

# Illness Perceptions, Cognitions, and Beliefs on COPD Patients' Adherence to Treatment – A Systematic Review

Valentina Poletti <sup>1</sup>, Francesco Pagnini <sup>1</sup>, Paolo Banfi <sup>2</sup>, Eleonora Volpato <sup>1,2</sup>

<sup>1</sup>Department of Psychology, Università Cattolica Del Sacro Cuore, Milan, Italy; <sup>2</sup>IRCCS Fondazione Don Gnocchi, Milan, Italy

Correspondence: Valentina Poletti, Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy, Email [valentina.poletti@unicatt.it](mailto:valentina.poletti@unicatt.it)



**Background:** Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory lung disease characterized by persistent respiratory symptoms and airflow limitation. Besides its irreversibility, COPD is a treatable condition, and patients would strongly benefit from being adherent to their treatments. However, almost half of them are non-adherent, and, according to several recent studies, the way the patient perceives the disease might influence this variable.

**Aim:** This systematic review provided a synthesis of studies about the relationships between illness perceptions (IP), cognitions, beliefs, and adherence in COPD.

**Methods:** English language publications were searched in PubMed, Medline, Scopus, ResearchGate, PsycINFO, and Cochrane Library databases from November 2022 to February 2023, following PRISMA guidelines. The reference lists of eligible studies were also searched. Data extraction and critical appraisal were undertaken by two reviewers working independently.

**Results:** A total of 14 studies were included. Adherence to treatment in COPD is confirmed to be low, using both self-report questionnaires and objective assessment systems. Most studies concluded that COPD is perceived as a moderate threat destined to last forever, even if many participants referred to little disease knowledge. This perception did not change between adherent and non-adherent groups. Those who considered more necessary to take their medicines and had a caregiver were more adherent and less concerned about their future. On the other side, forgetfulness, lack of trust in medications, and difficulties in understanding how to take them were perceived as the main causes of non-adherence. Other predictors of non-adherence, like depression, low self-efficacy, and severity of disease were confirmed.

**Conclusion:** The systematic review highlights the variability of the relationship between IP, cognitions and beliefs, and COPD treatment adherence. A new level of awareness of the relationship between patients' subjective point of view and treatment adherence may inform future treatment options and promote a more personalized intervention.

**Keywords:** illness perception, COPD, adherence to treatment, illness cognition, illness belief

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is an irreversible but treatable condition characterized by chronic bronchitis, airway thickening, and emphysema.<sup>1</sup>

Worldwide, COPD is considered the most frequent chronic respiratory disease and a leading cause of chronic morbidity and mortality, affecting above 391.9 million people aged between 30 and 79 years, with a higher prevalence among tobacco smokers.<sup>1</sup>

In addition to tobacco smoking, several risk factors have been studied to improve COPD management, such as indoor and outdoor air pollution, occupational hazards, and infections.<sup>2</sup> For this reason, a crucial part of COPD treatment consists of lifestyle changes: like quitting smoking, avoiding triggers like dust and pollution, eating a healthy diet, and avoiding respiratory infection.<sup>2</sup>

Typical treatments for COPD include medications: bronchodilators, corticosteroids, antibiotics, and mucolytics, commonly used to open the airways, reduce inflammation, and clear mucus;<sup>3</sup> oxygen therapy, used to help patients who have low oxygen levels;<sup>4</sup> non-invasive ventilation (NIV), a form of respiratory support that uses a mask to deliver air or oxygen without the need for an invasive procedure (like intubation);<sup>5</sup> pulmonary rehabilitation, a program of exercise and education that helps to improve breathing and muscle strength<sup>6</sup> and surgery, which may be recommended to remove damaged parts of the lungs or to repair a collapsed lung.<sup>7</sup>

However, if on the one hand, medicine continues to introduce many treatments which can improve patient's quality of life and disease acceptance, on the other hand, what makes a difference is their adherence rate, that is the extent to which a person's proactive behavior coincides with medical or health advice<sup>8</sup> which is generally low in patients with COPD.<sup>9</sup>

Studies have reported that the percentage of COPD patients who adhere to their treatment regimens ranges from as low as 30% to as high as 80%<sup>9-11</sup> and these differences are often due to two main reasons.

First, there is no consistency in the method by which adherence is assessed in studies on COPD and, consequently, the use of different methods of assessing adherence provides different results.<sup>12</sup> Second, inhaled drugs carry different implications for the evaluation of adherence than oral medications.<sup>13</sup>

However, as a multifactorial variable, several predictors had been studied to understand the mechanism behind these discouraging percentages. Researchers discovered that age,<sup>14</sup> higher levels of education,<sup>15</sup> and having a regular healthcare provider<sup>16</sup> are associated with better adherence rates; on the contrary, factors like the use of multiple medications or having complex treatment regimens<sup>14</sup> are associated with lower adherence.

In addition to this, considering the symptom burden in COPD patients (which may include cough, sputum production, wheeze, chest tightness, fatigue) and its impact on patient's psychological well-being,<sup>17</sup> more recent research led to a better understanding of some psychological aspects of it (such as psychiatric morbidity and cognitive impairment).<sup>18</sup>

Volpato et al,<sup>19</sup> for example, described the relationship between some psychopathological conditions, ie, anxiety and depression, and their impact on adherence to treatment.

Other researchers explored the role of perceived self-efficacy<sup>20</sup> and alexithymia<sup>21</sup> on COPD treatment, suggesting their consideration during the implementation of a personalized treatment plan.

Only in more recent times has literature begun to show interest in patients' perceptions of their condition.<sup>22</sup> This research has focused on the theoretical construct of Illness Perception (IP), which, according to the Self-Regulation Model (SRM),<sup>23</sup> consists of the patient's set of cognitive representations including beliefs about the cause, the duration, the impact, and the controllability of the illness.<sup>24</sup>

Following this line of research, Kaptein et al demonstrated that IP is a determinant of patient's quality of life, number of hospitalization, and medication use, even after controlling for the duration and objective severity of COPD,<sup>22</sup> reinforcing the thesis that an inaccurate perception of one's clinical condition might be associated to poorer treatment outcome.<sup>25</sup>

Moreover, other similar and related constructs are nowadays research objects, such as Illness Cognitions, and Beliefs.

Unlike IP, which refers to an individual's understanding and interpretation of his/her illness, cognition refers to mental processes such as thinking and memory and it defines how an individual learns something;<sup>26</sup> while belief refers to a conviction or acceptance that something that an individual knows is true, often without evidence.<sup>27</sup>

Considering the importance of actively involving the patient in his/her disease management, knowing the meaning patient attributes to the condition might be a first step to achieve a more detailed understanding of the relationship between patients' subjective point of view of their illness condition and treatment adherence. This relationship, moreover, may inform future treatment options in COPD and promote a more personalized clinical intervention.

## Aim

The aim of the present systematic review is providing an essential summary of the expanding literature characterizing the relation between IP, beliefs, and cognitions on treatment adherence in patients with COPD.

## Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed in conducting this systematic review.<sup>28</sup> The protocol was registered with PROSPERO international prospective register of systematic reviews (# CRD42022373141).

## Search Strategy, Eligibility Criteria, and Information Sources

Systematic searches were conducted from November 2022 to February 2023 following PRISMA guidelines.<sup>28</sup> The PubMed, Medline, Scopus, ResearchGate, PsycINFO, and Cochrane Library databases were consulted to capture free full-text, open-access human studies, from inception to the first of February 2023, that specified a relationship between illness perceptions/beliefs/cognition and adherence to treatment in COPD patients.

Considering that this is a Systematic Review of literature the ethics approval has been obtained by the original authors.

Inclusion and exclusion criteria, as well as comprehensive search terms, are presented below in Table 1 and 2.

Studies with populations with other illnesses besides COPD (eg, asthma) were included only if the results for the COPD group were highlighted and separated from other groups, considered the patient's point of view, not the physicians' or caregivers'.

## Study Selection

Titles, abstracts, and keywords were independently reviewed by two authors (VP; EV) excluding those that did not meet the eligibility criteria. A third author (FP) was consulted to resolve inconsistencies in screening decisions. Other articles were excluded because they were not available or not published.

Full-text articles assessed for eligibility were read by the researchers and assessed following inclusion/exclusion criteria. To identify additional relevant literature, a manual search was conducted.

**Table 1** Illness Inclusion and Exclusion Criteria

Criterion	Inclusion	Exclusion
<b>Time</b>	From inception to 1st February 2023	Studies outside these dates
<b>Language</b>	English (the recognized language of international scientific debate)	Non-English
<b>Type of Article</b>	Original research, published in a peer review journal. Qualitative or quantitative studies (Randomized Control Trials, Case Control Studies, Cross-Sectional Studies, Longitudinal Studies);	Articles that were not peer-reviewed, only abstracts available; grey literature; review; systematic review; narrative review; scoping review; meta-analysis; commentaries, letter, editorial
<b>Ethics Clearance</b>	Studies with approved ethics notification	Studies without approved ethics notification
<b>Study Focus</b>	Adherence to therapies (pharmacological therapies/Non-Invasive Ventilation (NIV)/Long Term Oxygen Therapy (LTOT), Pulmonary Rehabilitation (PR), etc) and its relationship with illness perceptions	Studies that do not consider the outlined relationship
<b>Literature Focus</b>	Studies that discuss the patient's point of view and his/her experience, beliefs, and perceptions, studies that present a clear theoretical framework on the patients' experience, studies that focus on the experience of using the treatment, in the context of chronic pathologies considered	Articles that did not make a passing or token reference to illness perceptions about therapies. The caregiver's and/or physicians' point of view
<b>Population and Sample</b>	Chronic Obstructive Pulmonary Disease (COPD)	All the other chronic diseases

**Table 2** Detailed Search Strategy

Database	Mesh Terms Combination	Filters
PubMed	“COPD” OR “Chronic Obstructive Pulmonary Disease*” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“adherence” OR “compliance”) AND (“NIV” OR “Non Invasive Ventilation” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	Humans; English; Full Text; Clinical Study; Clinical Trial; Controlled Clinical Trial; Meta Analysis; Observational Study; Randomized Controlled Trial; Review; Systematic Review; Comparative Study;
Medline	“COPD” OR “Chronic Obstructive Pulmonary Disease*” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“adherence” OR “compliance”) AND (“NIV” OR “Non Invasive Ventilation” OR “Oxygen” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “LTOT” OR “therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	N.A.
Scopus	“COPD” OR “Chronic Obstructive Pulmonary Disease*” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“adherence” OR “compliance”) AND (“NIV” OR “Non-Invasive Ventilation” OR “Oxygen” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “LTOT” OR “therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	Human/Humans; English; Article; Review; Journal; Psychology; Health Professions; Chronic Obstructive Lung Disease
ResearchGate	“COPD” OR “Chronic Obstructive Pulmonary Disease” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“adherence” OR “compliance”) AND (“NIV” OR “Non-Invasive Ventilation” OR “Oxygen” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “LTOT” OR “therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	English; Article; Review
PsycINFO	“COPD” OR “Chronic Obstructive Pulmonary Disease*” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“adherence” OR “compliance”) AND (“NIV” OR “Non-Invasive Ventilation” OR “Oxygen” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “LTOT” OR “therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	Humans; English
Cochrane Library	“COPD” OR “Chronic Obstructive Pulmonary Disease*” AND ‘Illness perception’ OR ‘Illness cognition’ OR ‘Illness belief’ AND (“NIV” OR “Non-Invasive Ventilation” OR “Oxygen Therapy” OR “Long Term Oxygen Therapy” OR “therapy” OR “pharmacological therapy” OR “medication*” OR “bronchodilator*” OR “inhalator*”	English; Trials; Review

## Data Extraction and Analysis

Data were extracted by two independent researchers (VP, EV) and confirmed by a third one (FP). Information gathered from each study considered the following data: title, authors, publication year, country, journal, keywords, kind of study, demographic description of participants (gender, mean age), objectives of the study, outcomes, setting, follow-up, drop-out rate, inclusion and exclusion criteria, analysis, instruments, explored themes and conclusions. Data from the final data extraction forms were tabulated and discussed in this review in a purely descriptive fashion.

Considering the heterogeneity of the data and the diversity of the clinical trial designs, no additional sub-analyses or meta-analyses were planned or performed.

## Quality Assessment of Studies

Methodological quality assessment of the included studies was completed with the NIH quality assessment tool, a general guidance, composed of 14 questions, for determining the overall quality rating of observational cohort and cross-sectional studies (see <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>).

Assessment of quality was evaluated according to these published checklists by two independent authors (VP; EV), and doubts were clarified with the help of a third one (FP).

No studies were excluded based on quality. Details about quality assessment are reported in Figure 1.

## Results

### Study Selection

The search strategy allowed the identification of 209 potentially relevant records: 116 articles were retrieved from MedLine, 32 from PubMed, 11 from Cochrane Library, 15 from Scopus, 17 from PsycInfo, and 18 from Web of Science (Figure 2).

After removing 68 duplicates, a total of 141 records' titles and abstracts were screened, and from these, other 58 articles were removed because they were not open-access or full-text available.

Eighty-three full-text articles were assessed for eligibility, and 69 of them were excluded for different reasons: the most common reasons for exclusion were no mention of illness perception, cognition or belief, or adherence or no reference to the relationship between these variables and no distinction between COPD patients and other chronic disease patients (in particular, asthmatics) in the data analysis.

Finally, 14 studies were included in this review (MedLine: 55.5%, PubMed: 15.3%, Web of Science: 8.6%, APA: 8.1%, Scopus: 7.2%, Cochrane Library: 5.3%).

### Samples Characteristics

The 14 included studies represent 8 different countries, including 3 from the Netherlands,<sup>29–31</sup> 3 from Italy,<sup>32–34</sup> 2 from Poland,<sup>35,36</sup> 2 from the USA,<sup>37,38</sup> and 4 from other countries.<sup>13,15,39,40</sup>

Most of the studies were conducted in university settings or pulmonary rehabilitation and communities.

Almost all the studies (n = 10) are cross-sectional designs, only 2 are longitudinal studies,<sup>29,30</sup> 1 is a multicenter, noninterventional (observational) cohort study<sup>33</sup> and 1 is an observational study.<sup>35</sup>

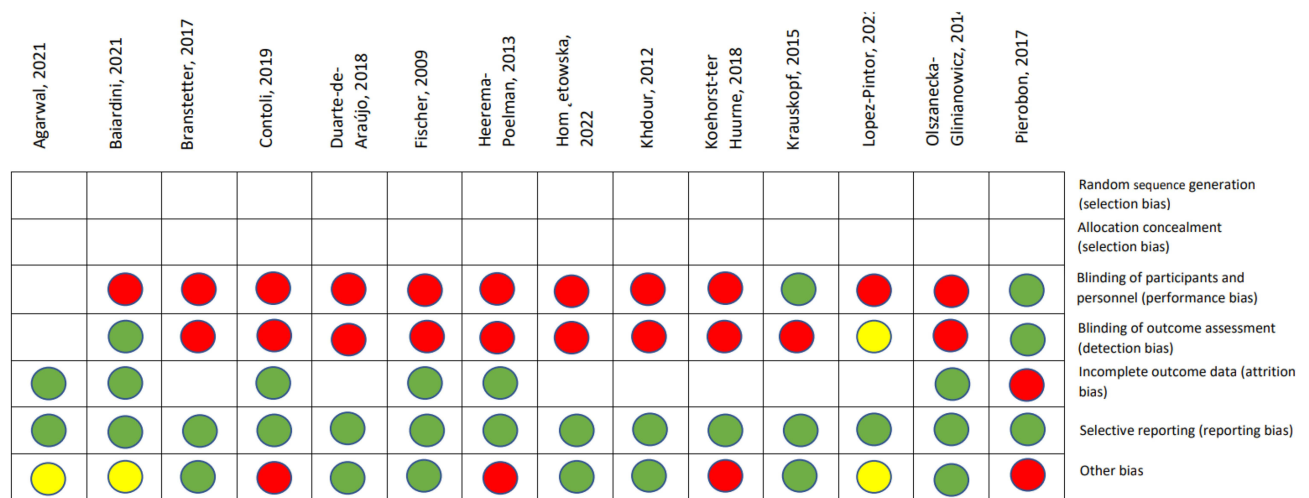
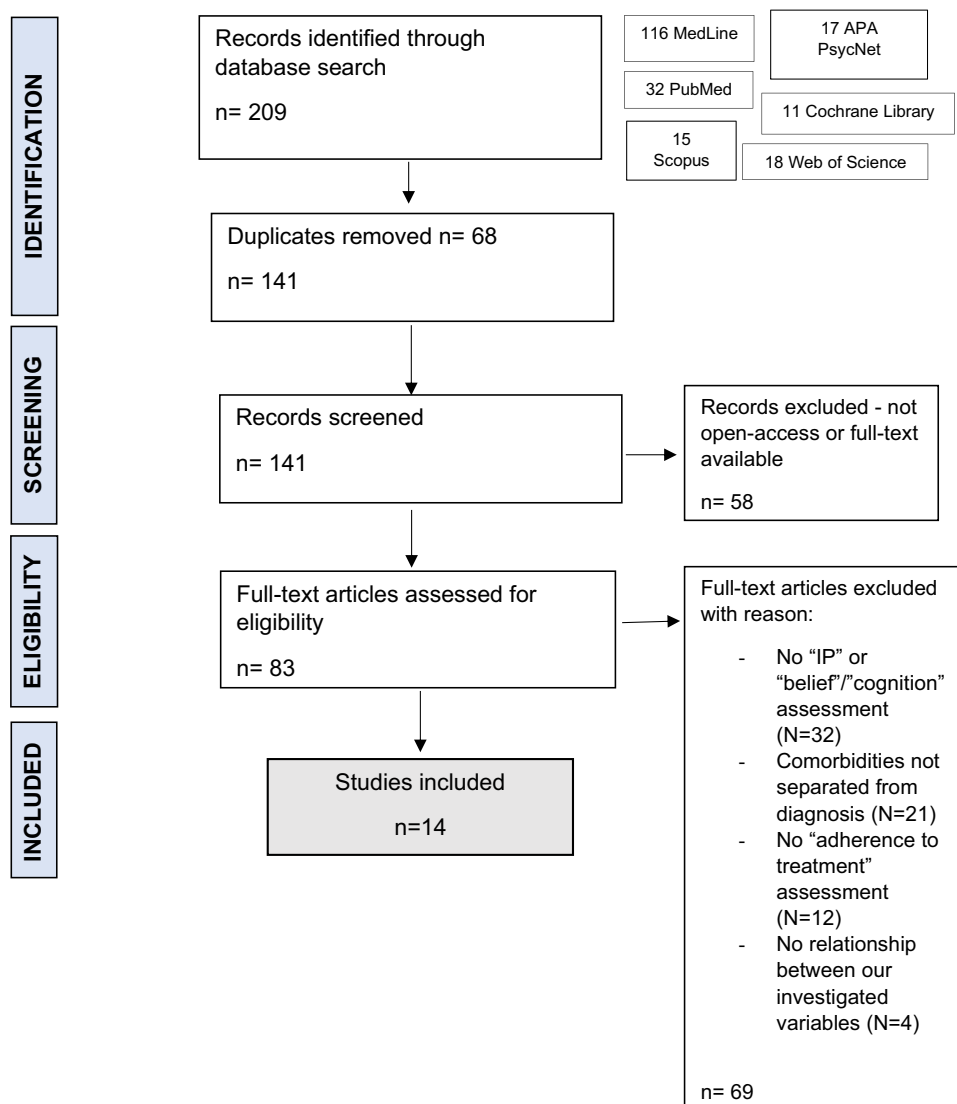


Figure 1 Risk of bias.



**Figure 2** Study selection process – eligibility graph.

The mean age is above 66.23 years old, with a range from 52 to 80 years. On average, males outnumber women (n/males: 3519 vs n/females: 2397).

The main characteristics of the included studies are shown in [Table 3](#).

## Measurements and Definition of Adherence

Adherence was assessed in many ways (see [Table 4](#)). For this reason, we decided to distinguish adherence to medication therapy from physiotherapy program, making explicit the scores and the tools used by each research group.

## Adherence to Medication Treatment

Three studies<sup>37–39</sup> administered the *Medication Adherence Report Scale* (MARS)<sup>41</sup> and results confirmed that more patients do not adhere to treatment than those who adhere (149 vs 245 non-adherent groups).

Three authors<sup>15,32,35</sup> administered the *Morisky Medication Adherence Scale*,<sup>42</sup> in its both versions, 4 and 8 items. Khdour et al<sup>15</sup> reported that “forgetfulness” as the main cause of non-adherence and results reported a little difference between adherence and non-adherence rate (1722 vs 1053 non-adherent groups).

Two research groups<sup>13,36</sup> used the *Test of Adherence to Inhalers'* (TAI),<sup>43</sup> a 12-item questionnaire, designed to assess the adherence to inhalers, and results reported a similar rate of adherence and non-adherence between the two samples (228 vs 236 non-adherent groups).

One author<sup>40</sup> used the *Measure of Treatment Adherence* (MTA), a psychometric tool derived from Morisky Medication Adherence Scale and found that 50 participants were non-adherent (vs 250); Pierobon et al<sup>34</sup> used the Morisky, Green, and Levine Adherence Scale (MGL Adherence Scale)<sup>42</sup> and the majority of the samples were adherent to treatment (70 vs 14 non-adherent groups).

Finally, Koehorst and collaborators<sup>31</sup> recorded therapy adherence with ICS from patients' pharmacy records: adherence was deemed good if it was 75%–125%, suboptimal between 50% and 75%, and poor below 50% (underuse) or above 125% (overuse).

## Adherence to Physiotherapy Program

Heerema-Poelman<sup>30</sup> assessed adherence as attending the maintenance program for 1 year after the Pulmonary Rehabilitation Program. [Dropouts at 6 months received the self-reported questionnaire, in which they were asked to describe the reasons for nonadherence, such as experiencing exacerbations, lack of motivation, financial burden, or distance problems, and exacerbations were the main cause] (38 vs 22 non-adherent groups).

Fischer et al<sup>29</sup> decided to focus on drop-out numbers from pulmonary rehabilitation to evaluate adherence to the rehabilitation program. Lack of motivation and hope of improvement were important barriers to adherence.

## Illness Perception in COPD Patients

Illness perception was generally assessed through *The Illness Perception Questionnaire* (IPQ)<sup>44</sup> and its different versions. The IPQ is a self-report tool which was specifically constructed to assess the five components of illness representation described in Leventhal's self-regulation model, which means beliefs about the cause, the duration, the impact, and the controllability of the illness.<sup>24</sup>

Five authors<sup>32,33,35,37,38</sup> assessed IP through *the Brief Illness Perception Questionnaire* (Brief-IPQ),<sup>45</sup> a nine-item version of the original self-report tool.<sup>44</sup>

Two authors<sup>29,30</sup> used *The Illness Perception-Revised* (IPQ-R),<sup>46</sup> a revised version which includes some additional subscales, like cyclical timeline perceptions, illness coherence, and emotional representations.

Finally, Huurne<sup>31</sup> decided to use a semi-structured interview inspired by the 5-factor model structure of the Illness Perception Questionnaire.

The mean score of The Brief Illness Perception Questionnaire was  $46.67 \pm 9$ , which, considering the cut-off (<42 indicates low threat, 42–49 indicates moderate threat, and  $\geq 50$  indicates high threat), represents a perception of illness as a moderate threat. In particular, according to Agarwal,<sup>37</sup> the highest scores were observed talking about the continuity of symptoms over time ( $M = 10$ ; (9, 10)) and the feeling of worry for the illness ( $M = 10$ ; (7, 10)).

Regarding the IPQ-R, we could not report an average score, because Fischer provided scores for the adherent group separately from the non-adherent group,<sup>29</sup> while Heerema-Poelman only reported the *Personal Control* ( $20.7 \pm 2.7$  vs  $20.4 \pm 4.4$ ) and the *Treatment Control Scores* ( $15.6 \pm 2.2$  vs  $16.2 \pm 3$ ), dividing the adherent group scores from the non-adherent one,<sup>30</sup> results explained that both adherent and non-adherent subjects perceived the same level of personal control on their illness condition, while beliefs about the possibility of being cured and able to control their illness through treatment is slightly higher in non-adherent people.

Huurne's findings were a general belief that COPD symptoms could not be cured, associated to a feeling of worry for the future; a general perception of limitation of participants' quality of life and daily routine activities; most of the participants reported that smoking and heredity were the main causes of their condition; and a general low acceptance of the disease.<sup>31</sup>

## Illness and Medication Beliefs and Cognitions in COPD Patients

Considering beliefs and cognition in COPD patients, we mainly observed the use of the following tools (See Table 5 for more details about the scores):

Table 3 Study Characteristics

ID	Citation (APA)	Author(s)	Publication Year	Journal	Search Engine	Key Words	Country	I/E Criteria	Sample (N, Gender, Age)
1	Krauskopf, K., Federman, A. D., Kale, M. S., Sigel, K. M., Martynenko, M., O'Connor, R., and Wisnivesky, J. P. (2015). Chronic obstructive pulmonary disease illness and medication beliefs are associated with medication adherence. <i>COPD: Journal of Chronic Obstructive Pulmonary Disease</i> , 12 (2), 151–164.	Krauskopf, K., Federman, A. D., Kale, M. S., Sigel, K. M., Martynenko, M., O'Connor, R., and Wisnivesky, J. P.	2015	COPD: Journal of Chronic Obstructive Pulmonary Disease	PubMed	Health beliefs, outcomes, self-management, vulnerable population	USA	Participants were excluded if they solely used as-needed bronchodilators, or did not use any COPD medication	188, 62 males (33%), 67 (62–74)
2	Brandtetter, S., Finger, T., Fischer, W., Brandl, M., Böhrer, M., Pfeifer, M., and Apfelbacher, C. (2017). Differences in medication adherence are associated with beliefs about medicines in asthma and COPD. <i>Clinical and Translational Allergy</i> , 7 (1), 1–7.	Brandtetter, S., Finger, T., Fischer, W., Brandl, M., Böhrer, M., Pfeifer, M., and Apfelbacher, C.	2017	Clinical and Translational Allergy	Scopus	Medication adherence, Compliance, Beliefs about medicines, Asthma, COPD, Chronic obstructive lung diseases	Germany - EU	Patients were eligible for participation in the study if asthma or COPD had been diagnosed by a physician at least 3 months ago, if they were adults, if they had sufficient knowledge of German and if they had no mental disorder (except affective disorders or anxiety).	206, 125 males (60.7%), 65.3 (8.85)
3	Duarte-de-Araújo, A., Teixeira, P., Hespagnol, V., and Correia-de-Sousa, J. (2018). COPD: understanding patients' adherence to inhaled medications. <i>International journal of chronic obstructive pulmonary disease</i> , 13, 2767.	Duarte-de-Araújo, A., Teixeira, P., Hespagnol, V., and Correia-de-Sousa, J. (2018).	2018	International journal of chronic obstructive pulmonary disease	MedLine	COPD, adherence, inhaled medications, adherence behaviors, beliefs	Portugal - EU	Stable patients over 40 years old and diagnosed as suffering from COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were consecutively included. <sup>13</sup> Exclusion criteria were refusal to participate and an inability to understand simple questionnaires.	319, 249 males (78.1), 67.7±10.26
4	Agarwal, P., Lin, J., Muellers, K., O'Connor, R., Wolf, M., Federman, A. D., and Wisnivesky, J. P. (2021). A structural equation model of relationships of health literacy, illness and medication beliefs with medication adherence among patients with chronic obstructive pulmonary disease. <i>Patient education and counseling</i> , 104(6), 1445–1450.	Agarwal, P., Lin, J., Muellers, K., O'Connor, R., Wolf, M., Federman, A. D., and Wisnivesky, J. P.	2021	Patient education and counseling	Scopus	COPD, Health literacy, Medication beliefs and adherence, Structural equation models, COPD illness	USA	We recruited community-dwelling, English or Spanish-speaking adults ≥55 years with physician-diagnosed COPD. Patients were excluded if they had asthma or another chronic respiratory illness, dementia, or other neurological and psychological conditions that would profoundly affect cognition (eg, stroke, advanced Parkinson's disease, schizophrenia).	393, 114 males, 67.23 + 8.06
5	Oliszanecka-Glinianowicz, M., and Almgren-Rachtan, A. (2014). The adherence and illness perception of patients diagnosed with asthma or chronic obstructive pulmonary disease treated with polytherapy using new generation Cyclohaler. <i>Advances in Dermatology and Allergy/Postępy Dermatologii i Alergologii</i> , 31(4), 235–246.	Oliszanecka-Glinianowicz, M., and Almgren-Rachtan, A.	2014	Advances in Dermatology and Allergy/Postępy Dermatologii i Alergologii	Research Gate	Asthma; chronic obstructive pulmonary disease; adherence; polytherapy; new generation C	Poland (EU)	The inclusion criteria were age ≥ 18 years; diagnosis of asthma or COPD; current polytherapy with fluticasone propionate and formoterol fumarate using the Fantasma inhaler at least 14 days prior to enrollment. The exclusion criteria included age below 18 years, inability to obtain the patient's answers to the questions included in the survey, patient's refusal	2602, 1491 males (52.3%), 60.0 ±13.5
6	Khdour, M. R., Hawwa, A. F., Kidney, J. C., Smyth, B. M., and McElinay, J. C. (2012). Potential risk factors for medication non-adherence in patients with chronic obstructive pulmonary disease (COPD). <i>European journal of clinical pharmacology</i> , 68(10), 1365–1373.	Khdour, M. R., Hawwa, A. F., Kidney, J. C., Smyth, B. M., and McElinay, J. C.	2012	European journal of clinical pharmacology	MedLine	Adherence; COPD; Health beliefs; Depression; Self-efficacy; Disease knowledge	Ireland	IC: confirmed diagnosis of COPD for at least 1 year, having an FEV1 value of 30–80% of the predicted normal value and being over 45 yo. Patients who had a HI, moderate to severe learning difficulties, severe mobility problems, terminal illness or who had attended a pulmonary rehabilitation programme in the last 6 months were excluded from the study.	173, 75 males (43.4%), 66.6 (9.7)



AIM -Research Question	Variables	Study Design	Main Outcome (Our Interest)	Secondary Outcome	Tool(s)	Analysis	Drop Out	Conclusion
1) to further characterize illness and medication beliefs in patients with COPD; 2) to assess the association of these beliefs with self-reported adherence to medications.	1) Illness beliefs; 2) Medication beliefs; 3) self-reported adherence to medication;	Cross-Sectional Study	Non-adherent participants reported being more concerned about their COPD (p = 0.011; Cohen's d = 0.43), more emotionally affected by the disease (p = 0.001; Cohen's d = 0.54) and had greater concerns about COPD medications (p < 0.001, Cohen's d = 0.81). In adjusted analyses, concerns about COPD medications independently predicted non-adherence (odds ratio: 0.52, 95% confidence interval: 0.36-0.75). In this cohort of urban minority adults, concerns about medications were associated with non-adherence.	n.a.	1) Brief Illness Perception Questionnaire (B-IPQ); 2) Beliefs about Medications Questionnaire (BMQ); 3) Medication Adherence Report Scale (MARS)	Logistic regression analysis	x	Identifying mechanisms that reinforce and improve medication adherence in patients with COPD will likely improve disease-related outcomes.
1) to examine the associations between beliefs about medicines and self-reported medication adherence in people with chronic obstructive lung disease	1) Medication beliefs; 2) self-reported adherence to medication;	Cross-Sectional Study	34% of COPD patients were completely adherent to their prescribed medication; specific beliefs about the necessity of medicines were positively associated with medication adherence in patients	- health related quality of life, Short Form Health Survey (SF-12) - anxiety and depression, Hospital Anxiety and Depression Scale (HADS) -self-efficacy, Generalized Self-Efficacy Scale (GSE), - COPD control, COPD assessment test (CAT)	1) Beliefs about Medications Questionnaire (BMQ); 2) Medication Adherence Report Scale (MARS)	Multivariable logistic regression models were computed for all five BMQ subscales.	x	This study demonstrated high rates in medication non-adherence in patients with chronic obstructive lung disease. Beliefs in the specific necessity of prescribed medications were found to be associated with medication adherence in patients with COPD and suggest a modifiable target for improving patient-doctor consultations when prescribing medicines
1) to assess whether demographic variables, clinical and functional severity of COPD, and beliefs about inhaled medications are associated with patients' adherence to inhaled medications.	1) Medication beliefs; 2) self-reported adherence to medication;	Cross-Sectional Study	The mean BMQ Necessity score was higher in adherent patients (P=0.000), but the mean Concern score was similar for both (P=0.877).	n.a.	1) the Beliefs about Medications Questionnaire (BMQ); 2) The Measure of Treatment Adherence (MTA).	Binary logistic regression	x	Adherence is related to need perception and to the functional severity of the disease. A non-adherent patient is usually a current smoker with lower degree of airflow limitation and lower perception of medication necessity. New information obtained was related to the patterns and reasons for different adherence behaviors, which are based on three major groups of patient related-determinants: health-related experiences, health-related behaviors and health-related beliefs.
1) to examine the pathways linking Health Literacy, through medications and illness beliefs, with COPD medication adherence	1) Medication and illness beliefs; 2) self-reported adherence to medication; 3) health literacy	Cross-Sectional Study	Those with low medication adherence had higher BIPQ illness score (45 [39, 51] vs 42 [34, 50], p = 0.01) and medication concern score (14 [10,18] vs 11 [10,14], p < 0.0001) as compared to those who were adherent to the medications.	- No association was observed between HL and overall illness beliefs (p = 0.08). - there were differences among individual illness belief scores. Individuals with limited HL were more likely to report that COPD affected their life (7 [5,9] vs 6 [4,8], p < 0.001), they experience more symptoms from COPD (7 [5,10] vs 6 [4,8], p < 0.001), and they think that COPD affects them emotionally (7 [4,10] vs 6 [3,9], p = 0.03). - Low adherence to COPD medications was observed among 208 subjects (53%). Participants with limited HL were more likely to have low medication adherence than those with adequate HL (67% vs 49%, p < 0.0001; Table 3)	1) B-IPQ; B;MQ 2) Medication Adherence Rating Scale (MARS); 3) Short Test of Functional Health Literacy in Adults (S-TOFHLA)	Chi-squared tests and Wilcoxon rank sum tests	x	n.a.
1. To assess the adherence in patients diagnosed with asthma and COPD treated with polytherapy with fluticasone propionate and formoterol fumarate using the Fantasma inhaler in relation to primary diagnosis and illness perception. 2. To assess patients' and doctors' opinion about this form of therapy.	1) Adherence to medication; 2) illness perception	Observational study	During the observation, the adherence rate increased significantly in the COPD group (61.5% vs.73.0%; p < 0.01). A negative correlation between total MMAS-8 and BIPQ scores was observed (R = -0.15; p < 0.001).	During the observation, a percentage of patients who believed that the administration of the two drugs in a single inhaler considerably facilitates their use increased significantly in both study groups. In addition, an increased percentage of doctors believed that this therapeutic option facilitated education of patients and decreased the number of errors made by the patients.	1) MMAS-8; 2) B-IPQ	Separate groups were compared using the $\chi^2$ test and $\chi^2$ test for trend and T-test. The assessment of associations between variables was done with Spearman correlation	x	The illness perception, younger age, disease duration and severity are predictors of adherence to treatment with fluticasone propionate and formoterol fumarate using the Fantasma inhaler among patients with asthma and COPD. The positive opinion of patients and doctors about administration of fluticasone propionate and formoterol fumarate using the Fantasma inhaler increased during observation.
1) 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.	1) self-reported adherence to medication; 2) Depression; 3) COPD knowledge; 4) Health beliefs; 5) COPD self-efficacy; 6) Medication effectiveness	Cross-Sectional Study	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, ie 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).	n.a.	1) Morisky scale; 2) Hds-D; 3) COPD knowledge questionnaire; 4) Health beliefs model questionnaire; 5) COPD self-efficacy questionnaire; 6) Medication effectiveness (interview)	Binary stepwise conditional logistic regression analysis	x	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.

(Continued)

Table 3 (Continued).

ID	Citation (APA)	Author(s)	Publication Year	Journal	Search Engine	Key Words	Country	I/E Criteria	Sample (N, Gender, Age)
7	López-Pintor, E., Grau, J., González, I., Bernal-Soriano, M. C., Quesada, J. A., and Lumbrales, B. (2021). Impact of patients' perception of COPD and treatment on adherence and health-related quality of life in real-world: study in 53 community pharmacies. <i>Respiratory Medicine</i> , 176, 106.280.	López-Pintor, E., Grau, J., González, I., Bernal-Soriano, M. C., Quesada, J. A., and Lumbrales, B.	2021	Respiratory Medicine	Research Gate	Chronic obstructive pulmonary disease; Adherence; Persistence; Inhaler medication; Health-related quality of life	Spain (UE)	COPD patients, adult patients	318, 239 males, 71.32 (9.24)
8	Koehorst-ter Huurne, K., Brusse-Kaizer, M., Van Der Valk, P., Movig, K., Van Der Palen, J., and Bode, C. (2018). Patients with underuse or overuse of inhaled corticosteroids have different perceptions and beliefs regarding COPD and inhaled medication. <i>Patient preference and adherence</i> , 12, 1777.	Koehorst-ter Huurne, K., Brusse-Kaizer, M., Van Der Valk, P., Movig, K., Van Der Palen, J., and Bode, C.	2018	Patient preference and adherence	PubMed	COPD; adherence; illness perceptions; medication beliefs; in-depth interviews	Netherlands (UE)	In order to study nonadherence, 10 patients who underused and 10 patients who overused their ICS were selected from the COMIC cohort and were invited for an in-depth interview.	20, 10 males (50%), 60.5
9	Homętowska, H., Świętoniowska-Lonc, N., Klekowski, J., Chabowski, M., and Jankowska-Polańska, B. (2022). Treatment Adherence in Patients with Obstructive Pulmonary Diseases. <i>International Journal of Environmental Research and Public Health</i> , 19(18), 11.573.	Homętowska, H., Świętoniowska-Lonc, N., Klekowski, J., Chabowski, M., and Jankowska-Polańska, B.	2022	International Journal of Environmental Research and Public Health	PubMed	Treatment adherence; compliance; chronic obstructive pulmonary disease; beliefs	Poland (EU)	The inclusion criteria were as follows: provision of informed written consent to take part in the study, diagnosis of an obstructive pulmonary disease, patients aged over 18, patients who had been using at least one inhaled medication for at least 6 months, cognitive status sufficient to understand the purpose and methods of the study and complete questionnaires	325, 166 males (51.08%), 63 ± 11

AIM -Research Question	Variables	Study Design	Main Outcome (Our Interest)	Secondary Outcome	Tool(s)	Analysis	Drop Out	Conclusion
1) We aimed to assess the impact of patients' perception of their treatment and disease on adherence and Health-Related Quality of Life (HRQL) in patients attending a community pharmacy, where usually subjects have a better condition than those in clinical settings.	1) Adherence to inhaled medication; 2) persistence; 3) Health related quality of life; 4) treatment perception	Cross-Sectional Study	SGRQ score was significantly worse in patients with intermediate/poor adherence ( $p = 0.036$ ) and in those who thought the inhaler's effectiveness was fair/poor ( $p < 0.001$ ).	Persistence was achieved by 78.6% of the patients and 58.5% had good adherence. Patients having a multidose DPI and those with MDI showed a 2.8-fold and 4.1-fold increased association, respectively, with intermediate/poor adherence in comparison with those having a single dose DPI. Those patients who did not have knowledge about COPD (aOR 2.106, $p = 0.006$ ) and those who thought that the inhaler effectiveness was fair/poor (aOR 2.361, $p = 0.006$ ) were more likely to have intermediate/poor adherence.	1) Test of Adherence to Inhalers test; 2) persistence interview; 3) St George's Respiratory Questionnaire (SGRQ); 4) treatment perception interview	Logistic regression	x	The type of inhaler and patients' knowledge and perceptions of their disease and treatment were associated with good adherence and higher HRQL. Clinicians should promote shared-decision making in the choice of inhaler depending on patients' individual abilities and beliefs.
1) To study perceptions and beliefs regarding COPD and inhaled medication in COPD patients with poor adherence.	1) Adherence to medication; 2) illness perception according to IRM-Leventhal	Cross-Sectional Study	Overusers and underusers showed a different pattern in perceptions and beliefs regarding inhaled medication and COPD.	(see the illness representation Model – 5 sections answers to the semi-structured interview)	1) patients' pharmacy records; 2) semistructured in-depth interviews, about mental and physical health, illness perceptions, knowledge regarding COPD, and experience with, knowledge of, and acceptance of COPD medication and inhalation devices	x	x	Non-adherence in COPD is a multifactorial problem encompassing behavioral issues possibly caused by perceptions and knowledge of patients. Underusers and overusers showed a different pattern in perceptions and beliefs on inhaled medication.
1) The aim of the study was to evaluate the level of treatment adherence to inhaled therapy in patients with obstructive pulmonary diseases.	1) beliefs about medications; 2) adherence to medication	Cross-Sectional Study	The patients were uncertain about the overuse of medicines by doctors (a mean of 3.19 points per question) and about the harmful effects of medicines (a mean of 2.82 points per question) and did not know if they were concerned about taking their medication (a mean of 3.33 points per question) (Table 2). The respondents tended to be convinced of the necessity of their medication (a mean of 3.87 points per question), king medications as prescribed ( $13.41 \pm 4.44$ ) and adherence to refills on schedule ( $7.74 \pm 2.21$ ). A total of 74.15% of patients demonstrated sporadic non-compliance, 59.69% exhibited deliberate non-compliance and 11.38% exhibited unconscious non-compliance with inhaled medications.	Belief that medicines are overused by doctors, belief that medicines are harmful and concerns about medicines were significantly ( $p < 0.05$ ) and positively ( $r > 0$ ) correlated with the total ARMS score and the two subscales of the ARMS. Therefore, the greater the belief that medicines are overused by doctors, the lower the level of adherence (the higher the score on the ARMS) in all dimensions (Table 2). Belief that medicines are overused by doctors was significantly ( $p < 0.05$ ) and negatively ( $r < 0$ ) correlated with the lack of sporadic, deliberate and unconscious non-compliance. Belief in the necessity of medication was significantly ( $p < 0.05$ ) and positively ( $r > 0$ ) correlated with the lack of sporadic and unconscious non-compliance and was significantly and negatively ( $r < 0$ ) correlated with the total ARMS score and the two subscales of the ARMS. Therefore, the stronger the belief in the necessity of medication, the higher the level of adherence (the lower the score) in all dimensions. Belief that medicines are harmful and concerns about medicines were significantly ( $p < 0.05$ ) and negatively ( $r < 0$ ) correlated with the lack of sporadic, deliberate and unconscious non-compliance. Therefore, the greater the concerns about medicines, the poorer the adherence to inhaled medications.	1) Beliefs about Medicines Questionnaire, 2) Test of Adherence to Inhalers and Adherence to Refills and Medications Scale.	Linear regression	x	The number of hospital admissions due to exacerbations of the disease over the last year and belief that medicines are harmful are independent determinants of poorer medication adherence.

(Continued)

Table 3 (Continued).

ID	Citation (APA)	Author(s)	Publication Year	Journal	Search Engine	Key Words	Country	I/E Criteria	Sample (N, Gender, Age)
10	Pierobon, A., Bottelli, E. S., Ranzini, L., Bruschi, C., Maestri, R., Bertolotti, G., and Giardini, A. (2017). COPD patients' self-reported adherence, psychosocial factors and mild cognitive impairment in pulmonary rehabilitation. <i>International journal of chronic obstructive pulmonary disease</i> , 12, 2059.	Pierobon, A., Bottelli, E. S., Ranzini, L., Bruschi, C., Maestri, R., Bertolotti, G., and Giardini, A.	2017	International journal of chronic obstructive pulmonary disease	Scopus	Depression; anxiety; mild cognitive impairment; adherence; COPD; pulmonary rehabilitation	Italy (UE)	The exclusion criteria were severe medical conditions that did not allow assessment, no Italian education or relapse into illiteracy, severe visual-perceptive deficits, low subjective motivation or refusal to undergo the evaluation, severe psychiatric disorders and severe cognitive deterioration	117, 63 males (75%), 70.2 (7.0)
11	Baiardini, I., Contoli, M., Corsico, A. G., Scognamiglio, C., Ferri, F., Scichilone, N., and Braido, F. (2021). Exploring the relationship between disease awareness and outcomes in patients with chronic obstructive pulmonary disease. <i>Respiration</i> , 100(4), 291–297.	Baiardini, I., Contoli, M., Corsico, A. G., Scognamiglio, C., Ferri, F., Scichilone, N., and Braido, F.	2021	Respiration	Research Gate	Awareness; Chronic obstructive pulmonary disease; Adherence; Patient-reported outcomes	Italy (UE)	COPD patients, adult patients	367, 74.2% males, 72.0 (67.0–77.0)
12	Contoli, M., Rogliani, P., Di Marco, F., Braido, F., Corsico, A. G., Amici, C. A., and Santus, P. (2019). Satisfaction with chronic obstructive pulmonary disease treatment: results from a multicenter, observational study. <i>Therapeutic advances in respiratory disease</i> , 13, 1753.466.619.888.128.	Contoli, M., Rogliani, P., Di Marco, F., Braido, F., Corsico, A. G., Amici, C. A., and Santus, P.	2019	Therapeutic advances in respiratory disease	Scopus	Adherence, COPD, treatment satisfaction	Italy (UE)	The main exclusion criteria included patients naive/without chronic, inhaled treatment, concomitant diagnosis of asthma.	401, 299 males (74.6%), 71.7±7.6
13	Heerema-Poelman, A., Stuive, I., and Wempe, J. B. (2013). Adherence to a maintenance exercise program 1 year after pulmonary rehabilitation: what are the predictors of dropout? <i>Journal of cardiopulmonary rehabilitation and prevention</i> , 33(6), 419–426.	Heerema-Poelman, A., Stuive, I., and Wempe, J. B.	2013	Journal of cardiopulmonary rehabilitation and prevention	PubMed	Adherence maintenance program pulmonary rehabilitation	Netherlands (UE)	Excluded were patients with progressive diseases interfering with short-term life expectancy, such as malignancies and unstable heart disease.	70, 32 males (45.7%), 61.3 (10.2)
14	Fischer, M. J., Scharloo, M., Abbink, J. J., van't Hul, A. J., van Ranst, D., Rudolphus, A., and Kaptein, A. A. (2009). Drop-out and attendance in rehabilitation: the role of clinical and psychosocial variables. <i>Respiratory medicine</i> , 103(10), 1564–1571.	Fischer, M. J., Scharloo, M., Abbink, J. J., van't Hul, A. J., van Ranst, D., Rudolphus, A., and Kaptein, A. A.	2009	Respiratory medicine	PsycINFO	Attendance; Chronic obstructive pulmonary disease; Drop-out; Illness perceptions; Pulmonary rehabilitation	Netherlands (UE)	Patients who had already started rehabilitation or had primary lung conditions other than COPD were excluded from the study.	217, 122 males (56%), 63.4 (9.4)

Note: x means "not available".

AIM-Research Question	Variables	Study Design	Main Outcome (Our Interest)	Secondary Outcome	Tool(s)	Analysis	Drop Out	Conclusion
1) The aims of the study were to describe a COPD population in a rehabilitative setting as regards the patients depressive symptoms, anxiety, mild cognitive impairment (MCI) and self-reported adherence and to analyze their relationships; to compare the COPD sample MCI scores with normative data; and to investigate which factors might predict adherence to prescribed physical exercise	1) depression; 2) anxiety; 3) MCI; 4) self-reported adherence; 5) disease perception and self-efficacy in following medical prescriptions	Observational cross-sectional study	They struggled with disease acceptance (30.9%) and disease limitations acceptance (28.6%). Most of them received good family (89%) or social (53%) support. Non-pharmacological adherence, depression, anxiety and MCI showed significant relations with 6-minute walking test, body mass index (BMI) and GOLD.	Depression was related to autonomous long-term oxygen therapy modifications, disease perception, family support and MCI. In the multivariate logistic regression analysis, higher BMI, higher depression and lower anxiety predicted lower adherence to exercise prescriptions (P=0.0004, odds ratio =0.796, 95% CI =0.701, 0.903; P=0.009, odds ratio =0.356, 95% CI =0.165, 0.770; and P=0.05, odds ratio =2.361, 95% CI =0.995, 5.627 respectively).	1) HADS; 2) HADS-3 MMSE, MOCA 4) MGL adherence scale; 5)asicold-r	Linear regression	x	In COPD patients, focusing on pharmacological and non-pharmacological adherence enhance the possibility of tailored pulmonary rehabilitation programs.
1) The aim of this analysis was to explore the association between COPD optimal and suboptimal awareness, clinical parameters, and the following patient-reported outcomes: modified Medical Research Council (mMRC), Treatment Satisfaction Questionnaire (TSQM-9), COPD Assessment Test (CAT), Morisky Medication-Taking Adherence Scale (MMAS-4), and Brief Illness Perception Questionnaire (B-IPQ).	1) Treatment satisfaction; 2) Medication adherence; 3) illness perception	Cross-Sectional Study	At enrollment, no difference between the 2 groups was found in terms of age, age at COPD diagnosis, and MMAS scores. Overall, patients with suboptimal awareness, compared to those in which awareness was optimal, had a higher median CAT score (difference: 5.0 points; p value = 0.0001), a higher median mMRC score (difference: 1.0 point; p value = 0.0031), a lower median duration of COPD (difference: 1.4 years; p value = 0.0428), a lower median TSQM-9 effectiveness score (difference: 5.6 points; p value = 0.0002), a lower median TSQM-9 convenience score (difference: 11.1 points; p value < 0.0001), a lower median TSQM-9 global satisfaction score (difference: 14.3 points; p value < 0.0001), and a higher median B-IPQ total score (difference: 9.0 points; p value < 0.0001).	At enrollment, the proportion of patients who had exacerbations during the previous year was higher in patients with suboptimal COPD awareness (DACQ total score <80) than in those with an optimal level of awareness (42.8 vs.21.4%, p value = 0.0009). At the 12-month follow-up, the proportion of patients with an optimal awareness (DACQ total score ≥80) was significantly higher in the group of those with CAT <10 than in the group of those with CAT ≥10 (p = 0.0022)	1) Treatment satisfaction Questionnaire; 2)MMAS-4; 3)B-IPQ	Linear regression	x	The results of our post hoc analysis suggest that patients' awareness of their COPD disease is related to both clinical outcomes and how they perceive and manage their condition.
1) The primary endpoint was to describe patients' satisfaction with COPD medical treatments by means of the TSQM-9 during a 12-month observation period in a real-world setting 2) The secondary endpoints included: (a) disease perception, adherence to treatment, health status, and dyspnea over the 12-month observation period; and (b) identification of factors associated with patient satisfaction with COPD medical treatments.	1) satisfaction with MT; 2) illness perception; 3) adherence to treatment; 4) health status; 5) adherence	Multicenter, noninterventonal (observational) cohort study	A significant negative association ( $\beta = 0.4709$ , $p < 0.0001$ ) emerged between the scores to all items of the TSQM-9 questionnaire recorded at the end of the study and the disease perception (B-IPQ) score. COPD patients with poor/suboptimal adherence to treatment (MMAS-4 scores 0-3) had a lower mean convenience score (about 6.6 points less; $p < 0.0001$ ) and lower global satisfaction score (of about 4.6 points; $\beta = 4.5608$ , $p < 0.002$ ) compared with patients with optimal adherence (MMAS-4 score = 4). Moreover adherence and satisfaction were positively correlated.	Similar levels of TSQM-9 scores were found during the 12-month follow-up period between patients who changed (switchers, n=73) and who did not change (nonswitchers, n=231) their pharmacological inhalatory regimens	1) TSQM-9 2) B-IPQ 3) MMAS-4 4) CAT 5) mMRC questionnaire	correlation	x	The results of this real-life study showed that the patients' satisfaction with treatments is only moderate in COPD. A high grade of patients' satisfaction is associated mainly with a low perception of the disease, high adherence to treatment and lower level of dyspnea.
1) To evaluate adherence to a maintenance exercise program in patients with chronic obstructive pulmonary disease (COPD) and explore predictors for adherence.	1) exercise capacity (walking test) 2) exercise self-efficacy; 3) illness perception; 4) health related quality of life; 5) anxiety and depression; 6) duration of pR; 7) Exacerbations; 8) Patient-reported reasons for nonadherence 9) Adherence to programme	Longitudinal Study	Health-related quality of life, anxiety, self-efficacy, exacerbations, and illness perceptions were found not to be predictive for adherence, probably due in part to shared variance with other variables, for example, FEV 1.	The most frequently patient-reported reason for dropout was exacerbations. The logistic model showed that especially (1) worse disease (lower FEV 1), (2) more depressive symptoms, and (3) shorter duration of the rehabilitation program predicted dropout from our maintenance exercise program	1) shuttle walking test; 2) exercise self-regulatory efficacy scale; 3) IPQ 4) HRQL questionnaire 5)HADS 6) n of exacerbation 7) self report questionnaire 8) drop out	Logistic regression analysis	22	Adherence to a maintenance exercise program, after PR, is quite reasonable for patients with COPD. Nonetheless, about one-third of patients dropped out during the first year. Experiencing exacerbations was the most reported reason for dropout. Greater health impairments, that is, poorer lung function and more symptoms of depression, appeared to be predictive for dropout. Taking these factors into account may help in early identification of possible dropouts.
1) The purpose of this prospective study is to investigate drop-out and attendance rates during rehabilitation programmes for patients with COPD and to provide an overview of reasons for drop-out and non-attendance. 2) A second aim of this study is to investigate whether patients' illness perceptions add to the prediction of drop-out and non-attendance after controlling for sociodemographic and medical variables.	1) illness perception; 2) clinical parameters (BMI, FEV, BORG CR10, walking test); 3) medical Research Council (MRC) dyspnoea scale	Longitudinal Study	The present study showed that patients' adherence to a pulmonary rehabilitation programme is high. More than 75% of the referred patients who participated in this study completed the rehabilitation course. The results of this study demonstrated a relationship between attendance during rehabilitation and patients' perceptions about the effectiveness of treatment. These perceptions are influenced by the patient-provider interaction, which suggests that communication between patient and healthcare provider may profit from an exploration and discussion of patients' illness and treatment perceptions during the referral or intake phase. Although on average patients demonstrate high attendance, creating a positive yet realistic expectation of the rehabilitation appears to be an important objective if one aims to optimise patients' adherence during rehabilitation.	Non-completion and non-attendance were often attributable to medical causes. Where the patient decided not to start or continue the rehabilitation programme, reasons were often practical (eg time constraints) or related to dissatisfaction with the organisation of care. Drop-out or decline was not related to medical and psychosocial variables. Patients' attendance however, was related to their fat free mass and their perception of effectiveness of the treatment.	1) Drop out rehabilitation programme - attendance; 2) illness perception;	Hierarchical logistic regression analyses	50	In general, adherence in rehabilitation is high. However, paying attention to patients' nutritional status and creating a positive expectation of treatment during referral and intake appear to be important, if one aims to optimise patients' attendance during rehabilitation.

**Table 4** List of Included Studies That Discussed Different Kinds of Adherence

Authors	Adherence Tool	Adherent vs Non-Adherent participants	Score
Agarwal, 2021 <sup>36</sup>	MARS	134 vs 208	NA
Brandstetter, 2017 <sup>38</sup>	MARS	70 vs 136	NA
Contoli, 2019 <sup>40</sup>	MMAS-4	n.a.	3.4±0.9 (n=401) 95% CI 3.3–3.5
Duarte-de-Araújo, 2018 <sup>39</sup>	MTA	210 vs 90	NA
Fischer, 2009 <sup>28</sup>	Drop-out numbers from pulmonary rehabilitation	80 vs 79	NA
Heerema- Poelman, 2013 <sup>29</sup>	Maintenance program for 1 year after the pulmonary rehabilitation	38 vs 22	NA
Hom, Etowska, 2022 <sup>35</sup>	ARMS	NA	21.15 ± 6.23–74%
	TAI	Sporadic non-compliance 74.15% Deliberate non-compliance 59.69% Unconscious non-compliance 11.38%	NA
Khdour, 2012 <sup>14</sup>	MMAS	122 vs 51	NA
Huurne, 2018 <sup>30</sup>	Patients' pharmacy records	10 vs 10	This was expressed as a percentage and adherence was deemed good if it was 75%–125%, suboptimal between 50% and 75%, and poor below 50% (underuse) or above 125% (overuse)
Krauskopf, 2014 <sup>37</sup>	MARS	79 vs 109	NA
López-Pintor, 2021 <sup>12</sup>	TAI	143 vs 96	NA
Olszanecka-Glinianowicz, 2014 <sup>34</sup>	MMAS-8	1600 vs 1002	Adherence: ≤4; Non-Adherence: ≥4
Pierobon, 2017 <sup>33</sup>	MGL	70 vs 14	NA

- The Belief about Medicines Questionnaire (BMQ),<sup>47</sup> is a 10 items self-report tool for evaluating people's beliefs about medicines, through a 5 points Likert scale. Items are divided into two subscales: "Medication Necessity score" and "Concerns about medication score"; scores range from 5 to 25: higher score indicates greater belief that COPD medications are necessary and greater worry about COPD medications.
- The Health Belief Model (HBM) Questionnaire, a 5-point Likert scale self-report tool, is widely used as a conceptual framework to explain and predict health behaviors by focusing on the beliefs and attitudes of individuals. It includes four primary variables: perceived susceptibility (eg, 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 (eg, individual's belief in the efficacy of the prescribed medication in reducing disease severity or susceptibility) and perceived barriers (eg, stigma of taking medication or denial of having serious illness).<sup>48</sup>
- The Medication Effectiveness Belief questionnaire,<sup>15</sup> a ad hoc questionnaire in which patients were 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.
- An ad hoc questionnaire about the perception of ease of use of the inhaler medications.<sup>13</sup>

**Table 5** List of Included Studies That Discussed Different Kinds of Illness Beliefs and Cognition Tools

Authors	Beliefs-Cognitions Tool(s)	Score	Notes
Krauskopf et al, 2015 <sup>37</sup>	BMQ	Necessity: 14.4±4 vs 14.1±4.7 p=0.54	Adherent vs Non-adherent
		Concerns: 11.4±3.2 vs 14.4±4.1 p<0.001	
Brandstetter et al, 2017 <sup>38</sup>	BM	Overuse: 3.2 (0.7)	Scores ranges from 1 to 5 for each scale, with higher values indicating stronger beliefs.
		Harm: 2.5 (0.7)	
		Utility: 3.9 (0.7)	
		Necessity: 2.6 (0.8)	
		Concerns: 4.1 (0.7)	
Duarte-de-Araújo et al, 2018 <sup>39</sup>	BMQ	Necessity: 20.58±4.104 vs 15.75 ±5.777 p<0.001	Adherent vs Non-adherent
		Concerns: 10.76±4.265 vs 10.65 ±4.383 p=0.87	
Agarwal et al, 2021 <sup>36</sup>	BMQ	Necessity: 14 (10–18)	
		Concerns: 12 (10–16)	
Khdour et al, 2012 <sup>15</sup>	Medication Effectiveness Belief questionnaire	Totally/mostly effective: 107 (63.7) Little/not effective: 61 (36.3)	
López-Pintor et al, 2021 <sup>12</sup>	Perception of ease of use of IT;	Easy: 307	
		Difficult: 10	
		Medication Effectiveness Belief questionnaire	Totally/mostly effective: 232 Little/not effective: 86
Homietowska et al, 2022 <sup>35</sup>	BMQ	Overuse: 12.74 ± 3.18	Overuse: 4–20
		Harm: 11.29 ± 2.70	Harm: 4–20
		Necessity: 19.35 ± 2.97	Necessity: 5–25
		Concerns: 16.67 ± 3.25	Concerns: 5–25

## The Relationship Between IPs, Cognitions and Beliefs and Adherence to Treatment in COPD Patients

Below, in [Table 6](#), we reported all the relationships (with the used statistical analysis techniques) we found, between adherence to treatment and illness perceptions, beliefs, and cognitions.

## Other Considered Variables and Their Relationship with Adherence to Treatment

Considering that adherence to treatment is a multifactorial variable, we decided to make explicit those predictors that have been most cited by the authors, such as some physical conditions (disease severity,<sup>38</sup> smoking status,<sup>36</sup> body mass index<sup>29</sup>) or some psychological variables like self-efficacy or health-related quality of life.<sup>39</sup> Below, in [Table 7](#), we reported all the cited predictors of adherence to treatment in COPD patients we found in our selected studies.

**Table 6** Relationship Between IP, Beliefs, and Cognitions and Adherence to Treatment in COPD Patients

Authors	Data Analysis Technique	Scores
Agarwal et al, 2021 <sup>36</sup>	Chi squared test IPQ, BMQ - adherence	Those with low adherence had higher BIPQ scores [45 (39, 51) vs 42 (34, 50) $p=0.001$ ] and medication concern score [14 (10, 18) vs 11 (10, 14) $p<0.001$ ] as compared to those who were adherent
Brandstetter et al, 2017 <sup>38</sup>	Logistic regression analyses of medication adherence on beliefs about medicines	Beliefs about the necessity of medicines were significantly associated with medication adherence (OR 2.46, CI 1.36–4.42), with stronger beliefs increasing the chance for adherence. Medication concern was not significantly associated with adherence.
Duarte-de-Araújo et al, 2018 <sup>39</sup>	Chi squared test BMQ - adherence	Necessity: Adherent 20.58±4.104 vs non-adherent 15.75 ±5.777 $p<0.001$ Concerns: Adherent 10.76±4.265 vs non-adherent 10.65 ±4.383 $p=0.87$
Fischer et al, 2009 <sup>28</sup>	MANOVA	The poor and high attendance group differed in their illness perceptions (MANOVA $F(8, 142) Z 2.47, p < 0.05$ ). Treatment control was higher in the adherent group (16.3 vs 15.4 $p=0.04$ ).
Heerema-Poelman et al, 2013 <sup>29</sup>	Descriptive statistics	IPQ-R personal control: adherent 20.7 (2.7) vs non-adherent 20.4 (4.4) IPQ-R treatment control: adherent 15.6 (2.2) vs non-adherent 16.2 (3.0)
Homietowska et al, 2022 <sup>35</sup>	Correlation analysis between beliefs about medicines (BMQ) and treatment adherence (ARMS, TAI)	Belief that medicines are overused, harmful and concerns about medicines were significantly ( $p<0.05$ ) and positively correlated with the total ARMS score. Therefore, the greater the belief that medicines are overused by doctors, the lower the level of adherence in all dimensions. Belief in the necessity of medication was significantly ( $p<0.05$ ) and positively correlated with the lack of sporadic and unconscious non-compliance and was significantly and negatively correlated with the total ARMS score. Therefore, the stronger the belief in the necessity of medication, the higher the level of adherence in all dimensions. Belief that medicines are harmful and concerns about medicines were significantly ( $p<0.05$ ) and negatively correlated with the lack of sporadic, deliberate and unconscious non-compliance. Therefore, the greater the concerns about medicines, the poorer the adherence to inhaled medications.
Khdour et al, 2012 <sup>15</sup>	Student's <i>t</i> -test	A significant association ( $p<0.01$ ) was found between self-report of the effectiveness of medication and adherence behavior, ie those patients who felt that their medications were totally or mostly effective were more likely to report adherence to their medications.
Koehorst-ter Huurne et al, 2018 <sup>30</sup>	Qualitative analysis – ATLAS.it	Most patients perceived their condition as stable, there was no difference between under- and over users in described symptoms or problems with everyday activities, in perceived causes or in perceived control. The majority of the non-adherent patients were not able to accept their disease and the accompanied treatment.

(Continued)



Table 6 (Continued).

Authors	Data Analysis Technique	Scores
Krauskopf et al, 2015 <sup>37</sup>	Unadjusted comparisons of beliefs according to self-reported adherence	Non-adherent participants reported being more concerned about their COPD ( $p=0.01$ ; Cohen's $d=0.43$ ). Non-adherent participants also had higher scores in the concerns subdomain of the BMQ, indicating increased worries about COPD medications ( $p<0.0001$ ; Cohen's $d=0.81$ ), adherent 11.4 (3.2) vs non-adherent 14.4 (4.1)
Lopez-Pintor et al, 2021 <sup>12</sup>	Chi squared test	Patients who thought that inhaler's effectiveness was good (145, 62.5% vs 41, 47.7%, $p = 0.017$ ) showed a good adherence rate.
Magdalena Olszanecka-Glinianowicz et al, 2014 <sup>34</sup>	$\chi^2$ test	The mean total score of illness perception was significantly higher in adherence than non-adherence group. $55.4\pm 10$ vs $53.2\pm 9.8$ $p<0.001$
Pierobon et al, 2017 <sup>33</sup>	Student's t-test	No significant relations were found.

Table 7 Predictors of Adherence to Treatment in COPD Patients

Authors	Variable(s)	Tool(s)	Score
Agarwal et al, 2021 <sup>36</sup>	Health Literacy	Short Test of Functional Health Literacy in Adults (S-TOFHLA)	$\beta=-0.003$ , $p=0.003$
Brandstetter et al, 2017 <sup>38</sup>	Depression;	HADS-D;	5.2 (4.1) vs 8.3 (4.6) $p<0.01$
	Disease severity;	COPD assessment test (CAT);	n.a.
	Health related quality of life	12-item Short Form Health Survey (SF-12);	Phy: 31.8 (9.7) $p<0.01$ ; Mental: 38.0 (14.3) $p<0.01$
	Self-efficacy	Generalized Self-Efficacy Scale (GSE)	28.2 (6.6) $p<0.01$
Contoli et al, 2019 <sup>32</sup>	Treatment satisfaction	Treatment Satisfaction Questionnaire, 9 items (TSQM-9)	$\beta=4.5608$ , $p<0.002$
Duarte-de-Araújo et al, 2018 <sup>39</sup>	Smoking status		Odds ratio: 2.4–2.4 times more risk of non-adherence for current smokers
Fischer et al, 2009 <sup>28</sup>	Body mass index (BMI)		$p=0.04$
Heerema-Poelman et al, 2013 <sup>29</sup>	Forced Expiratory Volume in the 1st second (FEV1)		$p=0.025$
Homietowska et al, 2022 <sup>35</sup>	Smoking status (non-smoker);		$p=0.023$
	Place of residence (rural area)		$p=0.004$
Khdour et al, 2012 <sup>15</sup>	Co-morbid illness;		$p<0.05$
	Depression;	HADS-D	$p<0.01$
	Perceived barriers to taking medication	Health Belief Model (HBM) scale	$p<0.05$
	Knowledge of COPD		$p<0.01$

(Continued)

**Table 7** (Continued).

Authors	Variable(s)	Tool(s)	Score
<b>Krauskopf et al, 2015</b> <sup>37</sup>	Education;		p=0.002
	Disease severity;	CAT	p=0.04
	Monthly income		p=0.02
<b>Lopez-Pintor et al, 2021</b> <sup>12</sup>	Physical activity;		p=0.035
	Smoking status;		p=0.049
	Knowledge of COPD;		p=0.003
	Receiving explanation about inhalers;		p=0.032
<b>Pierobon et al, 2017</b> <sup>33</sup>	BMI;		p<0.001
	Depression;	Beck Depression Inventory (BDI-II)	p<0.001

## Discussion

Finding a definition of “adherence” continues to be a complex matter.

In 2001, the WHO defined it as

the extent to which a person’s behavior taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a health care provider<sup>49</sup>

Giving patients a passive role, which, considering the importance of patients’ point of view about his/her illness condition, does not correspond to reality.

However, as Hughes specified, adherence is not just a dichotomous variable (ie, adherent/non-adherent), but a really more complex concept: for this reason, a common situation might be a COPD patient who may choose to stop taking some medications for no apparent reason.<sup>50</sup>

In this sense, adherence to treatment is also determined by patients’ choices of following medical directions, considering that, during a clinical experience, patient could build personal theories about it.

This latter aspect involves a real active position of the patient, whose theory about adherence, for example, might depend on whether patients are outcome-oriented, for example, “feeling better”, or process-oriented, like being more regular with the medication use.<sup>11</sup>

Therefore, by changing our perspective and assuming that the patient, in all respects, plays an active role in his/her treatment, it is easier to understand the importance of being aware of his/her point of view, through the knowledge of perceptions, cognitions, and beliefs about pathology.

To fill this research gap, we decided to focus our attention on adherence to treatment, which is considered, according to COPD guidelines,<sup>51</sup> one of the most important aspects of COPD self-management. However, as previous studies confirmed,<sup>9</sup> low rates of treatment adherence are common in COPD and they are also typically associated with several adverse health outcomes and a general patient’s quality of life reduction.<sup>16</sup>

Looking at our selected studies we could confirm a generally low rate of adherence, with only one exception,<sup>33</sup> who reported a suboptimal level.

In any other case, no matter which assessment tool was chosen, no relevant differences had been found between results, reporting a general low rate of adherence, even using different ranges and cut-off. Moreover, on the contrary, two studies<sup>38,39</sup> even found that their sample consisted of a majority of people who did not adhere to their treatment at all.

Poor adherence rates were also found when considering adherence to physiotherapy program, especially after one year;<sup>30</sup> whereas perceived physiotherapy treatment effectiveness demonstrated to be a strong predictor of patients' adherence behavior in rehabilitation, offering a first demonstration of the importance of considering patient's perceptions.<sup>29</sup>

In light of this finding, factors that can improve the level of adherence should be considered during the treatment selection process and be part of a self-management program focusing on the patient's role.

Starting from these considerations, we investigated patients' perceptions and beliefs about their condition and their treatment, as well.

As Pierobon et al<sup>34</sup> explained, being aware of one's condition is essential for consciousness and long-term management of chronic diseases, such as COPD. Many patients, in fact, deny their diagnosis or prognosis, to protect themselves.<sup>52</sup> At the same time, awareness is also considered a crucial competency for healthcare providers and public health practitioners.<sup>37</sup> This makes it easier for them to understand why one patient may be more adherent than another and enables them to provide appropriate support to at-risk patients.<sup>37</sup>

Brandstetter et al,<sup>39</sup> for example, discovered that COPD patients' beliefs about medication overuse by doctors and the harm of medicines reduced adherence rates to about 40%, while patients with stronger beliefs about the necessity of their medicines were three times as likely to be completely adherent. Similar results were also collected by Khdour et al,<sup>15</sup> Olszanecka-Glinianowicz et al<sup>35</sup> and Duarte-de-Araújo et al,<sup>40</sup> who also asked their participants to provide some justifications of their (non)-adherent behavior. According to COPD patients, for example, having a caregiver and easy access to medications were predictors of adherent behavior, while a lack of trust in medication (and its effectiveness) was a risk factor.<sup>40</sup> Regarding this, López-Pintor et al<sup>13</sup> found that receiving information about medication from clinicians before starting treatment might improve patients' level of adherence. This aspect was also described by Olszanecka-Glinianowicz<sup>35</sup> who reported "Poor understanding of instructions from the doctor" and "The method of taking the drug is complicated" (p. 240) as frequent affirmations of non-adherent group.

According to Krauskopf et al<sup>38</sup> and Koehorst-ter Huurne,<sup>31</sup> even negative emotions (like depression, "Half of our nonadherent patients also reported depressed mood" p. 1782<sup>31</sup>) and concerns about COPD and its impact on life were predictive of a low adherence rate. In line with the above point, Koehorst-ter Huurne et al<sup>31</sup> discovered that illness acceptance is a crucial variable to take into account talking about adherence to treatment, reporting that those patients who had a greater understanding about their illness were those with a greater level of acceptance and an increased adherence level.

Considering illness perceptions according to Leventhal's model,<sup>23</sup> we discussed each dimension, case-by-case.

In general, COPD is perceived as a moderate threat.

Focusing on "Identity" – How a person views his/her illness,<sup>23</sup> many participants<sup>13,15,31,37</sup> could not give a clear definition of it; in particular, some of them even talked about a general airway obstruction.<sup>31</sup> However, considering adherent and non-adherent groups separately, a higher rate was found in the non-adherent participants, which means that non-adherent people perceived their symptoms more than adherent participants.<sup>38</sup>

Talking about "Timeline" – How the patient believes the illness will develop over time<sup>23</sup> - several studies,<sup>35,37</sup> found that concerns about the future were very common, even between adherent people.<sup>31</sup>

From "Illness consequences" dimension – How the patient believes that the severity of illness will impact on physical, social, and psychological functioning<sup>23</sup> - emerged that both adherent and non-adherent patients had many problems in daily activities;<sup>31–34,37,38</sup> however, Khdour et al<sup>31</sup> specified that those with a good level of COPD self-efficacy perceived less negative consequences on their life than other participants and were more likely to be classified as adherent to treatment. On the other side, most reported "causes" were smoking, genetics, and environmental factors like pollution.<sup>15,31,37,39</sup>

Finally, we explored "Control", which is divided in "Treatment control" - How a person perceived that medication could control his/her condition - and "Personal control" - How a person perceived to be able to control his/her condition.<sup>23</sup>

Contrary to expectations, Heerema-Poelman et al,<sup>30</sup> who specifically focused on "control" dimension and its relationship with adherence to treatment, discovered that adherent people perceived to have more treatment control than others,

but no difference was reported between groups when asking about personal control. This finding, however, might be explained by the “timeline” perception of a “forever” lasting condition,<sup>35</sup> which persists even in the adherent group.<sup>29</sup>

## Limitations

As for limitations, it is useful to note that the considered sample was quite small ( $n = 14$ ) and this was also since we decided to consider only open-access articles, so the external validity of our results can be threatened. In addition, only two of the studies have longitudinal design, so it would be interesting if future research will investigate whether and how these constructs change over time.

## Conclusions

Adherence to treatment remains a challenge to the health and quality of life of COPD patients, as, both using objective and self-report tools, rates are low. In the light of the findings regarding the perceived threat of non-adherence and the consideration of patients’ subjective views, future interventions should try to consider the extent of the perception of disease and the beliefs that patients have about their treatment so that the level of awareness and adhesion can be improved.

However, having ascertained the interest and the novelty of this fertile research area, future research should choose to use both types of tools for the assessment of adherence to treatment, to obtain a more complete overview of the situation; moreover, and focus more on the impact these constructs have in clinical practice, for example, through the validation of new specific tools.

## Abbreviations

BDI, Beck Depression Inventory; B-IPQ, Brief Illness Perception Questionnaire; BMI, Body mass index; BMQ, Beliefs about medicines questionnaire; CAT, COPD assessment test; COPD, Chronic obstructive pulmonary disease; FEV1, Forced Expiratory Volume in the 1st second; GSE, Generalized Self-Efficacy Scale; HADS, Hospital Anxiety Depression Questionnaire; HBM, Health Belief Model; IP, Illness Perception; IPQ, Illness Perception Questionnaire; IPQ-R, Illness Perception Questionnaire Revised; LTOT, Long-Term Oxygen Therapy; MARS, Medication Adherence Report Scale; MMAS, Morisky Medication Adherence Scale; MTA, Measure of Treatment Adherence; NA, Not available; NIV, Non-Invasive Ventilation; PR, Pulmonary Rehabilitation; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SRM, Self-Regulation Model; S-TOFHLA, Short Test of Functional Health Literacy in Adults; TAI, Test of the adherence to inhalers; TSQ-9, Treatment Satisfaction Questionnaire, 9 items; WHO, World Health Organization.

## Author Contributions

All authors 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; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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