Original Research

Treatment Preferences of Patients with Chronic Obstructive Pulmonary Disease: Results from Qualitative Interviews and Focus Groups in the United Kingdom, United States, and Germany

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Running Head: Treatment Preferences of Patients With COPD

Abbreviations: chronic obstructive pulmonary disease, COPD; short-acting β2-agonist, SABA; long-acting β2-agonist, LABA; long-acting muscarinic antagonist, LAMA; inhaled corticosteroid, ICS; Global Initiative for Chronic Obstructive Lung Disease, GOLD; single-inhaler triple therapy, SITT; multiple-inhaler triple therapy, MITT; discrete choice experiment, DCE; United Kingdom, UK; United States of America, USA; COPD Assessment Test, CAT; modified Medical Research Council, mMRC; health-related quality of life, HRQoL; standard deviation, SD.

Keywords: chronic obstructive pulmonary disease (COPD); discrete choice experiment (DCE); interview; qualitative research; treatment preferences; focus group; multi-country

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This article has an online data supplement.
Abstract

**Background:** A wide range of therapeutic regimens, including single-inhaler triple therapies (SITTs), are now available for the maintenance treatment of chronic obstructive pulmonary disease (COPD). Thus, an improved understanding of patient preferences may be valuable to inform physician prescribing decisions. This study was performed to assess the factors considered by patients when making decisions about their COPD treatments using qualitative techniques.

**Methods:** In the UK, USA, and Germany, individual qualitative interviews (n = 10 per country) and focus groups (one per country; [UK, n = 4; USA, n = 6; Germany, n = 6 participants]) were conducted. Interviews and focus groups were semi-structured, lasting approximately 60 minutes, and focused on treatment preferences. Data were analyzed according to emerging themes identified from the interviews; qualitative thematic analysis of the data was performed using specialist software.

**Results:** In interviews and focus groups, efficacy, ease of use, and lower frequency of use were favored attributes for current treatment, while side effects, medication taste, and more complex administration techniques were key dislikes. In interviews, most participants would consider a switch in medication, mainly for improved efficacy, but also to reduce medication frequency or following physician advice. Overall, efficacy and ease of use were the two most important attributes reported in interviews in all three countries.

**Conclusion:** Patients with COPD have preferences for certain attributes of medication, highlighting the multi-faceted nature of treatment effectiveness and the importance of the delivery device. These results were subsequently used to inform the design of a discrete choice experiment.
Introduction

Despite the availability of current treatments, chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality globally.\(^1\) Key clinical features of COPD are shortness of breath (dyspnea), cough, sputum overproduction, and exacerbations, which are defined as episodes of worsening respiratory symptoms.\(^1\,2\)

The aims of treatment for COPD are to alleviate symptoms, improve health status and exercise tolerance, and to reduce the frequency and severity of exacerbations.\(^1\) Currently, the main classes of inhaled treatment for COPD include β\(_2\)-adrenergic agonists (which may be short-acting [SABA] or long-acting [LABA]), long-acting muscarinic antagonists (LAMA), and inhaled corticosteroids (ICS).\(^1\) The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends triple therapy (ICS + LAMA + LABA) for patients who are on a LAMA/LABA or ICS/LABA treatment and continue to have exacerbations.\(^1\) Triple therapy with ICS + LAMA + LABA improves lung function, patient-reported outcomes, and, in particular, exacerbation risk versus ICS/LABA in patients with COPD.\(^3\,7\) Randomized clinical trials have also reported the benefit of triple therapy compared with LAMA monotherapy\(^8\) and LAMA/LABA combination therapy.\(^9\,10\)

Until recently, patients were required to use at least two inhalers to receive inhaled triple therapy; however, single-inhaler triple therapies (SITTs; ICS/LAMA/LABA) are now available.\(^11\,13\) Evidence shows that SITT provides patient benefits over multiple-inhaler triple therapy (MITT), including enhanced efficacy and lower direct costs.\(^14\,15\) Higher rates of treatment persistence and adherence have been reported for patients who use a single inhaler, compared with those who use multiple inhalers,\(^16\) potentially due to increased convenience and ease of use. Such increased...
adherence is related to better quality of life status among patients with COPD,\textsuperscript{17} and reduced healthcare resource utilization.\textsuperscript{18}

Given the wide variety of existing treatments for COPD, which can differ in terms of the regimen and number of inhalers, an improved understanding of patient preferences may inform physician prescribing decisions. Moreover, patient perceptions are a major factor in determining treatment compliance/adherence, which may impact on treatment efficacy and the risk of hospitalization.\textsuperscript{19-22}

One well-established method of evaluating patient preferences is a discrete choice experiment (DCE); a number of studies have previously utilized this approach to quantify preferences for COPD treatments from the perspectives of patients\textsuperscript{23-25} and nurses\textsuperscript{26} in different settings. Qualitative research is required to inform the development of a DCE.

The objective of this study was to identify relevant, patient-determined attributes of COPD treatment in the United Kingdom (UK), United States of America (USA), and Germany. The relative importance of each attribute, patient preferences, priorities, and treatment goals was also explored. While obtaining valuable qualitative data on treatment preferences, this information was also used to define the relevant attributes and levels for inclusion in a subsequent online DCE, which allowed a quantitative evaluation of patient preferences and relative importance of attributes of inhaled treatments for COPD. The methodology and results for this DCE have been reported in a separate publication.\textsuperscript{27}

Materials and Methods

Study Populations
Patients with a self-reported physician diagnosis of moderate-to-severe COPD were enrolled by a specialist recruitment agency (Global Perspectives) via the established channels in each country, including the recruiter's proprietary patient database, consumer recruiter networks, medical recruiter networks, support groups and nurses, as well as patient key opinion leaders and social media. Inclusion criteria were: a self-reported physician diagnosis of moderate-to-severe COPD, a COPD Assessment Test (CAT) score of ≥ 10 or a modified Medical Research Council (mMRC) Dyspnea Scale score of ≥ 2 at enrollment; current prescription of either an ICS/LABA, LABA/LAMA, or ICS + LABA + LAMA combination, or a LAMA alone; age ≥ 40 years; current residency in the UK, USA, or Germany; adequate written and oral fluency in the language of their country of residence; and the ability to participate in an interview or focus group, including access to the internet. Individuals were excluded if they had a current diagnosis of asthma (patients with a prior history of asthma were eligible if they had a current diagnosis of COPD) or any comorbidity that would inhibit their ability to provide informed consent or participate.

In this qualitative survey analysis, the sample size was determined according to data saturation i.e., no further interviews were conducted once no new themes or concepts were emerging. Data saturation was expected to be reached after approximately 15 interviews, therefore a total qualitative sample of 45 patients was expected to be adequate to reach data saturation for all three countries. If saturation was not reached, the sample number would have been increased accordingly. Saturation was assessed using a documented codebook approach and saturation tables, documenting the rigor of the qualitative methods.
Clinical experts were recruited via Global Perspectives, using a database of individuals who had previously taken part in research or had expressed interest in doing so. The recruited clinical experts were registered clinicians in the UK, USA, or Germany, specializing in respiratory medicine and currently treating patients with COPD.

Institutional review board (Salus IRB, Texas, USA) approval of the study protocol was obtained prior to commencement. Informed consent was obtained from all participants prior to study initiation.

**Development of Interview and Focus Group Discussion Guides**

A targeted literature review focusing on the use of SITT and MITT in COPD was used to structure qualitative interview guides and focus group discussion guides for the patient research (Supplementary Tables S1 and S2). In addition, three expert clinician interviews were conducted to obtain the perspective of treating physicians on relevant disease and treatment factors, including aspects of the patient experience of COPD, current treatment, patient satisfaction, ideal treatment attributes, and cost implications of treatment. This was used to refine the discussion guides intended for the patient research; no data are presented in this manuscript.

Interview topics covered the experience of current treatments, attitudes towards switching treatments, treatment preferences and priorities, treatment goals, symptoms, and health-related quality of life (HRQoL). Interview participants were also asked to individually provide what they consider to be the three most important attributes of COPD medication from a list (ease of use, effectiveness, frequency of use, speed of effect, impact on sleep, side effects, exacerbations, and cost) and rank...
them by importance on a scale of one to three, with one being the most important. Participants were also invited to comment on any additional important aspects of treatment that had not already been discussed.

**Participant Interviews and Focus Groups**

Eligible participants took part in a telephone interview or a face-to-face focus group conducted by experienced, trained interviewers from ICON plc. (UK and USA) or Global Perspectives (Germany). Interviews were conducted with a total of 30 participants, 10 from each country (UK, USA, and Germany), and three focus groups were conducted (one per country) with a total of 16 participants (UK, n = 4; USA, n = 6; Germany, n = 6). Interviews and focus groups followed distinct semi-structured interview guides and lasted approximately 60 minutes.

**Data Analysis**

All interviews and focus groups were audio recorded and transcribed verbatim. Each transcript was checked for quality and coded using a code book, in which codes were grouped under categories generated from topics in the interview guide. Qualitative thematic analysis of the interview data was performed by the study staff using specialist software (MAXQDA version 11, VERBI Software GmbH). The overall ranking of the top three attributes reported in the interviews was calculated by allocating a score based on each attribute’s rank, with a ranking of first, second, and third allocated scores of three, two, and one, respectively (the highest ranking of importance received the highest score). The cumulative score of each attribute was then calculated and used to rank the attributes in order of overall importance.
Results

Participant Characteristics

The demographics, clinical characteristics, and current medication of participants who took part in individual interviews (N = 30) and focus groups (N = 16) are presented in Table 1. Overall, participants had a mean (standard deviation [SD]) age of 56.9 (10.4) years and 52.8 (9.1) years in the interviews and focus groups, respectively. There was a similar proportion of male and female interview participants (53% and 47%, respectively), but participants were predominantly male in the focus groups (75% male versus 25% female). Regarding medication, participants were on a broad range of treatments; the most common treatments patients received as part of their regimen were ICS/LABA or SABA in individual interviews (50% each) and LAMA/LABA in the focus groups (63%). Some patients took more than one treatment.

Qualitative Results

The results presented in this section cover patients’ perceptions of their current treatments, attitudes towards switching treatments, and treatment preferences. Quantitative results related to the most frequently reported symptoms, HRQoL factors and other outcomes are provided in the Supplementary Materials (see Supplementary Figures S1 and S2), while illustrative participant quotes are shown in Table 2.

Perception of Current Medication
Across individual interviews, current treatments were reported and discussed. Approximately half of the interview participants (UK, n = 4/10; USA, n = 5/10; Germany, n = 6/10) stated that efficacy was the most important attribute of their medication(s). Similar proportions were reported in UK and USA focus groups, with 5 participants specifically referring to relief of symptoms. Around half of the interview participants (UK, n = 3/10; USA, n = 7/10; Germany, n = 4/10) also reported that they liked how easy their inhaler was to use, with 4 participants liking that they were able to see how many doses were left and three referring to the number of steps required to use their inhaler, with an apparent preference for fewer steps. 3 participants also stated that they liked the frequency with which they had to take their medication, 2 of whom took their medication once-daily. Similar responses regarding the frequency of medication use were reported in the UK and USA focus groups, with participants reporting that they preferred to take their medication once per day.

Regarding aspects of their current treatment that participants did not like, the largest proportion of participants stated side effects (n = 7 interviews and discussed by the UK and USA focus groups), followed by the taste of the medication (n = 5 interviews and discussed by the USA focus group), and the lack of user friendliness of the inhaler in the context of the number of steps required for use (n = 5 interviews). The next most disliked aspects were higher required frequency of use (n = 4 interviews), the powder formulation of their medication (n = 3 interviews), lack of efficacy (n = 3 interviews), and having to take medication in general (n = 3 interviews and discussed in the USA and German focus groups). A total of 18 interview participants spontaneously reported the occurrence and type of side effects they had experienced with their current and previous COPD treatment, including sore throat (n
= 5), headache (n = 4), and dry mouth (n = 3). In contrast, 12 interview participants did not think they had experienced any side effects. In the focus groups, reported side effects included dry mouth, sore throat, headache, thrush, “runny nose”, and hives. Although avoiding side effects was considered important, participants reported that they could accept them if their COPD symptoms were relieved. A large proportion of participants in the USA interviews (n = 9/10) and 5 participants each in Germany and the UK reported that they had concerns about their current medication, specifically regarding side effects (n = 10), tolerability (n = 7), and lack of efficacy (n = 5). A large proportion of interview participants across the three countries (n = 24/30) stated that they would be willing to switch medication, mostly in search of improved efficacy (n = 21), to reduce medication frequency (n = 7), on advice from their doctor (n = 6), to increase ease of use (n = 4), or to reduce cost (n = 4).

**Preferences for Attributes of Treatment**

Treatment preferences were also discussed. Illustrative participant quotes are presented in Table 2. Overall, a large proportion of interview participants (n = 25/27) across the countries referred to treatment effectiveness as either “important”, “very important”, or “extremely important”. When asked to define “treatment effectiveness”, 4 interview participants referred to a treatment that “works”, while other definitions were related to “symptom relief” (n = 16 interviews and discussed by the German focus group), and “speed of effect” (n = 14 interviews and discussed by the USA and German focus groups). References were also made to “exacerbations” (preventing occurrence and/or reducing the number/length; n = 5 interviews and discussed by the UK and USA focus groups), “improved HRQoL” (n = 5 interviews) and
“prevention of disease progression” (n = 5 interviews, plus the USA focus group).

Although preference for “speed of effect” of medication (rescue or maintenance) varied in interviews, “fast” (n = 6) and “immediately” (n = 5) were the most common responses.

Ease of use was reported in interviews to be an important aspect of medication; this included the number of steps required to use an inhaler (n = 13), with an apparent preference for fewer steps, and the size and shape of an inhaler (n = 10), with 8 participants stating a preference for a smaller inhaler. While the length of time that participants stated it took them to use their inhaler ranged from seconds (2–30 seconds, n = 12 interviews) to minutes (1 minute, n = 2 interviews; 2–5 minutes, n = 10 interviews), no participants stated that they had a problem with the length of time it took to use their device. Across the three countries, most interview participants (n = 26) stated that they would prefer to take their medication less often, with participants in the UK focus group stating once per day, while participants in the USA focus group stated a preference for less than once per day. The majority of interview participants indicated that they would prefer either a one- or two-inhaler treatment regimen (n = 19 interviews). The remainder would prefer not to use any inhalers (participants that preferred oral tablet formulations: n = 2), use three inhalers (n = 1), or did not specify a preference (n = 5).

Cost Implications

While medication costs vary greatly across and within countries, interview participants reported in general that they would be willing to pay more for their medication for increased efficacy (n = 16, plus participants in the UK, USA, and...
German focus groups), fewer, or no, side effects (n = 5), increased ease of use (n = 4), and once-a-day frequency (n = 4).

**Attribute Ranking**

When interview participants were asked to rank attributes of medication by importance, efficacy and ease of use were the two most important attributes in all three countries, with speed of effect (UK), cost (USA), and side effects (Germany) ranked third (Table 3).

**Attributes Identified as Relevant for the DCE**

Six treatment attributes were identified as being appropriate for inclusion in a subsequent DCE, each with three associated levels, indicated in parentheses. These were ease of use (likely to make no/some/a lot of mistakes); exacerbations (likely to have no exacerbations/1 exacerbation/2 exacerbations in the next year); number of times per day required to take the medication (1/2/3 times); number of inhalers (1/2/3); side effects (likely to experience no/some/a lot of side effects); and out-of-pocket costs per month (no change/5% decrease/10% decrease; Germany and USA only, as treatment cost is not relevant in the UK [most patients with COPD in the UK pay a standard per-prescription fee, regardless of treatment type]).

**Discussion**

This study provides a unique perspective and helps to further our understanding of the preferences that patients with COPD have for attributes of their treatment. It employed a cross-country analysis to understand if, and how, participant opinions
differ across different countries (UK, USA, and Germany), to provide a broader perspective compared with previous single-country studies. Focus groups were included to supplement the individual interviews and to allow further elaboration through patient–patient interactions.

As anticipated, individuals with COPD had preferences for certain attributes relating to improvement of their medication, the most prominent of which were efficacy in reducing symptoms, ease of use, few side effects, and fast onset of effect. While side effects are an important consideration and are preferably avoided, participants appeared willing to make a trade-off and accept some side effects if a medication could effectively reduce COPD symptoms. Most, but not all, participants indicated that they would be prepared to switch to a new treatment option with improved attributes, especially one offering enhanced efficacy and fewer side effects.

Responses were broadly similar between different countries, though there was some variation in preference for particular attributes. When asked to rank attributes by importance, efficacy and ease of use were the two most important in all three countries, though the attribute ranked third varied (speed of effect in the UK, cost in the USA, and side effects in Germany). Most interview participants stated that they would prefer to take their medication less often, though the UK focus group preferred once per day and the US group preferred less than once per day.

While the medication preferences of participants with COPD have previously been evaluated, the treatment landscape has since changed considerably. It is therefore important to re-evaluate participant preferences in the context of newer
treatments that offer the possibility of improved efficacy, more convenient dosing, and the need for fewer inhalers.

The importance of each of the positive attributes consistently identified across all three countries (efficacy in reducing symptoms, ease of use, few side effects, and fast onset of effect), along with other important factors highlighted in this study, such as frequency of use and cost, has previously been reported for individuals with COPD and asthma. Telephone interviews and focus groups of patients with asthma and COPD (N = 72) in a UK study revealed that treatment preferences were linked to reducing the impact of disease, with improved sleep, and speed of onset and duration of treatment effect highlighted as key factors of treatment. Quantitative findings from a study of adult patients with COPD (N = 300) in Germany investigating disease-related preferences also highlighted the importance of reducing disease impact, through reduced breathlessness, and improved sleep quality and performance capability. Conversely, onset, frequency of use, and the emotional effects of medication were considered to be of minor importance.

This study had some limitations. Participants self-reported a physician diagnosis of moderate-to-severe COPD coupled with CAT or mMRC dyspnea scores that indicated significantly impaired health status or breathlessness-induced disability: there was no clinician confirmation of the diagnosis for the study. However, a detailed screening script was employed by the recruiting agencies in order to avoid potential patient misrepresentation where possible. In addition, treatment patterns and symptoms described by the patients during the research were consistent with the COPD population, indicating the included patients represent an appropriate sample for this population.
The recruitment techniques, small patient samples and qualitative methodologies used mean that the results may be of limited generalizability to the wider COPD patient population. As an example, the gender of patients in the focus groups was predominantly male (75%), which may have affected the overall perception of the most important treatment attributes. It should be noted, however, that the results of the focus groups were similar to those from the individual interviews, in which gender was more balanced. Furthermore, the participants recruited for the interviews and focus groups were notably younger than the typical clinical population of patients with COPD: previous meta-analyses have estimated that COPD is most prevalent in older age groups (≥ 60 years of age), while the mean ages of the participants in these interviews and focus groups were 56.9 years and 52.8 years, respectively. For this reason, extrapolation of these preferences to older patient populations should be approached with caution. The subsequent DCE, informed by the present results, provides quantitative data on patient preferences and the relative importance of COPD treatment attributes in larger patient populations from the three countries and may therefore be expected to include a broader patient population and have greater generalizability.

Additionally, recruitment of participants from a database of individuals who had previously taken part in research, or had expressed interest in doing so, may have created selection bias, which again could limit the wider application of these findings. The proportions of patients with higher level education (30% and 50% in interviews and focus groups, respectively, had completed university) were greater than may be expected in a broad COPD population. In a previous DCE in patients with COPD, which recruited patients from an opt-in internet survey panel, levels of
higher education were similarly high, with 39% of patients having attended college and 31% of patients with a college or higher degree.\textsuperscript{36} Selection bias may have also had an impact on the diversity of patients who participated in the focus groups: patients with more severe COPD may not have been able or willing to travel to take part in these discussions.

In other studies, a sample size of 10 participants per country with a total of 30 may be considered small; however, as a qualitative survey analysis, the sample size was determined through assessment of saturation on the data already collected, as described by Kerr et al.\textsuperscript{28} A total of 45 patients for all three countries was expected to be sufficient to reach saturation but, in practice, saturation was reached with a population size of 30 patients (10 per country).

This study was conducted to elicit aspects of care that patients deem important. The results of our study also provide valuable insight into the parameters most appropriate for inclusion in a future DCE. A DCE is an effective quantitative method for evaluating treatment preferences. For example, a DCE performed in the USA (N = 515) reported that efficacy and safety were the most important attributes to COPD patients, and that less frequent use of rescue medication, overall ease of use, and perceived speed of effect were also important.\textsuperscript{29} Similarly, our study resulted in the inclusion of the following as attributes in our future DCE: number of exacerbations (efficacy), number of times per day medication is required (frequency of use), and side effects (safety), in addition to number of inhalers and ease of use.

**Conclusion**
This study provides a valuable up-to-date insight into the medication attributes that are important to patients with COPD in the UK, USA, and Germany, particularly given the availability of newer treatments such as SITT. Results indicate that for patients with COPD in these countries, efficacy and safety remain priorities, whilst also revealing the importance of ease and frequency of use, and number of inhalers required. These results informed the definition of relevant attributes and levels for inclusion in a subsequent online DCE, which provides further valuable information on treatment preferences of patients with COPD.

Patient perception of “treatment effectiveness” is multi-faceted, considering factors such as speed of onset/duration of effect, HRQoL, symptom relief, exacerbation reduction, and prevention of disease progression. Healthcare providers should support patients by considering the key attributes that are important to each individual, with the aim of improving adherence and thus overall treatment effectiveness.
Acknowledgments
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Author contributions
Author contributions were as follows: MS, KH, LE, NG, JM, PJ, and ASI take responsibility for the study conception or design. MS, KH, LE, SB, JM, and ASI take responsibility for data collection. All authors take responsibility for data analysis or interpretation, writing/reviewing, and final approval of the manuscript.

Declaration of Interest
The authors declare the following conflicts of interest during the last 3 years in relation to this article: MS, ASI, NG, and PJ are employees of, and hold shares in, GlaxoSmithKline plc. ASI is also unpaid faculty at McMaster University, Canada. SB,
LE, KH, and JM were employees of ICON plc. while the study was conducted. ICON plc. received funding from GlaxoSmithKline plc. to conduct this study but were not paid for the development of this publication.
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disease illness and medication beliefs are associated with medication

and quantification of treatment preferences for patients with asthma or COPD
using discrete choice experiment surveys. Respir Med. 2017;132:76-83. doi:

inhaler attributes in asthma and chronic obstructive pulmonary disease in
10.1186/s12890-017-0439-x.


Table 1. Demographics, Clinical Characteristics, and Current Medication of Patients in the Individual Interviews and Focus Groups

<table>
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<th>Characteristic</th>
<th>Interviews (N = 30)</th>
<th>Focus Groups (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age, years</td>
<td>56.9 (10.4)</td>
<td>52.8 (9.1)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
<td>16 (53)</td>
<td>12 (75)</td>
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<tr>
<td>Female</td>
<td>14 (47)</td>
<td>4 (25)</td>
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<tr>
<td>Ethnicity, n (%)</td>
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<tr>
<td>White or Caucasian</td>
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<td>12 (75)</td>
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</tr>
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<td>Hispanic or Latino</td>
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<td>0 (0)</td>
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<tr>
<td>Employment status, n (%)</td>
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<tr>
<td>Employed full-time</td>
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<td>9 (56)</td>
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</tr>
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<td>Retired</td>
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<td>3 (19)</td>
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<td>Stay-at-home</td>
<td>2 (7)</td>
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<tr>
<td>Other</td>
<td>0 (0)</td>
<td>1 (6)</td>
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<tr>
<td>Marital status, n (%)</td>
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<tr>
<td>----------------------</td>
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<tr>
<td>Married</td>
<td>17 (57)</td>
<td>8 (50)</td>
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<td>Divorced/separated</td>
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<td>0 (0)</td>
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<td>1 (3)</td>
<td>2 (13)</td>
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<tr>
<td>Widowed</td>
<td>1 (3)</td>
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<tr>
<td>Single</td>
<td>7 (23)</td>
<td>6 (38)</td>
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<thead>
<tr>
<th>Highest level of education, n (%)</th>
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<tbody>
<tr>
<td>No formal education</td>
<td>2 (7)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Left school at 16 with qualifications</td>
<td>1 (3)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>Left school at 18 with qualifications</td>
<td>7 (23)</td>
<td>0 (0)</td>
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<tr>
<td>Technical/vocational qualifications from a college or job</td>
<td>10 (33)</td>
<td>2 (13)</td>
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<tr>
<td>Completed university</td>
<td>9 (30)</td>
<td>8 (50)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3)</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smoker, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>6 (20)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>No</td>
<td>3 (10)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Former</td>
<td>21 (70)</td>
<td>13 (81)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pet owner, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>11 (37)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>No</td>
<td>15 (50)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Former</td>
<td>4 (13)</td>
<td>4 (25)</td>
</tr>
</tbody>
</table>
Median (range) time since diagnosis, years | 5 (1–20) | 5 (0.75–21)

Current medication, n (%)

<table>
<thead>
<tr>
<th>Medication</th>
<th>UK (n)</th>
<th>USA (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS/LABA</td>
<td>15 (50)</td>
<td>7 (44)</td>
</tr>
<tr>
<td>LAMA/LABA</td>
<td>5 (17)</td>
<td>10 (63)</td>
</tr>
<tr>
<td>LABA</td>
<td>8 (27)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>LAMA</td>
<td>9 (30)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>ICS</td>
<td>2 (7)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>SABA</td>
<td>15 (50)</td>
<td>3 (19)</td>
</tr>
</tbody>
</table>

ICS=inhaled corticosteroid; LABA=long-acting β2-agonist; LAMA=long-acting muscarinic antagonist; SABA=short-acting β2-agonist; SD=standard deviation

Table 2. Illustrative Patient Quotes

<table>
<thead>
<tr>
<th>Topic</th>
<th>Example Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
</tbody>
</table>
| Description | “Lightheaded and very chesty, very ‘mucusy’ in the chest, that type of thing. That is it, in the main, really” (UK).
|        | “My main symptoms are definitely – and I’m probably going to cough through this interview, so you’ll have to excuse me. It’s definitely coughing and being out of breath, heaviness in my chest, wheezing, particularly if I do anything in any way physical that I don’t usually do” (USA).
|        | “And my lungs generally frequently don’t feel clear. You know, I always feel like you could clear your throat but, you know, I feel like I have something in it. I seem to start getting, like, chest
infections more frequently, but then I get real careful when that occurs” (USA).

“I would – you know, generally I feel weak” (USA).

<table>
<thead>
<tr>
<th>HRQoL</th>
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</table>
| “If I was very breathless, yes, it would be every time. Like, even putting on my socks and shoes, I struggle because I feel as if my stomach’s squashing my lungs. That would be the best way to describe it” (UK).

“Generally, I fall asleep easily and I have a deep sleep but sometimes I suddenly wake up and have a coughing attack. Everything is congested with mucus and I have to get up. Sometimes I am awake up to 1 hour and I have to take my medication. This is really disturbing and I experience it about 5 to 6 times per week. Maybe there is one night when I have a good night’s sleep” (Germany).

“Well, I can’t be involved too much with any physical activity that’s, like, sports related. I can’t play basketball. I mean, I don’t even try. I mean, I tried and it just makes me, you know, wheeze, you know, out of breath. And I couldn’t do hikes and I can’t do, like, I can’t do any sprints, but I can do, like, light jogging, but I can’t do it for a long period of time and can only do – so very limited. It just restricts my activities. So, it’s – that’s frustrating to me. I don’t like that” (USA focus group).
“I go to a lot of family events. I’ve got – I belong to a big family and when you’re having, yeah, you know, a flare-up, it’s embarrassing. You have to go away, because they, “Hey, is he okay, is everything – should we call 911?” I’m like, “No, I’m okay.” And then to have to explain that, that’s a little bit tiring and it’s embarrassing” (USA focus group).

“I mean, you guys, I don’t know anybody here, but I’m just going to throw it out there because…I have a great wife, but it’s like one in 4 times, or one, maybe 2 times, it’s like, I – you know, the issue with – like, I really feel like something’s squeezing my – something and it’s, like, it won’t – I want to, like, take something and the medicine doesn’t affect it, but there’s something squeezing my airways and it’s like I’m trapped. That’s how I feel and like she said, you know, it causes the panic, you know. But that’s the – that’s probably the worst thing for me is that part of – that aspect of it, ‘cause it’s like, I got – if I didn’t have a patient wife, I’d be divorced, you know. Actually, I’m just throwing it out there” (USA focus group).

<table>
<thead>
<tr>
<th>Current Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
</tr>
<tr>
<td>&quot;Yeah, it’s – one of the things I do like about it is, I take it once a day. It’s pretty easy to take. You just, kind of, flip it open, breathe in slowly, and count to, like, I don’t know, five or seven</td>
</tr>
</tbody>
</table>
and then breathe out and that is my, what I call my maintenance inhaler” (USA).

“Well, I take a – I use a pump and really, I mean, it does work and it’s not curing the COPD, but it’s clearing the airways so I can start to breathe properly. So, yes, it’s – but it is a, sort of, Elastoplast cure, isn’t it?” (UK focus group).

“I’m okay about using it, but I really don’t see the effects from it, whether it’s because I’m taking it and it is having [an] effect and I don’t realize it” (UK).

“Well, you know, I mean, it’s like the best thing that I have to use right now. There’s nothing better that I have” (USA).

“Concerns? Rather not. I don’t worry too much about it, I hope in the back of my mind that the pharmaceutical industry will produce pharmaceuticals soon, which are maybe more effective, better, with better results” (Germany).

[Anything else about it that concerns you?] “No, not necessarily, ’cause that would be, like, my main concern, you know, like bad side effects of course” (USA).

“I think that it’s always a concern with everybody is that your body’s going to start to become immune to it, because it’s, you know, it’s so used to it that it’s not going to function anymore with it” (USA).
### Switching

“Well, right now you would have to prove to me that this new drug would have some big improvement over what I’m feeling now […] I would have more energy. I’d be able to breathe better […] you take it once a day. The benefit for me would be taking it once a day, or if it’s some kind of release, where it was released over time” (USA).

“No, just if somebody said to me there’s a new medicine they’re trying out that they say that it’s very good and it’s more beneficial, I’d be begging for it” (UK).

“I would switch treatments if they could find a treatment that would cure it. But otherwise, there’s no point in me switching treatments, ‘cause what I’m taking once a day does work. So, it’s – yeah. So, unless they’re going to come up with something that actually – and so far, they haven’t come up with anything that cures it totally” (UK focus group).

### Treatment Preferences

| Treatment effectiveness | “I mean, if it’s not effective then what’s the point, you know?”
|-------------------------|---------------------------------------------------------------------
<p>|                         | (USA).                                                              |
|                         | “Oh, that [treatment effectiveness], 100 out of 100. I mean, that’s what it’s really all about” (USA). |
| Exacerbations           | “I mean, that’s the main thing, trying to avoid a flare-up, you know?” (UK focus group). |</p>
<table>
<thead>
<tr>
<th>Ease of use</th>
<th>“Yeah, I mean, the inhaler ease of use, it’s got to be easy to use, you know, ‘cause it’s not – yeah, it’s got to be easy to use. It’s your breathing, you know…” (UK focus group). “Not having to prick it but only open something, breathe in, and close it and be done” (Germany).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication frequency</td>
<td>“I wish I didn’t have to take it every day. I wish – I’m happy that it’s only once a day, compared to 2 times a day or 3 times a day, so that part I’m happy with. I wish I could take it once a week. I wish I could take it once a month. That would make me even happier. You know, that’s another thing psychologically, every time I take it, it reminds me that I have this medical disease. It just reminds me again that I’m living with this, which is a real downer” (USA).</td>
</tr>
<tr>
<td>Number of inhalers</td>
<td>“Now I got three different pharmaceuticals applied with three different inhalers, naturally it would be better to take only one inhaler and one pharmaceutical” (Germany).</td>
</tr>
<tr>
<td>Side effects</td>
<td>“I’m not really too bothered about side effects and I would rather cope with side effects than cope with breathlessness” (UK).</td>
</tr>
</tbody>
</table>
“Nobody needs side effects because the disease itself keeps you busy enough and if you additionally have to deal with side effects it would be tough as you would have to decide with which you deal first: your disease or the side effects” (Germany).

| Costs       | “A little more money for a lot more efficiency, sure. A little bit of money – ‘cause money is a huge factor” (USA focus group). |

*quotes are from individual interviews unless otherwise indicated

COPD=chronic obstructive pulmonary disease; HRQoL=health-related quality of life; UK=United Kingdom; USA=United States of America
Table 3. Ranking of COPD Treatment Attributes by Country From Individual Interviews

<table>
<thead>
<tr>
<th>Rank</th>
<th>UK</th>
<th>USA</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ease of use</td>
<td>Efficacy</td>
<td>Efficacy</td>
</tr>
<tr>
<td>2</td>
<td>Efficacy</td>
<td>Ease of use</td>
<td>Ease of use</td>
</tr>
<tr>
<td>3</td>
<td>Speed of effect</td>
<td>Cost</td>
<td>Side effects</td>
</tr>
<tr>
<td>4</td>
<td>Medication frequency</td>
<td>Side effects</td>
<td>Reduction of sleep disturbance</td>
</tr>
<tr>
<td>5</td>
<td>Reduction of exacerbation frequency</td>
<td>Speed of effect</td>
<td>Reduction of exacerbation frequency</td>
</tr>
<tr>
<td>6</td>
<td>Number of inhalers</td>
<td>Reduction of sleep disturbance</td>
<td>Medication frequency</td>
</tr>
<tr>
<td>7</td>
<td>Reduction of sleep disturbance</td>
<td>Reduction of exacerbation frequency</td>
<td>Speed of effect</td>
</tr>
<tr>
<td>8</td>
<td>Side effects</td>
<td>Cost</td>
<td></td>
</tr>
</tbody>
</table>

Not ranked by any patient: Cost, Medication frequency, Number of inhalers

Ease of use and efficacy were ranked first or second in each country (underlined)

Not all patients provided three attributes
Supplementary Materials

Results

Participant Responses – Symptoms

Across the individual interviews, a range of symptoms was reported (see Figure S1; illustrative participant quotes are also provided in Table 2 in the main manuscript). Shortness of breath was most commonly reported as a main symptom (n = 29 [n = 28 spontaneously reported]), followed by cough (n = 27 [n = 12 spontaneously reported]), and mucus (n = 22 [n = 11 spontaneously reported]) (Figure S1). Shortness of breath was the most concerning and most frequent symptom reported in all three countries (concerning: n = 16 [UK, n = 5; USA, n = 8; Germany, n = 3]; frequent: n = 14 [UK, n = 4; USA, n = 5; Germany, n = 5; data not shown]).

When describing exacerbations and reported symptoms, the terminology for “frequency” and “duration” varied across the individual interviews and focus groups. Five out of the 10 participants who spontaneously reported an “exacerbation” referred to a worsening of their symptoms, which required hospitalization, antibiotics, and/or steroids, that lasted more than 1 day and occurred between once every few weeks to once or twice per year. The remaining 5 participants referred to episodes of shorter duration (up to half an hour or until a rescue medication was used), which occurred between 3 times per month to once or twice per year.

Participant Responses – Health-Related Quality of Life (HRQoL)
A range of different impacts of chronic obstructive pulmonary disease (COPD) on everyday life were described by participants in the individual interviews. Most common was the impact on the ability to carry out physical activities, followed by social life and sleep (Table 2 in the main manuscript and Figure S2). Physical activities impacted by COPD included walking (n = 14), climbing stairs/steps (n = 12), running (n = 10), walking uphill (n = 7), playing football (n = 3), playing golf (n = 2), and a range of other sports/activities (n = 1 each). Participants reported that coughing (n = 10), breathing difficulties (n = 8), wheezing (n = 5), and chest tightness (n = 1) were the symptoms that impacted their sleep. COPD was reported to impair sleep in two main ways: waking up (n = 17 [UK, n = 6; USA, n = 8; Germany, n = 3]) and difficulty getting to sleep (n = 3 [n = 1 in each country]). In addition to coughing, wheezing, and difficulty breathing, one participant from the UK stated that the “fear of losing your breath” also kept them awake.

Participant Responses – Other Outcomes

Notable results from the UK focus group were that participants would like a dose counter on inhalers and increased monitoring between visits to the doctor. While they stated that pharmacies were useful to discuss their condition, they believed that pharmacists lacked “COPD training”. In the USA, participants highlighted the benefit of a “pulmonary physical therapy program/pulmonary respiratory program”, the desire for an inhaler where the user does not have to rinse their mouth after use, and a desire for alternatives to an inhaler (e.g., a pill or an injection). Comparatively, participants in Germany discussed the benefit of “lung sport” (a special sport for pulmonary diseased people), a similar desire for an alternative to an inhaler (e.g., a
pill) and the categorization of medications by insurance companies into a “completely unsuitable category of agents”, which impacted on whether medications were available to patients living with COPD.
Figure S1. Most Frequently Reported Main Symptoms in Individual Interviews
(N = 30; n = 10 per country)

SoB=shortness of breath; UK=United Kingdom; USA=United States of America

*a*chest tightness, pain, or pressure
Figure S2. Impacts of COPD on Daily Life Reported in Individual Interviews (N = 30; n = 10 per country)

ADL = activities of daily living; COPD = chronic obstructive pulmonary disease;
UK = United Kingdom; USA = United States of America
## Table S1. Qualitative Individual Interview Guide

### Symptoms

1. When were you formally diagnosed with COPD?

2. How is your condition at the moment?

3. What are the main symptoms that you experience with COPD? *(Probe into any of the symptoms below which have not already been mentioned by participant.)*
   - Shortness of breath
   - Coughing
   - Coughing up mucus (can change color/thickness during exacerbation)
   - Wheezing
   - Chest tightness, pain, or pressure
   - Trouble sleeping
   - Frequent chest infections

4. Which symptom concerns you the most?
   a) Why?

5. Which symptoms do you experience the most frequently?

6. Which symptoms are the least frequent?

### HRQoL

7. How does COPD affect your everyday life? *(Probe into any impacts below which have not already been mentioned by participant.)*
- Physical activities – ability to exercise, climbing stairs, walkable distance
- Social life – ability to visit family and socialize with friends, join social clubs
- Hobbies – ability to do all desired activities
- Sleep – effect of COPD on sleep, ability to sleep through the night
- Psychological – depression, fear of exacerbations

8. What are the reasons why you cannot do [insert activity]? [Probe: physical restrictions of COPD or psychological (e.g., fear of exacerbation, worried or embarrassed about taking medication).]

9. How have these impacts changed over time since you were diagnosed?
   a) When did you first notice [insert activity] was becoming more difficult to do?
   b) How did the change start?
   c) How does this make you feel?

Current Treatment

We are now going to talk about the treatments that you currently take for your COPD. These can either be long-term treatments which are taken primarily to prevent a recurrence of your symptoms, or short-term rescue/relief treatments which you take when your symptoms may have become particularly bad, this is often referred to as a flare-up or an exacerbation of symptoms. First, I would like to find out about your long-term/preventer medication.

10. How do you feel about using your current long-term/preventer medication?
a) How do you feel about the way it controls your COPD symptoms?

b) What do you like about your current medication?

c) What do you dislike about your current medication?

d) Have you ever been on a different type of treatment than your current one? [Probe for oral tablet, inhaler, other.]

   i. How does it compare? [Probe: dosage frequency, symptom-free period, side effects, taste, ease of use.]

11. Do you feel that your current medication works well to manage your COPD symptoms?

   a) Do you ever worry about your medication not working?

      i. Why?

12. How often has your doctor told you that you should take the treatment? [If the participant takes more than one treatment, ask for all.]

13. At times, some people miss taking their medication as often as their doctors has told them to take it, for a range of different reasons. Have you ever missed taking your preventer medication?

   a) [If Yes:] How often do you miss taking your medication? What are the reasons you have missed taking your medication?

   b) Does taking your medication affect your daily routine? [Probe for: differences between weekdays and weekends, during holidays.]

   c) Are there any times that you are more or less likely to miss a dose?

14. Are there any features of your medication that affect how you take your
medication? [Probe for taste, side effects.]

15. How often do you or your doctor discuss your treatment and how it is going for you?
   a) How do you feel about how often you have these discussions?
   b) Considering your current situation, how willing to switch to a new therapy would you be?
      i. What would influence your willingness to switch?

16. Next I want to discuss your reliever/rescue medication. Do you ever need to use a reliever/rescue medication?
   a) How often do you need it? [Probe: frequency, e.g., daily, weekly, monthly, every 3 months.]
   b) Can you describe the kinds of situations when you typically need rescue medication?
   c) How well does the reliever/rescue medication work to manage your symptoms?
   d) How quickly does your treatment take effect, i.e., you have relief of symptoms?

17. Overall, do you have any other concerns about your medication(s)? [Probe for potential side effects, becoming tolerant, how often they need to take the medication, picking up infections.]
[If not already done so, ask participant if they would like to take a break. Pause recorders if necessary – inform participant if/when recorders have been stopped and restarted.]

Treatment Preferences

Now I would like to ask you about how important different aspects of COPD treatment are to you if you had a range of treatments to choose between.

18. How important is it that your inhaler is easy to use?
   a) Is your current inhaler(s) easy to use?
   b) How long does it take to use each time you take your treatment?
      i. How do you feel about this?

19. How important is treatment effectiveness to you?
   a) What does ‘effective treatment’ mean to you?
   b) How long do you have relief from your symptoms (i.e., no shortness of breath or difficulty in breathing) when you use your current treatment?
      [Probe: hours, days.]
   c) Do you always have relief from your symptoms for the same periods of time?
      i. If not, please describe.
   d) Are there times during the day/week that your COPD symptoms seem better controlled? [Probe: mornings versus evenings, weekdays versus weekends.]

20. How important is how often that you are supposed to take your
maintenance/preventer medication?

a) Would you prefer to take medication more or less often? Why?
b) Are there specific times of the day when you prefer to take your medication?
c) How do you feel about taking your medication in public or in front of friends/family?

21. How important is the number of inhalers that you have to use?

a) How many inhalers do you currently need to use as part of your COPD treatment?
b) What would be your ideal number of inhalers?

22. How important is the speed with which you can feel the medication working?

a) How quickly can you feel your treatment take effect, i.e., you have relief of symptoms? [Probe: specific length of time, e.g., 15 min, 30 min, 1 hour.]
b) How is this different for rescue and maintenance medication?

23. How important is it that COPD does not disturb or wake you during the night?

a) Is your sleep impacted by your COPD? If so, how?
b) Do you ever wake up in the night needing your medication? If yes, please describe.
   i. Does your medication give you relief?

24. How important are side effects to you?

a) Do you experience any side effects due to treatment? [Probe: dry mouth,
hoarseness, sore throat/tongue, thrush, nausea, headache, skin effects, pneumonia, tremor, other.

i. If yes, please describe [Probe: frequency, severity.]

b) How do these side effects impact your daily life? [Ask for each side effect.]

c) Are you anxious of side effects potentially occurring?

25. How important is avoiding exacerbations of your COPD to you?

a) Do you ever experience flares/severe attacks/exacerbations due to COPD? An exacerbation is when your symptoms may have become particularly bad, this often referred to as a flare or an exacerbation of symptoms.

b) Which symptoms do you experience?

c) How long do you experience them for?

d) How often do you experience an exacerbation?

e) What is the outcome of a typical attack? [Probe: calling for a doctor, need to go to hospital, other.]

f) Has an exacerbation or hospitalization ever led to a change in treatment?

g) How does an exacerbation impact you? [Probe: emotional impact, activities they are unable to do.]

h) Are you anxious of exacerbations potentially occurring?

26. How important is cost of medication/prescription to you?

a) How do you currently pay for your medication? [Probe on insurance, co-payments.]
b) Does this impact on how often you take your medication?

c) [If participant does not pay:] Would you be willing to pay for your medication? If so, for what reasons? [Probe for ease of use, symptom control, frequency, speed of relief, sleep, side effects etc.]

d) [If participant does pay:] Would you be willing to pay more for your medication? If so, for what reasons? [Probe for ease of use, symptom control, frequency, speed of relief, sleep, side effects etc.]

27. So far we have discussed how easy it is to use your inhaler, treatment effectiveness, how often you take your medication, speed of feeling relief, sleep disturbance, side effects, exacerbations of your COPD, and cost. Out of those, which three aspects do you consider to be the most important in terms of your COPD treatment?

28. In addition to those we have discussed [list aspects again if necessary], do you think there are any aspects that may be important and we haven’t discussed today? [Probe: why are they important?]

29. That’s all of my questions. Is there something else you would like to talk about in relation to your COPD treatment and lifestyle or do you have any other questions or concluding remarks?

[Text] are cues for the interviewer

COPD=chronic obstructive pulmonary disease; HRQoL=health-related quality of life
Table S2. Focus Group Discussion Guide

Instructions

1. First, I would like to start by going around the group; please could you tell me your first name and complete this sentence “My COPD is…” using one or a few words. [Proceed with introductions.]

Symptoms

2. Can you describe the main symptoms that you experience with COPD?

Symptoms to probe for:
- Shortness of breath
- Coughing
- Coughing up mucus (can change colour/thickness during exacerbation)
- Wheezing
- Chest tightness, pain or pressure
- Trouble sleeping
- Frequent chest infections

3. Which of these symptoms are the most severe to you or affects your life the most?

HRQoL

4. How does COPD or the treatments you have to take for it affect your everyday life? [Probe into any impacts below which have not already been mentioned. Also, probe for reasons they can/cannot do things; due to physical restrictions]
of COPD or psychological (e.g., worried or embarrassed about having taking medication, their moods/emotions).]

- Physical activities – ability to exercise, climbing stairs, walkable distance
- Social life – ability to visit family and socialize with friends, join social clubs
- Hobbies – ability to do all desired activities
- Sleep – effect of COPD on sleep, ability to sleep through the night
- Psychological – depression, fear of exacerbations

5. What is the worst aspect of having COPD? [Can include anything including the symptoms, HRQoL impacts, tasks or activities they find difficult or are unable to do or aspects of treatment they do not like about their treatment.]

Current Treatment

We are now going to talk about the treatments that you currently take for your COPD. These can either be long-term treatments which are taken primarily to prevent a recurrence of your symptoms, or short-term rescue/relief treatments which you take when your symptoms may have become particularly bad; this is often referred to as a flare or an exacerbation of symptoms.

6. How do you feel about using your current treatment? When answering please let us know which kind of treatment you use (for example oral versus inhaler, more than one treatment).

   a) What are the main factors that you like about your current treatment?
   b) What are the main factors that you dislike about your current treatment?
c) What would be the main thing(s) you would like to change about your current treatment?

d) How often do you have to use additional medication to control your symptoms during a flare up/exacerbation?

i. How does this affect you?

e) Considering your current situation, how willing to switch to a new therapy would you be?

**Treatment Preferences**

Now, thinking about your current medication, I would like to discuss how important different aspects of COPD treatment are to you. *Use the following list to allow discussion and probe for why they are important/not important.*

- Inhaler ease of use
- Treatment effectiveness *Probe: what does treatment effectiveness mean to you?*
- Frequency that you are supposed to take your medication
- The number of inhalers you have to use as part of your COPD treatment
- How quickly you can feel your medication working
- Being disturbed or woken up during the night due to your COPD
- Treatment side effects
- Avoiding exacerbations
- Cost of medication/prescription

7. Do you think there are any aspects that may be important about COPD and the
treatment of COPD that we haven’t discussed here today?

8. To close the focus group, we will go around the group again. I would like you to imagine an ideal treatment which would have all the best aspects in it for you and tell the group one or two of those best aspects. This can be anything that we have discussed, or any other aspects that come to mind.

[Text] are cues for the interviewer

COPD=chronic obstructive pulmonary disease; HRQoL=health-related quality of life