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Predicting the costs of managing patients with chronic obstructive pulmonary disease ☆

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Summary The economic consequences of chronic obstructive pulmonary disease (COPD) are considerable, although the factors that best predict costs are largely unknown. This study used a population-based cohort to identify the clinical factors during an index year that were most predictive of increased direct medical costs in the subsequent year, and to develop a predictive model that described the cost variations in COPD.

The medical records of 2116 patients enrolled in one regional health system who had COPD and healthcare resource utilisation data for 1998 and 1999, were abstracted for information about symptoms, smoking history, chronic illnesses, and pulmonary function data. All inpatient, outpatient and pharmacy utilisation data for each subject for 1999 were extracted from the database. Total costs for each individual were transformed to a log scale. Potential causes of cost variability (predictor variables) were defined and classified into sets (or domains). Multiple linear regression models were fitted for each domain.

The study demonstrated that severity of airflow obstruction, as assessed by FEV_1% predicted, is a significant but weak predictor of future healthcare resource utilisation—prior hospitalisation and home oxygen use, the presence of comorbid conditions and symptoms of dyspnoea are better predictors of costs. Those interested in the economic benefits of new COPD treatments and disease management programs need to carefully account for these factors.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a multi-component disease involving airway inflammation, muco-ciliary dysfunction, airway and parenchymal structural changes, and expiratory airflow obstruction.[1] These components result in a complex of symptoms and physiological changes which affect the ability of patients to function, and ultimately, threaten survival.

There is growing awareness of the burden of COPD. In 2000, COPD was the fourth leading cause of death in the USA[2] and the fifth leading cause of mortality worldwide.[3] Furthermore, mortality from COPD is projected to increase to the third leading cause of mortality by 2020.[4] Likewise, morbidity from COPD is considerable, with the disease predicted to be the fifth leading cause of disability worldwide by 2020.[5] The economic consequences of COPD are considerable, due both to the high healthcare resource utilisation required by sufferers, and to indirect costs from work loss and mortality.[6–9] Exacerbations of the disease are particularly costly and contribute to increased disease progression, thereby increasing the likelihood of further exacerbations.[10,11] In the USA in 1995, the hospitalisation cost of managing acute exacerbations of chronic bronchitis was almost 40 times higher ($1592 million) than the outpatient cost (just under $40 million).[12]

Fortunately, a number of new COPD treatments have been investigated in clinical trials finding positive results in a range of outcomes including lung function parameters, exacerbation rates and health status.[13–15] However, healthcare payers increasingly are charged with making their decisions based on solid clinical evidence, and proving the cost–benefit of new treatments is problematic.[16] Most cost analyses are based on randomised clinical trial data, which invariably use highly selective inclusion and exclusion criteria and thus may not accurately reflect COPD patients treated in the general population. Even the basic systems of defining COPD severity are suspect because of their lack of validation in prospective, cross-sectional, or population-based studies.[17] One efficient approach to this problem is to compare the results of randomised clinical trials to cross-sectional population-based data. Retrospective analysis of administrative databases has proved highly useful in obtaining information about associations between treatments, health outcomes and healthcare resource utilisation in real-life populations.[18–20]

This study aimed to identify the factors most predictive of future costs in COPD, and to develop a model that best determined the causes of cost variations in this disease, based on data derived from a large population-based cohort of patients enrolled in a regional managed care system. A secondary aim was to examine how well the severity system recommended by the current GOLD guidelines predicted future costs.[1]

Methods

Patients

The model was based on data extracted from the Lovelace Health Plan (LHP), a health management organisation that serves over 200,000 members in the New Mexico area of the USA. Study subjects were required to have each of the following: (1) a diagnosis of COPD, defined as having had at least two outpatient encounters or one hospital admission coded as chronic bronchitis (491.x), emphysema (492.x), or chronic airway obstruction (496) during calendar year 1998; 2) be age 40 or older as of January 1, 1998; and, (3) have continuous enrolment in the LHP during the study period (January 1, 1998–December 31, 1999). A total of 2182 patients were identified who were classified as having COPD and had at least some healthcare resource utilisation during 1998. Of these, a total of 2116 patients also recorded some healthcare resource utilisation during 1999, with three patients recording no healthcare resource utilisation in 1999 and the remaining patients assumed to have died or left the LHP. The medical records of these 2116 patients were abstracted for information about symptoms, smoking history, radiographs, and pulmonary function data. Over 95% of this cohort had documentation of a least two clinical factors consistent with COPD (spirometry data, chronic respiratory symptoms or frequent bronchitis episodes, radiographic changes consistent with COPD, or cigarette smoking), so we conclude that our case ascertainment system was reliable.

Cost and comorbidity data

Data for all inpatient and outpatient encounters and prescription drug fulfillment for each study subject during the study period were abstracted from LHP administrative data. Data elements extracted from outpatient billing records included the date and location of service, principal and secondary diagnoses, and total charges. For inpatient records, we also extracted the date of admission and discharge, length of stay, diagnosis related group, and surgical procedures, if any.

Inpatient and outpatient costs were taken directly from the charge data. Data extracted from pharmacy records included fulfillment date, drug, amount, strength, average wholesale price, and therapeutic classification. Pharmacy costs were based on the average wholesale price of each prescription drug fulfillment. A detailed summary of these costs has been published elsewhere.[19]

The LHP administrative data was also used to identify and classify comorbidies. We used a modified version of the Charlson–Deyo index for our classification scheme, requiring that a patient have at least two outpatient codes or one inpatient code within a category to be counted as having that disease.[21,22]

Model development

The goals of the model development were to identify the clinical factors during calendar year 1998 that were predictive of total healthcare costs in 1999, and then to develop predictive models that identified which of these factors had the strongest association with costs and best explained the causes of cost variability. Total costs for the sample of 2116 individuals were transformed to a log scale to shorten the long right tail, lessen heteroscedasticity and decrease the influence of outliers,[23] and plotted to examine the distribution. Potential causes of cost variability (predictor variables) were defined and classified into sets (or domains), with each predictor assigned a binary code (Table 1). Multiple linear regression models were fitted for each domain, using SAS software (SAS Institute, Cary, NC, USA). Factors having a significant impact on cost variability were defined as those with a *P*-value of <0.05. The natural antilog of the regression coefficient was used to calculate the ratio of costs compared with the reference group.

Predictive power of fitted models

The predictive power of the proposed model was evaluated by randomly selecting 100 individuals from the sample of 2116 to use as a validation data set. A regression model, using all possible subsets

Table 1 Domains and predictive factors.

Domain	Binary code for predictive factors (abbreviation)	
	1	0
Demographic characteristics	Age less than 50 years	Age 50 years or over
	Male	Female
Smoking status	Former smoker	Never/current smoker
	Current smoker	Never/former smoker
Prior utilisation (in 1998)	Admitted to hospital	Not admitted
	Used home oxygen	No home oxygen
Clinical characteristics (in 1998)	Complained of dyspnoea	No complaint of dyspnoea
	Complained of wheeze	No complaint of wheeze
	Complained of cough	No complaint of cough
Comorbidities (in 1998)	Cardiovascular disease*	No such diagnosis
	Rheumatic conditions†	No such diagnosis
	Peptic ulcers, gastritis, reflux	No such diagnosis
	Psychiatric conditions	No such diagnosis
	Diabetes	No such diagnosis
	Malignancy	No such diagnosis
	Cerebrovascular conditions	No such diagnosis
	Renal disease	No such diagnosis
	Dementia	No such diagnosis
	Hepatic disease	No such diagnosis
Disease severity (FEV% predicted in 1998)	50–80%	>80%
	35–50%	>80%
	<35%	>80%

*Includes coronary artery disease, congestive heart failure, cor pulmonale, arrhythmias, peripheral vascular disease.
†Includes moderate to severe degenerative or osteo-arthritis, auto-immune disease such as lupus, rheumatoid arthritis.

of predictive domains, was fitted to the remaining patients. The fitted model was then used to generate predicted costs for each individual in the validation data set. Two measures of the overall predictive power of the fitted regression model were used: the square root of the mean squared prediction error (RMSPE) and the mean of the absolute prediction error (MABSPE). RMSPE gives an estimate of the true average deviation between predicted and observed costs for any subsequent patients with COPD, and is calculated as

$$\text{RMSPE} = \frac{\sqrt{\sum(C_{\text{observed}} - C_{\text{predicted}})^2}}{n_{\text{validation}}}.$$

The MABSPE provides a more intuitive measure of the variability around the estimate that is less sensitive then the RMSPE to outliers in the validation set, and calculated as

$$\text{MABSPE} = \frac{\sum_i |C_{\text{observed}} - C_{\text{predicted}}|}{n_{\text{validation}}}.$$

Each measure of prediction error was used to select the five models that resulted in the smallest error. This procedure was repeated ten times, using a different set of individuals in the validation data set. The predictors for the models for each validation data set were recorded, and the proportion of models including these predictors assessed.

Results

Patients

Demographic and clinical characteristics of the patients used to develop the model are shown in Table 2. Smoking status was not available for 144 men and 162 women, while spirometry results were not available for 537 men and 533 women. Fig. 1 summarises the costs incurred in managing the patients. A histogram of the costs incurred by each individual in the analysis, transformed to the log scale, is shown in Fig. 2. The marginal distribution of log(cost) was approximately Gaussian, though some slight degree of right skew was apparent. Consequently, the conditional distribution of log(-cost) was modelled assuming normal errors.

Modelling

The factors identified as having a significant impact in multiple linear regression models when individual domains were examined are summarised in

Table 2 Demographic and clinical characteristics.

Characteristics	Males ($n = 1074$)	Females ($n = 1042$)	Total ($n = 2116$)
Age in 1999 (years)	70.9 (range 34–98)	71.2 (range 32–99)	71.1 (range 32–99)
Former smokers (%)	61.3%	50.0%	55.8%
Current smokers (%)	28.4%	29.4%	28.9%
Mean pack years/smoker	56.8	46.9	52.2
Home oxygen (%)	32.1%	31.9%	31.6%
Dyspnoea (%)	60.4%	53.7%	57.1%
Wheeze (%)	38.6%	37.8%	38.2%
Cough (%)	9.5%	9.8%	9.6%
Mean no. comorbid conditions*	2.3 (range 0–9)	2.4 (range 0–10)	2.3 (range 0–10)
Cardiovascular disease (%)	42.9%	35.0%	39.0%
Rheumatic conditions (%)	26.4%	42.2%	34.2%
Peptic ulcers, gastritis, reflux (%)	30.6%	29.8%	30.2%
Psychiatric conditions (%)	17.4%	24.5%	20.9%
Diabetes (%)	11.8%	13.5%	12.7%
Malignancy (%)	8.1%	7.6%	7.8%
Cerebrovascular conditions (%)	6.9%	4.5%	5.7%
Renal disease (%)	5.6%	4.3%	5.0%
Dementia (%)	3.9%	4.2%	4.1%
Hepatic disease (%)	3.7%	2.8%	3.3%
FEV_1% predicted	60.1% (range 43–77%)	51.2% (range 36–65%)	55.5% (range 39–71%)

*Excluding COPD.

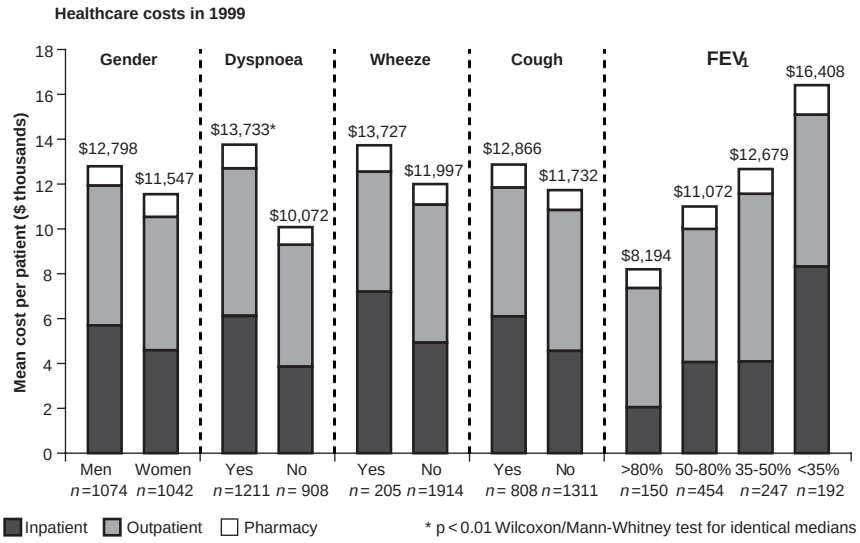

Figure 1 Healthcare costs in 1999.

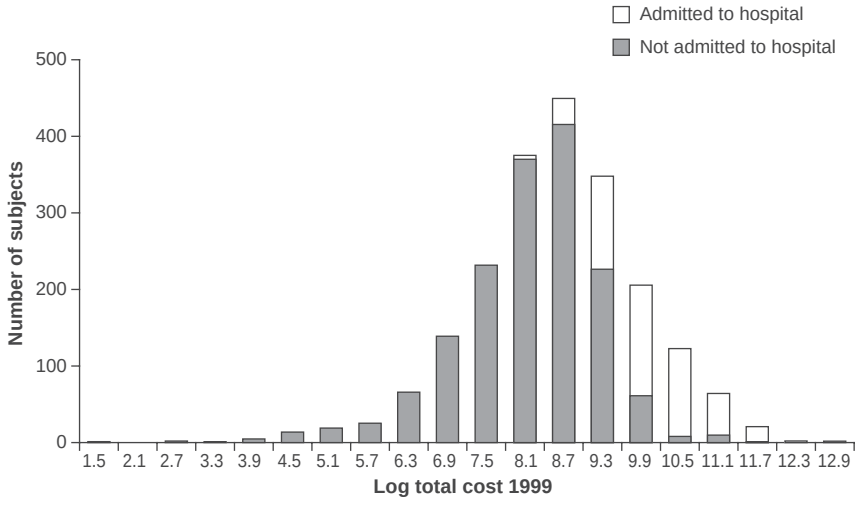

Figure 2 Distribution of costs.

Table 3. Patients using home oxygen or with a hospital admission in 1998 were 79% and 64% more costly, respectively, than those who did not require these resources in 1998. Costs increased progressively as lung function declined. Males and those aged less than 50 years were less costly than the comparator group by 12% and 51%, respectively. Current smokers were associated with a significant reduction in costs (by 40%), while former smokers were 21% more expensive than the comparator group.

Combining domains resulted in loss of significance of some factors, due to multi-colinearity (e.g. all patients using home oxygen also being former smokers, age and dyspnoea being positively correlated with increased disease severity) and reduced data (e.g. loss of significance of cerebrovascular conditions). Table 4 shows the factors that had a significant effect on the model to account for variability of costs, when all predictive domains were included. In this analysis, males showed a significant reduction in costs of 14% compared with females, while current smokers showed a 31% reduction in costs over the comparator group. Costs were increased by around 40% in those using home oxygen or having a hospital admission in the previous year, and in those with comorbid conditions.

As hospital admissions are a key cost driver, the probability of being admitted to hospital in 1999 was also modelled. Age, gender, smoking status and disease severity were found not to be significant predictive factors. However, a hospital admission in the previous year, use of home oxygen, reported

Table 3 Predictive factors in multiple linear regression models by domains.

Domain	Predictive factor	Regression coefficient	Ratio of costs	*P*-value
Demographic characteristics	Male	−0.12329	0.88	0.0310
	Age less than 50 years	−0.70503	0.49	<0.0001
Smoking status	Former smoker	0.19384	1.21	0.0237
	Current smoker	−0.51790	0.60	<0.0001
Prior utilisation	Admission	0.49733	1.64	<0.001
	Home oxygen	0.58119	1.79	<0.001
Clinical characteristics	Dyspnoea	0.43242	1.54	<0.001
Comorbidities	Cardiovascular disease	0.49744	1.64	<0.001
	Rheumatic conditions	0.24188	1.27	<0.001
	Peptic ulcers, gastritis, reflux	0.24274	1.27	<0.001
	Psychiatric conditions	0.29775	1.35	<0.001
	Diabetes	0.24790	1.28	0.0031
	Malignancy	0.48889	1.63	<0.001
	Cerebrovascular conditions	0.26867	1.31	0.0259
	Renal disease	0.26834	1.31	0.0390
FEV_1% predicted	50–80%	0.22097	1.25	0.0473
	35–50%	0.39201	1.48	0.0014
	<35%	0.53718	1.71	<0.001

Table 4 Predictive factors in multiple linear regression models, combining all domains.

Domain	Predictive factor	Regression coefficient	Ratio of costs	*P*-value
Demographic characteristics	Male	−0.14918	0.86	0.0338
Smoking status	Current smoker	−0.37082	0.69	0.0020
Prior utilisation	Admission	0.37429	1.45	<0.0001
	Home oxygen	0.30035	1.35	<0.0001
Comorbidities	Cardiovascular disease	0.33038	1.39	<0.0001
	Rheumatic conditions	0.20805	1.23	0.0039
	Peptic ulcers, gastritis, reflux	0.18884	1.21	0.0090
	Psychiatric conditions	0.32713	1.39	0.0001
	Diabetes	0.36711	1.44	0.0005
	Malignancy	0.59836	1.82	<0.0001
	Renal disease	0.36177	1.44	0.0287
FEV_1% predicted	35–50%	0.22952	1.26	0.0496

dyspnoea and some comorbid conditions were all significant factors predictive of hospital admission (Fig. 3).

Predictive power of fitted models

While dyspnoea and demographic characteristics were included in under half of the best predictive models (44% and 46%, respectively), prior healthcare resource utilisation (hospital admissions and home oxygen use) was included in 62% and comorbid conditions included in 68% of the best predictive models, indicating that these latter factors are most strongly predictive of future costs. However, the average prediction error was very high. Using RMSPE, the average deviation between the predicted and expected costs over the validation data set ranged from $11,253 to $61,655, with marked variation between validation sets used. Likewise, there was considerable variation in prediction error calculated using MABSPE.

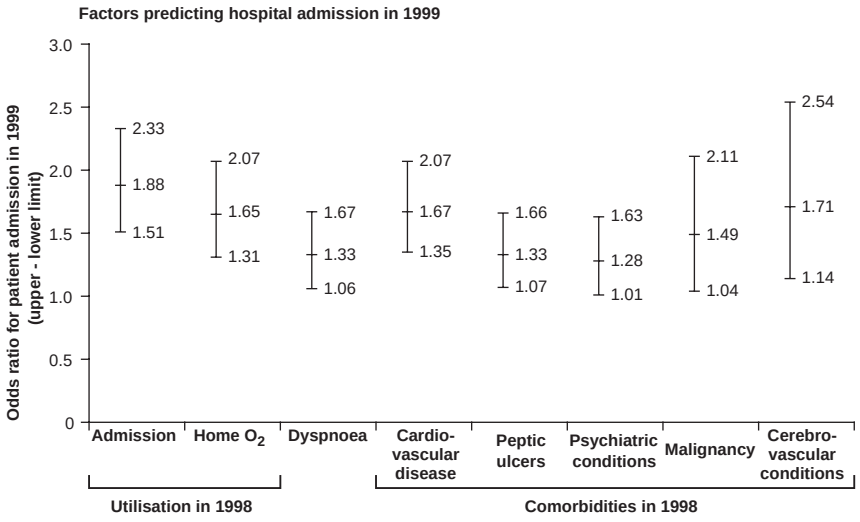

Figure 3 Factors predicting hospital admission in 1999.

Discussion

The study demonstrated that the currently recommended system for staging airflow obstruction[1] is a valid but weak predictor of future healthcare resource utilisation—prior hospitalisation and home oxygen use, the presence of comorbid conditions and symptoms of dyspnoea are better predictors of costs.

The patients enrolled in the LHP used as the basis for the model present a typical population of patients with COPD. In this study, 58% of patients had FEV_1 of 50% predicted or more, with 24% having lung function of 35–49% predicted and 18% with FEV_1 less than 35% predicted, comparable to populations of patients with COPD derived from the Health Survey for England[24] and from the Third National Health and Nutrition examination Survey (NHANES III) in the USA.[25] Furthermore, use of home oxygen (a factor with a significant impact on costs) was comparable in the present study and in that reported by US patients in the confronting COPD study.[26] Consequently, the findings of the present study are likely to be applicable to other populations.

The present study used information derived from a large database covering a population of some 200,000 people. Thus, the study population reflects real world data, encompassing patients suffering from multiple comorbid conditions—such patients may be excluded from randomised controlled clinical trials. The use of an administrative database also allows investigation of outcomes of interest to healthcare decision-makers, namely inpatient, outpatient and pharmacy costs. Such database studies are proving of great value in the study of COPD, as they allow the capture of information about intermittent severe events, such as exacerbations, which may be difficult to study in short-term studies that exclude many patients at greatest risk of experiencing these adverse events.[27] Exacerbations of COPD have been shown to have a major impact on patient quality of life, as well as on disease progression, mortality and costs.[10,28–30]

A standard methodology for the handling of data with skewed distribution was used in this study.[23] Cost data was transformed logarithmically, with exclusion of data from the three patients who did not have healthcare resource utilisation during 1999 (i.e. zero cost). Analysis of utilisation data on a log scale also facilitates the use of a multiplicative model for interaction between potential predictive factors because the exponential of the regression coefficients provides estimated ratios of costs. Other methods of analysing skewed data, such as Cox regression, result in regression coefficients that are more difficult to interpret in the context of medical costs, as they pertain to hazard ratios.[23]

One limitation of this analysis is that we required all patients to be continuously enrolled throughout the study period, thus excluding persons who died. We did this because of the profound increase in costs that occur at the end of life, which cause these patients to be statistical outliers with disproportionate effects on the overall results if included in the analysis. Therefore, our analysis assumes that all patients will survive the following year, and that is an important consideration when comparing our results to other populations. We have conducted a separate analysis of the

healthcare costs incurred in the last 12 months of life among persons treated by the LHP, and found that COPD patients had an average total cost of $48,384, which was approximately four times greater than that of the survivors. However, it is likely that the main findings of this study still apply to COPD patients who die. In studies of COPD survival, some of the main predictors of death have included most of the same factors that we found to be predictive of increased costs, such as advanced age, hospitalisations, and the presence of comorbidities.[31–33]

Regression analysis, although unsatisfactory for predicting healthcare utilisation of an individual, can be used to give meaningful predictions for a population. Such models are useful for healthcare planners and decision-makers. By identifying the factors that have the largest influence on future costs, they can direct decision-makers to the most appropriate outcomes for evaluation of potential treatments. This study showed that previous healthcare resource utilisation (prior hospitalisation or home oxygen use) was the most important determinant of future cost. Prior hospitalisations are usually the result of an exacerbation,[34] while failure of therapy to prevent exacerbations progressing to hospitalisation has been demonstrated to result in costs of $100/exacerbation.[30] Our study suggests that management strategies for COPD should put greater emphasis on reducing exacerbations and hospitalisations and on controlling chronic symptoms, as opposed to simply focusing on how treatments effect the FEV_1.

The severity of airflow limitation, as measured by % predicted FEV_1 and used in classifications of disease stages, was shown in this study to be a valid but weak predictor of healthcare utilisation. However, it should be noted that only the patients who survived the full period of 1998 and 1999 were included in the analysis, excluding those who died during the study period. Several studies have highlighted the link between disease stage and mortality risk, with lung function both an independent predictor of mortality and a marker for other changes.[35,36] Those who died during the period were likely to be those with most severely impaired lung function. As many costs are incurred in the period shortly before death, this would have the effect of blunting the predictive effect of lung function on healthcare resource utilisation.

Interestingly, this study found that current smokers were associated with lower costs, and former smokers with higher costs, than the comparator groups. A similar finding has also been reported in studies of completely different design, such as the large scale international patient survey, Confronting COPD.[37] This finding is likely to be due to the impact of the 'quitting ill' effect, in which smokers quit only after the onset of severe symptoms.[26]

Although the present study clearly identified the factors that are predictive of future costs, the magnitude of the prediction error was considerable. This means that the impact of these factors cannot be readily assigned a monetary value. The degree of error was largely determined by the composition of patients within the validation data set. When the validation set included some patients who incurred high costs, then the prediction error was correspondingly large. When such patients were not included in the validation data set, then the prediction error was relatively small. The predictive model does not account for factors that could influence whether an individual is in a high cost group or not. In the future, this may be addressed by refining the model to incorporate two stages: firstly, predicting whether or not hospitalisation would occur, then secondly, assessing the subsequent costs.

In conclusion, the study showed that the key predictors of future healthcare costs for a population of patients with COPD are prior hospitalisation and use of home oxygen. With the increasing prevalence and high cost of managing COPD, the study underlines the need for management strategies that reduce the frequency and severity of exacerbations, thereby reducing the need for hospitalisation and delaying disease progression.

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