ORIGINAL RESEARCH

Association of Patients' Knowledge on the Disease and Its Management with Indicators of Disease Severity and Individual Characteristics in Patients with Chronic Obstructive Pulmonary Disease (COPD): Results from COSYCONET 2

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Background: In patients with chronic diseases, including those with chronic obstructive pulmonary disease (COPD), knowledge on the disease and its self-management is considered as relevant for improving disease control and long-term outcome. We studied to which extent components of knowledge depended on potential predictors, such as participation in educational programs and disease severity. For example, the perception of exacerbations or GOLD grade might modulate the content and reliability of COPD understanding.

Methods: Data from the German COSYCONET 2 COPD cohort was used, and 13 questions addressing knowledge and self-management were analyzed.

Results: Overall, 310 patients with the diagnosis of COPD of GOLD grades 1/2/3/4 as well as the former grade 0 were included (39.7% female, median age 66.0 years). The answers to 3 questions (knowledge of term exacerbation, pursed lip breathing technique, criteria for contacting a doctor) were improved ($p < 0.05$ each) when patients had had moderate-to-severe exacerbations, and to one question (breathing exercise) when having COPD grade 3/4 versus 0/1/2. The other 9 responses did not depend on disease severity, but most of the knowledge was improved when having participated in an educational COPD program. This was particularly true for knowledge that also depended on exacerbations, or if the treating physician was a pulmonary specialist. In some responses, the proportion of correct answers was significantly reduced in males compared to females. The dependence on education level, existence of a treatment plan, self-reported level of risk aversion and low depression score was weak and heterogeneous.

Conclusion: These findings suggest that part of the disease-related knowledge in patients with COPD was reinforced by the experience of exacerbations, especially knowledge regarding criteria on contacting a physician. These observations might help in focusing education on those parts of knowledge that are considered as important by patients based on their own experience.

Keywords: COPD, symptom exacerbation, patient acuity, education, knowledge

Introduction

It is well known that patients with chronic obstructive pulmonary disease (COPD) suffer from progressive worsening and severity of disease. Their clinical state can be described via different indices, such as the spirometric lung function impairment (GOLD grades 1–4)[1] or the occurrence and severity of exacerbations. There is a broad spectrum of pharmacological and non-pharmacological therapeutic interventions for COPD, as documented in international guidelines.[1] In addition, it is assumed that patients benefit from a profound understanding of their disease and from awareness of their clinical state, which might allow for better disease control and reduce the likelihood of severe outcomes. This characteristic is also observed in other chronic diseases such as diabetes[2–7] and cardiac disorders.[8,9] Based on this, efforts have been undertaken to implement educational programs to improve patients' knowledge on their disease. Numerous data indicate the clinical effectiveness of such programs in diabetes[2–7] and cardiac disease.[8–10] Similar effects are suggested by studies performed in COPD.[11–16] As COPD is a multi-faceted disease, a comprehensive knowledge probably needs to cover a broad spectrum of topics, ranging from more theoretical ones such as pathophysiological mechanisms to more practical ones such as the response to deteriorations or the intake of medication.

Educational programs contribute to increased knowledge in COPD patients. However, it is also reasonable to assume that personal experiences, especially events such as exacerbations, play a role, either by reinforcing knowledge acquired through education or by motivating patients to gather additional knowledge from other sources. This raises the question, which part of COPD knowledge is influenced by the severity of the disease, and which is not. Dissecting the impact of different types of patients' knowledge (for example "personal experience" versus "educational") is not only of interest per se but might guide educational efforts towards the clinically most relevant topics. Patients' experience of disease severity might be quantified by indicators of acute experience, for example, exacerbations, or by indicators of persistent experience, such as lung function impairment. In a previous study, we identified determinants of knowledge in the COSYCONET 1 cohort,[17] but only for two simple questions.[13] There are many studies that utilized summary scores to identify determinants of knowledge and self-management in COPD.[18–20] They did not investigate, however, which questions were related to disease severity and which were not. Thus, the aim of this study was to identify the impact of disease severity, acute exacerbations and other clinical characteristics of patients with COPD on disease-related knowledge.

For this purpose, we used the answers to a panel of questions on COPD knowledge and self-management and investigated whether the answers showed different relationships to disease severity, educational interventions, modalities of treatment and individual characteristics including self-rated risk aversion. The analysis was performed using data from the German COSYCONET 2 COPD cohort, which is a continuation of COSYCONET 1.[17,21]

Methods

Study Population

The analyzed data set of the COSYCONET 2 cohort comprised 310 patients with the diagnosis of COPD, who were recruited between 2020 and 2024 in 12 German study centers that had already participated in COSYCONET 1.[17] Inclusion and exclusion criteria, as well as basic assessments, were the same as in COSYCONET 1.[17] COSYCONET 1 was a large German COPD cohort study, with recruitment from 2010 to 2013 and regular follow-up visits. At these visits, a comprehensive functional and clinical characterization was performed.[17] Based on the experiences from COSYCONET 1, COSYCONET 2 was designed, including some omissions and some extensions such as the introduction of the questions used in the present analysis. COSYCONET 2 had been approved by the ethical committees of all study centers and all patients gave their written informed consent. The study complies with the Declaration of Helsinki (2013). Its identifier in the German Register of Clinical Studies (DRKL) is DRKS00015884.

Questionnaires Used

COSYCONET 2 had been designed based on the experiences from COSYCONET 1. While some assessments were omitted as they had turned out to be uninformative, others had been additionally included as potentially informative. Among these were questions regarding the knowledge and self-management of COPD as listed in Figure 1, together with

Number	Questions	Answer options	Shortcuts
Q1	Do you know the term "exacerbation"?	O Yes O No	Term exacerbation
Q2	For the pursed lip breathing technique, I have to breathe out through almost closed lips.	O Right O False O Don't know	Pursed lip breathing technique
Q3	I have clear criteria for when to contact the doctor in the event of a deterioration	O Yes O No	Criteria for contact with doctor
Q4	I do breathing exercises (e.g. abdominal breathing) when I don't feel shortness of breath.	O Yes O No	Breathing exercise
Q5	Do you know the term "FEV_1"?	O Yes O No	Term FEV_1
Q6	How satisfied are you with your knowledge and understanding of COPD?	scale from 0= not at all to 6= very satisfied	High satisfaction with knowledge
Q7	On average, patients with COPD do not have more other diseases (concomitant diseases) than patients without COPD. *(wrong)*	O Right O False O Don't know	Comorbidities in COPD patients
Q8	I know exactly what medication to take for certain symptoms such as shortness of breath or a general worsening of my condition.	O Yes O No	Which medication for symptoms
Q9	Extensive, consistent exercise in everyday life (e.g. climbing stairs, going shopping) can already cover a large part of the necessary physical activity.	O Right O False O Don't know	Daily exercise
Q10	If I get short of breath during physical activity, I should not take it easy, but continue to exert myself as much as possible.	O Right O False O Don't know	Dyspnea during exercise
Q11	Has your doctor reviewed your inhalation technique in the last 12 months?	O Yes O No	Check of inhaler technique
Q12	When I am prescribed new medication, I ask the doctor or pharmacy exactly how often, how and for how long I should take it.	O Yes O No	Information about new medication
Q13	Have you ever received instructions on the correct inhalation of medication?	O Yes O No	Instructions for inhaler

Figure 1 Questions, answer options and shortcuts used in the text and the diagrams. By cutting the last column, the table could be used as a questionnaire.

their shortcuts and options for answers. These questions were partly taken from COPD knowledge questionnaires from other countries,[16,22,23] partly from a novel German questionnaire on COPD knowledge and self-management that was still in the development process during the time of COSYCONET 2 and is now available for use.[24]

Four of the questions (Q1, Q5, Q11, Q13) could only be answered by "Yes" or "No". Regarding other categorical questions (Q2, Q7, Q9, Q10), patients had the options "correct", "false" or "do not know". For the purpose of analysis, "do not know" was pooled with "false", resulting in two categories. Questions about self-management or attitude (Q3, Q4, Q8, Q12) were addressed using a Likert scale from 1 ("Do not agree at all") to 4 ("Agree entirely"); for analysis, binary responses were formed in terms of 3/4 versus 1/2.

Assessments

Patient characteristics, clinical history, lung function parameters and questionnaires on the state of the disease were collected as in COSYCONET 1.[17] For the present analysis, we only considered spirometry in terms of forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and their ratio (FEV_1/FVC). Predicted values were taken from the Global Lung Function Initiative (GLI).[25] Questionnaires comprised the COPD Assessment Test (CAT),[26] the modified Medical Research Council scale (mMRC),[27] and the screening questionnaire for depression PHQ-9.[28] Higher CAT and mMRC scores indicate more burden from the disease, and higher PHQ-9 scores a higher likelihood for a clinical diagnosis of depression. The patients' willingness to take risks was assessed using a Likert scale ranging from 0 to 10, where 0 indicated a high level of risk aversion, and 10 indicated a high willingness to take risks.

Patients with a ratio FEV_1/FVC <0.7 were categorized into spirometric GOLD grades 1–4,[1] while patients with a diagnosis of COPD but not fulfilling this criterion were termed "COPD 0" as previously.[29] Patients were also categorized into GOLD groups A, B and E, based on symptoms and exacerbation history (in the last year) as proposed[1] and used in previous analyses of COSYCONET data.[30–32] For the distinction between groups A and B, the mMRC[27] was used, as it yielded more balanced results than the CAT. Education was grouped into three categories based on the years of school education (low (0–9 years), secondary (9–11 years) and high (>11 years)) as previously.[11]

Data Analysis

Median values and quartiles, or numbers and percentages were used to describe the results, depending on the type of data. Potential predictors of knowledge and self-management had been identified in previous studies.[13,23,33–39] The set of predictors comprised the occurrence of at least one moderate or severe exacerbation, the presence of severe spirometric deterioration (GOLD grades 3/4 versus the others), previous participation in educational COPD programs, treatment by a pulmonary specialist (versus other physician), education (high (>11 years) versus lower), male sex, existence of a treatment plan (as reported by the patients), very low indication of depression (PHQ-9 ≤4 on a scale ranging from 0 to 27), and low willingness to take risks (scores 0–4 on a scale ranging from 0 to 10). Each of the 13 questions was then taken as dependent variable in binary logistic regression analyses. Depending on the findings of these single association analyses, sum scores of two sets of questions were computed (see Results). Please note that these two sum scores were only a tool to better understand the results of the present study and not intended for general use. The sum scores were investigated using linear regression analysis and the same set of predictors. All analyses were performed using the software package SPSS (Version 29, IBM Corp., Armonk, NJ, USA). Statistical significance was assumed for $p < 0.05$.

Results
Study Population

Among the 310 patients, 39.7% were female and 38.4% current smokers. GOLD grades 3/4 comprised 22.8% of patients and GOLD 0 20.9% of patients, while group A comprised 51.3%, group B 28.6% and group E 18.1%. Further characteristics are given in Table 1. Figure 2 shows the frequencies of correct answers or high approval to the 13 questions chosen for the present analysis.

Table 1 Patient Characteristics. GOLD Groups A/B/E Were Defined Using the mMRC Scale

Variable	Numbers (%) / Median [quartiles]
Male/Female	187/123 (60.3%/39.7%)
Age	66.0 [61.0, 73.0]
FEV$_1$% predicted (GLI)	67.1 [51.0, 81.6]
FVC % predicted (GLI)	85.7 [72.1, 98.2]
CAT (score 0–40)	17 [12, 23]
mMRC (score 0–4)	1 [1, 2]
Previous educational training on COPD (yes)	51 (16.5%)
GOLD grades 0/1/2/3/4	63/47/123/59/10 (20.9%/15.6%/40.7%/19.5%/3.3%)
GOLD groups A/B/E	159/81/53 (54.3%/27.6%/18.1%)
Number of cardiac comorbidities (0/1/2/3)	113/145/45/7 (36.5%/46.8%/14.5%/2.2%)
Number of vascular comorbidities (0/1/2)	269/40/1 (86.8%/12.9%/0.3%)
Number of respiratory comorbidities (0/1/2)	201/92/15 (65.3%/29.9%/4.8%)
Number of metabolic comorbidities (0/1/2/3)	138/112/44/16 (44.5%/36.1%/14.2%/5.2%)
Treatment plan for COPD (yes)	23 (7.4%)
Participation in COPD disease management program (yes)	58 (18.7%)
Time since diagnosis of COPD (years)	6 [2, 10]
Treating physician pneumologist (yes)	201 (64.8%)
Education level (basic/secondary/higher)	127/91/81 (42.5%/30.4%/27.1%)
Smoker status (currently/before/never)	119/181/10 (38.4%/58.4%/3.2%)
PHQ9 score	5 [3, 10]
Low PHQ9 score (0–4)	124 (40.0%)
Willingness to take risks (on a scale from 0 to 10)	5.0 [3.3, 7.0]
Low willingness to take risks (0–4)	101 (32.6%)

Abbreviations: FEV$_1$, forced expiratory volume in 1 s; FVC, forced vital capacity; GLI, Global Lung Function Initiative; mMRC, modified Medical Research Council scale; GOLD, Global Initiative for Chronic Obstructive Lung Disease; PHQ9, Patient Health Questionnaire.

Associations of Questions with the Set of Predictors

Logistic regression analyses were performed for each single question and the results represented in a heatmap in Figure 3 (p-values < 0.1 color-coded). Questions Q10 to Q13 (dyspnea during exercise, check of inhaler technique, information about new medication, instructions for inhaler) showed only weak associations with the predictors, whereas the strongest associations were seen for Q1 and Q2 (term exacerbation, pursed lip breathing technique). Exacerbations were significantly ($p < 0.05$) associated only with Q1 to Q3, while participation in educational programs was associated with questions Q1, Q2, Q4-Q7. Treatment by a pneumologist was positively linked to questions Q1, Q2, Q5 and Q8. A high (versus medium/low) degree of education was only linked to Q1 and Q7, and existence of a treatment plan only to Q9 and Q11 (daily exercise, check of inhaler technique).

There were also associations with male sex (Q1, Q2, Q8, Q9, Q10), most of them inverse (Q1, Q2, Q8) meaning that male sex was linked to a lower percentage of positive answers. A low depression score was inversely correlated with Q2 (pursed lip

Percentages of correct answers/Yes/High approval
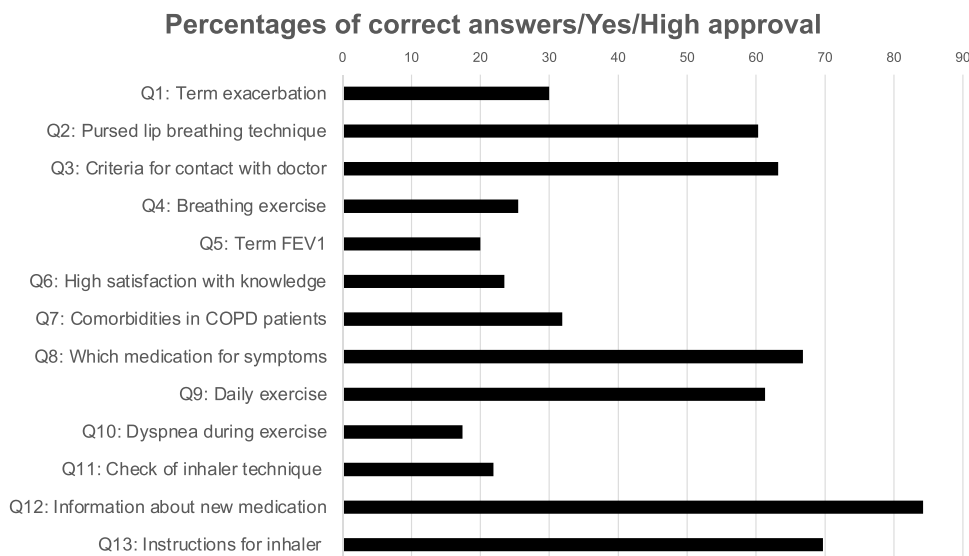
Figure 2 Percentages of knowledge on questions 1 to 13 in terms of correct answers/high approval/Yes. The full questions and their answer options can be found in Figure 1. Non-categorical questions Q3, Q4, Q8, Q12 were rated positive for answers "Rather agree" or "Agree entirely".

Predictors	Questions													Sum Scores	
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	S1-4	S5-13
Exacerbations	0,037	0,049	0,018	0,088	0,29	0,192	0,968	0,146	0,286	0,414	0,261	0,906	0,707	0,001	0,144
GOLD grade 3 or 4	0,348	0,327	0,76	0,015	0,27	0,553	0,223	0,103	0,559	0,259	0,098	0,439	0,692	0,059	0,212
Participation in educational program	0,001	0,001	0,262	0,044	0,001	0,026	0,005	0,098	0,716	0,145	0,437	0,248	0,071	0,001	0,001
Treated by pulmonary specialist	0,012	0,026	0,062	0,316	0,048	0,118	0,97	0,048	0,165	0,586	0,406	0,062	0,241	0,003	0,149
High education	0,004	0,845	0,041	0,59	0,185	0,137	0,022	0,35	0,238	0,22	0,057	0,722	0,433	0,668	0,319
Male	0,001	0,001	0,915	0,081	0,105	0,128	0,061	0,009	0,003	0,02	0,154	0,631	0,052	0,002	0,078
Treatment plan	0,348	0,18	0,532	0,312	0,544	0,705	0,331	0,993	0,031	0,627	0,002	0,65	0,383	0,387	0,107
Low PHQ9 score (0-4)	0,633	0,04	0,439	0,415	0,627	0,002	0,257	0,171	0,096	0,561	0,277	0,037	0,625	0,698	0,039
Low willingness to take risks (0-4)	0,104	0,924	0,375	0,733	0,171	0,143	0,446	0,059	0,771	0,276	0,67	0,693	0,986	0,29	0,055

Figure 3 Heat map of the associations between the answers to each of the 13 questions (independent variable, columns) and the set of predictors (rows). P-values from logistic regression analyses (questions) and linear regression analyses (sum scores) are shown. P-values <0.1 are coloured in order to make potential patterns more clear. The intensity of the colouring shows the significance of the association, while the colour indicates the direction (blue coloured cells for negative regression coefficients, red for positive regression coefficients). The shortcuts for the questions are: Q1: Term Exacerbation; Q2: Pursed lip breathing technique, Q3: Criteria for contact with doctor; Q4: Breathing exercise; Q5: Term FEV1; Q6: High satisfaction with knowledge; Q7: Comorbidities in COPD patients; Q8: Which Medication for symptoms; Q9: Daily Exercise; Q10: Dyspnoea during exercise; Q11: Check of inhaler technique; Q12: Information about new Medication; Q13: Instructions for inhaler; S1-4: sum score first four questions; S5-13: sum score questions Q5-13. The full questions can be found in Figure 1.

breathing technique), and positively with Q6 (high satisfaction with knowledge) and Q12 (information about new medication). Having a low willingness to take risks (ie, high degree of risk aversion) showed a tendency (p = 0.059) to be negatively associated with Q8 (which medication for symptoms). Although this pattern was complex, it clearly indicated that the questions Q1-Q4 were of a different kind than the other questions regarding their association with indicators of disease severity.

In order to check for multi-collinearity, bivariate correlation analyses were performed (data not shown). There were no strong correlations between the variables used as predictors. The highest correlation coefficient (Pearson) was 0.16 between treatment by a pulmonary specialist and previous participation in educational programs.

Based on the results for exacerbations and GOLD grades, we formed the two sum scores "S1-4" comprising Q1-Q4, and "S5-13" comprising Q5-13. We then determined their association with the same set of predictors via linear

regression analysis. The results are included in the last two columns of the heatmap (Figure 3) and underline that only the sum score from the first four questions Q1-Q4 showed a positive relationship ($p < 0.05$) to disease severity in terms of the occurrence of moderate or severe exacerbations. In addition, the sum score was significantly ($p < 0.05$) associated with previous participation in an educational program and with being treated by a pulmonary specialist. The sum score of the remaining questions Q5-Q13 was only dependent ($p < 0.05$) on the educational program but not on exacerbations or other predictors. The negative association between male sex and knowledge remained in the first sum score.

Discussion

The present study investigated the association between disease-related knowledge of patients with COPD and factors that might influence this knowledge, especially disease severity. Our findings confirmed that knowledge strongly benefits from participation in educational programs,[13,18–20,34,40–46] underlining the validity of our data. The novel insight was that much of the knowledge was not linked to the patient's chronic clinical state in terms of disease severity, and thus appeared to maintain a more "theoretical" status. In contrast, another part of knowledge seemed to be enhanced by experience of moderate or severe exacerbations in the prior year. Therefore, this part might be considered as more "important" or "useful" from the patients' perspective. Four out of 13 analyzed questions fell into this category. Although the cause for this association cannot be determined from our data, a reasonable explanation could be that potentially life-threatening experiences such as severe exacerbations either help to reinforce certain aspects of disease knowledge because patients focus more on the disease, or patients might be more motivated to seek knowledge from sources beyond such dedicated programs. The assumption of additional sources of knowledge is in accordance with the observation that knowledge of the exacerbation-associated questions was higher when the treating physician was a specialist. This probably improves the acquisition of relevant knowledge compared to a non-specialist, since pulmonologists may provide more specific advice or have more time for the patients.

The present analysis used data from COSYCONET 2 which is a continuation of the COSYCONET 1 study.[17] In contrast to the previous cohort, COSYCONET 2 enabled a more intricate analysis of patients' knowledge by incorporating a larger set of questions dealing with disease-related knowledge and self-management. While COSYCONET 2 builds on the same comprehensive set of assessments as COSYCONET 1,[17] we included only information considered potentially relevant for COPD knowledge in our analysis. Following GOLD,[1] we categorized exacerbations as A/B versus E, as well as lung function impairment according to spirometric results. One might assume the presence and number of comorbidities as additional factors relevant for disease-related knowledge, surprisingly; however, no association with COPD knowledge was found in additional analyses (data not shown). The same was true for symptoms in terms of low (A) versus high (B) symptom burden according to GOLD categories defined via the mMRC.[27] This seems to be consistent with the observation that high spirometric GOLD grades that are often associated with a higher symptom burden, only played a minor role compared to the occurrence of moderate-to-severe exacerbations.

One might assume that patients with higher number or severity of exacerbations participated in more educational training programs on COPD. Indeed, there was a correlation, yet these two variables were still statistically independent predictors. In addition, the duration of COPD in terms of the time since diagnosis might be assumed as a factor related to knowledge, but this was also not significant, again underlining the importance of the other factors including exacerbations. Knowledge might also be related to the occurrence of depression and the degree of risk aversion. Therefore, we included data on the PHQ-9, which is a well-introduced screening score for depression. To avoid a bias of PHQ-9 from COPD severity,[47] we specifically looked for the opposite end of very low scores. The presence of very low PHQ-9 scores was positively linked to a higher satisfaction with the patients' own knowledge, which appears a plausible finding.

Risk aversion was determined via a generic question not specifically addressing COPD, and we expected higher aversion to be associated with a greater amount of knowledge. This was not the case; on the contrary, there was a tendency for less knowledge regarding the intake of medication for specific purposes, which is a surprising result. Although personality traits were not the topic of our study, the lack of association, or even a negative association, was unexpected and showed that assessment of determinants of COPD knowledge was not as straightforward as it might seem. Conversely, the result that some of the answers were strongly dependent on the occurrence of exacerbations,

underlines the common wisdom that personal experiences can act as strong educators that reinforce certain though not all knowledge on the disease. It is remarkable, however, that the knowledge on criteria for contacting a physician in case of deteriorations was much more strongly related to exacerbations than to participation in an educational program.

Our study has some limitations due to the type of cross-sectional analysis that we performed. This did not allow causal inferences. It is, however, much more likely that exacerbations have driven knowledge compared to the alternative that knowledge has driven exacerbations. As one of the benefits from improved knowledge, one might expect an improved clinical state and course of the disease. This can only be assessed in prospective trials including a control group without educational efforts. It seems questionable, however, whether such a trial would be considered as ethical and, in view of the information available via the internet, realistic. Additionally, we did not evaluate the type of educational program, and potential differences in effectiveness between different educational programs were not assessed. Apart from depression and risk aversion, there may be other personality traits and patient characteristics that could influence patients' knowledge and that were not included in the analysis. We also focused on correct answers and did not differentiate between incorrect answers and the patients' statement of lack of knowledge.

Conclusion

In patients with COPD, part of the disease-related knowledge was dependent on the previous occurrence of moderate-to-severe exacerbations. Overall, knowledge was improved after participation in educational programs and partially by being treated by a pulmonary specialist. Noteworthy, the associations with exacerbations were present although patients with exacerbations also had more often participated in educational programs. Other parts of knowledge were not dependent on disease severity and exacerbations. These observations suggest that personal experiences might be relevant for the acquisition and maintenance of COPD knowledge that is relevant for the patient. Possibly, this could be considered in programs in COPD.

Data Sharing Statement

COSYCONET 2 data are not intended to be available without demand. If there is interest in the analysis of specific questions, however, there is a formalized procedure for submitting an application to the study office, which will be evaluated by the steering committee on scientific grounds. There is no limitation for this application except proven expertise in COPD studies. The contact details and application process can be found here: http://www.asconet.net/html/cosyconet/projects.

Ethics Approval and Consent to Participate

The study protocol was approved by the central ethical committee in Marburg (Ethikkommission FB Medizin Marburg) and the respective local ethical committees: Borstel (Ethikkommission Universität Lübeck); Coswig (Ethikkommission TU Dresden); Gießen (Ethikkommission Fachbereich Medizin); Greifswald (Ethikkommission Universitätsmedizin Greifswald); Großhansdorf (Ethikkommission Ärztekammer Schleswig-Holstein); MHH Hannover/Coppenbrügge (MHH Ethikkommission); Heidelberg Thorax/Uniklinik (Ethikkommission Universität Heidelberg); Homburg (Ethikkommission Saarbrücken); München LMU/Gauting (Ethikkommission Klinikum Universität München); Nürnberg (Ethikkommission Friedrich-Alexander-Universität Erlangen Nürnberg); Solingen (Ethikkommission Universität Witten-Herdecke); Würzburg (Ethikkommission Universität Würzburg). The study was performed in accordance with the declaration of Helsinki, and all participants gave their written informed consent.

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Author Contributions

All authors of this manuscript meet all of the following criteria required for authorship, as they 1) made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas, 2) have drafted or written, or substantially revised or critically reviewed the article, 3) have agreed on "Patient Preference and Adherence" as the Journal to which the article is to be submitted, 4) reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage, and 5) agree to take responsibility and be accountable for the contents of the article.

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