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# Predictive accuracy of patient-reported exacerbation frequency in COPD

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**ABSTRACT: Chronic obstructive pulmonary disease (COPD) exacerbation frequency is important for clinical risk assessment and trial recruitment. In order to accurately establish exacerbation frequency, patients need to be followed for 1 yr, although this is not always practical. 1) Patient recall of exacerbation number during the year prior to recruitment to the London COPD cohort was compared with the number of exacerbations recorded on diary cards during the subsequent year; and 2) patient recall of their exacerbation number after 1 yr of follow-up was compared with documented exacerbations over the same year.**

**A total of 267 patients (forced expiratory volume in 1 s 1.14 L) recorded worsening of respiratory symptoms on daily diary cards for 1 yr. Exacerbations were defined according to previously validated criteria.**

**There was no difference between the exacerbation number recalled by patients prior to recruitment and the number detected during the first year (median 2.0 (interquartile range 1.0–4.0) and 2.0 (1.0–4.0); expected agreement 76.4%; agreement 84.6%; $\kappa$=0.3469). There was no difference between the number of exacerbations remembered by patients and the number recorded on diary cards over the same 1-yr period (2.0 (1.0–4.0) for both groups; expected agreement 74.9%; actual agreement 93.3%; $\kappa$=0.6146).**

**Patients remember the number of exacerbations they have in a year. Accuracy is increased when comparing the same 1-yr period. Patient recall is sufficiently robust for stratification into frequent and infrequent exacerbator groups for subsequent years.**

**KEYWORDS: Chronic obstructive pulmonary disease, exacerbation frequency, exacerbations, patient perception**

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Exacerbations of chronic obstructive pulmonary disease (COPD) are episodes of acute symptomatic, physiological and functional deterioration. Exacerbations have important consequences for patients and healthcare providers; they cause a negative impact on health-related quality of life [1, 2], decline in pulmonary function [3], increased utilisation of healthcare resources [4] and decreased survival [5]. The frequency with which patients have exacerbations remains relatively stable from year to year [6], but there are large differences in yearly exacerbation incidence rates between patients of similar COPD severity [1]. Some individuals appear more susceptible to developing exacerbations and are termed frequent exacerbators [1]. One of the clearest factors predictive of frequent exacerbations is a high number of exacerbations during the previous year [1, 7]. Frequent exacerbators show worse quality of life [1], greater limitation of their daily activity, less time spent outdoors [8], faster disease progression [3, 9, 10] and greater airway inflammation [11] than patients with less frequent exacerbations. They also exhibit increased mortality [12] and are at higher risk of hospitalisation.

Knowledge of exacerbation frequency is important for assessment of clinical risk and stratification into trials, especially where exacerbation interventions are being evaluated [13, 14]. It is essential that the patient population is generalisable and that it is divided equally, in terms of exacerbation frequency, between drug and placebo groups. Shorter-term studies examining interventions on exacerbation must also be cost-effective by recruiting individuals who will exacerbate during the follow-up period [15, 16]. However, in order to determine an accurate exacerbation frequency, patients ideally need to be prospectively followed for $\geqslant$12 months to allow for effects of seasonality on exacerbations [17]. In most situations, this is not practical when recruiting for clinical trials. Thus, at an initial clinical assessment or during study recruitment,

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patient recall of the number of exacerbation events is the standard method for assessing exacerbation risk and so determining exacerbation frequency [15, 16]. It is not known how accurately this patient recall relates to the genuine number of events.

Therefore, the main objectives of the present study were as follows.

1) To investigate whether patients with COPD, when interviewed, can accurately remember the number of exacerbations they have had in the past year. Patient estimates of their exacerbation number during the year before they entered the London COPD cohort were compared with the number of exacerbations recorded on daily symptom diary cards collected subsequently during the first year of study in this cohort, where close monitoring of patients is routine.

2) Subsequently to evaluate whether exacerbation frequency stratification remained unchanged over these 2 yrs by comparing the exacerbation frequencies determined from analysis [1].

3) In order to further validate the use of patient recall, in a subset of patients, patient estimates of their exacerbation number during the first year of study were compared with the number of exacerbation events at the end of the same 1-yr period of daily diary card data collection. Patient recall of exacerbation events over this time period was further analysed by comparing patient recall with all exacerbation events recorded on diary cards and comparing patient recall with healthcare utilisation events alone.

## METHODS

### Patient recruitment

A total of 267 patients were studied between January 1, 1995 and March 31, 2008. These patients had mild to severe COPD, with varying numbers of exacerbations. They are, therefore, representative of COPD patients commonly seen in a clinical setting and recruited into clinical trials. The recruitment and monitoring of patients in the London COPD study has previously been described [1, 3, 8, 11, 18–21], but the present analysis is entirely novel. Patients were selected for this analysis from the London COPD cohort if they had remained in this study for $\geqslant$1 yr and had had $<$30 days (nonsequential) of missing diary card data over the period of study. The study was approved by the Royal Free Hospital Research Ethics Committee (Royal Free Hospital, London, UK) and patients gave written informed consent.

All patients had COPD as defined by a forced expiratory volume in 1 s ($FEV_1$) of $\leqslant$80% and $FEV_1$ to forced vital capacity ratio of $<$70%, with $\beta_2$-agonist reversibility of $<$15% or $<$200 mL. Patients were excluded if they had other significant respiratory diseases. Patients were recruited when stable, with no exacerbations reported in the preceding month. At the initial visit, daily respiratory symptoms, smoking history, drug history, sex and comorbid conditions were recorded. Patients were also asked how many lower respiratory tract infections/exacerbations they had had in the preceding year. Information was collected regarding social contacts (*i.e.* living alone, living with spouse and contact with children). Height and weight were measured along with baseline lung function using a volumetric storage spirometer (Vitalograph 2160; Vitalograph, Maids Moreton, UK).

### Exacerbations

Patients completed daily diary cards, recording any increase in daily respiratory symptoms. They were asked to contact the study team if they experienced an increase in their daily respiratory symptoms, and were usually reviewed within 24 h. Exacerbations were defined according to the previously validated criteria of two symptoms (one of which must be major) for 2 days consecutively, or, if in the opinion of the attending clinician, the patient had an exacerbation [11]. Major symptoms were increased dyspnoea, sputum volume or sputum purulence and minor symptoms increased cough, wheeze, sore throat or coryzal symptoms. This exacerbation definition has been validated against changes in quality of life [1], inflammatory markers [11] and $FEV_1$ decline [3].

### Validation substudy

A subset of 100 patients from the main cohort who had no missing diary card data between May 1, 2007 and April 30, 2008 were studied in more detail. These patients were called within 6 weeks of completion of the study (April 30, 2008), after the diary cards had been collected, and asked a standardised scripted question: ''How many exacerbations have you had in the last year? By this I mean infections, bad attacks of your chest/worsening of symptoms?'' The number of exacerbations they remembered was recorded. If a patient gave a range, *e.g.* ''four or five'', then the lower number was taken. This question deliberately avoided asking about treatment and so permitted capture of information on treated and untreated exacerbations.

Diary cards were further evaluated in these patients such that both the total number of exacerbations recorded and the number of exacerbations that were treated with antibiotics and/or a course of oral steroids were counted separately. If the patient was not seen by a healthcare professional at the time of an exacerbation (usually a member of the study team, but also their own general practitioner or in an emergency department), this was considered to be an unreported exacerbation. All of these data were obtained from the diary cards. The end of an exacerbation was taken as the last day of recorded lower airway symptoms. Patients had to be symptom-free for $\geqslant$5 days before a new exacerbation onset was defined. Patients had no input into the definition of exacerbation and no education on classification of exacerbations, and, as such, this could not impact on their predictive accuracy and influence results. These patients also completed a St George's Respiratory Questionnaire (SGRQ), a disease-specific measure of health status during this 1-yr period [22].

### Exacerbation frequency

Exacerbation frequency was determined in the three following ways depending upon the analysis. 1) Using patient estimates of exacerbation number in the year before they entered the cohort. This permitted assessment of recall prior to diary card intervention. 2) Exacerbations were counted from diary cards. 3) Using patient estimates of exacerbation number at the end of the first year of study. When using this method to determine exacerbation frequency grouping, the grouping did not change

for any patient by taking the lower number recalled, *i.e.* no patient gave an answer of ''two or three''.

Patients were defined as frequent exacerbators if they had three or more exacerbations, or infrequent exacerbators if they had less than three exacerbations. Three exacerbations was chosen since both treated and untreated exacerbations were included in the present definition.

### Statistical analysis

Data were analysed using SPSS version 11 (IBM Corporation, Somers, NY, USA) or STATA version 8.2 (StataCorp, College Station, TX, USA). The Kolmogorov–Smirnov test of normality was applied. Normally distributed data were expressed as mean±SD, and skewed data as median and interquartile range (IQR). Comparisons between exacerbations counted in the different ways were made using a weighted kappa score, and the results were reported as a summary kappa statistic [23]. This weighting adjusts for the importance of the agreement. A perfect match is 1, with the smallest weight for the biggest disagreement. These data were analysed using STATA, which gives weights for agreement, rather than weights for disagreement. Pearson's correlation was used to assess parametric data, and Spearman's rank correlation to assess nonparametric correlations. One-way ANOVA was used to compare the SGRQ score by exacerbation frequency determined in the three different ways. The Wilcoxon signed-rank test was used to compare the difference between the number of exacerbations recorded on diary cards and patient estimates of exacerbation number prior to recruitment to the cohort, and the number of exacerbations recorded on diary cards *versus* patient estimates over the first year of study for those in the cohort for ⩾3 yrs. For all statistical tests, a p-value of ⩽0.05 was taken as significant.

## RESULTS

### Baseline patient characteristics

A total of 267 patients were studied, 179 male and 88 female. Of these, 165 were classified as infrequent exacerbators (<3 exacerbations·yr$^{-1}$) and 102 as frequent exacerbators (⩾3 exacerbations·yr$^{-1}$) using diary card data collected over the first year of participation in the London COPD cohort. The baseline characteristics of the cohort are reported in table 1. The patients exhibited a mean $FEV_1$ of 1.14 L or 45.4% of the predicted value.

### Comparison of patient estimates of exacerbation number in year preceding recruitment and exacerbation number over subsequent year

A total of 654 exacerbations were recorded on diary cards over the first year of study. Patient estimates of their exacerbation number in the year preceding recruitment to the London COPD cohort accurately predicted the number of exacerbations detected on diary cards over the coming year. There was no significant difference between the number of patient-recalled exacerbations in the year prior to recruitment to the cohort and the number of exacerbations recorded on diary cards in the first year of the study (median 2.0 (IQR 1.0–4.0) for both groups, and mean±SD 2.34±2.17 and 2.45±2.2, respectively; p=0.21). If patient estimates and genuine exacerbation number were random, 76.4% agreement would be expected. However, they agreed by 84.6% (κ=0.3469). This amount of agreement indicates that the hypothesis that patient estimates of their exacerbation number in the year prior to recruitment and the exacerbation number recorded on diary cards was determined randomly can be rejected (fig. 1).

When examining each exacerbator group separately, there was a difference between the number of patient-estimated exacerbations in the year preceding recruitment and the number of exacerbations recorded on diary cards during the first year of study. Frequent exacerbators underestimate the annual number of exacerbations by 1.23 exacerbations·yr$^{-1}$ (26.3%; p<0.001) and infrequent exacerbators overestimate their exacerbations by 0.59 exacerbations·yr$^{-1}$ (59.0%; p<0.001).

### Validation substudy

The baseline characteristics of the 100 patients studied from May 2007 to April 2008, who were telephoned at the end of the study, are representative of the main cohort and shown in table 1.

#### *Patient estimates of exacerbation number over first year of study and exacerbation number recorded on diary cards*

The number of exacerbations recorded on diary cards over the first year of participation in the study were compared to estimates of exacerbation number over that same 1-yr period when patients were asked at the end of the study. A comparison of these exacerbation numbers is shown in figure 2. There was no significant difference between the number of exacerbations recorded on diary cards and patient estimates of their exacerbation number over the same 1-yr period (median 2.0 (IQR 1.0–4.0) for both groups; p=0.36; mean±SD 2.4±2.2 and 2.3±2.1, respectively). If patient estimates of exacerbation number and genuine exacerbation number over this same time period were random, 74.9% agreement would be expected. However, they agreed by 93.3% (κ=0.6146). This amount of agreement indicates that the hypothesis can be rejected that there is a difference between patient estimates of their exacerbation number and the number of exacerbations recorded on diary cards over the same 1-yr period. Frequent exacerbators underestimate the annual number of exacerbations by 0.55 exacerbations·yr$^{-1}$ (11.8%; p=0.051) and infrequent

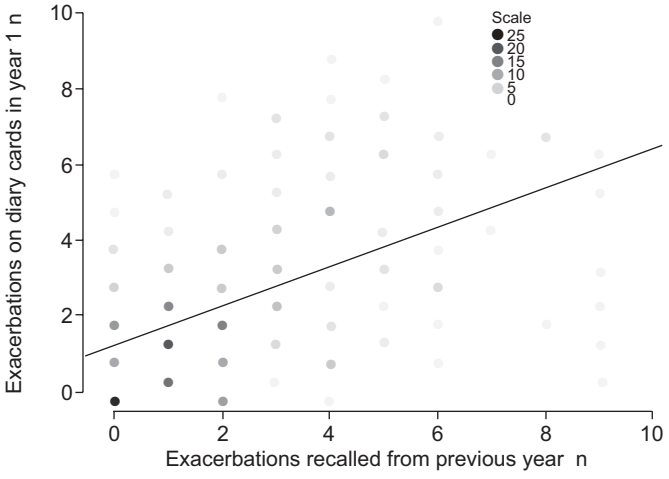


**FIGURE 1.** Scattergram of correlation showing the number of exacerbations recorded on diary cards in the first year of study and the number of exacerbations remembered by the patient to have occurred in the year before the study (n=267). Agreement 84.6%; κ=0.3469.

**TABLE 1** Baseline characteristics of patients in the study and those in the validation substudy

| | |
|---|---|
| **Study** | |
| Subjects n | 267 |
| Age yrs | 69.1±8.2 |
| $FEV_1$ L | 1.14±0.50 |
| $FEV_1$ % pred | 45.4±18.2 |
| FVC L | 2.49±0.83 |
| BMI kg·m$^{-2}$ | 25.2±5.8 |
| Smoking history pack-yrs | 49.2±33.4 |
| $Sa,O_2$ % | 94±2 |
| **Validation substudy** | |
| Subjects n | 100 |
| Age yrs | 71.4±8.3 |
| $FEV_1$ L | 1.14±0.51 |
| $FEV_1$ % pred | 46.4±17.1 |
| FVC L | 2.52±0.85 |
| BMI kg·m$^{-2}$ | 26.4±5.0 |
| Smoking history pack-yrs | 48.9±36.0 |
| $Sa,O_2$ % | 95±2 |
| SGRQ score | |
| Total | 49.1±17.1 |
| Activity | 66.1±21.5 |
| Impact | 35.8±19.2 |
| Symptoms | 60.2±19.9 |
| MRC dyspnoea score | 3.0 (2.0–4.0) |

Data are presented as mean± SD or median (interquartile range), unless otherwise stated. $FEV_1$: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; BMI: body mass index; $Sa,O_2$: arterial oxygen saturation; SGRQ: St George's Respiratory Questionnaire; MRC: UK Medical Research Council.

exacerbators overestimate their exacerbations by 0.18 exacerbations·yr$^{-1}$ (18%; p=0.27).

*Treated exacerbation number compared to patient estimates of exacerbation number*

A total of 240 exacerbations were recorded on diary cards over this 1-yr period; 181 of these were treated. Previous findings were confirmed that patients do not report all of their exacerbations to healthcare professionals [1, 24, 25] Overall, there was a difference between the number of treated exacerbations and the number of exacerbations remembered by the patient over the same 1-yr period (median 1.0 (IQR 0.0–3.0) and 2.0 (1.0–4.0), respectively; p<0.001; mean±SD 1.8±1.8 and 2.3±2.1, respectively) (fig 3). If patient estimates of their exacerbation number and the number of treated exacerbations were random, 74.1% agreement would be expected. However, they agreed by 88.6% (κ=0.5605). Frequent and infrequent exacerbators have fewer exacerbations treated then they remember over the same time period by 1.14 exacerbations·yr$^{-1}$ (31.4%; p<0.001) and 0.49 exacerbations·yr$^{-1}$ (71.0%; p<0.001), respectively.

### *Relationship between SGRQ and exacerbation frequency determined using patient recall and recorded on diary cards*

SGRQ data were collected on all 100 substudy patients during the year of follow-up. There was no significant difference in any of the baseline characteristics reported in table 1 between frequent and infrequent exacerbators, except for SGRQ total score and all subcomponents of the SGRQ, which is consistent with previous work [1]. Table 2 shows that these differences were similar when frequent and infrequent exacerbators were classified according to exacerbation frequencies determined by: 1) the number of exacerbations recorded on diary cards, 2) the number of exacerbations remembered by patients to have occurred over the year of diary card collection, and 3) the number of exacerbations remembered by patients to have occurred in the year before participation in the cohort. Comparison of SGRQ total score and all subgroups (activity, impact and symptoms) calculated in the three different ways was made in frequent exacerbators (p=0.99, 1.00, 0.99 and 0.68, respectively (ANOVA)). Similarly, for the infrequent exacerbators, there was no difference (p=0.86, 0.93, 0.88 and 0.84, respectively (ANOVA)).

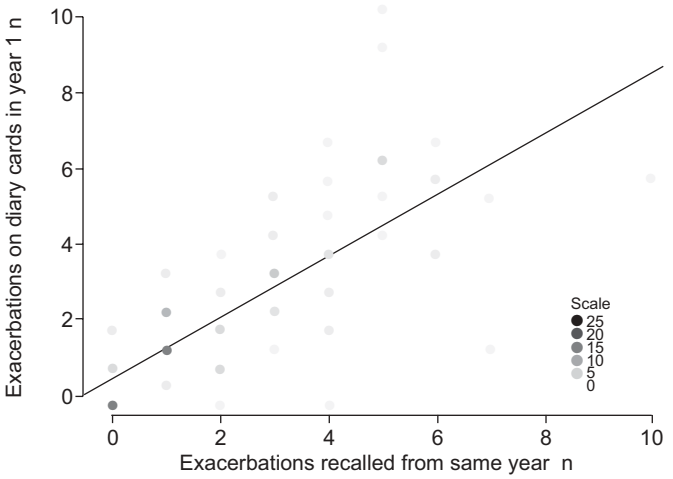


**FIGURE 2.** Scattergram of correlation showing the number of exacerbations recorded on diary cards in the first year of study and the number of exacerbations remembered by the patient to have occurred over the same 1-yr period (n=100). Agreement 93.3%; κ=0.6146.

### *Predictive accuracy of exacerbation recall*

There were no factors, *i.e.* $FEV_1$, smoking history, sex, comorbid conditions or social contacts (living alone, living with spouse and contact with children), that were predictive of an individual having poor recall of their number of exacerbations (p>0.05 for all). There was no difference in SGRQ total score or any subgroups between those that recalled the same number of exacerbations recorded on diary cards and those with poor recall (p>0.05 for all).

### *Patient recall and length of time in the cohort*

It was also investigated whether length of time in the cohort (*i.e.* diary card intervention) affected patient recall of exacerbations. Patients' recall of their exacerbations was not more accurate with increased length of time in the cohort. In 19 patients from the 100 patient subset, the time between the first year of diary card data and the 2007–2008 follow-up was >3 yrs. This was chosen as the cut-off as it was felt that, if there were a difference with diary card intervention, it would be seen with patients in the London cohort after this amount of

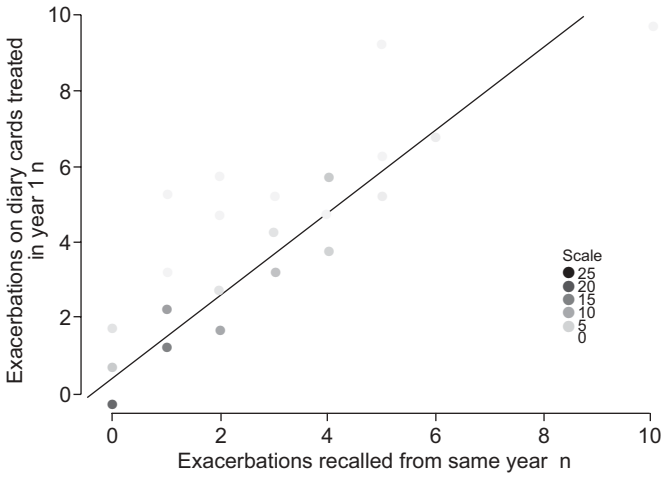


**FIGURE 3.** Scattergram of correlation showing the number of exacerbations recorded on diary cards in the first year of study that were treated and the number of exacerbations remembered by the patient to have occurred over the same 1-yr period (n=100). Agreement 88.6%; $\kappa$=0.5605.

time. In these patients, there was no difference in the difference between the number of exacerbations recorded on diary cards during the first year of the study and the number of exacerbations remembered to have occurred in the year prior to recruitment, and the difference between the number of exacerbations remembered over the first year of the study and the number recorded on diary cards over that same time period (mean±SD difference -0.05±1.99 and -0.32±2.08 exacerbations·yr$^{-1}$; p=0.74 (Wilcoxon)).

## DISCUSSION

This is the first study to prospectively show that COPD patients can reliably estimate the number of exacerbations they have had in the preceding year and that this patient-reported exacerbation frequency can be used to accurately stratify patients into frequent and infrequent exacerbator groups in subsequent years. This study is also unique in that it was possible to capture information on both treated and untreated exacerbations. The findings are important for a number of reasons. First, from the patient perspective, frequent exacerbators exhibit reduced quality of life [1], increased mortality [12], faster decline in lung function [3, 9], reduced physical activity [8] and increased depression [26]. The present study shows that patients can recognise themselves to be frequent exacerbators and that these individuals may benefit from self-management plans or increased patient education [24, 25, 27]. Secondly, for clinicians, as frequent exacerbators experience more frequent hospitalisations [12] and increased healthcare costs, identification of these patients early on may affect management. Patients with frequent exacerbations may be specifically targeted for more aggressive therapy and exacerbation prevention in order to help prevent disease progression [28, 10] and improve quality of life [29], and the present data suggest that simply asking patients about their exacerbations is sufficient to categorise them. Thirdly, as exacerbation

**TABLE 2** St George's Respiratory Questionnaire (SGRQ) scores in frequent and infrequent exacerbators

| | Frequent exacerbators | Infrequent exacerbators | p-value |
|---|---|---|---|
| **Exacerbations on diary cards** | | | |
| Subjects n | 38 | 62 | |
| SGRQ score | | | |
| Total | 55.6±16.0 | 45.4±16.1 | 0.003 |
| Activities | 73.1±18.2 | 62.8±20.6 | 0.015 |
| Impact | 41.5±19.2 | 31.7±19.0 | 0.011 |
| Symptoms | 68.4±16.3 | 56.6±21.0 | 0.010 |
| **Exacerbations recalled in same year** | | | |
| Subjects n | 40 | 60 | |
| SGRQ score | | | |
| Total | 56.0±15.6 | 44.6±16.0 | 0.001 |
| Activities | 73.2±18.0 | 62.2±20.6 | 0.009 |
| Impact | 41.4±19.7 | 31.3±18.6 | 0.008 |
| Symptoms | 70.5±14.8 | 54.5±20.8 | <0.001 |
| **Exacerbations recalled in previous year** | | | |
| Subjects n | 32 | 68 | |
| SGRQ score | | | |
| Total | 55.8±14.8 | 46.1±16.8 | 0.008 |
| Activities | 73.3±15.8 | 63.6±21.4 | 0.04 |
| Impact | 40.7±19.2 | 33.0±19.4 | 0.04 |
| Symptoms | 71.5±15.4 | 56.2±20.3 | 0.001 |

Data are presented as mean±SD, unless otherwise stated. Exacerbation frequencies were determined by: 1) the number of exacerbations recorded on diary cards, 2) the number of exacerbations remembered by patients to have occurred over the year of diary card collection, and 3) the number of exacerbations remembered by patients to have occurred in the year before participation in the cohort.

frequency is often controlled for or used as a criterion for selection [15, 16], stratification into frequent and infrequent exacerbator groups may be necessary at the time of recruitment into trials. Incorrectly defining patients into these two groups may lead to a marked effect on trial outcome.

It was found that, overall, the number of exacerbations recorded on diary cards in the first year of participation in the London COPD cohort was comparable to the number of exacerbations remembered by patients to have occurred in the year preceding recruitment. There was a difference between frequent and infrequent exacerbators in their ability to recall their exacerbations. Perception became less accurate at the extremes of numbers of exacerbations, with the majority of patients who have 1–3 exacerbations·yr$^{-1}$ being the most accurate. Frequent exacerbators underestimate and infrequent exacerbators overestimate the number of their exacerbations. It is possible that, as frequent exacerbators are symptomatic more of the time, multiple exacerbations overlap into one, and so they recall fewer, whereas in infrequent exacerbators, who are well more of the time, symptom deteriorations are more acute and thus memorable events. Although this difference in perception exists, in terms of recruitment to clinical trials, the underestimation of exacerbations in frequent exacerbators and overestimation in infrequent exacerbators at the extremes of exacerbation number would not affect exacerbation frequency grouping but instead affirms their position in the correct group. This is unlikely to be a regression to the mean effect as exacerbations are not random events [30].

The present comparison of patient estimates of exacerbation number prior to recruitment to the London COPD cohort with the number of exacerbations recorded on diary cards was validated by also comparing patient recall of exacerbations over the 1-yr period in which daily diary card data had been collected. It was found that, for each patient, the total number of exacerbations (both treated and untreated) on diary cards accurately compared to the number estimated by the patient over that period, and was more accurate than comparing exacerbation number prior to recruitment to the cohort and over the first year of study. Once more, frequent exacerbators underestimated and infrequent exacerbators overestimated the number of exacerbations experienced.

The present cohort is unique in that it was possible to study untreated and unreported exacerbations [1, 3, 6], as most studies lack consistent information on these events. Previous studies have used treatment definitions to predict exacerbations in the next year [31]. However, it has been shown that unreported exacerbations have an important impact on health status in COPD [1, 32, 33]. Although, as stated above, patient recall of exacerbation number accurately matched the number of exacerbations recorded on diary cards, patient estimates of exacerbation number did not match the number of exacerbations treated during the year when considering the exacerbator subgroups alone. Both groups remembered more exacerbations than they had treated. Therefore, it appears that patients count unreported exacerbations as important events, even if they do not seek treatment for these episodes. They may not seek treatment due to difficulty in obtaining access to healthcare providers [34], or, more likely, they feel that the episode is self-limiting and they will improve without therapy. This finding is also important from a trial recruitment perspective. Recruiting patients using a healthcare utilisation definition as an outcome could lead to over-recruitment of patients with a lower rate of healthcare-utilisation-defined exacerbations. This, in turn, may affect trial outcome. As frequent exacerbators exhibit worse quality of life [1] and, by definition, spend a greater proportion of their time symptomatic with exacerbations, it is likely that they recognise these events and seek treatment. It is possible that frequent exacerbators are more likely to have courses of emergency treatment (antibiotics and steroids) at home and so are more likely to have treated exacerbations.

It has previously been shown that there are significant differences in health status between frequent and infrequent exacerbators [1], and this has been confirmed in the present study. Similar differences have also been shown in both exacerbator groups, regardless of which definition of exacerbation was used in the classification analysis. This, again, supports the data showing that patients are able to accurately classify themselves into frequent and infrequent exacerbator groups.

Exacerbation frequency is stable in individual patients from year to year [6]. It has now been shown that patient recall can be used to stratify patients as frequent or infrequent exacerbators in the following year. It is appreciated that not all COPD patients fill in diary cards. Therefore patient estimates of exacerbation number prior to recruitment to the London COPD cohort were compared with estimates after recruitment. The kappa score was higher when comparing the number of exacerbations recorded on diary cards and number of exacerbations remembered by patients over the same year of study ($\kappa$=0.6146) with the number of exacerbations recorded on diary cards and the number of exacerbations remembered by patients to have occurred in the year before ($\kappa$=0.3469), suggesting that participation in the cohort improved patient recognition of exacerbations. However, it is possible that patients did not have exactly the same number of exacerbations in the year before participation as they had in that next year. It is also possible that patient education on cohort recruitment improved recognition of these events. It was found that patients who had been in the cohort for $\geqslant$3 yrs did not show a change in their ability to recall their exacerbations, suggesting that filling in diary cards does not provide reinforcement or more accurate recall of exacerbations later on. The fact that patient recall did not become more accurate with increased time spent in the cohort implies that cohort patients have a good understanding of their disease at commencement in studies. This emphasises the importance of patient education about the nature of COPD exacerbations. Factors were investigated that could affect patient recall of their exacerbations, and found no factors that predicted poor recall. Specifically, there was no relationship with disease severity, exacerbation frequency or quality of life.

An important strength of the present study is the accurate data collection and uniqueness of ability to detect all types of exacerbation. A validated and consistent definition of exacerbation [1, 3, 8, 11, 18–21] was used, with the same individuals asking the questions. Consistent attempts were made to obtain

information on all exacerbations, including information on untreated events.

In summary, the present study, using daily patient exacerbation monitoring, shows, for the first time, that COPD patients can accurately recall the number of exacerbations that they have experienced in the past year, and that this recall is sufficiently robust for stratification of COPD patients into frequent and infrequent exacerbator groups. This finding has important implications for the performance of clinical trials in COPD patients and also in clinical practice when stratification of COPD patients at risk of exacerbation is required.

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## STATEMENT OF INTEREST

None declared.

## REFERENCES


1 Seemungal TA, Donaldson GC, Paul EA, *et al.* Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; 157: 1418–1422.
2 Spencer S, Jones PW. Time course of recovery of health status following an infective exacerbation of chronic bronchitis. *Thorax* 2003; 58: 589–593.
3 Donaldson GC, Seemungal TAR, Bhowmik A, *et al.* Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002; 57: 847–852.
4 O'Brien JA, Ward AJ, Jones MKC, *et al.* Utilization of health care services by patients with chronic obstructive pulmonary disease. *Respir Med* 2003; 97: S53–S58.
5 Groenewegen KH, Schols AMWJ, Wouters EFM. Mortality and mortality related factors after hospitalisation for acute exacerbation of COPD. *Chest* 2003; 124: 459–467.
6 Donaldson GC, Seemungal TAR, Patel IS, *et al.* Longitudinal changes in the nature, severity and frequency of COPD exacerbations. *Eur Respir J* 2003; 22: 931–936.
7 Ball P, Harris JM, Lowson D, *et al.* Acute infective exacerbations of chronic bronchitis. *QJM* 1995; 88: 61–68.
8 Donaldson GC, Wilkinson TM, Hurst JR, *et al.* Exacerbations and time spent outdoors in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 171: 446–452.
9 Kanner RE, Anthonisen NR, Connett JE. Lower respiratory illnesses promote FEV1 decline in current smokers but not ex-smokers with mild chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001; 164: 358–364.
10 Celli BR, Thomas NE, Anderson JA, *et al.* Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary disease: results from the TORCH Study. *Am J Respir Crit Care Med* 2008; 178: 332–338.
11 Bhowmik A, Seemungal TAR, Sapsford RJ, *et al.* Relation of sputum inflammatory markers to symptoms and lung function changes in COPD exacerbations. *Thorax* 2000; 55: 114–120.
12 Soler-Cataluna JJ, Martinez-Garcia MA, Roman Sanchez P, *et al.* Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005; 57: 137–141.
13 Powrie DJ, Wilkinson TM, Donaldson GC, *et al.* Effect of tiotropium on sputum and serum inflammatory markers and exacerbations in COPD. *Eur Respir J* 2007; 30: 472–478.
14 Seemungal TAR, Wilkinson TMA, Hurst JR, *et al.* Long term erythromycin therapy is associated with decreased COPD exacerbations. *Am J Respir Crit Care Med* 2008; 178: 1139–1147.
15 Wedzicha JA, Calverley PMA, Seemungal TA, *et al.* The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. *Am J Respir Crit Care Med* 2008; 177: 19–26.
16 Calverley P, Pauwels R, Vestbo J, *et al.* Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003; 361: 449–456.
17 Donaldson GC, Seemungal T, Jeffries DJ, *et al.* Effect of temperature on lung function and symptoms in chronic obstructive pulmonary disease. *Eur Respir J* 1999; 13: 844–849.
18 Hurst JR, Perera WR, Wilkinson TMA, *et al.* Systemic and upper and lower airway inflammation at exacerbation of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2006; 173: 71–78.
19 Wilkinson TMA, Hurst JR, Perera WR, *et al.* Effect of interactions between lower airway bacterial and rhinoviral infection in exacerbations of COPD. *Chest* 2006; 129: 317–324.
20 Seemungal TAR, Harper-Owen R, Bhowmik A, *et al.* Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001; 164: 1618–1623.
21 Seemungal TAR, Donaldson GC, Bhowmik A, *et al.* Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 161: 1608–1613.
22 Jones PW, Quirk PH, Baveystock CM, *et al.* A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992; 145: 1321–1327.
23 Keene ON, Calverley PMA, Jones PW, *et al.* Statistical analysis of exacerbation rates in COPD: TRISTAN and ISOLDE revisited. *Eur Respir J* 2008; 32: 17–24.
24 Bourbeau J, Julien M, Maltais F, *et al.* Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003; 163: 585–591.
25 Gadoury MA, Schwartzman K, Rouleau M, *et al.* Self-management reduces both short- and long-term hospitalisation in COPD. *Eur Respir J* 2005; 26: 853–857.
26 Quint JK, Baghai-Ravary R, Donaldson GC, *et al.* Relationship between depression and exacerbations in COPD. *Eur Respir J* 2008; 32: 53–60.
27 Monninkhof E, van der Valk P, van der Palen J, *et al.* Effects of a comprehensive self-management programme in patients with chronic obstructive pulmonary disease. *Eur Respir J* 2003; 22: 815–820.
28 Zheng JP, Kang J, Huang SG, *et al.* Effect of carbocisteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomised placebo-controlled study. *Lancet* 2008; 371: 2013–2018.
29 Calverley PM, Anderson JA, Celli B, *et al.* Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007; 356: 775–789.
30 Hurst JR, Donlaldson GC, Quint JK, *et al.* Temporal clustering of exacerbations in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2009; 179: 369–374.
31 Niewoehner DE, Lokhnygina Y, Rice K, *et al.* Risk indexes for exacerbations and hospitalizations due to COPD. *Chest* 2007; 131: 20–28.
32 Langstemo L, Platt RW, Ernst P, *et al.* Underreporting exacerbation of chronic obstructive pulmonary disease in a longitudinal cohort. *Eur Respir J* 2008; 177: 396–401.
33 Vijayasaratha K, Stockley RA. Reported and unreported exacerbations of COPD: analysis by diary cards. *Chest* 2008; 133: 34–41.
34 Garcia-Aymerich J, Hernandez C, Alonso A, *et al.* Effects of an integrated care intervention on risk factors of COPD readmission. *Respir Med* 2007; 101: 1462–1469.