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Relation between illness acceptance and quality of life in patients with chronic obstructive pulmonary disease (COPD)

The authors declare no financial disclosure.

Abstract

Introduction: Despite the advances in medicine, COPD is still leading, incurable and chronic respiratory disease. It greatly restricts the functioning of patients in terms of physical, emotional and social aspects, reducing significantly their quality of life. The study into quality of life in patients with COPD is becoming increasingly important as a valuable complement to the assessment of clinical status of the patient, the effects of therapy, effectiveness of educational programs, clinical evaluation of drugs, including the patient's acceptance of the disease and treatment. Acceptance or lack thereof, can affect the healing process, result in the lack of cooperation and conscious participation of the patient in the therapeutic process, correlate negatively with different variables of treatment and may lead to the lack of cooperation between the patient and a therapeutic team.

The aim of this study was to determine the correlation of acceptance of disease with quality of life in patients with chronic obstructive pulmonary disease.

Material and methods: The study included 105 patients (including 29 women). Analysis was used to examine the medical records, the Acceptance of Illness Scale (AIS) and the World Health Organization Quality of Life-BREF (WHOQOL-Bref).

Results: The results showed a significantly higher quality of life, in all domains of the questionnaire in patients with COPD who accept their illness to a high degree (AIS > 29). In the physical health domain, group I (lack of acceptance AIS 8–18) won 23.4 ± 13.7, group II (mean acceptance AIS 19–29) 47.9 ± 11.2, group III (high acceptance AIS > 29) 68.9 ± 12.8; p < 0.001. In the psychological domain, group I achieved 40.4 ± 9.2; group II 63.9 ± 9.7; group III 74.9 ± 10.1, in the social relationships domain, group I 48.4 ± 12.5; group II, 69.6 ± 12.7; group III 74.9 ± 10.1, in the environmental domain, group I 45.4 ± 10.7; group II, 62.3 ± 11.6; group III 71.5 ± 10.0 (p < 0.001). Patients with COPD highest rated their quality of life in the domain of social relationships 46.7 ± 19.6, and lowest in the domain of physical health 68.8 ± 18.4.

Conclusions: Acceptance of the disease has a significant impact on the level of assessment of quality of life in patients with COPD — the higher acceptance, the higher rating of quality of life.

Key words: chronic obstructive pulmonary disease, quality of life, the level of acceptance of disease

Pneumonol Alergol Pol 2016; 84: 3–10

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the major problems of public health. It is estimated that 8–10% of Europeans suffer from the disease [1]. It means that there are approximately 2 million patients with COPD in Poland. 3.6% of persons hospitalised constitute

people with COPD. The number of deaths due to COPD and direct complications related to the disease in Poland amounts to about 14–15,000 annually. It is estimated that in 2020, COPD will be the third cause of death [2]. The primary objective of treatment for COPD is to slow the progression of the disease, reduce intensity of symptoms, decrease the number of exacerbations

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DOI: 10.5603/PiAPa.2015.0079

Received: 02.11.2014

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ISSN 0867–7077

and prevent late complications, i.e. complete respiratory failure and pulmonary hypertension [3]. Treatment should also improve lung ventilation and limit annual FEV₁ decline. While starting therapy, the degree of severity of the disease should be taken into account, then treatment should be modified depending on the intensity of symptoms [4]. Therapy should be patient-tailored, adjusted to the intensity of symptoms and response to treatment. Appropriate treatment, adherence to prescribed regimen and smoking cessation may considerably influence the patient's quality of life and hamper further progression of disease [4]. Of crucial importance are prevention efforts, rehabilitation, psychological and family support [5]. Despite continuous progress in medicine, COPD still remains leading, incurable and chronic disease of the respiratory system. It considerably limits patients' functioning in physical, emotional and social aspects, significantly lowering their quality of life. Researches into quality of life in COPD patients are rising in importance as a valuable supplement to the assessment of clinical status of the patient, effects of the current treatment, evaluation of the effectiveness of educational programmes, clinical assessment of drugs, including the patient's acceptance of illness and the method of treatment. Acceptance or the paucity thereof may affect the process of treatment, lead to lack of cooperation and aware participation of the patient, negatively correlate with various variables related to treatment, thus - it may result in the lack of cooperation between the patient and a therapeutic team. The disease forces the patient to change his or her previous functioning, eliminate bad habits, introduce a healthy diet, get involved in physical activity and adhere to long-term therapy [6, 7]. There are data about quality of life of COPD patients in the literature, but there are no papers concerning the acceptance of disease and its relation to self-assessed quality of life.

The aim of the study was to determine the correlation of acceptance of disease with quality of life in patients with COPD.

Material and methods

The study included 105 patients (inclusive of 29 women) hospitalised between September 2013 and March 2014 due to exacerbation of COPD in the Independent Public Clinical Hospital No.1 in Wrocław at the Department and Teaching Hospital of Internal Diseases, Geriatrics and Allergology. According to the Recommendations of the Polish

Respiratory Society concerning diagnosis and treatment of chronic obstructive pulmonary disease, diagnosis of disease was based on patients' history, physical examination, spirometric and radiological tests of the chest [8]. Participation in the study was voluntary and anonymous. The patients qualified for the study were informed about its objective, methods and the possibility to withdraw at any stage. The Bioethical Committee of the Wrocław Medical University consented to the study (no. KB 593/2013). The subjects were divided into three groups depending on Acceptance of Illness Scale (AIS) score:

- Group I (AIS 8–18) — n = 25
- Group II (AIS 19–29) — n = 57
- Group III (AIS > 29) — n = 23

Inclusion criteria:

- diagnosis of COPD and determination of COPD severity according to the GOLD guidelines [8]
- above 18 years of age
- consent to the participation in the study

Exclusion criteria:

- under 18 years of age
- concomitance of severe chronic diseases that could interfere with the study (severe asthma, neoplastic diseases of the lungs, respiratory failure).

The study used the following tools:

- a dedicated questionnaire and the analysis of medical documentation
- the Acceptance of Illness Scale questionnaire (AIS)
- a general questionnaire evaluating quality of life — an abbreviated version of the World Health Organization Quality of Life (WHOQoL-BREF).

The dedicated questionnaire comprised 18 questions. The survey's questions and data from medical documentation allowed to determine a sociodemographic and clinical profile of the patient. Information about severity of the disease and received treatment was collected.

The Acceptance of Illness Scale is an instrument of measurement in promotion and psychology of health. It consists of eight statements describing negative impact of poor health status and its consequences for functioning in the world. The respondents were evaluating statements on a scale from 1 (poor adaptation to the disease) to 5 (full acceptance of the disease). The acceptance of illness scale was drawn up by Felton, Revenson and Hinrichsen and translated into Polish by Juczyński. The survey comprises 8 statements describing difficulties and limitations

that are negative effects of poor health status. The limitations are the result of the illness, the feeling of dependency upon other people, lack of self-sufficiency and self-esteem. The answers are scored on a five-point scale with 1 meaning “I definitely agree”, and 5 — “I definitely do not agree”. The total score oscillates between 8 and 40. It is a general assessment of the level of acceptance of illness. The lower score, the poorer acceptance of disease and more severe restrictions caused by condition. A high score means acceptance of own health status and lack of negative emotions related to illness. The Polish version of AIS has a high Cronbach alpha coefficient — 0.82, which is in accordance with the original version of the scale. The consent to conduct the study with this instrument was granted by the Psychological Test Laboratory [9]. The participants of the study were divided into three groups depending on the achieved AIS score: < 29 — great acceptance of illness, 19 — 29 average acceptance, and 8–18 — lack of acceptance.

The WHOQoL-BREF is a questionnaire prepared by WHO to assess the position in life of the individual both in case of healthy people and that being the result of illness and the received therapy. The abbreviated version contains a total of 26 questions examining four domains of life: physical health, psychological, social relationships and environment. The physical health domain includes pain and discomfort, activities of daily living, sleep and rest. The psychological domain concerns negative feelings and bodily image and appearance. The social relationships domain involves personal relationships and social support. The environmental domain deals with safety, financial resources, home environment, accessibility to health and social care. According to the WHO recommendations, raw scores obtained for particular domains were converted to transformed scores to a 0–100 scale [10].

Statistical analysis:

All quantitative parameters (age) were verified in terms of conformity of their distribution with normal distribution. Conformity was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests. $P = 0.05$ was assumed as statistically significant.

Mean values, standard deviations, medians and extreme values (minimum and maximum) were calculated for all measurable parameters.

The significance of differences of mean values in the two groups (women and men) for parameters with normal distribution and homogenous

variances was verified with *t*-Student test. In the cases when the distribution of a variable diverged from normal, non-parametric Mann-Whitney U test was applied.

The significance between the differences of the mean values of quantitative parameters in more than two groups (e.g. in groups differing in education) was verified with analysis of variance (ANOVA).

For unmeasurable variables (qualitative ones, e.g. sex, nicotine use etc.), the numbers (n) and percentage (%) were calculated and gathered in contingency tables.

Hypotheses about the paucity of correlation between qualitative parameters were verified using Pearson's chi-square test. When in a four-field table (2×2) the number in the table cell was 5 or less, Fisher's exact test was applied. $P < 0.05$ was assumed as significant correlation between the variables.

Calculations were made with the help of the EXCEL spreadsheet and the STATISTICA software v.10 PL.

Results

The study on the influence of acceptance of illness on quality of life in patients with chronic obstructive pulmonary disease was carried out among 105 subjects (29 women) (mean age 64.8 ± 11.5). $P < 0.05$ were assumed as statistically significant.

No statistically significant correlation was observed between the level of acceptance of illness and patients' sex. Among the surveyed women (36.8%) and men (63.2%), people with average acceptance of disease prevailed. The level of acceptance of illness is abating together with age. In the group accepting the disease well, the mean age was 60.6 ± 11.1 , in the group of average level of acceptance — 64.3 ± 10.7 , and in the group not accepting the illness — 69.8 ± 12.4 ($p = 0.018$).

Significant relation of the level of acceptance of illness to patients' education was found ($p < 0.01$). The higher education, the higher level of acceptance of disease. In group III (AIS < 29) individuals with higher education made up 56.5% of the respondents, in group II — 22.8%, and in group I — 28%. The majority of the study group lived in a town or city (72.4%), no statistically significant relation was noted between the place of living and the level of acceptance of disease. 22.9% of the respondents were current smokers, and more than half of them (55.2%) quit smoking. It was observed that in the group with great accep-

tance of illness, those who never smoked (34.8%) prevailed, whereas current smokers constituted the smallest part (17.4% vs 21.1% in group II vs 32% in group III) (ns). Duration of illness was an important variable that correlated with acceptance of disease. Here inversely proportional dependence was observed — the shorter duration of illness, the higher level of acceptance thereof (group I — 9.8 ± 5.8 vs group II — 7.5 ± 4.2 vs group III 4.9 ± 3.0 ; $p = 0.001$). A lowered level of acceptance of disease was connected with the number of hospitalisations due to COPD exacerbations. All subjects with low level of acceptance of disease were hospitalised due to exacerbations. Whereas in group II and III, 91.2% of the respondents were hospitalised (ns). Inversely proportional dependence of the number of hospitalisations and the level of acceptance of disease was also revealed. The higher number of hospitalisations, the smaller acceptance of illness (group I — 4.2 ± 2.1 , group II — 2.5 ± 1.8 , group III — 1.5 ± 1.2 ; $p < 0.001$). Basing on the recommendations of the Polish Respiratory Society, a moderate form of disease was diagnosed in nearly half of the subjects (48.6%). Statistically significant correlation was discovered between the stage of disease and its level of acceptance. In group I, there were 44% of people with a severe form of COPD and 16.0% with a very severe form. In group II, patients with a moderate form of disease prevailed (50.9%), in group III — with a moderate form (60.9%) and the mild one (34.8%) ($p = 0.001$). A comparable correlation concerned the frequency of intensity of dyspnoea and the level of acceptance of illness. Among the subjects with low acceptance of disease, those suffering from dyspnoea several times a day predominated (48%), in the group with moderate acceptance, dyspnoea occurred several times a day in 22.8% of the respondents, and in the group with high acceptance of disease — merely in 4.3% of the subjects ($p < 0.001$). Elementary sociodemographic and clinical data are presented in Table 1.

The impact of acceptance of disease on the patient's quality of life

The results of the study have shown significantly higher quality of life in all domains of the questionnaire among COPD patients who accepted their disease to a great extent (AIS > 29). In the physical domain, group I (lack of acceptance, AIS 8-18) achieved 23.4 ± 13.7 , group II (average acceptance, AIS 19–29) — 47.9 ± 11.2 , group III (high acceptance, AIS > 29) 68.9 ± 12.8 ($p < 0.001$). In the psychological domain, group

I — 40.4 ± 9.2 , group II — 63.9 ± 9.7 , group III — 74.9 ± 10.1 , in the social relationships domain, group I — 48.4 ± 12.5 ; group II — 69.6 ± 12.7 ; group III — 74.9 ± 10.1 , in the environmental domain, group I — 45.4 ± 10.7 ; group II — 62.3 ± 11.6 ; group III — 71.5 ± 10.0 ($p < 0.001$). COPD patients rated their quality of life highest in the social relationships domain — 46.7 ± 19.6 , and lowest — in the physical health domain — 68.8 ± 18.4 . The above data are presented in Table 2.

Discussion

Chronic conditions, including COPD, due to their progressive character and course with unpleasant symptoms, markedly influence biopsychosocial functioning of population. They produce big changes to elementary roles of patients. They create barriers in physical and mental spheres. Difficulty with accepting disease and its effects play a crucial role in perceiving his or her quality of life [11, 12].

The objective of the study was to present the correlation between the acceptance of illness and quality of life in patients with diagnosed chronic obstructive pulmonary disease. The impact of many factors on the level of acceptance of disease was examined. The results of the study have shown that COPD patients have low quality of life at every stage of the disease, which has been confirmed by other authors. The study by Ferrer et al. included 321 subjects. Contrary to expectation, even patients with a mild form of disease had a considerably lower quality of life [13].

63.2% of the respondents constituted men, which corresponds to epidemiological data indicating that males more frequently suffer from COPD [14]. In the present study patients with average acceptance of illness prevailed, similarly, in the research by Kupcewicz and Abramowicz who examined 96 subjects with diagnosed COPD, the mean rate of acceptance amounted to 19.00 ± 6.9 , which reflects average acceptance of disease [15].

According to the WHOQoL-Bref questionnaire, all four life domains of the subjects who did not accept the disease, considerably affected their quality of life. As maintained by Bał-Drabik and Ziora [16], quality of life of COPD patients was also vitally reduced in all domains of functioning. Its decline is affected by progressing bronchial airflow limitations related to the progression of disease, physical activity restrictions, intensity of dyspnoea and poor education. These studies have not noted significant correlation between age, sex or tobacco smoking and QoL [16].

Table 1. Analysis of sociodemographic and clinical patients with COPD with respect to Illness Acceptance Scale (AIS)

Variable	AIS				p-value test
	All	Group I Low AIS 8–18	Group II Moderate AIS 19–29	Group III High AIS > 29	
Gender:					
female	29 (27.6%)	3 (12.0%)	21 (36.8%)	5 (21.7%)	0.053
male	76 (72.4%)	22 (88.0%)	36 (63.2%)	18 (78.3%)	
Age (years)					
M ± SD	64.8 ± 11.5	69.8 ± 12.4	64.3 ± 10.7	60.6 ± 11.1	0.018
Me (Q1; Q3)	66 (56;74)	74 (60;78)	66 (56;71)	61 (54;66)	
Education:					<0.001
primary	6 (6.7%)	6 (24.0%)	1 (1.8%)	0 (0.0%)	
basic vocational	31 (29.5%)	6 (24.0%)	18 (31.6%)	7 (30.4%)	
secondary	34 (32.4%)	6 (24.0%)	25 (43.9%)	3 (13.0%)	
higher	33 (31.4%)	7 (28.0%)	13 (22.8%)	13 (56.5%)	
Place of residence:					
town	76 (72.4%)	15 (60.0%)	42 (73.7%)	19 (82.6%)	0.206
village	29 (27.6%)	10 (40.0%)	15 (26.3%)	4 (17.4%)	
Smoking:					0.120
I never smoked	23 (21.9%)	7 (28.0%)	8 (14.0%)	8 (34.8%)	
I do not smoke anymore	58 (55.2%)	10 (40.0%)	37 (64.9%)	11 (47.8%)	
currently smoke	24 (22.9%)	8 (32.0%)	12 (21.1%)	4 (17.4%)	
Number of cigarettes smoked (pcs./day)					0.885
M ± SD	8.3 ± 3.1	7.9 ± 3.5	8.6 ± 2.7	8.5 ± 4.0	
Me (Q ₁ ; Q ₃)	8 (5;10)	8 (5;9)	10 (6;10)	8 (5;12)	
Duration of COPD diagnosis:					0.001
M ± SD	7.5 ± 4.7	9.8 ± 5.8	7.5 ± 4.2	4.9 ± 3.0	
Me (Q ₁ ; Q ₃)	7 (4;10)	8 (6;14)	7 (4;10)	4 (2;7)	
Hospitalization due to exacerbations:					0.310
no	7 (6.7%)	0 (0.0%)	5 (8.8%)	2 (8.7%)	
yes	98 (93.3%)	25 (100%)	52 (91.2%)	21 (91.3%)	
Hospitalization rates:					<0.001
M ± SD	2.7 ± 2.0	4.2 ± 2.1	2.5 ± 1.8	1.5 ± 1.2	
Me (Q ₁ ; Q ₃)	2 (1;4)	4 (2;6)	2 (1;3)	1 (1;2)	
Stages of COPD:					0.001
mild COPD	24 (22.9%)	2 (8.0%)	14 (24.6%)	8 (34.8%)	
moderate COPD	51 (48.6%)	8 (32.0%)	29 (50.9%)	14 (60.9%)	
severe COPD	25 (23.8%)	11 (44.0%)	13 (22.8%)	1 (4.4%)	
very severe COPD	5 (4.8%)	4 (16.0%)	1 (1.7%)	0 (0.0%)	
The frequency of exacerbations: shortness of breath					< 0.001
never (0)					
only after physical effort (1)	7 (6.7%)	0 (0.0%)	1 (1.8%)	6 (26.1%)	
several times a week (2)	23 (21.9%)	3 (12.0%)	14 (24.6%)	6 (26.1%)	
once daily (3)	26 (24.8%)	4 (16.0%)	16 (28.1%)	6 (26.1%)	
several times daily (4)	23 (21.9%)	6 (24.0%)	13 (22.8%)	4 (17.4%)	
	26 (24.8%)	12 (48.0%)	13 (22.8%)	1 (4.3%)	

M — mean, Me — median, Q — quartile

Majda et al. in their study [17] used the Acceptance Illness Scale (AIS). 50% of patients had great acceptance of disease. There were 18% of women and 32% of men among subjects with good acceptance. The average level of acceptance was found in 33% of the subjects, including 11% of women and 22% of men. Low level of acceptance was noted in 17% of men [17]. In the present stu-

dy, the biggest group comprised the respondents with average level of acceptance, including 36.8% of women and 63.2% of men. Good level of acceptance was shown in 21.7% of women and 78.3% of men, and the lack of acceptance — in 12% of women and 88% of men. Both the present study and the research by Bąk-Drabik have shown that sex does not impact materially on quality of life

Table 2. Median scores (interquartile ranges) on individual WHOQoL Bref domains stratified according to the Acceptance of Illness Scale (AIS) scores of patients with chronic obstructive pulmonary disease

AIS	Quality of life domains (WHOQoL Bref)			
	Physical Health	Psychological	Social	Environmental
Group I Lack Of Acceptance (8–18 pts)	23.4 ± 13.7	40.4 ± 9.2	48.4 ± 12.5	45.4 ± 10.7
Group II Average Acceptance (19–29 pts)	47.9 ± 11.2	63.9 ± 9.7	69.6 ± 12.7	62.3 ± 11.6
Group III High Acceptance > 29	68.9 ± 12.8	74.9 ± 10.1	88.9 ± 11.3	71.5 ± 10.0
ANOVA:	p < 0.001	p < 0.001	p < 0.001	p < 0.001
Total (Groups I, II and III)	46.7 ± 19.6	60.7 ± 15.5	68.8 ± 18.4	60.3 ± 14.3

in COPD patients [16]. However, it should be underlined that in the study by Majda et al., the patients who accepted the disease well made up half of the respondents, whereas in the present study, subjects with average level of acceptance predominated. A comparable result concerned persons with the paucity of acceptance. In the research by Majda et al., the comparison of particular age groups has shown that the highest level of acceptance was achieved by people aged 51–60 years [17], whereas the study by Bąk-Drabik has not noted the influence of age on quality of life in COPD patients [16]. Yet Manguera et al. have observed that quality of life was poorer in younger patients, compared to the older ones [18]. Nevertheless, the research conducted among 202 COPD patients in Sweden produced opposing findings — lower QoL was observed in patients at more advanced age [19]. In the study by Martin et al., which included 9,405 subjects (79% of men, mean age 68 years), patients at the age of 60 perceived their quality of life worse than the subjects aged 40–59 years [20].

In the present study, age significantly impacts on the level of acceptance of disease. The level of acceptance is abating together with age. The highest level of acceptance of illness was achieved by people aged 54–66 years (mean age 60.6). Furthermore, significant correlation between the level of acceptance of disease and patients' education was observed. The higher education, the higher level of acceptance of disease. In the studies by other authors, the group of patients with university education assessed higher their quality of life in the social relationships domain, compared to people with secondary, vocational or elementary education. The results confirmed the thesis that poor level of education affects negatively quality of life of patients with COPD [16].

The research by Majda et al. has demonstrated the highest rate of acceptance of disease in the subjects with university education [17]. Comparable results were obtained by Kołcz et al. [21]. A significantly higher quality of life was noted in the subjects with university education, compared to those with secondary, vocational or elementary education [21].

Taking into account the COPD classification, 24 patients were at mild stage of disease, 51 individuals had a moderate form of COPD, 25 — severe, and 5 — very severe. In the study by Ziętkowski et al., 25 persons had IV stage of disease, 24 — III, 29 — a moderate form of COPD, and 24 — the mild one [22]. According to Bąk-Drabik, higher quality of life was observed in the respondents with a mild form of COPD [16]. The present study has shown that the stage of disease strongly correlates with the level of acceptance thereof. Its lack occurs in patients at a very severe and severe stage of illness.

Taking into account the results of the study with regard to duration of disease, the number of hospitalisations due to exacerbations and taken inhaled drugs, it may be concluded that the intensity of these aspects of disease will impair patients' quality of life. The average duration of disease was 7.5 ± 4.7 years, and the level of acceptance of it decreases together with growing duration. The same regularity applies to the number of hospitalisations. The patients on average were treated 2.7 ± 2.0 times. Every stay in hospital reduces the level of acceptance. The patients using fast-acting inhaled drugs rarely, accept the disease well, contrary to the patients taking drug 3 or more times a day. In the study by Majda et al., a prominent part in their lives, thus their quality of life, was the appearance of exacerbations of COPD and their consequence

— hospitalisations. They occurred 2–3 times annually. In 30% of respondents, they occurred more often than 4 times per year [17]. The research conducted by Kieczka has shown that longer duration of illness results in a greater number of patients who are affected negatively by disease [23]. According to Kołcz et al. [21] the biggest impact on the lowering of QoL has progressive dyspnoea (80% of the respondents). Its frequent occurrence impairs physical activity in the majority of the subjects. It results directly in the reluctance to physical exercise related to rehabilitation of COPD patients. 60% of the subjects voiced concern for their health during exercise, also the one recommended by the physical therapist. They preferred aerobic exercise, which was bringing them relief. They have adopted similar attitude to inhalations and the necessary pharmacotherapy [21]. Progressive character of the disease favours the intensity of dyspnoea. According to the present study, the occurrence of dyspnoea significantly affects quality of life. Good acceptance of illness occurs with rare prevalence of dyspnoea. Of importance is also its influence on the activities of daily living. Lack of acceptance occurs significantly more frequently in patients in whom dyspnoea restricts their daily duties to a large extent. To reduce negative effects of disease, the patients were undertaking some activities such as physical exercise, aerobic exercise and oxygen therapy. This method of treatment is used more frequently by patients not accepting their condition. However, they more rarely stick to a healthy diet, compared to patients who accept the disease well.

Conclusions

1. The acceptance of disease significantly impacts on the perception of quality of life in patients with COPD — the greater acceptance, the higher rating of quality of life.
2. The acceptance of disease in COPD patients is vitally affected by: age, education, duration of illness, the number of hospitalisations due to exacerbations, the stage of disease and the intensity of dyspnoea.

Practical implications

There is the need to educate patients, in particular the elderly ones, those poorly educated and often hospitalised due to exacerbations, in order to engage them fully in therapeutic process.

Lack of acceptance of disease and lowered quality of life may result in negative attitude to

the process of treatment, it may hinder compliance and adherence, thus leading to exacerbations, which in turn contribute to negative behaviour.

Conflict of interest

The authors declare no conflict of interest.

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