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Title: Hidden morbidity: the results of a collaborative community Chronic Obstructive Pulmonary Disease screening initiative.

Running Title: Results of community COPD screening

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Abstract

Chronic obstructive pulmonary disease (COPD) often goes unrecognised resulting in people living with the disease without a diagnosis. Screening of asymptomatic individuals is not recommended but case-finding is encouraged to detect early disease. We investigated the characteristics, symptom burden and flow of participants taking part in a community-based COPD screening initiative in a city with high smoking prevalence.

Screening was undertaken during four events in public locations over a 2-week period. Participants completed symptom questionnaires and FEV-1/FEV-6 measurement. The criteria for being considered ‘screen positive’ were FEV-1 <80% predicted or FEV-1 ≥80% predicted and FEV-1/FEV-6 <0.72. Screen positive individuals were invited to attend one-stop clinics where they underwent diagnostic spirometry, respiratory physician review and consulted a smoking cessation specialist.
257 individuals participated (mean±SD age 58±16, 24% current smokers). 77/257 were screen positive with 59 referred and 27 ultimately attending a one-stop clinic. 18 individuals were confirmed to have COPD (7% of participants). The presence of ≥1 respiratory symptom and a prior smoking history were more common in screen positive individuals. The COPD Assessment Test score of participants with confirmed COPD was 19.3±11.4. Two-thirds had moderate airflow obstruction on spirometry.

The diagnosis rate in this screening initiative was comparable to trials of systematic case-finding approaches using primary care records. COPD patients identified through screening had a moderate to high symptom burden. Further research is required to explore the impact of COPD screening and early initiation of therapy on physical activity, quality of life and health care utilisation.

**Key Words:** case-finding, chronic obstructive pulmonary disease, screening, spirometry

**Introduction**

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable long term condition that places a high burden on patients, their carers and health services. It is recognised that there is a large population of individuals that would meet diagnostic criteria for COPD but remain undiagnosed either through lack of contact with health services or lack of consideration of the diagnosis by health care professionals.
A recent review of COPD screening by the US Preventive Task Force recommended against screening asymptomatic individuals, concluding that there is no net benefit.\(^1\) The UK Government’s strategy for COPD in England, published in 2011, supports opportunistic and systematic case-finding as well as improved awareness of symptoms and signs among the population and health care professionals to achieve early disease recognition and prevent late diagnosis.\(^2\) However, a subsequent report by the UK National Screening Council recommended against a national COPD screening programme. The reasons for recommending against screening are: limited evidence of benefit of interventions in early stage disease; inconclusive effects on smoking behaviour; and the limitations of spirometry in a population-wide setting.\(^3\) However, this report supports case-finding in symptomatic individuals with ‘more developed’ COPD.

The differentiation between screening and case-finding relates to the presence of symptoms prompting health service utilisation in the latter, where the former offers the screening test to all people in a population that meet certain criteria.\(^3\) It is sometimes assumed that participants in screening campaigns are asymptomatic or at least do not have sufficient symptoms to prompt contact with health services. However, there are a broad range of barriers that can prevent individuals from seeking healthcare and therefore this assumption may not be valid.

A cluster-randomised trial in the UK demonstrated that targeted case-finding in primary care was cost effective and identified more new cases than routine care.\(^4\) This intervention was defined as case-finding because only symptomatic individuals were invited for spirometry. In the ‘active’ case-finding group, questionnaires were sent to the homes of all eligible individuals, a strategy often utilised in screening. This ‘active’ case-finding approach identified more new cases of COPD and was more cost effective than ‘opportunistic’ case-finding that was only undertaken when eligible individuals attended the GP practice.
In 2016 there were 7,849 people with COPD in Hull and more than 5000 individuals estimated to have the disease that had not yet been diagnosed. We report the findings of a pilot, community-based COPD screening and public awareness initiative consisting of 4 screening events in public areas in Hull with the aim of characterising participants, evaluating flow through the screening pathway, and assessing participants symptom burden.

Materials and Methods

Screening Events

Four, one day screening events were undertaken as part of the British Lung Foundations (BLF) ‘Love Your Lungs’ campaign. Screening events occurred during a 2-week period in the summer of 2017. Events were publicised on social media, local radio and on posters and held in public places with high foot fall including supermarkets and shopping centres in high smoking prevalence areas within the city. Each screening event was attended by a BLF representative, a smoking cessation specialist and up to 3 clinicians trained in hand held spirometry.

Screening Procedures

Individuals were encouraged to undertake screening if they had a prior smoking history and respiratory symptoms but all attendees were welcome. Participants completed a questionnaire collecting lifestyle and symptom data including the COPD Assessment Test (CAT) questionnaire prior to performing Forced Expiratory Volume in 1 second (FEV-1) / Forced Expiratory Volume in 6 seconds (FEV-6) assessment (COPD-6, Vitalograph). Individuals were considered to be screen positive if their FEV-1 was <80% or if their FEV-1 was ≥80% and their FEV-1/FEV-6 ratio was <0.72. These criteria were selected to minimise false negative results and in recognition of the inherent limitations of performing FEV-1/FEV-6 measurements in a public setting. Participants that were
screen positive were made aware that this did not mean that they have COPD but they were provided with a date and time to attend a one-stop clinic appointment for further assessment.

One-stop Clinic

Screen positive participants were invited to attend a one-stop clinic appointment. One-stop clinics were held within health centres in the same locality as the screening events. During this appointment they saw a smoking cessation specialist, underwent diagnostic spirometry (MicroLab Mk8 Spirometer, Micro Medical) and had an appointment with a respiratory physician. A letter was sent to participants’ general practitioners detailing the clinic attendance and any proposed management. COPD diagnosis was made by a respiratory physician on the basis of compatible symptoms, relevant exposure history and spirometry evidence of airflow obstruction defined as $\text{FEV-1/FVC} < 0.7$. Consenting current smokers were enrolled into a smoking cessation program.

Data Analysis

Data are presented as mean (SD) or median (range) unless stated otherwise. For categorical data, 2x2 contingency tables and fishers exact test were used to identify between group differences. Otherwise, between group differences were analysed using two-tailed paired and un-paired t-tests as appropriate. The relationship between lung function parameters during screening and diagnostic spirometry were assessed using Pearson’s correlation coefficient. Receiver operating characteristic curve and Bland and Altman plot were produced using IBM SPSS (version 25).
Results

Patient Flow

A total of 257 people underwent screening during 4 community-based events. 82% of participants undertook screening because they were ‘passing’ an event with remaining participants having seen posters, heard about events using social media or been told by friends or family. Participants’ characteristics are detailed in Table 1.

Seventy-seven individuals met positive screening criteria and 59 were referred for review in a one-stop clinic. Reasons for not being referred to a one-stop clinic included participant choice (n=3), living outside the region (n=5), pre-existing COPD diagnosis (n=3), and health care professional choice (n=6). Thirty-two participants attended the one-stop clinic with 18 receiving a diagnosis of COPD. Of the 27 participants referred to a one-stop clinic that did not attend; 19 did not contact screening staff prior to non-attendance, 7 reported being unable to attend any of the dedicated one-stop clinics and were offered routine respiratory clinic appointments, and 1 cancelled and did not wish to be reappointed. In addition to the 18 patients that received a confirmed diagnosis of COPD, 13 participants received an alternative diagnosis as a cause for their symptoms either in addition to or instead of COPD.

Smoking Status

There was a higher proportion of current and ex-smokers in the screen positive cohort (81.8% versus 57.2% screen negative, p<0.001) with a higher pack-year smoking history than those that were screen negative (28.2±25.4 and 12.7±23.4 respectively, p<0.001). Similarly, those that received a COPD diagnosis had a higher pack year smoking history than those not diagnosed with COPD (40.2±30.5 pack years compared to 11.4±15.3 pack years, p<0.01).
**Respiratory Symptoms**

The proportion of individuals with at least 1 respiratory symptom was significantly higher in those that were screen positive compared to screen negative (92% compared to 62% respectively, p<0.001). The most common symptoms reported by screen negative individuals were shortness of breath and cough with phlegm (reported by 35% and 34% respectively). Shortness of breath and wheeze were the most frequently reported symptoms by screen positive individuals (both symptoms reported by 65%). Cough with phlegm was reported by 50% of screen positive individuals. Symptom data were unavailable for 3 individuals with confirmed COPD.

The CAT was used to evaluate the symptom burden experienced by participants of the screening programme. The CAT score was significantly greater in screen positive compared to screen negative individuals (16.9±1.0 and 9.5±7.7 respectively, p<0.001). However, there was no significant difference between patients attending the one-stop clinic that were diagnosed with COPD compared to those that were not (19.3±11.4 and 17.4±8.5, p=0.6).

**Spirometry**

FEV-1, FEV-6 and the FEV-1/FEV-6 ratio were significantly reduced in individuals that were screen positive compared to screen negative (See Table 1, p<0.001 for all measures). Paired screening and clinic spirometry data were available for 26 individuals. FEV-1 did not differ significantly between clinic and screening spirometry and strongly correlated (r = 0.91, 95% CI 0.80 to 0.96); Forced Vital Capacity (FVC) recorded during clinic attendance were significantly higher than FEV-6 recorded at screening (2.86±1.09L compared to 2.45±0.95L, p<0.001) but there was a strong correlation (r = 0.90, 95%CI 0.78 to 0.95). Similarly, the forced expiratory ratio was significantly lower on spirometry (0.67±0.14 versus 0.73±0.12 respectively, p<0.001) but strongly correlated (r=0.79, 95%CI 0.58 to
The relationship between FEV-1/FEV-6 and FEV-1/FVC is presented in Figure 1. The sensitivity of FEV-1/FEV-6 ratio of <0.72 to detect airflow obstruction defined as an FEV-1/FVC ratio <0.7 was 69% with a specificity of 80%. Receiver operating characteristic (ROC) analysis was performed to identify the performance of FEV-1/FEV-6 to identify airflow obstruction on diagnostic spirometry (FEV-1/FVC <0.7) (Figure 2). The area under the ROC curve (AUC) is 0.86 (95% CI 0.70 – 1.00; SEM 0.08).

Discussion

The following key observations are worthy of discussion: 1. A community-based screening and public awareness campaign is capable of identifying previously undiagnosed COPD patients with new diagnosis rates comparable to targeted case-finding approaches; 2. Respiratory symptoms are common among individuals that self-select to participate in screening and the individuals identified to have COPD during this initiative had a moderate to high symptom burden; 3. Current smokers engage in screening but maintaining contact and achieving cessation is challenging; and 4. The sensitivity and specificity of FEV-1/FEV-6 ratio of 0.72 to identify airflow obstruction in this patient cohort was lower than previously reported.

The COPD diagnosis rate in this pilot, community-based COPD screening initiative was 7%. However, the true COPD rate within the screened population may be higher due to the likelihood that some cases were missed as a result of the high non-attendance rate at one-stop clinics amongst current and ex-smokers. Published reports of primary care based targeted COPD case-finding demonstrate a diagnosis rate of between 2% and 20%. There are however fundamental differences in methodology, with the screening intervention we describe being short term, labour intensive and combined with a public awareness campaign. Indeed, our screening initiative was opportunistic and involved patient self-selection rather than identifying at risk populations through GP registries. It is
also important to consider regional variation in smoking and COPD prevalence when considering the effectiveness of different case-finding initiatives. Practice-based targeted case-finding in the UK has been demonstrated to be cost effective. No cost effectiveness analysis was performed as part of our evaluation. However, our findings suggest that in high smoking prevalence areas, short term, community screening initiatives can result in a proportion of new COPD cases being identified that is comparable to that obtained through practice based approaches.

COPD screening is contentious because there is a lack of evidence that early identification of patients alters disease outcomes. Early initiation of COPD treatment has never conclusively been demonstrated to alter disease trajectory or long-term outcomes. However, a recent randomised trial conducted in China suggested that Tiotropium might reduce the rate of lung function decline in mild COPD patients compared to placebo. This was also observed in a sub-group analysis of young COPD patients participating in UPLIFT. If confirmed in further cohorts this would strengthen the argument for early COPD diagnosis through screening.

Participants diagnosed with COPD in this study had a mean age of 64 years and mean FEV-1 of 70% predicted. The majority of confirmed COPD cases (78%) had moderate or severe airflow obstruction on spirometry (GOLD grade 2-3) suggesting that community based screening initiatives identify patients with a spectrum of disease severities. The COPD patients that we identified were symptomatic with a mean CAT score of 19 suggesting moderate symptom burden with 6 participants having CAT scores in the severe or very severe range. Irrespective of impact on disease trajectory, there is potential to improve individual participant’s symptoms and quality of life with inhaled therapies and pulmonary rehabilitation.

Screening is not recommended in asymptomatic individuals. However, it is recognised that individuals with COPD modify their behaviour to minimise symptoms and that this begins prior to diagnosis. This has been observed in the form of reduced physical activity. It is therefore important to consider what is meant when categorising an individual as ‘asymptomatic’. Not having
previously reported symptoms to a health care provider does not imply a lack of symptoms. Indeed, an individual's perceived lack of symptoms does not mean that they have not altered their behaviour to maintain status quo. Further research is essential to explore the impact of COPD screening and early initiation of therapy on symptoms, physical activity, quality of life and health care utilisation.

Smoking cessation is associated with a plethora of health benefits and could be considered a valuable outcome for case-finding initiatives. The effect of spirometry screening on smoking cessation remains unclear. A randomised trial undertaken in general practices in England found that informing smokers of their ‘lung age’ in addition to advice and smoking cessation referral was associated with significantly improved quit rates at 1 year. However, other trials have found no benefit. 24% of individuals taking part in this screening initiative were current smokers with 61% of current smokers being screen negative. Although concerns that normal spirometry may reduce individuals' motivation to stop smoking are not evidence based, further research is required to assess the impact of normal spirometry on smoking behaviour. All smokers participating in screening events were provided with education and smoking cessation support including referral to the local smoking cessation service irrespective of their screening result. Of the current smokers that were screen positive, two-thirds did not attend their one-stop clinic appointment. Targeting smoking cessation in this cohort is therefore challenging.

FEV-1/FEV-6 measurement was well tolerated by health care professionals and participants. The sensitivity and specificity of an FEV-1/FEV-6 ratio of <0.72 to predict airflow obstruction on conventional spirometry (FEV-1/FVC <0.7) were lower in this study than previously reported. The receiver operating characteristics of FEV-1/FEV-6 in this cohort suggest that a higher cut-point of 0.76 would improve performance. However, the small number of participants with both screening and diagnostic spirometry results available and the fact that this population were pre-selected based on FEV-1 and FEV-1/FEV-6 criteria limits the generalisability of this finding and our ability to comment on its performance at a population level.
Inclusion of individuals with FEV\textsubscript{1} <80% predicted irrespective of the forced expiratory ratio ensured participants with abnormal lung function were not missed and resulted in other causes for respiratory symptoms to be identified and treated (for example, obesity, heart failure and obstructive sleep apnoea). It could be argued that using fixed spirometry cut points to define individuals as screen positive or to confirm airflow obstruction on spirometry is invalid in a population setting and that using lower limits of normal or z-scores would be preferred. However, this practice is not yet widely established in a primary care setting. Indeed, relying on spirometry in isolation to diagnose COPD is flawed in clinical practice given the variable quality in a real world setting. As such, we opted to adopt a pragmatic approach to COPD diagnosis that we believe reflects current practice within the United Kingdom and is supported by international guidelines \textsuperscript{8}.

Previously reported methods of COPD screening have utilised questionnaires and measures of airflow limitation either in isolation or combined\textsuperscript{16}. A combined approach appears to perform better than either alone when identifying individuals with COPD that are likely to benefit from existing therapies\textsuperscript{17}. However, there remains no gold standard method for COPD screening in a population setting.

When considering the limitations of this study it is important to understand that it is not designed to assess the merits of COPD screening. Instead it aims to characterise the population participating in a screening initiative, describe participant flow through the pathway, and assess the symptom burden of participants. In this regard, the main limitation is that it was conducted in a single city with high levels of deprivation and high smoking prevalence. This limits the generalisability to other areas with different population characteristics.

In conclusion, the COPD diagnosis rate in this community-based COPD screening initiative was comparable to that observed using a targeted, case-finding approach of at risk individuals identified through primary care records. Further research is needed to assess the impact of COPD case-finding
on patient outcomes. However, we demonstrate that community based screening identifies individuals with a spectrum of disease severity and prominent symptoms that warrant treatment.

Acknowledgements

Thank you to the British Lung Foundation for coordinating and project managing the screening events. This initiative involved the collaboration of Hull and East Yorkshire Hospitals NHS Trust, City Health Care Partnership, Hull Clinical Commissioning Group and Hull City Council.

References


Figure Legends

Figure 1. Bland and Altman plot of the relationship between FEV-1/FEV-6 and FEV-1/FVC. The mean difference (red line) and 95% CI (green lines) between FEV1/FEV6 and FEV1/FVC are illustrated.

Figure 2. Receiver operating characteristic analysis of FEV-1/FEV-6 ratio to identify confirmed airflow obstruction on diagnostic spirometry (FEV-1/FVC <0.7).
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Participants</th>
<th>Screen Negative</th>
<th>Screen Positive</th>
<th>Confirmed COPD</th>
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<tr>
<td>Number</td>
<td>257</td>
<td>180</td>
<td>77</td>
<td>18</td>
</tr>
<tr>
<td>Male:Female</td>
<td></td>
<td></td>
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<tr>
<td>Age: mean (SD)</td>
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<td></td>
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</tr>
<tr>
<td>- &lt;20</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>- 21-30</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>- 31-40</td>
<td>20</td>
<td>15</td>
<td>5</td>
<td>0</td>
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<tr>
<td>- 41-50</td>
<td>35</td>
<td>23</td>
<td>12</td>
<td>2</td>
</tr>
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<td>- 51-60</td>
<td>57</td>
<td>39</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>- 61-70</td>
<td>69</td>
<td>46</td>
<td>23</td>
<td>6</td>
</tr>
<tr>
<td>- 71-80</td>
<td>42</td>
<td>31</td>
<td>11</td>
<td>2</td>
</tr>
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<td>- &gt;80</td>
<td>14</td>
<td>9</td>
<td>5</td>
<td>2</td>
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<td>- Unknown</td>
<td>3</td>
<td>0</td>
<td>3</td>
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<tr>
<td>Smoking Status (%)</td>
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<tr>
<td>- Never</td>
<td>86 (33.5)</td>
<td>75 (41.7)</td>
<td>11 (14.3)</td>
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<tr>
<td>- Current</td>
<td>105 (40.9)</td>
<td>66 (36.7)</td>
<td>39 (50.6)</td>
<td>12 (66.7)</td>
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<tr>
<td>- Ex</td>
<td>5 (1.9)</td>
<td>2 (1.1)</td>
<td>3 (3.9)</td>
<td>3 (16.7)</td>
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<td>17.1 (24.9)</td>
<td>12.7 (23.4)</td>
<td>28.2 (25.4)</td>
<td>40.2 (30.5)</td>
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<td>Pack Years – mean (SD)</td>
<td>2 (1-5)</td>
<td>2 (1-5)</td>
<td>3 (1-5)</td>
<td>4 (1-5)</td>
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<tr>
<td>COPD Awareness* Median (range)</td>
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<td></td>
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<tr>
<td>Symptoms – n (%)</td>
<td></td>
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<tr>
<td>Data available for:</td>
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<td></td>
<td></td>
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<tr>
<td>- Dyspnoea</td>
<td>108 (43.7)</td>
<td>60 (34.7)</td>
<td>48 (64.9)</td>
<td>10 (66.7)</td>
</tr>
<tr>
<td>- Cough</td>
<td>96 (38.9)</td>
<td>59 (34.1)</td>
<td>37 (50.0)</td>
<td>9 (60.0)</td>
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<td>- Phlegm</td>
<td>60 (24.3)</td>
<td>37 (21.5)</td>
<td>23 (31.1)</td>
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<td>51 (29.5)</td>
<td>48 (64.9)</td>
<td>10 (66.7)</td>
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<td>- Wheeze</td>
<td>12.0 (9.2)</td>
<td>9.5 (7.7)</td>
<td>16.9 (10.0)</td>
<td>19.3 (11.1)</td>
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<td>CAT Score – mean (SD)</td>
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<td></td>
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<td></td>
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<tr>
<td>Screening Spirometry</td>
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<tr>
<td>FEV-1 litres</td>
<td>2.56 (1.06)</td>
<td>2.87 (1.07)</td>
<td>1.86 (0.72)</td>
<td>1.78 (0.79)</td>
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<tr>
<td>% predicted FEV-1</td>
<td>94.89 (21.6)</td>
<td>104.87 (14.12)</td>
<td>71.79 (17.95)</td>
<td>66.21 (18.36)</td>
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<td>FEV-6</td>
<td>3.14 (1.02)</td>
<td>3.41 (0.97)</td>
<td>2.52 (0.86)</td>
<td>2.67 (0.91)</td>
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<td>% predicted FEV-1</td>
<td>0.81 (0.10)</td>
<td>0.84 (0.07)</td>
<td>0.75 (0.11)</td>
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<td>Clinic Spirometry</td>
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<tr>
<td>FEV-1</td>
<td></td>
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<td></td>
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<tr>
<td>%predicted FEV-1</td>
<td></td>
<td></td>
<td></td>
<td>1.92 (0.68)</td>
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<tr>
<td>FVC</td>
<td></td>
<td></td>
<td></td>
<td>70.06 (17.28)</td>
</tr>
<tr>
<td>% predicted FVC</td>
<td></td>
<td></td>
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<td>3.24 (1.04)</td>
</tr>
<tr>
<td>Ratio</td>
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<td></td>
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<td>94.22 (18.19)</td>
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<td>0.60 (0.11)</td>
</tr>
</tbody>
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Table 1. Participant characteristics and outcomes. CAT: COPD Assessment Test; FEV-1: forced expiratory volume in 1 second; FEV-6: forced expiratory volume in 6 seconds; FVC: forced vital capacity; SD: standard deviation.

* 1-5 Lickert Scale where 1 = ‘not at all aware’ and 5 = ‘very aware’.