

COPD Treatment Preference Study: A Conjoint Analysis of Preferred Drug Treatments

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Abstract

Objective: The goal of this study was to determine preferences and expectation of COPD patients about their drugs used.

Method: 46 patients with COPD were involved to the study. Preferences of patients relevant to the drugs they use for COPD and their expectations from this therapy were assessed under 6 categories. 16 alternative therapy forms were established for these groups by utilizing conjoint analysis. Patients sorted 16 types of therapy per order of preference.

Results: During the Conjoint analysis the major expectation of patients from the drugs they use was the choice of number of day without complaints is to be maximum (more than 20 days). 2nd major choice of patients' for their therapy was the choice of therapy cost to be minimum. Other choices of patients relevant to the drugs they use for therapy was respectively as follows; rapid commencing of effective period of drugs they use for reliever therapy, effective period of drugs they use for reliever therapy to be long, combined using of long term effective bronchodilator and inhaler steroid rather than separate form. In addition, the first choice of patients for inhaler for maintenance and acute symptoms was long acting-bronchodilator.

Conclusion: The major expectation and choice of COPD patients from their drug treatment were that the number of days without complaints was to be maximum with therapy. Other choices relevant to the drug therapy was combined forms rather than separate and long acting bronchodilator for maintenance treatment. Taking account of patient preferences when selecting COPD treatment may help to improve compliance with treatment.

Keywords: COPD; Conjoint analysis; Preferred drug treatments; Compliance of treatment

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease with poor clinical outcomes if not appropriately treated. Current guidelines for the management of COPD recommend the regular use of inhaled bronchodilator therapy in order to relieve symptoms and prevent exacerbations [1]. Patients' preferences for medications may be important in determining their compliance with therapy. Therefore, the appropriate treatment approaches can reduce symptoms due to disease. The factors associated with treatment such as drug characteristics, therapeutic effects, side effects, the onset and duration times of effects of drugs determine treatment preferences of patients. These preferences are increasingly important in evaluating outcomes in patients with COPD.

Conjoint analysis was originally developed for market research into consumer preferences, and is a method that investigates the relative importance of groups of attributes, eg, products with certain properties or more abstract concepts such as treatment procedures [2,3]. The method can thus be used to analyze patient preferences for various treatment alternatives. Conjoint analysis was used to determine preferences association with drug treatment in patients with asthma by Johansson et al in their study [4]. Furthermore, Osman et al examined by using conjoint analysis that patient weighting of importance of asthma symptoms [5]. Health benefits and patient preferences may play a key role in patient decision making about whether to take medication, which medication to take and whether to remain compliant and persistent. However, preferences drug treatment of patients was not examined by using conjoint analysis in patients with COPD.

We examined in this study by using conjoint analysis, COPD patients' preferences for different aspects of pharmacologic copd treatment such as efficacy, drug characteristics, and costs. The purpose of this study was to evaluate the relative importance for each of the

described attributes and the patient's preferences for different treatment concepts.

Methods and Subjects

Consecutive subjects admitted to the polyclinic at the Department of Chest Disease, patients with diagnosed COPD were included in this study. The diagnosed of COPD conformed to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [6]. To be included in the study, patients had to be in a stable condition and with no physical findings or symptoms suggestive of acute exacerbation or therapy modifications in the 6 weeks before enrollment and received optimal therapy according to guidelines. The age range of patients with COPD was 43-79. Pulmonary function tests (PFT) were performed with flow sensitive spirometer according to American Thoracic Society (ATS) guidelines [7]. Smoking packet/year was calculated and recorded by questioning history of smoke. Exclusion criteria were: severe congestive heart failure, other respiratory diseases such as asthma, interstitial lung disease, obstructive sleep apnea, acute infections and uncontrolled comorbidities such as malignancy, hepatic failure. A questionnaire on demographics, smoking history, medical history,

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and medications was completed. Dyspnea was evaluated using Medical Research Council (MRC) dyspnea scale [8]. CAT (COPD association test) was used to question the symptoms of the patients [9]. All subjects gave written informed consent to taking. The study was approved by the local ethics committee.

Statistical Analysis

All clinical parameters were summarized by descriptive statistics and results were expressed as mean $\pm$ standard deviation (SD). A value of $p < 0.05$ was considered statistically significant. Median values of CAT score and MMR dyspnea score were used as cut off value. Higher and lower scores were classified. The cut off value for CAT score was 18 and for MRC dyspnea score was 3. Patients with higher symptom score and lower symptom score according to CAT and MMR dyspnea scale were compared by using the chi-squared test.

Conjoint Analysis

In conjoint analysis, several attributes of treatment are chosen and a range of possible values are defined for each attribute. This analysis was used by Johansson et al. [4]. The analysis is used to create a number of treatment concepts. The selected attributes were as follows: type of maintenance treatment, need for an additional reliever inhaler, time to onset of action for reliever, duration of action for reliever, number of symptom-free days (SFD), and monthly out-of-pocket cost. The number of possible treatment concept that could be constructed from three attributes with two levels, and three attributes with four levels is $2^3 \times 4^3 = 512$. After than the number of treatment concept was reduced to 16. An SPSS package (ORTHOPLAN) was used to obtain the minimum number of scenarios needed to obtain utility scores for each the scenarios. The orthogonal design reduced the number of alternatives treatment. Each of these 16 treatment concepts was presented on a separated card. Sixteen of the cards were used to calculate preferences. Patients' preferences were presented with 16 different treatment concepts and an instruction folder explaining the ranking task. The treatment concepts included different combinations of medications and inhalers. The patients were wanted to rank the presented treatments according to their own choose about copd treatment. All patients received general information about copd treatment, focusing on the different use of inhaler corticosteroids and bronchodilators for maintenance and reliever therapy. A measure of preference often used in conjoint analysis is the term utility. The utility of a treatment concept is a function of the levels of the attributes in that concept. A higher level of utility expresses a greater preference for that treatment concept. For example, different patients are likely to favor different maintenance treatment concepts, eg, combination inhaler or separate inhalers. For other attributes, the treatment becomes more preferable with an increasing level of the attribute. The utility measure not only expresses which alternative is the most preferred, but also gives a measure of importance. A high relative level of utility indicated that the attribute was important to the patient and has had a high impact on the ranking of the treatments.

Results

Demographic and clinic parameters of patients with COPD

The study included 46 patients with COPD. The characteristics of the 46 patients are shown in Table 1. The study population consisted of 43 men and 3 women aged between 43 and 79 years (mean: 61 years). Using Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, 13% (6 patients) were classified as stage 1 COPD patients, 41.3% (19 patients) were stage 2, 28.3% (13 patients) were stage 3 and 17.4% (8 patients) were stage 4. Furthermore, according to revized 2011 GOLD criteria, 17.4% (8 patients) were classified as group A patients,

67.4% (31 patients) were classified as group B, 2.2% (1 patient) was classified as group C and 13.6% (6 patients) were classified as group D.

The attribute levels used in the conjoint analysis questionnaire was shown in Table 2. The most preferred as first choice was card with number 5. This card preferred as first choice by 22 patients (47.8%). The most preferred as last choice was card with number 4. This card preferred as last choice by 32 patients (69.6%) (Tables 3a and 3b).

Conjoint data

Patients ranked a total of 16 treatment concepts used to be estimate utility values and expressed their preferences for various attributes. These cards were sorted in order of preference. Validation of this model was acquired by calculating utility scores using each patient's utility function for all 16 treatments. Calculated scores were recorded and then rank ordered. Original rankings were compared pairwise with the theoretical rankings resulting from calculated utility scores.

The avarage relative importance of the attributes, based on invidual preferences, is presented in Table 4. SFD per mounth was the most important patient preference among the outcomes included in the study (56.3). Patients ranked the remaining treatment preferences as follows: Treatment cots (TL) (18.7), time to onset of reliever (8.4), duration of reliever (7.6), maintenance treatment (7.4), reliever inhaler (1.3). The utility scores indicated that the levels of patients's preferences. Higher utility values indicate higher levels of preferences. Each treatment concept ranked according to levels of preference. Accodngly, in concept of maintenance treatment: the most preferred concept was corticosteroid plus long acting bronchodilator in combi

	Patients with COPD Mean $\pm$ SD N: 46
Age	61.2 $\pm$ 8.7
Sex male/female	43/3
Smoke p/y	33.4 $\pm$ 13.1
FEV1%	55.1 $\pm$ 22.2
FVC%	63.9 $\pm$ 23.8
FEV1/FVC%	64.4 $\pm$ 15.2
PEF%	55.6 $\pm$ 22.4
MEF%	36.6 $\pm$ 21.3

SD: Standart deviasyon.

BMI: Body mass index.

Table 1: Demographic and clinic parameters of patients with COPD.

Attribute	Levels
Maintenance treatment	Only short acting bronchodilator [1] Only long acting bronchodilator [2] Corticosteroid plus long acting bronchodilator in combi inhalers [3] Corticosteroid plus long acting bronchodilator in saperate inhalers [4]
Reliever inhaler	Separate inhaler [1] Same as maintenance [2]
Time to onset, reliever	Within 3 minute [1] 10-15 minute [2]
Duration of reliever	3-6 hour [1] 12 hour [2]
Symptom free days per mounth	<10 days [1] 10-14 days [2] 15-20 days [3] >20 days [4]
Treatment cots per mounth (TL)	20 [1] 40 [2] 60 [3] 80 [4]

Table 2: Attribute levels used in the conjoint analysis questionnaire.

Inhaler for maintenance therapy	Only long acting bronchodilator [2]
Additional inhaler for acute symptoms	Yes. Separate inhaler for acute symptoms [1]
To time onset inhaler for acute symptoms	Within 3 minute [1]
Duration of reliever acute symptoms	12 hour [2]
Symptom free days per month	>20 days [4]
Treatment costs per month (TL)	60 TL [3]

Table 3a: The Card with Number 5: N: 22 (47.8%).

Inhaler for maintenance therapy	Only long acting bronchodilator [2]
Additional inhaler for acute symptoms	No. Same as maintenance inhaler for acute symptoms [2]
To time onset inhaler for acute symptoms	10-15minute [2]
Duration of reliever acute symptoms	3-6 hour [1]
Symptom free days per month	<10 days [1]
Treatment costs per month (TL)	80 TL [4]

Table 3b: The card with number 4: N: 32 (69.6%)

	1	2	3	4	Relative Importance to Attribute*
Maintenance treatment Utilities	Only short acting bronchodilator -0.6	Only long acting bronchodilator 0.2	Corticosteroid plus long acting bronchodilator in combi inhalers 0.5	Corticosteroid plus long acting bronchodilator in saperate inhalers -0.1	7.4
Reliever inhaler Utilities	Separate inhaler -0.1	Same as maintenance 0.1			1.3
Time to onset, reliever Utilities	Within 3 minute 0.6	10-15 minute -0.6			8.4
Duration of reliever Utilities	3-6 hour -0.6	12 hour 0.6			7.6
Symptom free days per month Utilities	<10 days -4.4	10-14 days -1.9	15-20 days 1.9	>20 days 4.5	56.3
Treatment costs (TL) Utilities	20 1.6	40 -0.09	60 -0.1	80 -1.3	18.7

*The difference in utility between the level with the highest utility and the level with the lowest utility for each attribute

Table 4: Utilities from a single hypothetical patient based on average in the study population.

inhalers (utility: 0.5). Others listed as follows in order of preference: only long acting bronchodilator (utility: 0.2), corticosteroid plus long acting bronchodilator in separate inhalers (utility: -0.1), only short acting bronchodilator (utility: -0.6). In the using of reliever inhaler concept, the most preferred concept was using of reliever inhaler which is same as maintenance (utility: 0.1). Other preference was using separate inhaler (utility: -0.1). In concept of time to onset of reliever: To started the effect of reliever in 3 minutes (utility: 0.6) was more preferred than to started the effect of reliever in 10 minutes (utility: -0.6). In the duration effect of reliever inhaler concept: the duration of the effect of reliever inhaler to 12 hour (utility: 0.6) was more preferred than duration of the effect of reliever innaler to 3-6 hour (utility: -0.6). In concept of symptom free days per month: the most of preferred concept was symptom free days per month >20 days (utility: 4.5). Other concepts were respectively, as follows: symptom free days per month: 15-20 days (utility: 1.9), symptom free days per month: 10-14 days (utility: -1.9), symptom free days per month: <10 days (utility: -4.4). In the concept of treatment costs (TL): The most of preferred concept was 20 TL cost (utility: 1.6). Other concepts were respectively, as follows: 20 TL cost (utility: 1.6), 40 TL cost (utility: -0.09), 60 TL cost (utility: -0.1), 80 TL cost (utility: -1.3).

The preferred treatment concept according to the conjoint analysis are presented in Table 5 in relation to current treatments of patients. Accordingly, 7 patients were not using treatment as maintenance and reliever. None of patients were using treatments of concept 1 and 2 as maintenance and reliever. The most common used current treatment by patients was concept 6.14 patients were currently receiving inhaler corticosteroid plus long-acting bronchodilator as maintenance and

long-acting bronchodilator as reliever according in this concept. Treatment concept 6 was rated as best by no patient in the conjoint analysis; treatment concept 4 was rated as best by 5 patients, treatment concept 5 was rated as best by 1 patient, treatment concept 7 was rated as best by 5 patients, treatment concept 9 was rated as best by 3 patients. In the example, 14 of 14 patients (%100) rated treatment concepts other than concept 6 (current treatment) as best, implying that they would prefer to switch to an alternative treatment. The treatment option of combination inhaler (corticosteroid plus long-acting bronchodilator) and long-acting bronchodilator for maintenance and as reliever (concept 7), and the treatment option of long-acting bronchodilator for both maintenance and needed (concept 3), had the lowest percentage of patients rating other treatments as best (50%). Over-all, a total 70% of the patients in the sample rated treatments other than their current treatment as best.

The used drug treatment as maintenance by patients with COPD was shown in Figure 1. 15.2% of patients (7 patients) were not using drug as maintenance. 84.8% of patients were using regularly inhaler drug as maintenance. None of the patients was used only short-acting bronchodilator as maintenance therapy. 15.2% of patients (3 patients) were using only long acting as maintenance therapy. 19.6% of patients (9 patients) were using corticosteroid plus long acting bronchodilator in combi inhalers as maintenance therapy. 17.4% (8 patients) were using corticosteroid plus long acting bronchodilator in separate inhalers as maintenance therapy. 19.6% of patients (9 patients) were using corticosteroid plus long acting bronchodilator in combi inhalers and long acting bronchodilator. 21.7% of patients (10 patients) were using corticosteroid plus long acting bronchodilator in saperate

Maintenance	Reliever		No	%	1	2	3	4	5	6	7	8	9
No Treatment	No Treatment	0	7	100	2			5					
SAB	SAB	1											
SAB	LAB	2											
LAB	SAB	3	1	100				1					
LAB	LAB	4	2	50				1			1		
Corticosteroid plus LAB	SAB	5	4	100				4					
Corticosteroid plus LAB	LAB	6	14	100				5	1		5		3
Combination	SAB	7	2	50				1			1		
Combination	LAB	8	8	100				5		1	2		
Combination	Combination	9	8	100	1			5			2		
				70%	6%	0%	0%	58%	2%	2%	23%		6%
			46		3	0	0	27	1	1	11		3

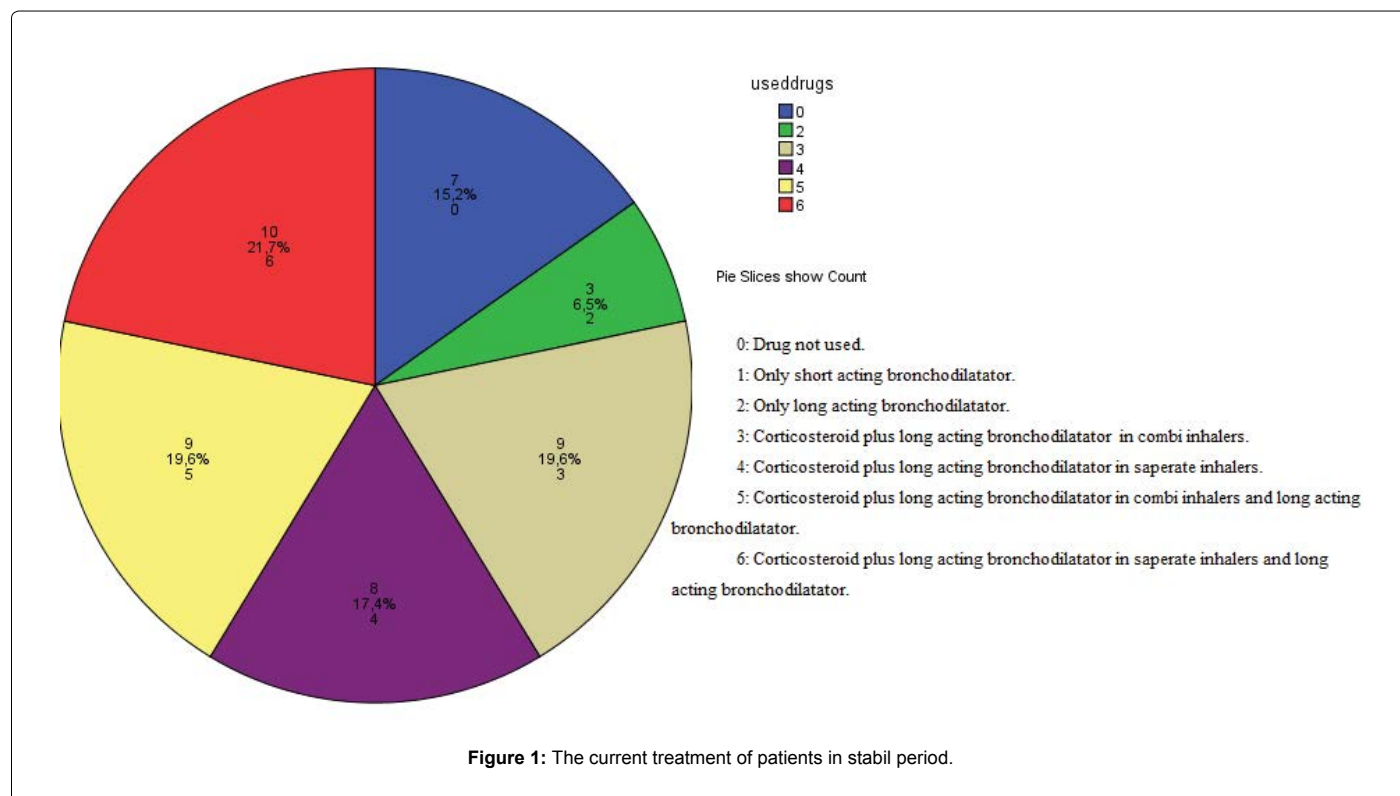
SAB: Short-acting bronchodilator.

LAB: Long-acting bronchodilator (long-acting b2-agonists or long-acting muscarinic antagonist).

Combination: Corticosteroid plus long acting bronchodilator in combi inhalers.

Corticosteroid plus LAB: Corticosteroid plus long acting bronchodilator in saperate inhalers.

Table 5: Patients by current treatment, the analysis of switching behavior from current treatment to best treatment according conjoint data.



inhalers and long acting bronchodilator (Figure 1). 15.2% of patients (7 patients) were using short-acting bronchodilator as reliever for acute symptoms in addition to maintenance therapy. 6.5% of patients (3 patiens) were using oral theophylline in addition to inhaler therapy.

The cut off value for CAT score was 18 and for MRC dyspnea score was 3. The comparison of patients with lower CAT score and higher CAT was performed according to preferences of patients. In patients with higher CAT score, the preference of corticosteroid plus long acting bronchodilator in combi inhalers was higher. In addition, in patients with higher MRC dyspnea score, preferences of use of corticosteroid plus long acting bronchodilator in combi inhalers and corticosteroid plus long acting bronchodilator in saperate inhalers were higher

than use of only bronchodilator. However, these differences were not significant (Tables 6 and 7).

Discussion

This study investigated preferences for different attributes of COPD treatment. The most important result of this study was that patients preferred the most SFD. The values of utilities was increasing with the increasing of SFD. This result has showed that the most expectation of patients with COPD from their treatments is to recover their complaints. It was showed the most expectation of patients with asthma from their treatments is the most of SFD in the study of Johansson et al. [4]. In our study, the frequency of COPD with modarate and severe stage was more great. Thus, these patients have often pulmonary symptoms such as

	Lower CAT score (CAT score<18) N (%)	Higher CAT score (CAT score ≥18) N (%)	P value
SAB	2 (9.1)	1 (4.2)	0.7
LAB	14 (63.6)	13 (54.2)	0.6
Combination	4 (18.2)	10 (41.7)	0.4
Corticosteroid plus LAB	2 (9.1)	0	-
Total	22	24	

CAT: COPD association test.

SAB: Short-acting bronchodilator.

LAB: Long-acting bronchodilator (long-acting b2-agonists or long-acting muscarinic antagonist).

Combination: Corticosteroid plus long acting bronchodilator in combi inhalers.

Corticosteroid plus LAB: Corticosteroid plus long acting bronchodilator in saperate inhalers.

Table 6: The comparison of patients with lower CAT score and higher CAT score according to preferences of patients.

	Higher MMR score (MMR score <3) N (%)	Lower MMR score (MMR score ≥ 3) N (%)	P value
SAB	2 (9.1)	1 (4)	0.7
LAB	14 (63.6)	13 (52)	0.4
Combination	5 (23.8)	9 (36)	0.7
Corticosteroid plus LAB	0	2 (8)	-
Total	21	25	

MRC: Medical Research Council (MRC) dyspnea scale.

SAB: Short-acting bronchodilator.

LAB: Long-acting bronchodilator (long-acting b2-agonists or long-acting muscarinic antagonist).

Combination: Corticosteroid plus long acting bronchodilator in combi inhalers.

Corticosteroid plus LAB: Corticosteroid plus long acting bronchodilator in saperate inhalers.

Table 7: The comparison of patients with lower MRC score and higher MRC score according to preferences of patients.

shortness of breath, cough, sputum production. Patients were suffered from these symptoms which may be worse quality of life of their. To improve the quality of life of these patients, it has been suggested that symptoms associated with COPD such as dyspnea, fatigue and sleep disturbance should be regulated and FEV1% predicted value should be increased [10].

The most important second parameter associated treatment for patient was cost of the treatment according to the study. A significant number of patients preferred the least cost of the treatment per month. The importance of cost of treatment for patients may show variability according to the economic conditions in each country.

The study showed that 70% of patients with COPD expressed preferences other treatments to their current treatments. The presented preference structure indicates variations in patient preferences that might need to be addressed in clinical practice [4]. The most used current treatment regimen by patient was corticosteroid plus long acting bronchodilator in saperate inhalers as maintenance and long acting bronchodilator as reliever. However, the most preferred treatment regimen by patient as first choice was long acting bronchodilator (58%) as both maintenance and reliever. Inhaled corticosteroids increase patients' quality of life more than long-acting bronchodilator as insignificantly. However, inhaled corticosteroids do not improve lung function as much as long-acting bronchodilator and significantly increase incidence of pneumonia [11]. On the other hand, long-acting bronchodilator and inhaled corticosteroids combinations had a class effect with regard to the prevention of COPD exacerbations

[12]. There could be several reasons for preferences of patients. The one of this reasons may be that using of long-acting bronchodilator by patient was easy. In addition, daily use of one-time of long-acting bronchodilator may be reason preferred by patients.

This study results showed that the highest-ranked treatment concepts included a reliever with fast onset and long duration according to the utility values in conjoint analysis. Furthermore, a combination inhaler for corticosteroid plus long acting bronchodilator was ranked higher than separate inhaler. In patients with higher symptom score according to CAT score and MRC dyspnea score, preference of use of corticosteroid plus long acting bronchodilator in combi inhalers was higher than in patient with lower symptom score but this difference was insignificant.

The major criticism about the study is the small sample size of 46 respondents. In addition, some patients was not using inhaler treatment for disease despite they have got more symptoms.

In conclusion, it was showed that highly rated patients (70%) preferred treatment other alternative inhaler treatment except their treatments in this study. A combination inhaler for corticosteroid plus long acting bronchodilator was preferred higher than separate inhaler. The first choice of patients for inhaler form for maintenance and acute symptoms was long acting bronchodilator. The highest preferences of patients of their treatment was increasing as the number of SFD increasing per month. Using highly inhaler preferred of patients may increase compliance of their treatment. Taking account of patient preferences when selecting COPD treatment may help to improve compliance with treatment, thus compliance of patients may decrease symptoms due to disease.

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