



Exacerbations of COPD: quantifying the patient's perspective using discrete choice modelling

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ABSTRACT: Patient-centred care is the current vogue in chronic obstructive pulmonary disease (COPD), but it is only recently that robust techniques have become available to determine patients' values and preferences. In this international cross-sectional study, patients' concerns and expectations regarding COPD exacerbations were explored using discrete choice modelling.

A fractional factorial design was used to develop scenarios comprising a combination of levels for nine different attributes. In face-to-face interviews, patients were presented with paired scenarios and asked to choose the least preferable. Multinomial logit (with hierarchical Bayes) methods were used to estimate utilities. A total of 125 patients (82 males; mean age 66 yrs; 4.6 mean exacerbations·yr⁻¹) were recruited.

The attributes of exacerbations considered most important were impact on everyday life (20%), need for medical care (16%), number of future attacks (12%) and breathlessness (11%). The next most important attributes were speed of recovery, productive cough and social impact (all 9%), followed by sleep disturbance and impact on mood (both 7%). Importantly, analysis of utility shifts showed that patients most feared being hospitalised, housebound or bedridden. These issues were more important than symptom improvement.

Strategies for the clinical management of chronic obstructive pulmonary disease should clearly address patients' concerns and focus on preventing and treating exacerbations to avoid these feared outcomes.

KEYWORDS: Chronic obstructive pulmonary disease, discrete choice modelling, exacerbations, patient perceptions

With the global move towards patient-centred care, there is an increasing need for valid and reliable methods to assess patient values, concerns and preferences. Discrete choice modelling, which was developed from conjoint analysis, is widely used in economics to identify individual preferences, but has only recently been applied to healthcare settings [1, 2]. The technique provides an attribute-based measure of benefit, based on the suppositions that interventions, services, policies or events can be described by their attributes (characteristics), and that an individual's valuation depends on the levels (nature) of these attributes [2]. As this technique is based on the belief that attributes considered jointly can be better measured than if considered individually, subjects are presented with a choice of scenarios that are described in terms of their attributes and associated levels. For each choice, they are asked to choose their preferred outcome. The modelled data provide

information on the importance of different attributes, the relative importance of levels, the rate at which respondents are willing to trade between levels and the overall benefit (utility) values for alternative scenarios [3].

The feasibility of this type of approach has been demonstrated in asthma, where discrete choice modelling [4] and conjoint analysis [5–8] have been used to assess patient preferences for symptoms, type of treatment and delivery of services. However, to the current authors' knowledge, there have been no such studies in chronic obstructive pulmonary disease (COPD).

Exacerbations of COPD clearly have a dramatic impact on patient outcomes [9–13]. However, there is considerable heterogeneity in the aetiology and manifestation of COPD exacerbations. A wide range of symptoms may be experienced, resulting in different physical and psychological consequences for individual patients [14, 15].

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Improved understanding of the relative importance and desired outcomes of different attributes of COPD exacerbations from the patient’s perspective may facilitate clinical management of this disorder. Although studies have shown that patients with COPD tend to underestimate the severity and impact of exacerbations [10, 11], patients’ relative value judgments regarding how they feel about different aspects of exacerbations have not been extensively studied. With this in mind, the current study used discrete choice modelling to describe, quantify and prioritise attributes associated with COPD exacerbations from the patients’ perspective.

METHODS

An international, face-to-face, cross-sectional study of patients’ values regarding the characteristics and burden of COPD exacerbations was conducted in France, Germany, Spain, Sweden and the UK. The study was conducted in accordance with the Declaration of Helsinki and approved by local ethics committees at each of the participating centres. All patients provided written informed consent to participate.

Patients

Males and females aged ≥50 yrs were eligible for the study if they had: 1) a diagnosis of COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [16]; 2) forced expiratory volume in one second/forced vital capacity of <70%; 3) experienced two or more exacerbations (defined as the worsening of respiratory symptoms so as to require medical intervention, *i.e.* oral corticosteroids and/or antibiotics and/or hospitalisation) during the previous year; and 4) at least one exacerbation within the past 6 months. Patients currently hospitalised and patients with lung cancer, chronic heart failure (not associated with COPD), asthma, a history of psychiatric disorders and any other condition considered likely to render the subject unable to participate in a face-to-face interview of 1 h duration were excluded. Each centre was scheduled to recruit 25 patients, of whom 50% should be aged 50–65 yrs and 50–75% should be male.

Data collection

Information concerning COPD and exacerbations was collected during semi-structured, face-to-face interviews with individual participants. During this visit, data were also collected on each subject’s COPD (sociodemographic status, clinical parameters, disease history, symptoms, treatment and exacerbation history, including medical resource consumption) using standardised case report forms.

During the interviews, each patient was shown a set of cards that described pairs of hypothetical profiles of their “next exacerbation” and asked to choose the profile within each set of two that would be the least desirable for them. Exacerbations were described *via* nine different attributes: 1) impact on everyday life; 2) level of medical care required as a consequence of the exacerbation; 3) number of future attacks; 4) breathlessness; 5) speed of recovery; 6) cough and phlegm/spit; 7) social impact; 8) sleep disturbance; and 9) impact on mood. Three or four levels were assigned to each of the nine attributes (table 1). Both the attributes and the levels were selected by the current authors, based on personal experience and published reports of exacerbations, as those that were considered important to patients and within the sphere of

TABLE 1 Attributes and levels included in the discrete choice model

Treatment attribute	Levels
Impact on everyday life	Little impact on household activities and able to go for a short walk Able to wash, dress and move around the house, but not able to walk outside Able to wash and dress, but little else; walking almost impossible Stay in bed and not able to do anything for myself
Medical care	No need to see a doctor Need to see a doctor Admitted to hospital
Number of future attacks	Fewer attacks in the future No change in the number of future attacks More attacks in the future
Symptoms	
Breathlessness	No worse than usual
Cough and phlegm/spit	Worse than usual
Social impact	Much worse than usual
Sleep disturbance	
Impact on mood	
Speed of recovery	<1 week 2 weeks ≥3 weeks

influence of practising physicians. Attributes and levels were tested in a small number of patients before proceeding to the main study.

Patients were divided randomly into four groups, with each group seeing a different set of cards. Each set had 12 choice tasks, with each task showing two different profiles of the patient’s “next exacerbation”. All outcome profiles included five of the nine attributes described above and each pair within each profile included the same five attributes, but with different levels. Each of the 12 pairs included a different set of five attributes so that all patients were exposed to all nine attributes. In total, each patient saw 24 different profiles (96 profiles in total) out of the full possible factorial design (3 × 3 × 3 × 3 × 3 × 3 × 3 × 3 × 4 = 26,244). In all cases, the 24 profiles were presented in 12 pairs with the question, “Which of these two descriptions of your next exacerbation would be the least desirable?” The questionnaire and examples of the question cards used in this study are shown in the Appendix.

Analysis

The experimental design was developed using Choice-Based Conjoint software from Sawtooth Software (Sequim, WA, USA), ensuring that both orthogonality and level balance requirements were met. The paired choice data were analysed using multinomial logit with hierarchical Bayes (HB) in order to determine utility values for the 28 possible features (three levels on eight of the attributes and four levels on one attribute) of a COPD exacerbation [17]. Although computationally

extensive, HB analysis can produce acceptable estimates of utility values for individuals with <12 tasks per respondent [18, 19]. HB analysis has been found to be consistently superior to ordinary least-squares regression with regard to its ability to recover the true population mean. It is particularly beneficial when the data are heterogeneous [17–19].

The mean utility values for levels were calculated on an *a priori* basis so that the value of one level within each attribute was zero. Superior (more preferable) levels were given a nonzero positive value. These utility values can be interpreted in two ways, both based on differences between values for levels within the attributes. The “utility shifts” indicate the weighting of patient preferences. A larger difference in utility values between one level and another indicates a stronger preference for this shift. The first interpretation allows conclusions to be made based on the values of transitions from one level to another within an attribute and also permits comparisons between transitions involving successive pairs of levels. The second interpretation allows conclusions to be made based on the relative importance of attributes. The relative importance of variation across the range of each of nine attributes was calculated for each individual respondent by use of the following formula [20]:

$$\text{Importance \%} = 100 \times (U_{\text{imax}} - U_{\text{imin}}) / \sum (U_{\text{imax}} - U_{\text{imin}}) \quad (1)$$

where U_{imax} = maximum utility value of levels within the *i*th attribute and U_{imin} = minimum utility value of levels within the *i*th attribute.

As part of this study, qualitative data were also collected to obtain knowledge about the burden of exacerbations on patients. These results are reported separately [21].

RESULTS

In total, 125 patients were recruited from France (n=25), Germany (n=25), Spain (n=27), Sweden (n=28) and the UK (n=20). Patient demographics and disease characteristics at baseline are shown in table 2. Of the 104 patients who underwent GOLD staging [16], 2.9% (n=3) were classified as stage I, 18.3% (n=19) as stage II, 44.2% (n=46) as stage III and 34.6% (n=36) as stage IV. The most common comorbid conditions were cardiovascular disease (49.5%; n=48), endocrine disorders (20.6%; n=20) and rheumatic disease (19.6%; n=19). As agreed prospectively, no inter-country comparisons would be made in view of the limited number of patients per country.

On average, patients had experienced 4.6 exacerbations during the previous 12 months and visited a healthcare professional 4.1 times. However, these numbers varied considerably between patients (table 2). There was also significant variability between patients with regard to the duration of their last exacerbation, time between exacerbations and time since their last exacerbation.

Utility scores and shifts calculated for each level of the exacerbation attributes are shown in figure 1 (n=122). The highest shifts in mean utilities were between the following attribute levels. 1) Impact on everyday life: between “having little impact on daily activities” and “being housebound”, and “being housebound with restrictions” and “being bedridden”.

TABLE 2 Patient demographics and disease characteristics at baseline[#]

Characteristic	Value
Male/female	82/43
Age yrs	66.3 ± 8.6
FEV1 % pred	40.9 ± 18.1
FEV1/FVC %	50.0 ± 14.0
Duration of COPD yrs	7.4 ± 7.4
Smoking history	
Ex-smoker	77 (61.6)
Smoker	39 (31.2)
Never smoked	9 (7.2)
Patients with ≥ 1 comorbidity	97 (77.6)
Number of exacerbations in the past 12 months	4.6 (1–50) [‡]
Time since last exacerbation days	93.6 (0–720) [‡]
Duration of last exacerbation days	12.7 (1–119) [‡]
Time between exacerbations days	115.6 (1–546) [‡]
Healthcare resource use per patient in the past 12 months	
Healthcare professional visits	4.1 (0–19)
Emergency room visits	1.1 (0–10)
Hospitalisations	0.8 (0–8)
Stays in intensive care unit	0.04 (0–1)

Data are presented as n, mean ± SD, n (%) or mean (range). FEV1: forced expiratory volume in one second; FVC: forced vital capacity; COPD: chronic obstructive pulmonary disease. #: n=125; †: data determined from patient responses. According to physician records, all patients met the inclusion criteria.

2) Medical care: between “no need to see a doctor” and “being hospitalised”. 3) Number of attacks: between “having fewer attacks in the future” and “no change in the number of attacks”, and “no change in the number of attacks” and having “more attacks in the future”. 4) Breathlessness: between “no worse than usual” and “worse than usual”. 5) Speed of recovery: between “<1 week” and “2 weeks”. 6) Cough and phlegm/spit: between “worse than usual” and “much worse than usual”. 7) Social impact: between “no worse than usual” and “worse than usual”, and “worse than usual” and “much worse than usual”. 8) Sleep disturbance: between “no worse than usual” and “worse than usual”. 9) Impact on mood: between “no worse than usual” and “worse than usual”.

The attributes of COPD exacerbations considered by patients to be the least desirable, determined as the mean of their importance for individuals, ranked in order of importance were: impact on everyday life and medical care, followed by number of attacks, breathlessness, speed of recovery, cough and phlegm/spit, social impact, sleep disturbance and finally impact on mood (n=122; fig. 2).

DISCUSSION

To the present authors' knowledge, this is the first study to examine patient preferences in COPD using discrete choice modelling (a robust method used for examining patient preferences, values and concerns in healthcare settings) [1, 2]. Within this setting, discrete choice modelling has provided a

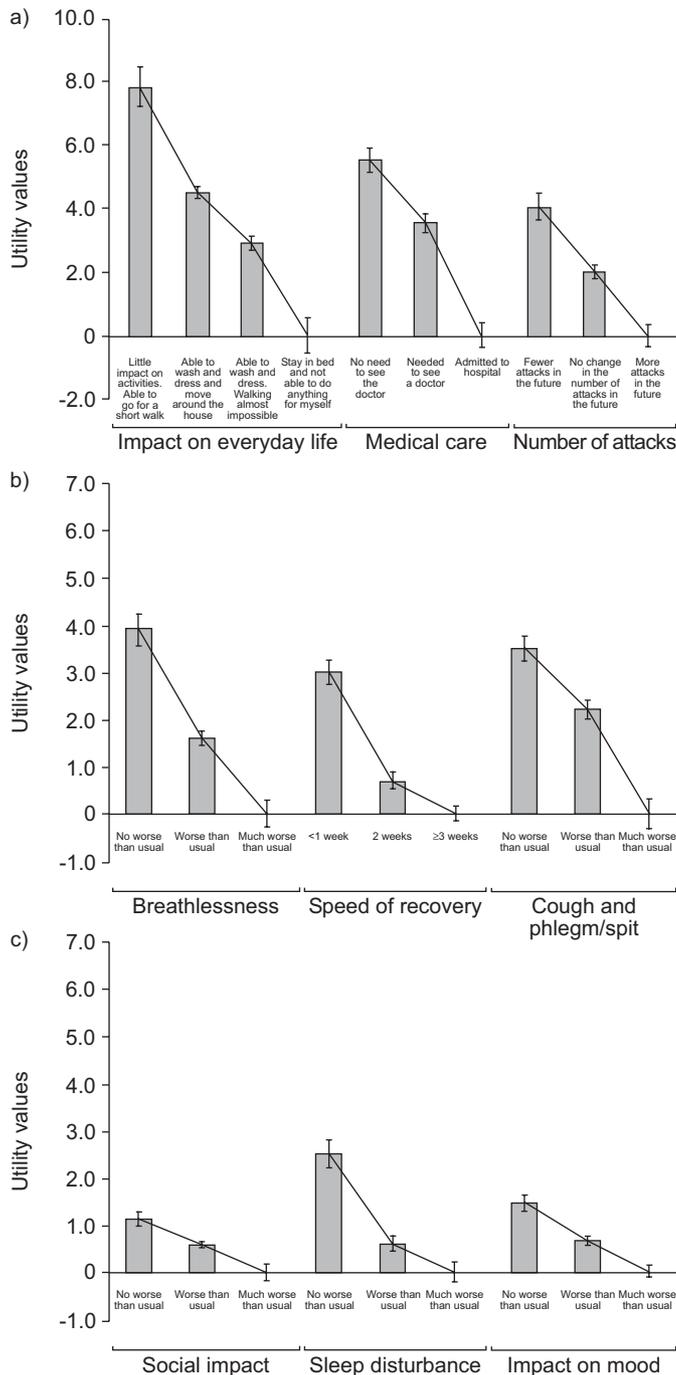


FIGURE 1. Utility values and shifts between levels for the attributes of chronic obstructive disease exacerbations: a) impact on everyday life, level of medical care and number of future attacks; b) breathlessness, speed of recovery, and cough and phlegm/spit; and c) social impact, sleep disturbance and impact on mood. Data were missing for three patients.

useful starting point for exploring patient preferences with regard to exacerbations of COPD and understanding the trade-offs patients are willing to make as new interventions are developed.

The results of this study indicate that the impact on daily activities and the level of medical care they require are

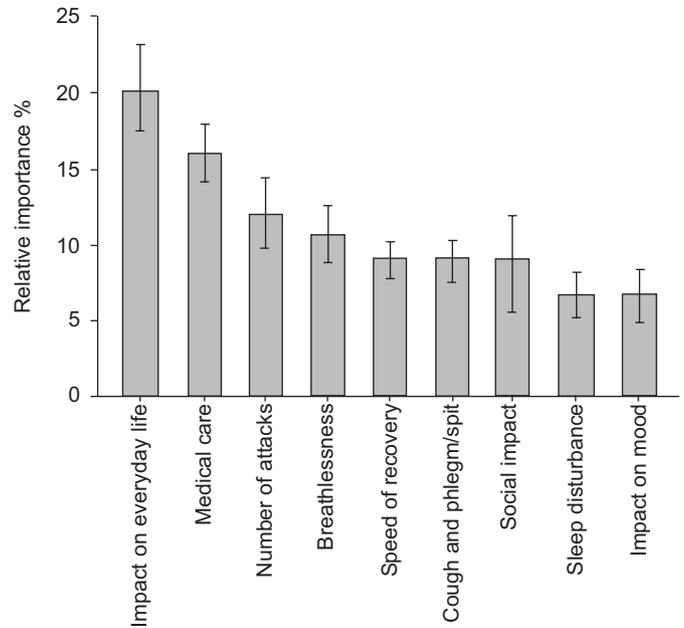


FIGURE 2. Relative importance (%) of different attributes of chronic obstructive pulmonary disease exacerbations, as ranked by patients. Data are expressed as mean \pm SEM. Data were missing for three patients.

paramount medical concerns for patients during COPD exacerbations, ranking higher than concerns over the number of future attacks and severity of breathlessness. The discrete choice modelling study results suggest that, in terms of the impact of exacerbations on daily life, being housebound is the major worry for patients. If housebound, patients consider the level of ambulatory restriction less important than being bedridden. Similarly, with respect to medical care, avoiding a physician visit is important to patients, but avoidance of being hospitalised is a highly valued outcome, having the largest utility shift seen in the study. Avoidance of being housebound, confined to bed or hospitalised appears to be more important to patients than improvement of breathlessness, productive cough or disturbed nights. Traditionally, physicians tend to be more concerned about symptoms, but results from this study suggest that symptoms are less important from the patient's perspective than the impact of exacerbations on everyday activities.

This finding is consistent with previous studies reporting the dramatic effect of exacerbations on patients' health-related quality of life and daily activities. In 1998, SEEMUNGAL *et al.* [22] demonstrated that health-related quality of life was related to the frequency of exacerbations in addition to disease severity in patients with moderate-to-severe COPD. A similar negative association between exacerbation frequency and health-related quality of life has been shown in other studies involving patients with moderate or moderate-to-severe COPD [12, 23, 24]. Reducing the frequency of exacerbations has been shown to be associated with beneficial effects on health-related quality of life [23, 25]. It is important to note that poor health-related quality of life is associated with an elevated risk of ensuing COPD-related hospitalisation and all-cause mortality [26–28]. Becoming housebound, confined to bed or hospitalised during

an exacerbation would clearly have an enormous impact on patients' daily activities and quality of life. Data from this study show that patients recognise this and are extremely concerned about these potential outcomes. Developments of strategies to avoid these potential outcomes are likely to be welcomed by patients.

For many patients, the only safe place during an exacerbation is in hospital, where they can receive specialist support, such as controlled oxygen therapy and noninvasive mechanical ventilation. However, for others, hospitalisation may not be necessary. The findings from the present study emphasise how much patients fear hospitalisation. It is likely that these patients would prefer to be managed at home and implementation of schemes such as "hospital at home" and early supported discharge may be congruent with their desire to avoid hospitalisation. These schemes appear to be safe, in that hospital re-admission rates and mortality in patients treated in this way are comparable with those in patients who are admitted to hospital [29–31]. Similarly, patients' preference to avoid the need to see their doctor when they experience an exacerbation may be assisted by a greater emphasis on self-management education and patient instruction. However, the benefits of this type of approach have not yet been proved in COPD [32].

A better approach to avoidance of hospitalisation and physician visits may be through prevention of exacerbations. The data from this study clearly show that the potential for fewer attacks in the future has considerable appeal for patients. Within this particular attribute, the impact of each level was found to be equally important from the patients' perspective. Prevention of exacerbations is already recognised in the GOLD guidelines as a key goal for COPD management [16], and long-term trials of new therapies (inhaled corticosteroids/long-acting β_2 -agonist combinations (budesonide/formoterol and fluticasone/salmeterol) and the long-acting anticholinergic agent, tiotropium) have included exacerbations as a primary end point, and have been shown to be effective [33–36]. Thus, there is evidence that treatments can help prevent future exacerbations of COPD.

Exacerbations are not short-term events. Indeed, several studies have shown that recovery from an exacerbation can take several weeks and some patients do not return to their previous state of health before they experience another exacerbation [10, 37, 38]. Data from this analysis indicate that a fast recovery (<1 week) from an exacerbation is an attractive outcome for patients. Achieving a fast recovery is likely to be heavily dependent on receipt of early and appropriate medical intervention at the onset of an exacerbation. A recent cohort study by WILKINSON *et al.* [39] supports this supposition. These workers found that earlier treatment (oral corticosteroids and/or antibiotics) for exacerbations was associated with a significantly faster recovery from exacerbation symptoms (regression coefficient 0.42 days/day delay). Moreover, patients who reported a higher proportion of exacerbations for treatment had improved health-related quality of life compared with patients who had more untreated exacerbations. Lack of reporting of exacerbations was also associated with an increased risk of hospitalisation.

Shifts between attribute levels in the current study also show that even small increases in the symptoms of breathlessness and sleep disturbance are important to patients. With regard to productive cough, a minor worsening of this symptom may be acceptable to patients but a significant worsening would not. These results imply that patients would value any intervention that provides symptomatic relief, particularly during periods of symptom worsening. For the attributes "social impact" and "impact on mood", patients might agree to trade a worsening in these attributes in order to gain an improvement in other attributes that they have ranked as more important. The utility shifts suggest that any intervention which affects a patient's mood or social relationships is unlikely to affect their preference for that intervention to any great extent.

Although these data reveal interesting and important findings, the conclusions that can be made are only tentative given the limited sample size in this study. The small sample size and recruitment procedure used meant that testing for statistical differences was not appropriate, nor was it possible, or ever the current authors' intention, to examine the influence of baseline characteristics on patient preferences. Despite these limitations, discrete choice modelling is a rigorous and validated method for determining preferences [3].

In conclusion, patient-centred care is becoming increasingly important in medicine today. If clinical management is tailored to service patient's desires, use of robust techniques to determine their values and preferences is essential. Discrete choice modelling has provided a useful starting point for exploring patient preferences with regard to exacerbations of chronic obstructive pulmonary disease. Using this methodology, it was found that impact on daily activities and the need for medical care are paramount concerns for patients during exacerbations. Being house-bound or hospitalised are the least favourable outcomes and are more important to patients than improvements in symptoms. Strategies for the clinical management of chronic obstructive pulmonary disease should clearly address patients' concerns, thus focusing on preventing and treating exacerbations to avoid these feared outcomes. Fewer exacerbations would likely reduce the burden and worry associated with chronic obstructive pulmonary disease.

APPENDIX: STUDY QUESTIONNAIRE AND EXAMPLE QUESTION CARDS

Study questionnaire

Discrete choice modelling exercise: Your next {USE PATIENT'S OWN WORD FOR EXACERBATION}

I am going to present you with 12 sets of cards. Each set of cards [SHOW HIM/HER THE CARD] describes 2 alternative ways in which you may experience an {USE PATIENT'S OWN WORD}. For each set of cards, I will ask you to choose between the 2 alternatives the one that is the worst for you. Please study each card in detail before answering the question.

THE FOLLOWING QUESTION IS TO BE ASKED AFTER EACH SET: The next time you have an {USE PATIENT'S OWN WORD}, which of these 2 descriptions of symptoms, treatment and duration of illness would be the worst for you?

Please WRITE the NUMBER on the card given by the patient in the appropriate box of TABLE 1. The numbers are EITHER 1 OR 2.

First choice. PLEASE WRITE THE NUMBER ON THE CARD (1 OR 2)
Example card A
CARD B
CARD C
CARD D
CARD E
CARD F
CARD G
CARD H
CARD I
CARD J
CARD K
CARD L
CARD M

Example question cards

An example of question cards given to the patients is shown below.

	Situation 1	Situation 2
Version 1 task 1		
Sleep disturbance	No worse than usual	Worse than usual
Speed of recovery	3 weeks and more	2 weeks
Impact on mood	Worse than usual	Much worse than usual
Social impact	No worse than usual	Much worse than usual
Impact on everyday life	Able to wash and dress myself but little else. Walking almost impossible	Able to wash and dress and move around the house but not to walk outside
Version 1 task 2		
Cough and phlegm/spit	No worse than usual	Worse than usual
Medical care	Admitted to the hospital	No need to see the doctor
Speed of recovery	Less than 1 week	3 weeks and more
Breathlessness	Worse than usual	No worse than usual
Number of attacks	More attacks in the future	Fewer attacks in the future
Version 1 task 3		
Cough and phlegm/spit	Worse than usual	Much worse than usual
Medical care	Admitted to the hospital	Needed to see a doctor
Impact on mood	Much worse than usual	No worse than usual
Breathlessness	Worse than usual	Much worse than usual
Impact on everyday life	Little impact on activities in the house and able to go for a short walk	Stay in bed and not able to do anything for myself

REFERENCES

- Ryan M, Gerard K. Using discrete choice experiments to value health care: current practice and future prospects. *Appl Health Econ Policy Analysis* 2003; 2: 55–64.
- Ryan M. Discrete choice experiments in health care. *BMJ* 2004; 328: 360–361.
- Ryan M, Bate A, Eastmond CJ, Ludbrook A. Use of discrete choice experiments to elicit preferences. *Qual Health Care* 2001; 10: Suppl. 1, i55–i60.
- McKenzie L, Cairns J, Osman L. Symptom-based outcome measures for asthma: the use of discrete choice methods to assess patient preferences. *Health Policy* 2001; 57: 192–204.
- Johansson G, Stallberg B, Tornling G, et al. Asthma treatment preference study: a conjoint analysis of preferred drug treatments. *Chest* 2004; 125: 916–923.
- Ratcliffe J, Van Haselen R, Buxton M, Hardy K, Colehan J, Partridge M. Assessing patients’ preferences for characteristics associated with homeopathic and conventional treatment of asthma: a conjoint analysis study. *Thorax* 2002; 57: 503–508.
- Osman LM, McKenzie L, Cairns J, et al. Patient weighting of importance of asthma symptoms. *Thorax* 2001; 56: 138–142.
- Balsbaugh TA, Chambers CV, Diamond JJ. Asthma controller medications: what do patients want? *J Asthma* 1999; 36: 591–596.

- 9 Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002; 57: 847–852.
- 10 Seemungal TAR, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 161: 1608–1613.
- 11 Rennard S, Decramer M, Calverley PM, *et al.* Impact of COPD in North America and Europe in 2000: Subjects' Perspective of Confronting COPD International Survey. *Eur Respir J* 2002; 20: 799–805.
- 12 Miravittles M, Ferrer M, Pont A, *et al.* Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax* 2004; 59: 387–395.
- 13 Vestbo J. What is an exacerbation of COPD? *Eur Respir Rev* 2004; 13: 6–13.
- 14 Wedzicha JA. The heterogeneity of chronic obstructive pulmonary disease. *Thorax* 2000; 55: 631–632.
- 15 Pauwels R, Calverley P, Buist AS, *et al.* COPD exacerbations: the importance of a standard definition. *Respir Med* 2004; 98: 99–107.
- 16 Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD). NIH publication No. 2701. Bethesda, MD, National Institutes of Health, 2001 (revised 2003).
- 17 Gelman A, Carlin JB, Stern HS, *et al.* Bayesian Data Analysis. Suffolk, Chapman & Hall, 2004; pp. 1–568.
- 18 Allenby GM, Arora N, Ginter JL. Incorporating prior knowledge into the analysis of conjoint studies. *J Mark Res* 1995; 32: 152–162.
- 19 Lenk PJ, DeSarbo WS, Green PE, *et al.* Hierarchical Bayes conjoint analysis: recovery of partworth heterogeneity from reduced experimental design. *Marketing Science* 1996; 15: 173–191.
- 20 Sawtooth Software Inc. CBC User Manual Version 2.0. Sawtooth Software Inc., Sequim, WA, USA, 1993.
- 21 Kessler R, Löfdahl C-G, Tornling G, Ståhl E. An evaluation of exacerbations in COPD. *Eur Respir J* 2004; 24: Suppl. 24, 89s–90s.
- 22 Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998; 157: 1418–1422.
- 23 Spencer S, Calverley PM, Burge PS, Jones PW. Impact of preventing exacerbations on deterioration of health status in COPD. *Eur Respir J* 2004; 23: 698–702.
- 24 Doll H, Grey-Amante P, Duprat-Lomon I, *et al.* Quality of life in acute exacerbation of chronic bronchitis: results from a German population study. *Respir Med* 2002; 96: 39–51.
- 25 Jones PW, Ståhl E. Reducing exacerbations leads to a better health-related quality of life in patients with COPD. *Eur Respir J* 2003; 22: Suppl. 45, 238s.
- 26 Fan VS, Curtis JR, Tu SP, McDonnell MB, Fihn SD, and the Ambulatory Care Quality Improvement Project Investigators. Using quality of life to predict hospitalization and mortality in patients with obstructive lung diseases. *Chest* 2002; 122: 429–436.
- 27 Soler JJ, Sanchez L, Roman P, Martinez MA, Perpina M. Risk factors of emergency care and admissions in COPD patients with high consumption of health resources. *Respir Med* 2004; 98: 318–329.
- 28 Osman LM, Godden DJ, Friend JAR, Legge JS, Douglas JG. Quality of life and hospital re-admission in patients with chronic obstructive airways disease. *Thorax* 1997; 52: 67–71.
- 29 Ram FS, Wedzicha JA, Wright J, Greenstone M. Hospital at home for patients with acute exacerbations of chronic obstructive pulmonary disease: systematic review of evidence. *BMJ* 2004; 329: 315.
- 30 Cotton MM, Bucknall CE, Dagg KD, *et al.* Early discharge for patients with exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. *Thorax* 2000; 55: 902–906.
- 31 Skwarska E, Cohen G, Skwarski KM, *et al.* Randomized controlled trial of supported discharge in patients with exacerbations of chronic obstructive pulmonary disease. *Thorax* 2000; 55: 907–912.
- 32 Monninkhof E, van der Valk P, van der Palen J, van Herwaarden C, Partridge MR, Zielhuis G. Self-management education for patients with chronic obstructive pulmonary disease: a systematic review. *Thorax* 2003; 58: 394–398.
- 33 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.
- 34 Calverley PM, Boonsawat W, Cseke Z, Zhong N, Peterson S, Olsson H. Maintenance therapy with budesonide and formoterol in chronic obstructive pulmonary disease. *Eur Respir J* 2003; 22: 912–919.
- 35 Szafranski W, Cukier A, Ramirez A, *et al.* Efficacy and safety of budesonide/formoterol in the management of chronic obstructive pulmonary disease. *Eur Respir J* 2003; 21: 74–81.
- 36 Casaburi R, Mahler DA, Jones PW, *et al.* A long-term evaluation of once-daily inhaled tiotropium in chronic obstructive pulmonary disease. *Eur Respir J* 2002; 19: 217–224.
- 37 Spencer S, Jones PW, and the GLOBE Study Group. Time course of recovery of health status following an infective exacerbation of chronic bronchitis. *Thorax* 2003; 58: 589–593.
- 38 Peach H, Pathy MS. Follow-up study of disability among elderly patients discharged from hospital with exacerbations of chronic bronchitis. *Thorax* 1981; 36: 585–589.
- 39 Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; 169: 1298–1303.