Eur J Clin Pharmacol (2012) 68:1365–1373
DOI 10.1007/s00228-012-1279-5

CLINICAL TRIAL

Potential risk factors for medication non-adherence in patients with chronic obstructive pulmonary disease (COPD)

Maher R. Khdour · Ahmed F. Hawwa · Joseph C. Kidney · Bronagh M. Smyth · James C. McElnay

Received: 25 November 2011 / Accepted: 18 March 2012 / Published online: 5 April 2012

Abstract
Aims To investigate the effect of a range of demographic and psychosocial variables on medication adherence in chronic obstructive pulmonary disease (COPD) patients managed in a secondary care setting.
Methods A total of 173 patients with a confirmed diagnosis of COPD, recruited from an outpatient clinic in Northern Ireland, participated in the study. Data collection was carried out via face-to-face interviews and through review of patients' medical charts. Social and demographic variables, co-morbidity, self-reported drug adherence (Morisky scale), Hospital Anxiety and Depression (HAD) scale, COPD knowledge, Health Belief Model (HBM) and self-efficacy scales were determined for each patient.
Results Participants were aged 67±9.7 (mean ± SD) years, 56 % female and took a mean (SD) of 8.2±3.4 drugs. Low adherence with medications was present in 29.5 % of the patients. Demographic variables (gender, age, marital status, living arrangements and occupation) were not associated with adherence. A range of clinical and psychosocial variables, on the other hand, were found to be associated with medication adherence, i.e. beliefs regarding medication effectiveness, severity of COPD, smoking status, presence of co-morbid illness, depressed mood, self-efficacy, perceived susceptibility and perceived barriers within the HBM ($p<0.05$). Logistic regression analysis showed that perceived ineffectiveness of medication, presence of co-morbid illness, depressed mood and perceived barriers were independently associated with medication non-adherence in the study ($P<0.05$).
Conclusions Adherence in COPD patients is influenced more by patients' perception of their health and medication effectiveness, the presence of depressed mood and co-morbid illness than by demographic factors or disease severity.

Keywords Adherence · COPD · Health beliefs · Depression · Self-efficacy · Disease knowledge

M. R. Khdour · A. F. Hawwa · J. C. McElnay (✉)
Clinical and Practice Research Group, School of Pharmacy, Medical Biology Centre, Queen's University Belfast, 97 Lisburn Road, Belfast BT9 7BL, UK
e-mail: j.mcelnay@qub.ac.uk

J. C. Kidney · B. M. Smyth
Department of Respiratory Medicine, Mater Hospital, Belfast BT14 6AB, UK

Present Address:
M. R. Khdour
Faculty of Pharmacy, Al-Quds University, Abu-Dies, Jerusalem P.O. Box 20002, Palestine

Introduction

Chronic obstructive pulmonary disease (COPD) is often associated with a constant deterioration in health leading to a belief among patients that they are not going to readily benefit from their treatment, and it has been shown that a significant proportion of COPD patients have poor adherence to prescribed treatment [1–5]. Poor adherence of COPD patients to drug therapy and disease management programmes has been identified as a major factor resulting in emergency hospitalisation in addition to sub-optimal clinical outcomes [6, 7]. Several factors could predispose COPD patients to non-adherence. First, the management of COPD is complex and requires several behavioural and lifestyle changes such as smoking cessation and adherence to exercise programmes and prescribed

medication [8]. In addition, multiple co-morbidities are common in COPD patients; they are often prescribed complex medication regimens comprising scheduled and as-needed medications, delivered by multiple administration routes. Depression, a common co-morbidity in patients with COPD, is also known as a potential risk factor for non-adherence [7, 9, 10].

Older age and disease duration are additional factors that may contribute to non-adherence since they are associated with increased risk of cognitive impairment and memory problems [11]. Interruptions or changes in normal routines, adverse side effects, running out of medication and polypharmacy have also been associated with non-adherence.

Strategies to improve COPD patient adherence include establishing a personal relationship or partnership in which the patient feels able to discuss their fears, concerns and personal goals. Synchronising dosing times and simplifying regimens can help improve non-adherence resulting from forgetfulness, but are unlikely to promote deliberate non-adherence due to barriers such as patient beliefs that medicines are no longer needed [12] or concerns about side-effects [13]. Patient education and provision of information about COPD and its treatment can play an important role in modifying beliefs and understanding, hence potentially improving adherence.

The aim of the present study was, therefore, to examine the effect of a range of potential clinical and psychosocial variables on adherence to medication in COPD patients managed in a secondary care setting.

Methods

Study subjects

A total of 173 patients (mean age 67; 56 % females), with moderate to severe COPD were recruited from the outpatient COPD clinic at the Mater Hospital, Belfast, Northern Ireland. All COPD patients who attended the clinic were invited to participate. Other inclusion criteria included confirmed diagnosis of COPD for at least 1 year by their hospital consultant, having an FEV_1 value of 30–80 % of the predicted normal value and being over 45 years old. Patients who had a heart failure, moderate to severe learning difficulties (as judged by hospital consultant), severe mobility problems, terminal illness or who had attended a pulmonary rehabilitation programme in the last 6 months were excluded from the study. All clinical data were obtained from patients' medical charts.

This study was part of a larger research project on a self-management intervention programme for COPD patients [14]. The study was approved by the Office of Research Ethics Committees in Northern Ireland (ORECNI; 06/NIR02/23).

Instruments

Various validated instruments were used in this study to investigate the potential effect of the tested variables, i.e. the self-reported adherence (Morisky scale), the Hospital Anxiety and Depression (HAD) scale, COPD knowledge questionnaire, the COPD self-efficacy scale, the perceived medication effectiveness scale and the Health Belief Model (HBM) questionnaire. Further details about these six instruments are presented below.

Self-reported adherence (Morisky scale) The self-report Morisky adherence scale [15] was used to measure patients' adherence to their COPD-related medications over the 4 weeks preceding their clinic visit. This scale measures adherence through four yes/no response items: forgetting, carelessness, stopping medication when feeling better and stopping medication when feeling worse. Each 'yes' response is given a score of one and each 'no' response is scored zero (total adherence scores range between 0 and 4). Two adherence classifications were used, i.e. high adherence (scores of 0–1) and low adherence (scores of 2–4). The Morisky scale has good validity and reliability; Cronbach's alpha=0.61 [15].

Hospital Anxiety and Depression (HAD) scale The HAD scale is a 14-item self-report questionnaire designed to detect psychological morbidity in medically ill patients [16]. It contains depression and anxiety subscales, each scoring 0–21. A score above 8 on either subscale can be used to screen for possible depression and anxiety and a score above 11 for a probable disorder. A score of less than 8 on the depression scale is considered normal, 8–10 is mild depression, 11–14 is moderate and 15 or above represents severe depression. The HAD scale is a valid measure of depression and anxiety with Cronbach's alpha values of 0.83 for anxiety and 0.82 for depression [17].

COPD knowledge questionnaire This instrument was developed by Scherer [18] to assess the effectiveness of patient education in COPD patients. It consists of 16 true/false items relating to the pathophysiology of COPD, breathing and exercise, energy conservation, medications, relaxation and stress control. Correct responses for each item are scored 1 and incorrect or unsure responses are scored 0 (total range 0–16). The instrument has been shown to be valid, with a Cronbach's alpha for internal consistency of 0.89 [18].

Health Belief Model (HBM) questionnaire The HBM has been widely used as a conceptual framework to explain and predict health behaviours by focusing on the beliefs and attitudes of individuals [19–22]. The model attempts to define the individual's motivation for adopting a

health-promoting behaviour. The model includes four primary variables: perceived susceptibility (e.g. belief of vulnerability to disease relapse as a result of not taking the medication when not experiencing symptoms directly), perceived severity (or seriousness of the health threat), perceived benefits (e.g. individual's belief in the efficacy of the prescribed medication in reducing disease severity or susceptibility) and perceived barriers (e.g. stigma of taking medication or denial of having serious illness) [19, 20]. The questionnaire rates variables on a 5-point Likert scale. The HBM questionnaire was completed only by the intervention group at baseline of the main study [14]; data were available for 83 (96.5 %) of that group.

COPD Self-Efficacy Scale (CSES) The CSES was used to assess the level of confidence of COPD patients in their ability to manage or avoid breathing difficulty while participating in certain activities [23]. The instrument contains 34 items (5-point Likert scale), with higher scores indicating greater perceived self-efficacy. These items are categorised into five subscales which include negative affect, intense emotional arousal, physical exertion, weather/environment and behavioural risk factors. Good test-retest reliability (r=0.77) and internal consistency (Cronbach's alpha=0.95) have been reported [23]. A mean score was calculated in the present study by summing the response scores for each item and dividing them by the number of items answered.

Medication effectiveness Patients were also asked to rate their perceived medication effectiveness and their faith in their prescribed medication as totally effective, mostly effective, partially effective or totally not effective.

All questionnaires were administered to patients via a face-to-face interview at the hospital clinic.

Data analysis

Statistical analyses were performed using SPSS version 19 (SPSS, Chicago, IL, USA). Associations between the dependent variable (adherence category) and other potential explanatory variables, the chi-squared test or the Fisher exact test were used, as appropriate, for categorical variables. Student's t-tests and the Mann-Whitney U-tests were used for parametric and non-parametric continuous variables respectively.

For further investigation of factors influencing the dependent variable, binary stepwise conditional logistic regression analysis was utilised. Variables with a probability of <0.25 in the univariate analysis were included in this latter analysis [24]. A p-value < 0.05 was considered statistically significant (two-sided test) in all cases.

Results

Demographics and disease characteristics

The demographic characteristics of participants are presented in Table 1. Completed questionnaires were available for all patients recruited (n=173). Medical and disease characteristics of the study population are shown in Table 2. The mean number (±SD) of prescribed medications per patient was 8.2 (±3.4). Most of the patients had moderate to severe disease according to the British Thoracic Society (BTS, 2006) guidelines and 21 % were active smokers.

Demographic variables and adherence to COPD medications

Of the 173 participants, 29.5 % (n=51) were classified in the low-adherence group (scoring 2–4 on Morisky scale). Figure 1 summarises patient responses to individual items of the scale. Missed dose (forgetfulness) was the most prevalent type of non-adherence, i.e. reported by 33 % of the respondents overall and by 68 % of the low adherence group. Statistical analyses indicated no significant correlations between adherence groups and demographic variables, including gender, marital status, age, living arrangements, occupation and level of education (Table 3).

Table 1 Characteristics of study population (n=173)

Variable	Frequency, n (%)
Gender	
Male	75 (43.4)
Female	98 (56.6)
Age (mean, SD, years)	66.6 (9.7)
Marital status	
Single	9 (5.4)
Married	103 (62.0)
Separate	15 (9.0)
Widowed	39 (23.5)
Living arrangements	
Independently	28 (16.8)
With friends	2 (1.2)
With family	119 (71.3)
24-h supervised accommodation/hostel	6 (3.6)
Alone but with support	12 (7.2)
Educational level	
Primary school	49 (28.3)
Secondary/tertiary	124 (71.7)
Occupation	
Low	110 (63.5)
Medium	38 (22.4)
High	25 (14.5)

Table 2 Medical and disease characteristics of study population (n=173)

Variable	Frequency, n (%)
Disease severity (BTS)	
Mild (60–79)	35 (20.5)
Moderate (40–59)	90 (52.6)
Severe (<40)	46 (26.9)
FEV_1 (mean, SD)	
L	1.17 (0.5)
% predicted	52.6 (16.8)
FEV_1/FVC	56.6 (10.0)
Number of prescribed medications (mean, SD)	8.2 (3.4)
Years of diagnosis (mean, SD)	6.5 (5.1)
Medications, n (%)	
Short-acting β2-agonists	163 (94.2)
Long-acting β2-agonists	137 (79.2)
Long-acting anti-cholinergic	130 (75.1)
Inhaled steroids	114 (65.9)
Oral steroids	16 (9.2)
Effectiveness of the medication	
Totally/mostly effective	107 (63.7)
Little/not effective	61 (36.3)
Co-morbid illness	
Co-morbid illness present	85 (49.1)
No co-morbidity	88 (50.9)
Smoking status	
Ex-smokers	113 (65.3)
Current smokers	37 (21.4)
Never smoked	23 (13.3)
HAD scores (mean, SD)	
Anxiety scores	8.28 (4.3)
Depression scores	8.27 (4.2)

BTS British Thoracic Stages, *HAD* Hospital Anxiety and Depression scale

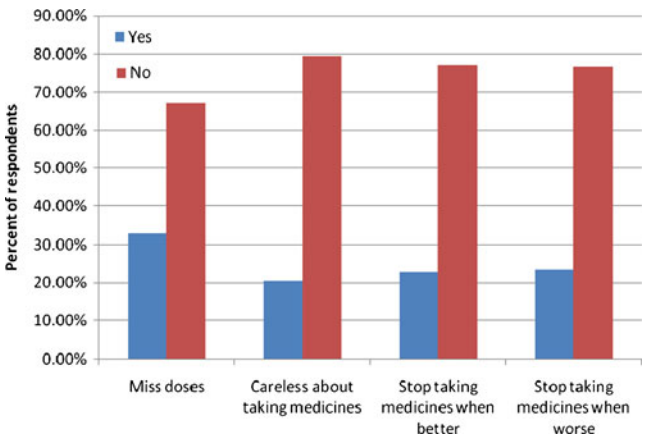

Fig. 1 Patient responses to self-report adherence items

Table 3 Univariate analysis of the association of potential demographic and clinical variables with self-reported adherence

Potential explanatory variables	p-value
Gender	>0.25[a]
Age	>0.25[b]
Marital status	>0.25[a]
Living arrangements	<0.25[a]
Occupation	>0.25[a]
Education	>0.25[a]
Smoking status	<0.05[a]
Disease and medication knowledge	<0.01[b]
Self-efficacy	<0.01[b]
Number of prescribed medications	>0.25[b]
Medication effectiveness	<0.01[a]
Disease severity	<0.05[a]
HAD anxiety	<0.25[b]
HAD depression	<0.01[b]
Co-morbid illness	<0.01[a]
Duration of COPD disease	<0.25[b]
HBM perceived susceptibility score	<0.01[b]
HBM perceived barriers score	<0.01[b]

HAD Hospital Anxiety and Depression scale, *COPD* chronic obstructive pulmonary disease, *HBM* Health Belief Model

[a] Chi-squared test or Fisher exact test, as appropriate

[b] Mann-Whitney U-Test or Student's t-test, as appropriate

Medical and disease characteristics and adherence to COPD medications

Disease severity and presence of co-morbid illnesses A significant association (p<0.05) was found between COPD disease severity stages (Table 3) and adherence groups. Review of patient charts revealed that 49.1 % had one or more co-morbid illness which required medications, including heart disease (21.4 %), osteoporosis (17.9 %) and hypertension (9.8 %). A significant relationship was also found between the presence of co-morbid conditions and adherence groups (p<0.01), i.e. higher percentage of the patients with no co-morbid illness were classified within the high adherence category.

Knowledge about COPD medications and disease management Patients who had lower knowledge scores were more likely (p<0.01) to be in the low-adherence group (Table 3; Fig. 2).

Effectiveness of the prescribed medications No significant association (p>0.05) was found between the mean number of prescribed medications and medication adherence. However, a significant association (p<0.01) was found between self-report of the effectiveness of medications and adherence

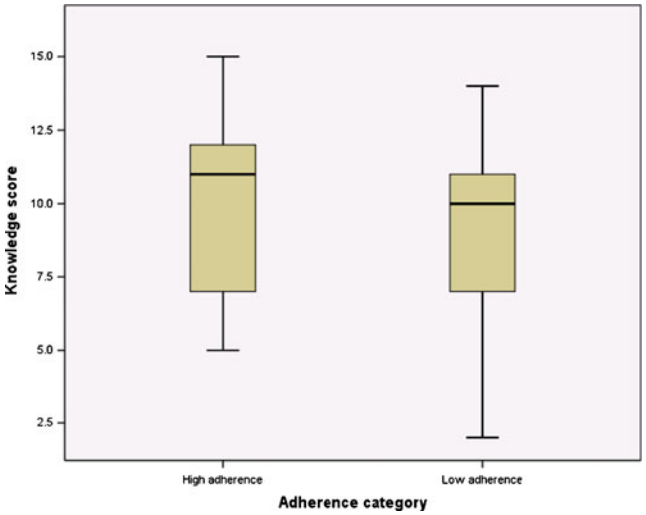

Fig. 2 Box and whisker plot of the association between COPD knowledge scores and self -reported adherence

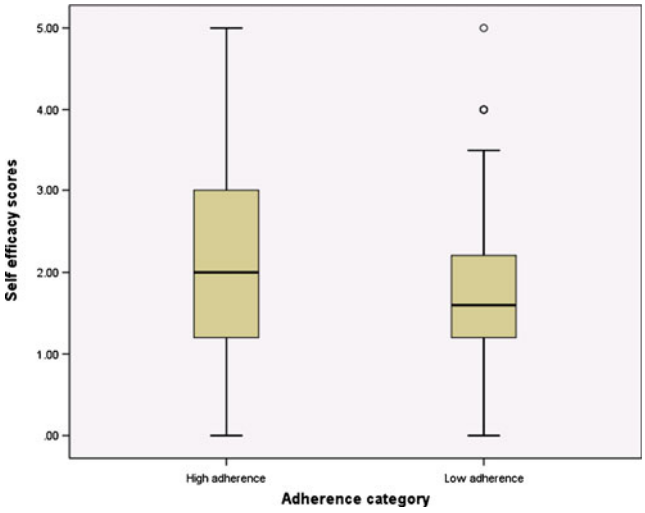

Fig. 4 Box and whisker plot of the association between COPD self-efficacy scores and self-reported adherence

behaviour (Fig. 3), i.e. those patients who felt that their medications were totally or mostly effective were more likely to report adherence to their medications.

Self-efficacy and smoking status Participants with higher COPD self-efficacy scores were more likely to be classified as adherent (Table 3; Fig. 4). Patients who still smoked were more likely to be non-adherent with their medication (Table 3).

Hospital anxiety and depression scale scores In the low adherence group, depression, i.e. HAD score of 11 or more, was evident in 52.4 % of patients versus 27.7 % in the high adherence group ($p<0.01$). There was no significant difference between high and low adherence group patients with regard to anxiety scores.

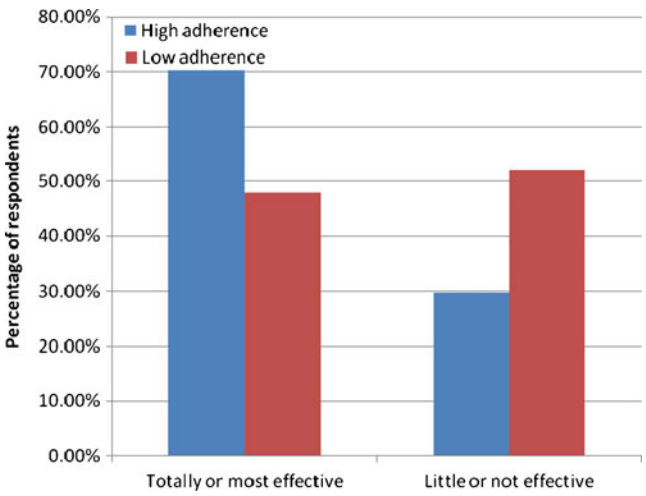

Fig. 3 Influence of self-reported medication effectiveness on self-reported adherence behaviour

Health Belief Model Medication adherence behaviour was correlated with the perceived susceptibility (e.g. relapse or exacerbation as a result of not taking the medication, $p<0.01$) and with perceived barriers to medication use (e.g. stigma of taking medications, concerns about side effects or denial of serious illness; $p<0.01$; Table 3). No association was found for perceived severity or benefits of medication use ($p>0.05$).

Binary logistic regression analysis of self-reported adherence

Following the modelling strategy of Homer and Lemeshow [24], the explanatory variables with a p-value <0.25 (Table 3) were subjected to logistic regression analysis to further explore associations between the potential explanatory variables and self-reported adherence.

The final model included depression status, views on medication effectiveness and presence of co-morbid conditions. Those who had HAD scores indicative of depression and those with co-morbid illness were 8.9 times and 5.0 times respectively more likely to be classified as non-adherent. Conversely those who believed that their medication was effective were more likely to be deemed adherent (OR=0.09 for non-adherence). A test of the final model against a constant only model was statistically reliable ($p<0.05$) indicating that the predictors were able to reliably distinguish between adherent and non-adherent participants in this sample. This model explained 45.8 % (Nagelkerke R^2) of the variation in adherence. A non-significant results ($p>0.05$) for the Hosmer test was evidence that the model has good fit to the data. An overall success rate of 83.6 % was found using the developed model, i.e. 90.0 % of adherent and 66.7 % of non-adherent were correctly

classified. A separate regression analysis of the sub-group of patients who answered the Health Belief Model revealed 'perceived barriers' as an additional significant variable in the final regression model. This model explained 51.9 % of adherence variability with an overall success rate of 83.0 %. Table 4 shows the estimated odds-ratios and the 95 % confidence intervals for each of the predictors in the two models.

Discussion

Adherence research in COPD has mainly focused on quantification of adherence, with few studies attempting to identify factors influencing non-adherence [2, 7, 8, 25]. Prior to the present study, the patient perspective relating to adherence had been largely neglected.

Although the sample size was reasonably small (n=173), this should be adequate to achieve reliability and confidence in the results obtained [26]. While self-report is an indirect measure of medication adherence, it has been shown to be as effective as other indirect measures, including pill counts and refill rates [10] and was the most practical for the present study. More precise estimates of medication adherence can be gained via direct methods (e.g. observation, drug or metabolites blood concentrations), however, such methods are expensive, burdensome or invasive [10].

Table 4 Final logistic regression models predicting self-reported adherence

Variables	OR (95 % CI)	p-value
Logistic regression analysis for the whole group (n=173)		
Medication effectiveness		
Totally or most effective	0.094 (0.017–0.517)	<0.01
Little or no effectiveness	Reference	
Co-morbid illness		
No presence of co-morbid disease	5.02 (1.0–25.2)	<0.05
Presence of co-morbid disease	Reference	
Depression category		
Depressed (score 11 or more)	8.95 (1.8–44.1)	<0.01
Not depressed (score less than 11)	Reference	
Logistic regression analysis for the subset who answered HBM (n=83)		
Medication effectiveness		
Totally or most effective	0.082 (0.015–0.46)	<0.01
Little or no effectiveness	Reference	
Co-morbid illness		
Presence of co-morbid disease	9.03 (1.6–49.9)	<0.05
No presence of co-morbid disease	Reference	
Depression category		
Depressed (score 11 or more)	8.77 (1.8–43.8)	<0.01
Not depressed (score less than 11)	Reference	
HBM perceived barriers		
Perceived barriers to taking medication	1.24 (1.02–1.5)	<0.05
No perceived barriers	Reference	

HBM Health Belief Model

Using the classification system described, 29.5 % of the study participants were placed within a low adherence group. This fell within the expected range reported in earlier studies [27, 28]. In agreement with a smaller study in this area [2], no significant associations were found between demographic variables (gender, age, marital status, living arrangements and occupation) and self-reported adherence.

Approximately half of the patients in the present study had co-morbidities; a significant relationship between non-adherence and co-morbidity presence was identified (odds ratio of 5.0 in the final logistic regression model; $p<0.05$). This was regardless of the number of medications patients received, which did not have sufficient association to be included in the multivariate analysis ($p>0.25$). Statistical analysis also failed to identify a significant relationship between duration of the disease and adherence group classification, although both of these factors have previously been found to negatively affect adherence [29]. Findings in the latter study, however, are not consistent across adherence research, e.g. Horne et al. found that the number of prescribed medications was unrelated to adherence in a group of hypertensive patients [30].

A significant association ($p<0.01$) was also found between COPD knowledge scores and adherence, with lower knowledge scores more likely within the low-adherence group (Fig. 2). This finding is consistent with the work of Johnson et al. [8] who concluded that COPD patients classified as adherent had a greater understanding about their illness and options for its management. There are, however, mixed findings in the literature regarding the relationship between knowledge and adherence. In a recent study by Scherer et al., higher education level was correlated with higher knowledge scores, however, attitudes and self-efficacy rather than knowledge had the most significant impact on adherence [31]. Studies evaluating the effect of educational interventions on adherence to medication in COPD patients have also shown varied and inconsistent results [32, 33]. Promising results, however, were reported recently by studies that offered educational programmes to COPD patients that emphasised illness control through health behaviour modification [34–36]. Such educational programmes have been shown to empower patients to self-manage their chronic health condition and to promote adherence [36]. In the present study, however, knowledge score did not have sufficient association to remain as an independent predictor of adherence in the final regression model.

The HBM model is widely accepted as a tool to measure patient motivations to accept, and subsequently adhere to, a prescribed preventive treatment. It lends itself to the prediction of medication adherence since it includes various psychological factors that influence the person's capacity to act [19, 20, 37]. The HBM suggests that a behavioural change is dependent upon perceived illness severity and perceived susceptibility to harm or serious health consequences if the disease is left untreated. In addition, the patient's perception of the effectiveness or benefit of the recommended treatment weighed against the perceived barriers to action (e.g. potential side effects of treatment or denial of illness) predicts the likelihood of taking or adhering to that treatment [19, 38]. Therefore, it has been concluded that higher adherence to a prescribed treatment (particularly in case of chronic conditions such as COPD) requires both an acceptance of the illness and confidence in medication effectiveness [7, 39–41].

In the present study, the HBM construct of perceived barriers was a better predictor of adherence than other components of HBM (perceived severity, susceptibility and benefits) or the objective severity of the disease (disease activity) in the multiple regression analysis. Perceived barriers contributed significantly to the final regression model and explained a significant percentage of the variance in adherence (7.1 %; $p<0.05$). Other HBM components and objective severity were not sufficiently associated to be included in the regression model, however, when considered in a bivariate relationship with adherence, both perceived susceptibility and objective disease severity were significantly associated with adherence ($p<0.01$ and $p<0.05$ respectively). These findings concur with earlier studies which suggest that a patient's perceived need for the treatment is not directly associated with the objective measures of severity of the disease [42, 43].

For chronic illnesses, self-efficacy, which relates to the person's perceived capability of carrying out an intended behaviour [44], can be an important predictor of adherence behaviour [45]. However, in the present study self-efficacy did not explain a significant proportion of the variance in adherence and, hence, was not incorporated in the final logistic regression model.

Thirty-five percent of the participants in the present study had HAD scores indicative of anxiety and 34.5 % had scores indicative of depression. A significant correlation was found between depression (but not anxiety) and low adherence behaviour ($p<0.01$). In addition, depression was a significant predictor of non-adherence in the regression model and explained 22 % of the variance in adherence (OR=8.95; $p<0.01$). In the UK, the National Institute of Clinical Excellence COPD Guidelines estimated the prevalence of depression in COPD to be 40 % (36–44 %) and suggested that anxiety symptoms may have a prevalence of 36 % (31–41 %) [9]. Having a co-morbid illness in the present study was found to increase depressive symptom scores, i.e. participants who did not have any co-morbidity had a mean HAD score of 7.08, whilst those who did have co-morbidity had a mean HAD score of 9.19 ($p<0.01$). Both co-morbidity and depression status remained significant in the final logistic regression model.

A meta-analysis has found that depression is associated with non-adherence to medical advice in a number of disease states [46]. Although there has been little research to date in COPD patients, the few studies which have been carried out have shown a significant relationship between depression and poor adherence [47]. Research is required to determine whether treating depression can enhance adherence to medical advice and reduce morbidity and mortality risk in COPD patients [47].

The results of the present study also revealed that those patients who felt that their medications were totally or mostly effective were more likely to be adherent ($p<0.01$), as predicted by the HBM. This is in line with research in other patient groups [7, 39–41].

Interestingly, the variance in adherence explained by the factors identified in the present study (45.8 % for the whole group and 51.9 % when HBM 'perceived barriers' were included in the regression model) was higher than that reported by other models of adherence [21, 30, 43, 48, 49]. For instance, a model described by George et al. [48] explained only 19.5 % of variance in non-adherence in a COPD population. Another recent study described a linear regression model explaining 31.8 % of variance in reported adherence to continuous positive airway pressure therapy in patients with COPD [43]. In the latter model, patients' beliefs about their medicines were the strongest predictors, accounting for 21.8 % of the variance. One possible reason for the low fraction of variance explained in any model of adherence could be the discrepancies between true and self-reported adherence, in that non-adherent subjects tend to exaggerate their degree of adherence [50]. This is supported by the fact that the classification success rate for the present model was 90 % in patients who were adherent to therapy, but was 66.7 % for those who were non-adherent to medication.

Conclusion

The key finding in the present study was that patient views on medication effectiveness and the presence of depression or co-morbid illnesses were found to be more powerful predictors of reported adherence than socio-demographic factors or other clinical factors. In addition, the present findings support the utility of HBM for the prediction of non-adherence to medication in COPD patients. Future research should focus on highlighting further variables, which may inform interventions aimed at improving adherence to COPD medication.

References

1. Osman L (1998) Health habits and illness behaviour: social factors in patient self-management. Respir Med 92:150–155
2. Dolce JJ, Crisp C, Manzella B, Richards JM, Hardin JM, Bailey WC (1991) Medication adherence patterns in chronic obstructive pulmonary disease. Chest 99:837–841
3. Make BJ (2003) Chronic obstructive pulmonary disease: developing comprehensive management. Respir Care 48:1225–1234
4. Breekveldt-Postma NS, Gerrits CM, Lammers JW, Raaijmakers JA, Herings RM (2004) Persistence with inhaled corticosteroid therapy in daily practice. Respir Med 98:752–759
5. Krigsman K, Nilsson JL, Ring L (2007) Refill adherence for patients with asthma and COPD: comparison of a pharmacy record database with manually collected repeat prescriptions. Pharmacoepidemiol Drug Saf 16:441–448
6. Antoniu SA (2010) Adherence to inhaled therapy in COPD: effects on survival and exacerbations. Expert Rev Pharmacoecon Outcomes Res 10:115–117
7. Earnest MA (2002) Explaining adherence to supplemental oxygen therapy: the patient's perspective. J Gen Intern Med 17:749–755
8. Johnson G, Kong D, Rambha K, Stewart K (2005) Factors associated with medication nonadherence in patients with COPD. Chest 128:3198–3204
9. Yohannes AM, Baldwin RC, Connolly MJ (2006) Depression and anxiety in elderly patients with chronic obstructive pulmonary disease. Age Ageing 35:457–459
10. Osterberg L, Blaschke T (2005) Adherence to medication. N Engl J Med 353:487–497
11. Salzman C (1995) Medication compliance in the elderly. J Clin Psychiatry 56(Suppl 1):18–22
12. Chambers CV, Markson L, Diamond JJ, Lasch L, Berger M (1999) Health beliefs and compliance with inhaled corticosteroids by asthmatic patients in primary care practices. Respir Med 93:88–94
13. Boulet LP (1998) Perception of the role and potential side effects of inhaled corticosteroids among asthmatic patients. Chest 113:587–592
14. Khdour MR, Kidney JC, Smyth BM, McElnay JC (2009) Clinical pharmacy-led disease and medicine management programme for patients with COPD. Br J Clin Pharmacol 68:588–598
15. Morisky DE, Green LW, Levine DM (1986) Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 24:67–74
16. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67:361–370
17. Bjellan I, Dahl AA, Haug T (2002) The validity of the hospital anxiety and depression scale: an updated literature review. J Psychosom Res 52:69–77
18. Scherer YK, Schmieder LE, Shimmel S (1998) The effects of education alone and in combination with pulmonary rehabilitation on self-efficacy in patients with COPD. Rehabil Nurs 23:71–77
19. Rosenstock I (1974) The health belief model and preventative health behaviour. Health Educ Monogr 1974:354–386
20. Becker MH (1974) The health belief model and personal health behavior. Health Educ Monogr 2:324–473
21. Becker MH, Maiman LA, Kirscht JP, Haefner DP, Drachman RH, Taylor DW (1979) Patient perceptions and compliance: recent studies of the health belief model. In: Haynes RB, Taylor DW, Sackett DL (eds) Compliance in healthcare. The Johns Hopkins University Press, Baltimore, MD, pp 78–109
22. Champion VL, Skinner CS (2008) The health belief model. In: Glanz K, Rimer B, Viswanath K (eds) Health behaviour and health education: theory, research and practice, 4th edn. Jossey-Bass, San Francisco, CA, p 45–66
23. Wigal JK, Creer TL, Kotses H (1999) The COPD self-efficacy scale. Chest 99:1193–1196
24. Hosmer DW, Taber S, Lemeshow S (1989) The importance of assessing the fit of logistic regression models: a case study. Am J Public Health 81:1630–1635
25. Incalzi RA, Pedone C, Onder G, Pahor M, Carbonin PU (2001) Predicting length of stay of older patients with exacerbated chronic obstructive pulmonary disease. Aging 13:49–57
26. Wangcharoen W, Nagrmask T, Wilkinson BH (2005) Snack product consumer survey: large versus small sample. Food Qual Prefer 16:511–516
27. Kyngas HA, Skaar-Chandler CA, Duffy ME (2000) The development of an instrument to measure the compliance of adolescents with a chronic disease. J Adv Nurs 32:1499–1506
28. Rand CS, Nides M, Cowles MK, Wise RA, Connett J (1995) Long-term metered-dose inhaler adherence in a clinical trial. The Lung Health Study Research Group. Am J Respir Crit Care Med 152:580–588
29. Stewart RB, Caranasos GJ (2000) Medication compliance in the elderly. Med Clin North Am 73:1551–1563
30. Horne R, Weinman J (1999) Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res 47:555–567
31. Scherer YK, Bruce S (2001) Knowledge, attitudes, and self-efficacy and compliance with medical regimen, number of emergency department visits, and hospitalizations in adults with asthma. Heart Lung 30:250–257
32. Effing T, Monninkhof EM, van der Valk PD, van der Palen J, van Herwaarden CL, Partidge MR, Walters EH, Zielhuis GA (2007) Self-management education for patients with chronic obstructive pulmonary disease. Cochrane Database Syst Rev 4:CD002990
33. Janssen DJ, Engelberg RA, Curtis JR (2010) Toward patient-tailored education in COPD. Patient Educ Couns 81:1–2
34. Gallefoss F, Bakke PS (2002) Cost-benefit and cost-effectiveness analysis of self-management in patients with COPD—a 1-year follow-up randomized, controlled trial. Respir Med 96:424–431
35. Incorvaia C, Riario-Sforza GG (2011) Effect of patient education on adherence to drug treatment for chronic obstructive pulmonary disease. Ann Thorac Med 6:242–243
36. Casey D, Murphy K, Cooney A, Mee L (2011) Developing a structured education programme for clients with COPD. Br J Community Nurs 16:231–237
37. Clark N, Becker M (1998) Theoretical models and strategies for improving adherence and disease management. In: Shumaker S, Schron E, Ockene J, McBee W (eds) The handbook of health behavior change, 2nd edn. Springer, New York, pp 5–32
38. Becker MH, Haefner DP, Kasl SV, Kirscht JP, Maiman LA, Rosenstock IM (1977) Selected psychosocial models and correlates of individual health-related behaviors. Med Care 15:27–46
39. Benson J, Britten N (2002) Patients' decisions about whether or not to take antihypertensive drugs: qualitative study. BMJ 325:873
40. Buston KM, Wood SF (2000) Non-compliance amongst adolescents with asthma: listening to what they tell us about self-management. Fam Pract 17:134–138
41. Remien RH, Hirky AE, Johnson MO, Weinhardt LS, Whittier D, Le GM (2003) Adherence to medication treatment: a qualitative study of facilitators and barriers among a diverse sample of HIV+ men and women in four US cities. AIDS Behav 7:61–72
42. Stepnowsky C, Marler M, Ancoli-Isreal S (2002) Determinants of nasal CPAP compliance. Sleep Med 3:239–247

43. Olsen S, Smith S, Oei T, Douglas J (2008) Health belief model predicts adherence to CPAP before experience with CPAP. Eur Respir J 32:710–717
44. Bandura A (1977) Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev 84:191–215
45. Harzke AJ, Williams ML, Nilsson-Schonnesson L, Ross MW, Timpson S, Keel KB (2004) Psychosocial factors associated with adherence to antiretrovira dications in a sample of HIV-positive African American drug users. AIDS Care 16:458–470
46. DiMatteo MR, Lepper HS, Croghan TW (2000) Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 160:2101–2107
47. Nasser EH, Overholser JC (2005) Recovery from major depression: the role of support from family, friends, and spiritual beliefs. Acta Psychiatr Scand 111:125–132
48. George J, Kong DC, Thoman R, Stewart K (2005) Factors associated with medication nonadherence in patients with COPD. Chest 128:3198–3204
49. Christensen AJ, Moran PJ, Wiebe JS (1999) Assessment of irrational health beliefs: relation to health practices and medical regimen adherence. Health Psychol 18:169–176
50. Turner J, Wright E, Mendella L, Anthonisen N (1995) Predictors of patient adherence to long term home nebulizer therapy for COPD. The IPPB Study Group. Intermittent Positive Pressure Breathing. Chest 108:394–400