ORIGINAL RESEARCH ARTICLE

Prioritization and Refinement of Patient-Informed Value Elements as Attributes for Chronic Obstructive Pulmonary Disease Treatment Preferences

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Abstract

Background and Objective Formative research studies can inform stated-preference instrument development to quantify the importance of various attributes of healthcare treatments. The objective of this study was to elicit from patients with chronic obstructive pulmonary disease the prioritization of an established set of patient-informed value elements.

Methods Using an iterative mixed-methods study design, we engaged individuals living with chronic obstructive pulmonary disease in Phase 1 value element elicitation and Phase 2 language refinement. Study participants were recruited from March to July 2019. Four guided activities, administered in an online instrument, elicited individual preferences for 40 disease-agnostic value elements that were aligned with treatment, outcomes, or care process. Responses from the guided activities were summarized and then presented to a patient advocate and additional patient participants for further refinement of the value elements and the phrasing.

Results Twenty-three participants, 18 male and five female, mean age of 66 years (standard deviation = 7) were enrolled in Phase 1. Participant responses informed the selection of eight elements as the key candidates for the Phase 2 language refinement: Side Effects, New Therapeutic Option, Available Treatment, Appropriateness of Care, Predictable Healthcare Needs, Physical Activities: Endurance and Symptom Control, and Explanation of Treatment. With feedback from a patient advocate and additional patient participants, elements were refined, rephrased, or modified and this list was narrowed to six value elements (Side Effects, New Therapeutic Option, Willingness to Pay, Physical Activities, Explanation of Treatment, and Access to Care) to serve as attributes in a conceptual framework for a future quantitative stated-preference instrument.

Conclusions This patient-engaged formative work identified patients with chronic obstructive pulmonary disease key attributes of value-based decision making that underpin benefit-risk trade-offs between physical endurance, treatment side effects, care access, and cost. This study illustrates an iterative process for eliciting and refining a comprehensive list of value elements, resulting in a subgroup of elements important to a specific patient population.

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1 Introduction

Chronic obstructive pulmonary disease (COPD) is a common progressive condition of the airways characterized by diminishing lung function and persistent respiratory symptoms. Chronic obstructive pulmonary disease has been the third leading cause of death in the world since 2016, with an estimated 3 million deaths (5.3% of all deaths) [1]. Numerous pharmacologic treatments in various combinations, formulations, and delivery options exist for COPD [2]. Newer treatments include dual- and triple-therapy inhalers, combining long-acting beta$_2$-agonists, muscarinic antagonists and/or inhaled corticosteroids, providing convenience but often with higher cost sharing for patients. Economic evaluations

Key Points

A comprehensive list of condition-agnostic value elements was tailored for patients with chronic obstructive pulmonary disease to reflect the element that matters most for their healthcare decision making.

We used an iterative process as formative work to develop attributes for stated-preference instrument development.

Patients with chronic obstructive pulmonary disease key attributes of value-based decision making are physical endurance, treatment side effects, care access, and cost.

of COPD treatments play an important role in ensuring access to pharmacologic treatments for patients with COPD.

Previous economic evaluations of treatments for COPD have focused on valuing outcomes such as exacerbations and lung function, as these are often the outcomes of major clinical trials of COPD treatment [3, 4]. While these outcomes are important to both patients and healthcare providers, patients may also value other aspects of treatment. Studies using stated-preference methods have revealed patients are concerned with other impacts of their condition [5]. Numerous studies have elicited preferences from patients with COPD, but these efforts have largely been directed at product development and future clinical studies [6–8]. Therefore, the attributes used in these prior investigations may not address the physical, social, and economic impact of treatment on a patient's daily life that are important for economic evaluations that comprise the patient's perspective.

Our ongoing research at the XXXX Center at the University of XXXX seeks to elicit elements of value important to patients. In our recent work, we identified, prioritized, and refined a core set of patient-informed value elements with continuous patient-stakeholder engagement [9]. These elements were condition agnostic and related not only to treatment effects, but also to the economic, physical, and social impact of treatment as well as to healthcare access [9]. The objective of the present study was to tailor the set of condition-agnostic, patient-informed value elements to individuals living with COPD by eliciting which of the elements are most important to them. This was a formative research study with the objective of eliciting and refining value elements for the development of a stated-preference instrument [10–12] for use in future quantitative evaluation of COPD treatment preferences. The focus of this paper is to describe the study process and how the results can be used to inform instrument development.

2 Methods

2.1 Study Design

In this study of patient preferences for COPD treatment, we elicited from individuals with COPD the value elements that were most important to them in making decisions about treatment to manage their condition. Using an iterative study design, we engaged individuals living with COPD in two phases of the research: Phase 1 value element elicitation and Phase 2 language refinement. In both phases, one-on-one guided interviews were conducted in person (Phase 1 only), by telephone, or by WebEx platform. We followed the established methods for attribute development and reporting guidance of formative qualitative study for stated-preference instrument development [11–13].

2.2 Participant Recruitment

Individuals were eligible to participate in the study if they were aged 18 years or older, were diagnosed with COPD, and had used or been offered medication for COPD. Phase 1 study participants were recruited from March to July 2019 primarily from two large, university medical center pulmonary clinics, as well as the COPD Foundation national advocacy organization. Study flyers were distributed at clinic offices and via e-mail as well as through word of mouth at COPD-specific advocacy events.

Participation was voluntary and individuals were informed that their decision to join the study would not affect their relationship with providers or their advocacy group membership. Individuals who were interested in the study contacted the research team by telephone or e-mail. A member of the research team screened by telephone all potential participants for eligibility, and those eligible were scheduled to attend one-on-one discussion and guided activity administered in person, by phone, or via WebEx. Eligible participants provided verbal consent prior to completing the study activity. A target sample of 30 participants was recruited across both phases. This work was conducted iteratively with patient and stakeholder input. This study was approved by the authors' institutional review board (Protocol number: HP-00083928).

2.3 Study Procedures

This study builds upon our previous work with continuous patient-stakeholder engagement that resulted in a comprehensive set of 42 patient-informed value elements. These elements were organized across 11 domains that included tolerability, disease burden, forecasting, accessibility of care/treatment, healthcare service delivery, cost incurred on the

patient, cost incurred on the family, personal well-being, stigma, social well-being, and personal values [9]. The goal of this prior work was to elicit directly from patient stakeholders, using an iterative guided process, the value elements that mattered most to them when making healthcare decisions. The resulting 42 patient-informed value elements reflect attributes of treatment decisions that may apply to a range of conditions. The goals of the present study were to determine which elements were most important to patients with COPD and to tailor the descriptions of the elements to fit the experience of patients with COPD. To execute this, we carried out this work in two phases.

2.3.1 Phase 1: Value Element Elicitation

Four guided activities, administered in an online instrument, elicited individual preferences for 40 of the 42 established patient-informed value elements. The 40 elements were categorized by relation to treatment, outcomes, or care processes [14]. We excluded two elements related to disease burden, i.e., age of onset and symptom importance, that were not specific to treatment effects, outcomes, or care processes. Two value elements, embarrassment/self-consciousness and fatigue, were categorized as both treatment- and outcome-related elements. In previously published COPD preference and patient-reported outcome studies, 'embarrassment' may relate to both an outcome (e.g., coughing) and the treatment itself (e.g., oxygen use in public). Similarly, fatigue may relate to an outcome (e.g., too tired to carry out daily activities) or the treatment (e.g., nebulizer treatment is often physically taxing). Administration of the four activities is described below and illustrated in the Electronic Supplementary Material (ESM; Appendix Fig. 1).

Activity 1 focused on eliciting domain importance. In the first activity, participants selected which of the 11 domains were important to them, and among those selected they were asked to choose the five most important to them. The goal of this activity was to inform which categories of elements would be most important to appear in a future stated-preference instrument. Activities 2–4 focused on the individual value elements nested within the domains and were categorized as treatment, outcome, and care process related, respectively. Each activity was administered one at a time. Participants were shown the list of patient-informed value elements within treatment, outcome, or care process, and similar to the first activity, were asked to select all of the elements important to them and then choose the five most important elements from those selected.

A brief demographic questionnaire was administered upon completion of the activities. Participants provided basic demographic (e.g., age, sex, race) along with health information (e.g., years living with COPD, current medications). The demographic questionnaire is provided in the ESM (Appendix Fig. 1). The guided activities and the demographic questionnaire were developed using Qualtrics, a platform that enables online survey deployment. A research team member guided the participants through activities either in person or over the phone/web conference.

Responses from the guided activities were summarized and then presented to a patient advocate in a leadership position with the COPD Foundation (study author xxx), who is a patient community partner affiliated with our center. The patient advocate, through her longstanding work in COPD advocacy and policy, was able to provide contextual meaning to the value elements identified as most important from the guided activities with the patients with COPD and offered suggestions for prioritizing or consolidating the selected elements. The goal was to refine, with patient stakeholder engagement, the list of value elements identified as most important that would most meaningfully reflect the COPD patient experience. The refined list forms the conceptual basis for attribute development to be incorporated in a stated-preference instrument. The goal was to retain approximately six to eight elements for such an instrument

2.3.2 Phase 2: Language Refinement

Phase 2 language refinement comprised patient interviews and literature synthesis. We recruited seven patient participants for Phase 2. Three of these patients had participated in Phase 1 and agreed to be re-contacted for Phase 2. Four additional patients that had not participated in Phase 1 were recruited through the COPD Foundation and online patient communities. We developed an instrument (Appendix Fig. 2 in the ESM) that first asked participants about the clarity of an overarching choice task question for the future stated-preference instrument. Next, we asked participants to consider a proposed statement for each of the elements retained after Phase 1, framed as attributes. For example, the attribute Side Effects could be described in terms of the tolerability or the likelihood of experiencing the side effect. Participants reviewed the language for each attribute and its description to ensure that the statement phrasing reflected the most relevant and meaningful experience to them. During the discussion, we asked participants to explain what the attribute meant to them and how it related to their own experience.

To identify best parameters for the attribute levels, participants were asked to comment on whether differences between levels for each attribute would influence their decision making. Throughout this process, we aimed to authentically reflect patient experiences as well as to accommodate varying levels of health literacy. Participants were also asked to comment on whether important concepts related to their healthcare decision making were missing from the attribute list. Finally, we elicited feedback on the preferred instrument

profile layout (e.g., two vs three profiles) for each choice task so as to assess the potential for response burden. It should be noted that participants were informed the layouts were for illustrative purposes only and the attributes and levels presented were not necessarily realistic.

Following Phase 2 interviews, we used multiple sources for language refinement of the attribute description. This is an important step in attribute development to ensure the phrasing is relevant to the experiences of individuals living with COPD. First, we reviewed literature on patient preferences for COPD treatment to identify the attributes and levels used in prior studies. The published studies were used to inform appropriate parameters for the attribute levels (e.g., extent of improvement in symptoms scores) so that our attribute levels would be grounded in realistic options. In addition, to capture the patient voice and specifically the terminology commonly used when referring to management of their COPD, we explored the COPD Foundation website COPD360social [15], which is an online communication forum about one's COPD illness and treatment experiences. Integration of the information from all of these sources resulted in a final language refinement for the attribute descriptions and levels. The COPD Foundation patient advocate and one patient who participated in Phase 2 reviewed the attribute phrasing and provided final input on the attributes for a future stated-preference instrument.

2.4 Data Analysis

The information collected for each of the four guided activities and the responses on the demographic questionnaire were downloaded from Qualtrics as an Excel file. Descriptive summaries included frequencies for categorical and binary variables and means for continuous variables. We evaluated agreement by a majority of participants (> 50%) rating the element as among the five most important.

3 Results

Figure 1 shows the number of participants in each study phase as well as changes in the selected value elements over the course of our two-phase study. 23 participants, 18 male and five female, mean age of 66 years (standard deviation = 7) were enrolled in Phase 1 of the study. Participants reported living with COPD for an average of 10.6 years (standard deviation = 8). Twelve participants (52%) self-reported as non-Hispanic white, ten (43%) as non-Hispanic black, and one (4%) as Asian/Pacific Islander (Table 1). Nearly half of the participants were married (n = 10, 43%), most were retired or not working (n = 21, 91%), and most

described their residence in an urban community (n = 12, 52%). All participants reported limited physical activities because of COPD. Twenty participants (87%) reported using two or more long-acting agents for treatment, and nine (39%) participants reported oxygen use.

3.1 Domain and Value Element Importance

Data are reported where more than 50% of participants selected an element as most important to the management of their COPD. Healthcare Service Delivery, Accessibility of Care/Treatment, Tolerability, and Cost Incurred on the Patient were the most important domains (Table 2). The elements rated by participants to be among the top five elements were Side Effects, Provider Relationship & Trust, and Medication Frequency. Physical Abilities, Maintain Social Activities, and Fatigue were reported to be the most important outcome-related elements. Physical Abilities was selected among the top five most important outcome-related elements by 22 of the 23 participants. Explanation of Treatment (Risks & Benefits), Provider Willing to Deliver Care, Proximity to Care Location, Consistency of Care, and Support Network were all among the top five most important care process elements (Table 3). Of the 40 value elements shown across Activities 2–4, 18 were retained as important to individuals living with COPD [i.e., Medication Frequency, Side Effects, New Therapeutic Option, Available Treatment, Appropriateness of Care, Fatigue (as both a treatment- and outcome-related factor), Length of Treatment, Physical Abilities, Predictable Healthcare Needs, Relationship with Family, Maintain Social Activities, Emotional Status, Ability to Plan, Life Expectancy, Explanation of Treatment (Risks and Benefits), Provider Willing to Deliver Care, Proximity to Care Location, and Consistency of Care (Fig. 1)].

With the goal of creating a stated-preference instrument with the resulting elements, we targeted retention of six to eight of the most important elements. Feedback from a discussion with the COPD Foundation patient advocate resulted in the removal of 11 elements (Fig. 1): medication frequency, fatigue (from both treatment- and outcome-related categories), length of treatment, relationship with family, maintain social activities, emotional status, ability to plan, life expectancy, provider willing to deliver care, proximity to care location, and consistency of care. The physical abilities element was split into two elements to more fully capture feedback from patients: endurance and symptom control. This left eight elements as the key candidates for language refinement.
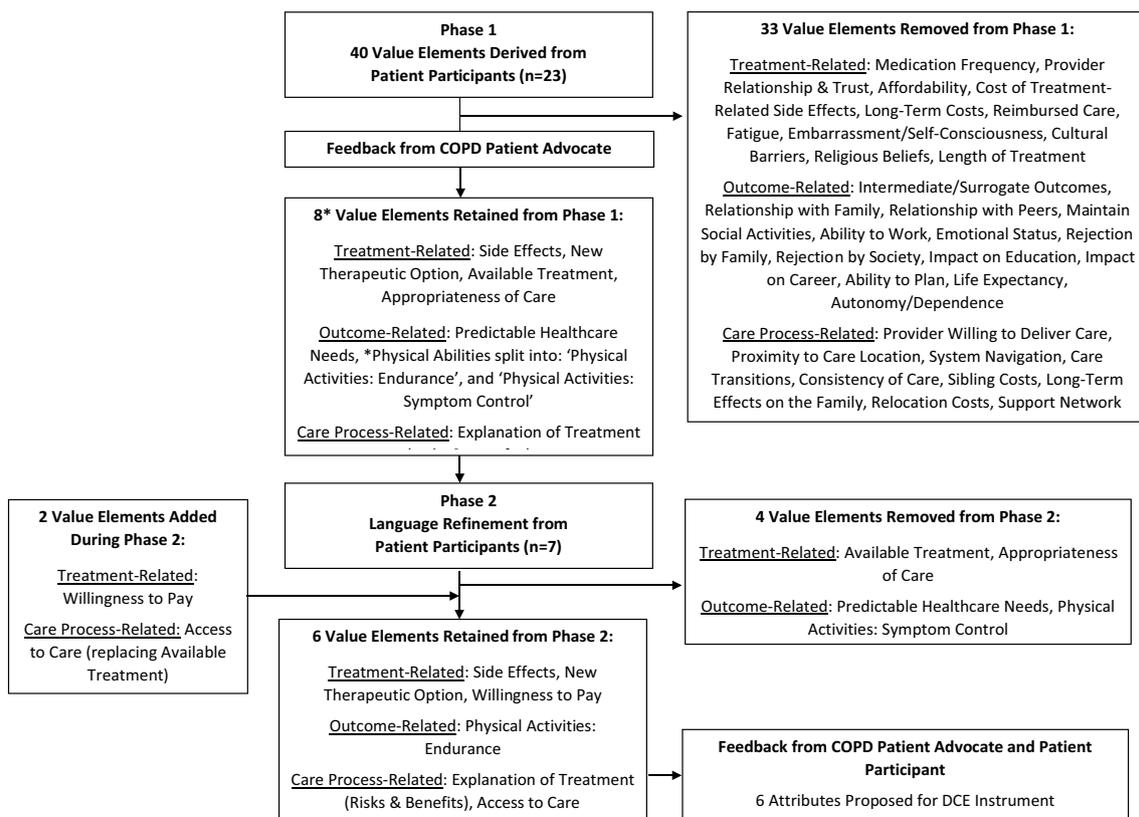
Fig. 1 Value element prioritization and refinement process among patients with chronic obstructive pulmonary disorder (COPD). *DCE* discrete choice experiment

3.2 Language Refinement

The phrasing and feedback from patient participants in the Phase 2 language refinement is shown in Table 4. Seven patient participants, through their feedback, provided key insights on comprehensiveness, redundancy or overlap of attributes, and suggested phrasing based on their experience. These participants were all over 60 years of age, located in the West, Midwest, and South areas of the USA. Their feedback indicated that the two physical activities attributes (endurance and symptom control) were related and could be combined. The suggested phrasing for "Available Treatment" related to both out-of-pocket costs and non-financial access to care, such as driving distance to a provider or timeliness of an appointment. Several participants commented that available treatment did not directly address the financial burden, which was an important attribute for decision making, and thus the availability should be expressed in terms of out-of-pocket costs. The phrasing elicited for Appropriateness of Care and Explanation of Treatment Benefits and Risks indicated that these elements could be combined. Based on the themes that emerged from Phase 2 interviews, we removed appropriateness of care, combined physical activities: symptom control and predictable healthcare

needs, and added two elements: access to care and willingness to pay (replacing available treatment), which resulted in a net reduction of the eight attributes to six. These participants also provided input on the question layout for the stated-preference instrument. Four of the seven participants preferred and recommended using the three-profile layout over the two-profile layout. Participants suggested removing the phrasing 'only options' and 'likely adhere to' from the overarching question framing as it implied that patients did not want to comply with recommendations.

Participant feedback and the COPD stated-preference literature informed the phrasing for the six attributes and attribute levels. The literature on COPD outcome measures and stated-preference instruments revealed a range of ways in which attributes have been phrased. The COPD360social platform [15] provided examples of phraseology related to COPD burden, treatment side effects, and access to care directly from patient experiences. In a real-time feedback session with the COPD Foundation patient advocate and a Phase 2 patient participant, we reviewed the list of attributes and proposed levels.

Based on their input and literature synthesis, the attributes parameters and levels were defined as follows. As we did not target a specific treatment, attributes such as side effects and

Table 1 Phase 1 interview participants' characteristics (*n* = 23)

Characteristics	Interview participants (*n* = 23)
Sex, *n* (%)	
Male	18 (78)
Female	5 (22)
Race, *n* (%)	
White, not of Hispanic origin	12 (52)
Black, not of Hispanic origin	10 (43)
Black, of Hispanic origin	0 (0)
Asian/Pacific Islander	1 (4)
Hispanic	0 (0)
Native American/Alaskan Native	0 (0)
Other	0 (0)
Marital status, *n* (%)	
Married	10 (43)
Never married	3 (13)
Divorced/separated	7 (30)
Widowed	1 (4)
Other	2 (9)
Highest level of education completed, *n* (%)	
Less than high school	4 (17)
High school	14 (61)
College	4 (17)
Postgraduate	1 (4)
Current work status	
Working	2 (9)
Not working	11 (48)
Retired	10 (43)
Family's yearly household income	
$15,000 or less	8 (35)
$15,001 to $35,000	5 (22)
$35,001 or over	8 (35)
Missing	2 (9)
Community of residence, *n* (%)	
Urban	12 (52)
Suburban	7 (30)
Rural	4 (17)
Age in years, mean (SD)	66.0 (7.1)
Age at COPD diagnosis, mean (SD)	54.8 (7.6)
Number of COPD hospitalizations in the past year, mean (SD)	1.8 (2.2)
Use of two or more long-acting agents for treatment, *n* (%)	20 (87)
Oxygen use, *n* (%)	9 (39)
Physical activities limited by COPD, *n* (%)	
Yes	23 (100)

COPD chronic obstructive pulmonary disorder, *SD* standard deviation

willingness to pay need to reflect a range of possible COPD treatments. Patients told us that what was most bothersome about Side Effects was whether they needed to change their regimen or add medication to manage side effects. Levels for the willingness to pay attribute were guided by the patient advocate's expert opinion and from our Phase 1 interviews where patients stated $200 was more than they were willing to pay for treatment. Thus, we knew this was an upper bound beyond which they would not consider trade-offs with other attributes. Access to care was parameterized as the

Table 2 Value element domains rated among the five most important to individuals with chronic obstructive pulmonary disorder ($n = 23$)

Domains	Number of votes (%)
Healthcare service delivery	17 (74)
Accessibility of care/treatment	16 (70)
Tolerability	14 (61)
Cost incurred on the patient	14 (61)
Personal well-being	11 (48)
Disease burden	8 (35)
Cost incurred on the family	7 (30)
Social well-being	6 (26)
Personal values	5 (22)
Forecasting	3 (13)
Stigma	1 (4)

Table 3 Value elements rated among the five most important to individuals with chronic obstructive pulmonary disorder ($n = 23$)

Value elements	Number of votes (%)
Treatment-related factors	
Side effects	15 (65)
Provider relationship and trust	15 (65)
Medication frequency	14 (61)
New therapeutic option	10 (43)
Available treatment	10 (43)
Affordability	10 (43)
Appropriateness of care	8 (35)
Long-term costs	8 (35)
Fatigue	8 (35)
Length of treatment	8 (35)
Cost of treatment-related side effects	5 (22)
Reimbursed care	2 (9)
Embarrassment/self-consciousness	1 (4)
Religious beliefs	1 (4)
Cultural barriers	0 (0)
Outcome-related factors	
Physical abilities	22 (96)
Maintain social activities	14 (61)
Fatigue	12 (52)
Life expectancy	9 (39)
Relationship with family	8 (35)
Emotional status	8 (35)
Predictable healthcare needs	8 (35)
Ability to plan	7 (30)
Intermediate/surrogate outcomes	6 (26)
Autonomy/dependence	6 (26)
Rejection by family	4 (17)
Ability to work	3 (13)
Impact on education	3 (13)
Relationship with peers	2 (9)
Impact on career	2 (9)
Rejection by society	1 (4)
Embarrassment/self-consciousness	0 (0)
Care process factors	
Explanation of treatment (risks and benefits)	21 (91)
Provider willing to deliver care	19 (83)
Proximity to care location	14 (61)
Consistency of care	14 (61)
Support network	14 (61)
Long-term effects on the family	7 (30)
System navigation	5 (22)
Care transitions	5 (22)
Sibling costs	2 (9)
Relocation costs	1 (4)

timeliness of contacting a care provider. New therapeutic option was parameterized as medication frequency, which emerged in Phases 1 and 2 as an important consideration. According to feedback in Phase 2, Explanation of Benefits and Risks reflected how patients learned about treatments. The attributes aligned with the most important domains stated in Phase 1, Activity 1: healthcare service delivery, accessibility of care/treatment, tolerability, and cost incurred on the patient.

To address patients' feedback that knowing their symptom score improved was the best indicator of Physical Activities attributes, we proposed using the COPD Assessment Test (CAT). The CAT operationalized improvement in physical endurance that directly related to symptom control. The CAT is a patient-completed questionnaire that quantifies the impact of COPD on the patient's health (cough, mucus, chest tightness, breathlessness, ability to perform activities, confidence in leaving home, sleep, and energy) [16]. This will require an introduction to the CAT prior to administration of the stated-preference instrument so that respondents have a baseline to gauge level changes described in the instrument. The CAT and stated-preference instrument can be easily incorporated into a survey instrument without imposing an excessive response burden. Table 1 in the ESM illustrates the final attributes and levels selected for the development of a stated-preference instrument for inclusion in a future study.

4 Discussion

This study revealed that, for individuals with COPD, their most important treatment, care, and outcomes concerns were healthcare service delivery, care accessibility, tolerability, and costs. Among individual value elements, > 75% of participants selected as the most important physical

Table 4 Key themes identified from Phase 2 interviews with patients with chronic obstructive pulmonary disorder (COPD) (*n* = 7)

Value element	Themes
Side effects	Side effects may lead to changes in treatment regimen
	Tachycardia and jitteriness are common side effects that may lead to patient discontinuation of medications
	It is a question of benefits vs risks that are acceptable to the patient
New therapeutic option	How is the new treatment better than existing options, e.g., less frequent dosing?
	Convenience
Available treatment	Affordability/insurance coverage
	Delay in access to treatment
	Geographic accessibility
Appropriateness of care	Physician knowledge/trust that they will prescribe appropriate treatment for the patient
Explanation of treatment benefits and risks	Patient knowledge/understanding of correct use of medication
	Informed decision making for oneself
Physical activities: endurance	Endurance and symptom control are related
	Ability to walk for longer
Physical activities: symptom control	Ability to go grocery shopping
	Level of assistance needed with activities
	Having energy throughout the day
Predictable healthcare needs	Ability to plan may depend on severity of COPD
	Difficult to predict whether it will be a "good day" or a "bad day"

abilities, explanation of treatment, and provider willingness to deliver care. Side effects and provider relationship and trust emerged as the most important treatment-related factors. Patient stakeholder engagement enabled attribute refinement to identify the key attributes and to use language that best reflected the patient experience.

Previous COPD patient preference studies report similar findings for treatment, care, and outcome factors. An internet-based survey conducted in the UK found that the most important treatment attributes to patients with COPD were the degree of daytime symptom control and the number of times a day medication is needed [17]. This is similar to our finding that medication frequency was reported as important to patients. A discrete choice experiment conducted in the Netherlands found that fatigue, limitations in moderate physical activities, number of exacerbations, dyspnea at rest, and fear of breathing getting worse contributed most to the burden of disease [18]. The condition-agnostic nature of our value elements enabled mapping them to COPD-specific measures. For example, symptom control and endurance were important to patients in this research, both of which are directly related to exacerbations and dyspnea. We also found that physical abilities and fatigue were important to patients, and while these are condition agnostic, we were able to tailor them to manifestations of COPD. Another qualitative study found that patients with COPD reported impacts including ability to socialize, similar to our finding, in addition to other emotional impacts such as embarrassment/stigma, fear, and anxiety [19]. Our study participants did not express

embarrassment or stigma to be a major factor, but emotional status was important to them. A meta-synthesis of qualitative data identified seven themes that describe the ongoing needs of individuals living with COPD and included better understanding of the condition [20], which corresponds to the explanation of treatment that ranked as important by nearly all our study participants.

While our study findings are similar to those reported in previous literature on patients with COPD preferences for maintenance treatment, our work adds substantially to the evidence on what patients with COPD consider important for treatment decision making. For example, previous studies reported the importance of treatment-related factors such as side effects from treatment and cost [17], and outcome-related factors, such as symptom control [21], which is in line with our findings. However, our findings indicate that in addition to treatment- and outcome-related factors, which have been the primary focus of previous COPD patient preference literature [21–23], the manner in which healthcare is delivered and the accessibility of care or treatment are also important considerations in treatment decisions. Furthermore, we were able to phrase and contextualize the attributes in the patient's voice, which is a significant contribution to the field.

This study of value element prioritization and refinement was conducted specifically to develop a stated-preference instrument to quantify patient treatment preferences. This research is relevant for its potential to include patient preferences in economic evaluations [11, 24–26]. While clinical

trial data are frequently used to compare the cost effectiveness of COPD treatments, our findings reveal that patients with COPD prioritize outcomes that are not typically measured in trials [27]. Clinical COPD trials typically include forced expiratory volume in 1 second, a measure of lung function, as an outcome. However, its use as an outcome measure has been criticized, as forced expiratory volume in 1 s is known to be poorly correlated with the severity of symptoms and does not fully reflect the burden of COPD on patients [27, 28]. A measure of lung function alone may not adequately describe the social impact of COPD and the effectiveness of treatments in reducing exacerbations, improving exercise capacity, or improving health-related quality of life, which may be as important or more important than changes in lung function [27]. There have been increased efforts in recent years to capture the patient voice in clinical trials, including the Patient-Focused Drug Development Initiative of the US Food and Drug Administration and the release of its final guidance for industry on the use of patient-reported outcomes to support labeling claims [29]. However, patient-reported outcomes, which are defined as, 'any report of the status of a patient's health condition that comes directly from the patient' [29], do not reflect patient preferences for treatment, and patient-reported outcomes included in trials may not necessarily be the outcomes that are most important to patients living with COPD.

This study describes a methodological approach for tailoring a condition-agnostic list of elements to a specific condition. This approach is useful for researchers who wish to tailor our 42 patient-informed value elements, or similar sets of attributes, in future research. Furthermore, the ability to refer to a common set of elements may enhance comparability among studies in a single condition, or studies of diverse conditions. Future studies will be able to build upon the methodologic foundation for tailoring the same set of patient-informed value elements to diverse medical conditions across the range of patient populations.

An economic assessment for COPD that incorporates patient preferences would more accurately represent value from the patient perspective. Economic evaluations that incorporate novel value elements and the patient perspective are a major focus of current efforts in the field. Methodologies such as an augmented cost-effectiveness analysis or a multi-criteria decision analysis as well as additions to the perspective used in the reference case have been described in the literature [25, 30]. Presently, there is a great interest in incorporating patient preferences into economic evaluations and decision making [24, 31, 32]. Our study will help guide instrument development to collect patient preference data on attributes that matter most to patients. As a formative study, we reflected on some of our methods that were useful in the attribute elicitation process as well as some aspects that researchers should reconsider in future research. First,

providing a list of elements within specific activities was useful for eliciting feedback across a span of domains. We found that several items were important to at least 70% of participants in Phase 1, suggesting that individuals were discriminating among the elements in a consistent manner. In the future, we aim to collect data from a condition-specific patient-reported outcome or generic health-related quality-of-life instrument to align preferences with an individual's health status. Additionally, health insurance type should be collected as this can influence the importance of cost-related value elements. Willingness to pay was added after Phase 2 based on the discussion with the seven individuals that cost was a major concern. It had not arisen in the 23 interviews mainly because many of these participants had fully subsidized, comprehensive healthcare coverage. Our Phase 2 instrument was very useful for gaining feedback not only for attribute phrasing but also for gaining insight on the overarching choice task question and profile layouts, even if they are only for illustrative purposes.

The main limitation of our study is that our findings are representative of a small sample of patients with COPD and may not reflect the priority of patients beyond those sampled here. Even so, alignment of our findings with prior studies and a clear prioritization of the elements was assuring. Our goal was to include patients with varying disease severity, time living with COPD, healthcare payer type, and geographic region. However, there are likely patients whose preferences are not captured in this study. The findings of this study may not be generalizable to the overall COPD population in the USA. One-fifth of the individuals that participated in Phase 1 were female. However, in the USA, COPD has been reported to be more prevalent among female than male individuals [33]. Additionally, none of the participants were of Hispanic ethnicity, and 52% of individuals resided in an urban area, which do not reflect the general COPD population [34]. Insurance status may have affected patients' perceived importance of the cost of treatment. Future partnership with advocacy organizations could help to engage populations that are more broadly representative. Furthermore, the results may not be generalizable to healthcare settings outside the USA. In particular, cost would likely not be an important factor to patients in countries with primarily government-sponsored healthcare.

Another limitation is that not all of the elements selected as important to individuals with COPD could be incorporated in the set of attributes for a stated-preference instrument. With the goals of minimizing cognitive burden and ensuring compensatory decision making, stated-preference instruments include at most 6–8 attributes. Our iterative process of patient-engaged feedback was intended to narrowly focus on the attributes that would be most sensitive to preferences in decision making. Thus, while not all attributes can be included, we used a rigorous approach to identify the

most meaningful attributes. Acknowledging this still has its limitations, the next stage of our research will be a pre-test of the stated-preference instrument with a new set of participants to ensure that we have excluded the appropriate attributes. While we have chosen to tailor the value elements for a stated-preference instrument, we acknowledge there are other economic evaluation methods, such as a health-state utility estimation or a multi-criteria decision analysis, where fewer or a greater number of elements could be considered for evaluation.

5 Conclusions

This study illustrates how our previously established value elements [9] can be used in an iterative process as formative work for stated-preference instrument development. Among 40 patient-informed value elements, six that related to side effects, new therapeutic option, willingness to pay, physical activities, explanation of treatment, and access to care were important to patients with COPD in managing their condition. Future work should investigate benefit/risk trade-offs as well as translation of these elements into an economic evaluation, such as a health-state utility estimation or a multi-criteria decision analysis.

Declarations

Conflict of Interest Julia F. Slejko reports grants from GSK Pharmaceuticals, Novartis Pharmaceuticals, and Takeda Pharmaceuticals and a teaching honorarium from Pfizer, all outside the submitted work. Susan dosReis reports grants from the National Institute of Mental Health, the Patient Centered Outcomes Research Institute, the US Food and Drug Administration, PhRMA Foundation, and GlaxoSmithKline. Yoon Duk Hong, Jamie L. Sullivan, and Robert M. Reed have no conflicts of interest that are directly relevant to the content of this article.

Availability of Data and Material The ESM provides the instrument used to collect all the data summarized at each phase of this formative work. This enables transparency and replication of this study in other populations. There are no software codes or analytical models related to this work.

Author Contributions JFS and SDR obtained funding for this work, conceptualized the design and data collection, led the data analysis, contributed to the interpretation of the findings, and drafted and edited all aspects of the manuscript. JLS and RMR contributed to participant recruitment, data interpretation and analysis, and reviewed and edited all versions of the manuscript. YDH assisted with the data collection and the summation of the findings and reviewed and edited all versions of the manuscript.

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