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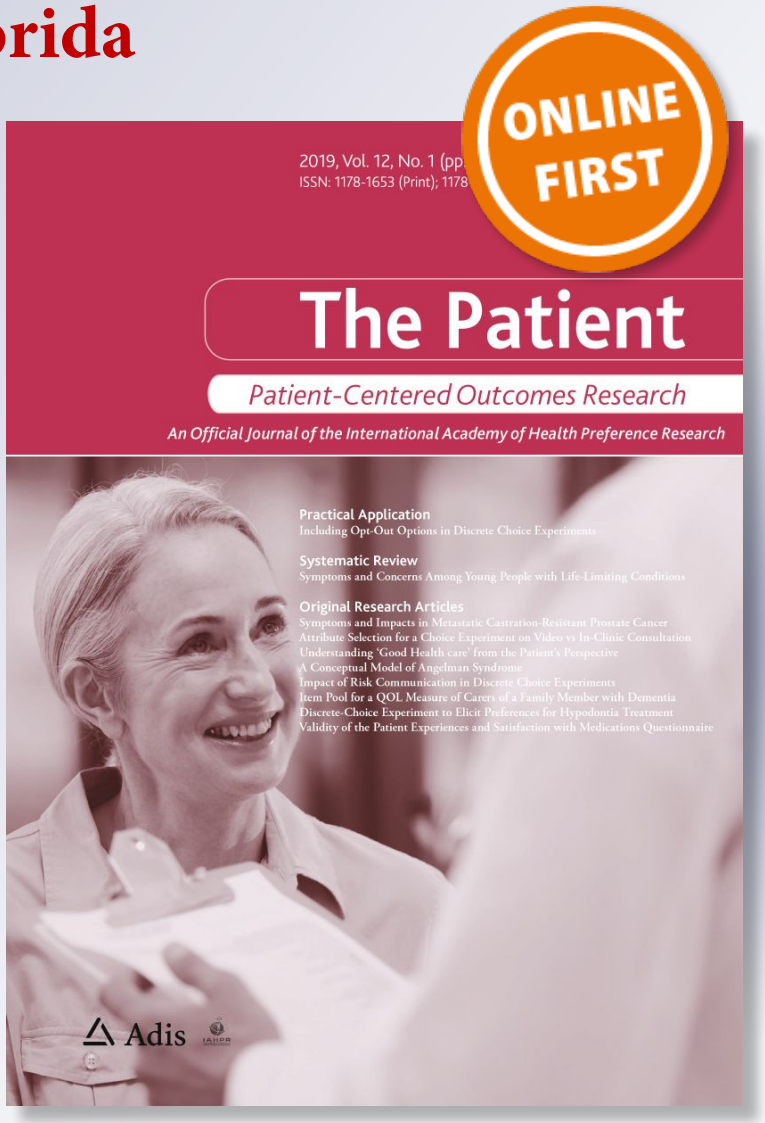

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ORIGINAL RESEARCH ARTICLE

Preferences for Use and Design of Electronic Patient-Reported Outcomes in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Objectives Collection of patient-reported outcome (PRO) measures is critical to fully understand chronic obstructive pulmonary disease (COPD) management and progression, as the impact on health-related quality of life is not well understood by objective measures alone. Electronic PROs (ePROs) are increasingly used because of their advantages over paper data collection, including elimination of transcription errors, increased accuracy and data quality, real-time data reporting, and increased compliance. The objective of this study was to characterize how patients with COPD prefer to use various types of technology to report disease symptoms, and their preferences for ePRO design and display.

Methods The sample consisted of subjects with COPD ($N = 103$) who completed in-person surveys on their ePRO preferences.

Results The majority of subjects prefer to use a form of electronic media over paper to report their disease symptoms. Of these electronic methods, subjects most often prefer to use a smartphone provided by their physician. Subjects were also interested in ePRO features, such as knowing estimated PRO completion time at the outset, tracking their progress in real time as they complete a questionnaire, seeing the data that they report in order to track their health status, being encouraged to complete their diary if they fall behind by positive messaging, and being thanked for their completion of a daily diary.

Conclusions Investigators should consider including these preferences when designing ePRO assessments. Incorporating patient preferences for ePRO design can ultimately help reduce patient burden and increase engagement, compliance, and improve data quality.

Key Points

Patients with chronic obstructive pulmonary disease (COPD) prefer to report disease symptoms using electronic methods versus paper methods.

Patients with COPD have preferences for the design and display of electronic patient-reported outcomes.

Clinical practice and clinical research trials should consider using electronic patient-reported outcomes to help decrease patient burden and increase compliance.

1 Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death worldwide and has a significant impact on patient quality of life [1, 2]. The principal methods for diagnosis and disease progression are lung function tests, such as spirometry, but these do not take into account the full impact of the disease on patient health status [2]. COPD has a major impact on patient activity levels, quality of life, and general well-being, which only show a weak correlation with objective measures such as lung function [3]. Self-reported health status is especially critical for chronic and progressive diseases like COPD because symptoms are not fully reversible with treatment and the impact on patient health-related quality of life can be life-long [2]. Therefore, collecting patient-reported outcome (PRO) measures in addition to objective measures is critical to get a more accurate picture of patients' health status.

Given the importance of PROs in documenting health status from the patients' perspective, integration of PROs into clinical practice is gaining increased attention [4]. In

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particular, PRO measures in COPD are important for both disease management in clinical practice and treatment success in clinical trials, and are recommended by both regulators and key opinion leaders [2, 5]. As PROs in COPD are becoming standard in both avenues, electronic data capture has become critical as a valid and reliable way to collect PRO measures [6–9]. Electronic methods can include smartphones provided to subjects in a trial, applications (apps) downloaded on a personal device, or web-based systems accessed via laptop or desktop computer. Electronic PROs (ePROs) have many advantages over paper, including elimination of transcription errors, increased accuracy, date- and time-stamped data, higher compliance, less missing data, and are recommended by regulatory agencies [10–16]. The use of ePRO assessments is both feasible and reliable in COPD clinical trials, showing 80–94% compliance rates for daily at-home diaries [7, 9]. ePRO has also successfully alerted providers of COPD subjects at risk of exacerbations [6, 8, 17]. Given the chronic nature of COPD and the importance of patient-reported health status for COPD disease management, it is crucial to have accurate and reliable measures of disease progress, and ePRO technology is a practical and valuable tool to accomplish this.

When using ePRO technology, it is important to consider usability and patient preference in order to maximize patient compliance and data quality. This is especially critical when using ePRO in clinical trials, where patient compliance and accurate data collection is imperative for evaluating evidence of treatment efficacy (i.e., endpoints) for drug approval. Whether an ePRO assessment is de novo or migrated from a validated paper form, the design and implementation of the assessment should follow ePRO best practices and recommendations [18]. The format and display of assessments should ideally improve usability, increase understanding, and motivate subjects to complete the assessment. The objective of this study was to characterize how patients with COPD prefer to use various types of technology to complete ePROs in a clinical trial. We aimed to characterize the preferences for specific aspects of ePRO display, including wording emphasis, question format, screen layout, and real-time feedback on completion time, progress, and compliance. Incorporating patient preferences to improve usability of ePRO in COPD clinical trials could ultimately reduce subject burden, improve compliance even further, and increase data quality.

2 Methods

2.1 Recruitment and Study Population

Subjects with COPD were recruited from the Boston area via online and newspaper advertisements. Eligible subjects were 18 years or older and able to complete in-person surveys alone and in English. All subjects reported that they had been told by a doctor or health professional that they had COPD. Subjects were excluded if they reported having a traumatic brain injury, dementia, schizophrenia, psychoses, or had current alcohol or drug dependence. Subjects provided a signed informed consent form that indicated an understanding of the study objectives and procedures and a willingness to participate. This study was approved by Copernicus Group IRB.

2.2 Study Design and Statistical Analysis

Subjects completed paper questionnaires that asked questions about demographics, experience with technology, and preference for technology in clinical trials. See Online Resource 1 (electronic supplementary material [ESM]) for questions examined in the current study. All questionnaires were developed by the authors. Subjects answered questions about their preference for how to report disease symptoms in a clinical trial (i.e., different types of electronic methodologies versus paper), what time of day they prefer to complete daily questionnaires, and whether audible alarms would be a helpful reminder to complete diaries or take medication. Subjects were also asked about their preference for ePRO design and display (i.e., text and screen formatting), and about their preference for types of real-time feedback they might receive on an ePRO device (i.e., questionnaire progress, compliance rate, health progress, and thank you screens). Variables were evaluated using a chi-square test. $p < 0.05$ was considered statistically significant.

3 Results

3.1 Demographics and Technology Experience

A total of 129 subjects were screened, and 103 subjects completed the study. See Table 1 for subject demographics and experience with technology. Subjects ranged from 32 to 86 years of age (median 55 years) and 55% were female. Almost half of subjects (44%) have a computer at home and 41% own a smartphone. Forty-two percent of subjects reported using the internet daily or weekly, while 43% reported not using the internet at all. Half of subjects (50%) have participated in a clinical trial.

3.2 Preference for the Use of Electronic Patient-Reported Outcome (ePRO) Measures in Clinical Trials

Subjects were asked how they would like to report their disease symptoms if they were reporting symptoms once a day for a clinical trial. Preference for how to report disease

Table 1 Subject demographics and experience with technology ($N = 103$)

Characteristic	*N* (%)
Age	
Median = 55 years	
Range = 32–86 years	
Gender	
Male	46 (44.7%)
Female	57 (55.3%)
What is your racial or ethnic background?	
White	51 (49.5%)
Black or African-American	42 (40.8%)
American Indian/Alaska Native	2 (1.9%)
Subjects selecting more than one response	8 (7.8%)
Do you have a computer (e.g., laptop, desktop, tablet) at home?	
Yes	45 (43.7%)
No	58 (56.3%)
Do you have a smartphone?	
Yes	41 (39.8%)
No	59 (57.3%)
No response	3 (2.9%)
How frequently do you use the internet?	
Daily	34 (33.0%)
Weekly	9 (8.7%)
Monthly	6 (5.8%)
I have used it, but do not recall when I used it	9 (8.7%)
I do not use the internet	44 (42.7%)
No response	1 (1.0%)
Have you ever participated in a clinical trial?	
Yes	51 (49.5%)
No	52 (50.5%)

symptoms varied significantly ($\chi^2_4 = 16.4$, $p < 0.01$; Fig. 1a). Reporting symptoms on a device provided by a physician was the most highly preferred method (36% of responses), while reporting symptoms on paper was one of the least preferred methods (16% of responses; Fig. 1a). Together, preference for one of the electronic methods to report disease symptoms made up 84% of responses. Although preference for paper was higher in those who did not own a smartphone or computer (32%) versus those who own a smartphone or computer (8%), the distribution of responses for how to report disease symptoms did not significantly differ between these two groups (Online Resource 2 [ESM]; $\chi_1 = 7.69$, $p = 0.10$). Similarly, the distribution of responses for how to report disease symptoms did not significantly differ between those who have participated in a clinical trial and those who have not participated in a clinical trial (Online Resource 2 [ESM]; $\chi_1 = 3.21$, $p = 0.52$).

Subjects also showed a significant variation in preference for what time of day they would want to complete a daily diary in a clinical trial ($\chi^2_6 = 19.8$, $p < 0.01$; Fig. 1b). The most preferred time was 8:00 am to noon (26%), followed by 8:00 pm to midnight (21%). In general, subjects preferred time combinations representing either the morning or evening, with only 11% preferring midday (noon to 4:00 pm). Participants were asked if they would find audible alarms helpful if they had to record symptoms and medication intake every day on a smartphone provided by their physician. There was a significant variation in responses (necessary, very helpful, helpful, not very helpful, and unnecessary), with most reporting that they would find alarms necessary, very helpful, or helpful to record symptoms (84%, $\chi^2_4 = 51.7$, $p < 0.0001$) or medication intake (80%; $\chi^2_4 = 35.3$, $p < 0.0001$; Fig. 1c).

3.3 Preference for ePRO Design and Display

See ESM for example screens presented in each question below.

Subjects were presented with four options for emphasizing key words in a question. Subjects reported that underlining (33%) and capitalization (33%) best drew attention to words, followed by bold (19%) and italicized (15%) lettering (Fig. 2a), demonstrating a significant difference in responses ($\chi^2_3 = 10.6$, $p < 0.05$). Subjects were shown screens of a multi-select question formatted to read left to right (question to the left of the answers) or top to bottom (question above the answers). Almost half of subjects (46%) reported that they could read and understand the screens equally. Of those subjects with a preference, significantly more subjects found the top to bottom format (63%) easier to read and understand than the left to right format (37%) ($\chi^2_1 = 6.76$, $p < 0.01$, Fig. 2b).

There was no significant preference for number of questions per screen, with 54% preferring one question per screen and 46% preferring multiple questions per screen ($\chi^2_1 = 0.64$, $p = 0.42$; Fig. 2c). The main reasons for preferring one question per screen were that the questions were easier to read (66%) and easier to understand (41%), while the reasons for preferring multiple questions per screen were that the questions were easier to read (51%) and faster to complete (40%). When 'back' and 'next' navigation buttons were presented to subjects either at the top or the bottom of the screen, 24% reported that it was equally easy to find the buttons in both versions. Of those with a preference, significantly more subjects (74%) preferred them at the bottom of the screen compared with the top of the screen ($\chi^2_1 = 23.0$, $p < 0.0001$, Fig. 2d).

3.4 Preference for Real-Time Feedback When Using ePRO

See ESM for example screens presented in each question below.

Subjects showed a significant preference for whether they liked or disliked a screen at the outset of a

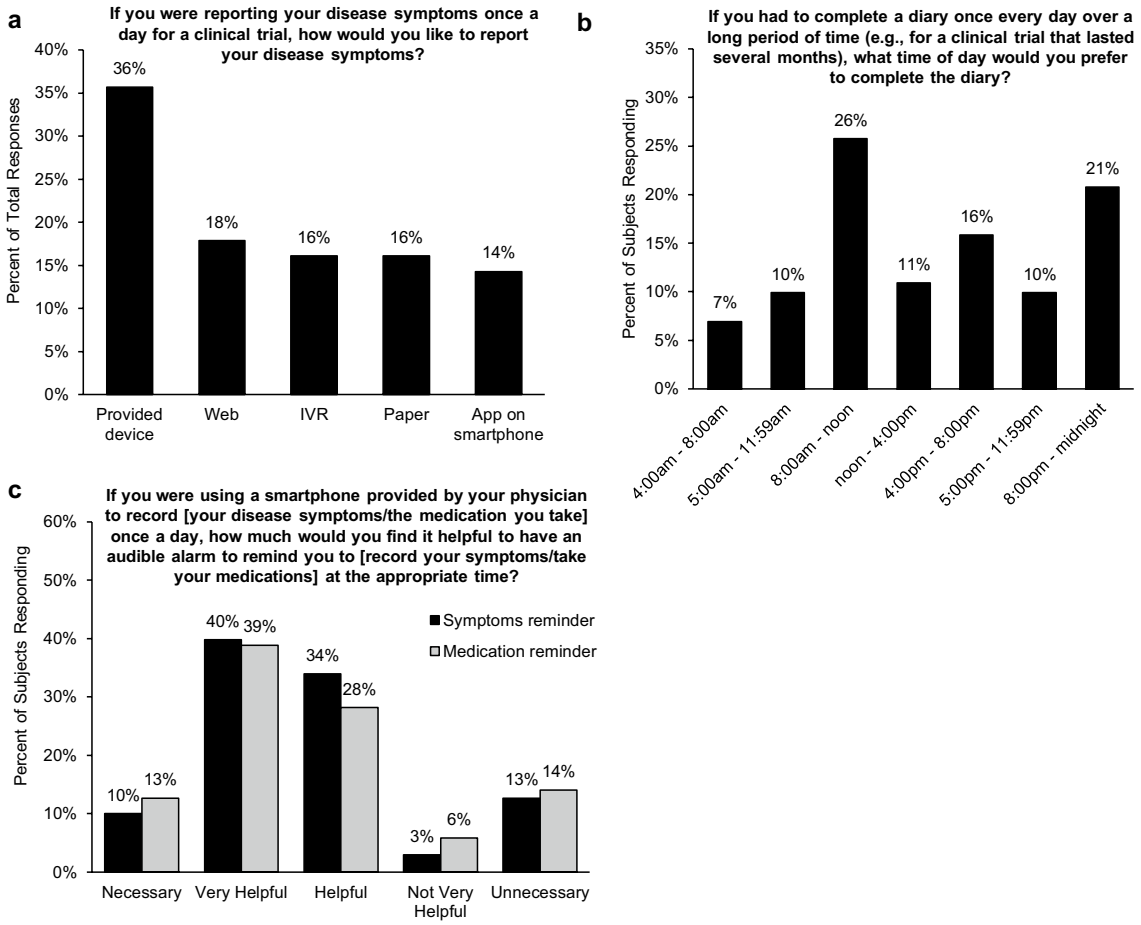

Fig. 1 **a** Subject responses on their preference for how to report disease symptoms. Subjects responding '4' from a scale of 0–4, where 4 = "I would most prefer to use this method" and 0 = "This is my least preferred method." Some subjects chose '4' for more than one response and/or did not include all ranking options. Only subjects with at least three rankings were included ($N = 41$). **b** Subject responses on their preference for time of day to complete a daily diary ($N = 101$). **c** Subject responses to whether they would find audible alarms helpful as a reminder to report disease symptoms and take medication ($N = 103$)

questionnaire that summarizes the number of items and estimated time for completion ($\chi^2_4 = 52.1$, $p < 0.0001$). Most subjects (69%) liked the screen a lot or a little, about a quarter (24%) neither liked or disliked the screen, and only 7% disliked the screen (Fig. 3a). Subjects also preferred to see some type of indicator to know their progress when completing questionnaires (84% of responses; Fig. 3b). Subject preferences were significantly different ($\chi^2_3 = 18.8$, $p < 0.001$), with a progress bar alone being the most preferred option (39% of responses), followed by a progress bar that also included a "Question X of Y" message (33% of responses).

Subjects were asked whether they would find it helpful to see a graph of their own responses to questionnaires on a regular basis in order to track their health status. They were shown a graph of fatigue scores over a 10-day period as an example. Subjects showed a significant preference for whether they would find this screen helpful or unhelpful ($\chi^2_4 = 39.1$, $p < 0.0001$), such that most subjects (81%) reported that it would be helpful, very helpful, or necessary to regularly receive this type of graph in order to track their health status (Fig. 3c).

Subjects showed a significant preference for whether they liked or disliked a screen at the end of each questionnaire with a smiley face saying, "Thank you for completing this questionnaire!" ($\chi^2_4 = 45.6$, $p < 0.0001$). The majority of subjects (59%) reported that they would like to see such a thank-you screen; about a quarter (27%) of subjects had no preference, and 14% reported disliking such a screen (Fig. 3d). Subjects were also shown screens that included various statements about their compliance and were asked how much these screens would motivate them to complete a diary each day. All screens included simple words of encouragement ("It is important to complete your diary every day"), accompanied by either their

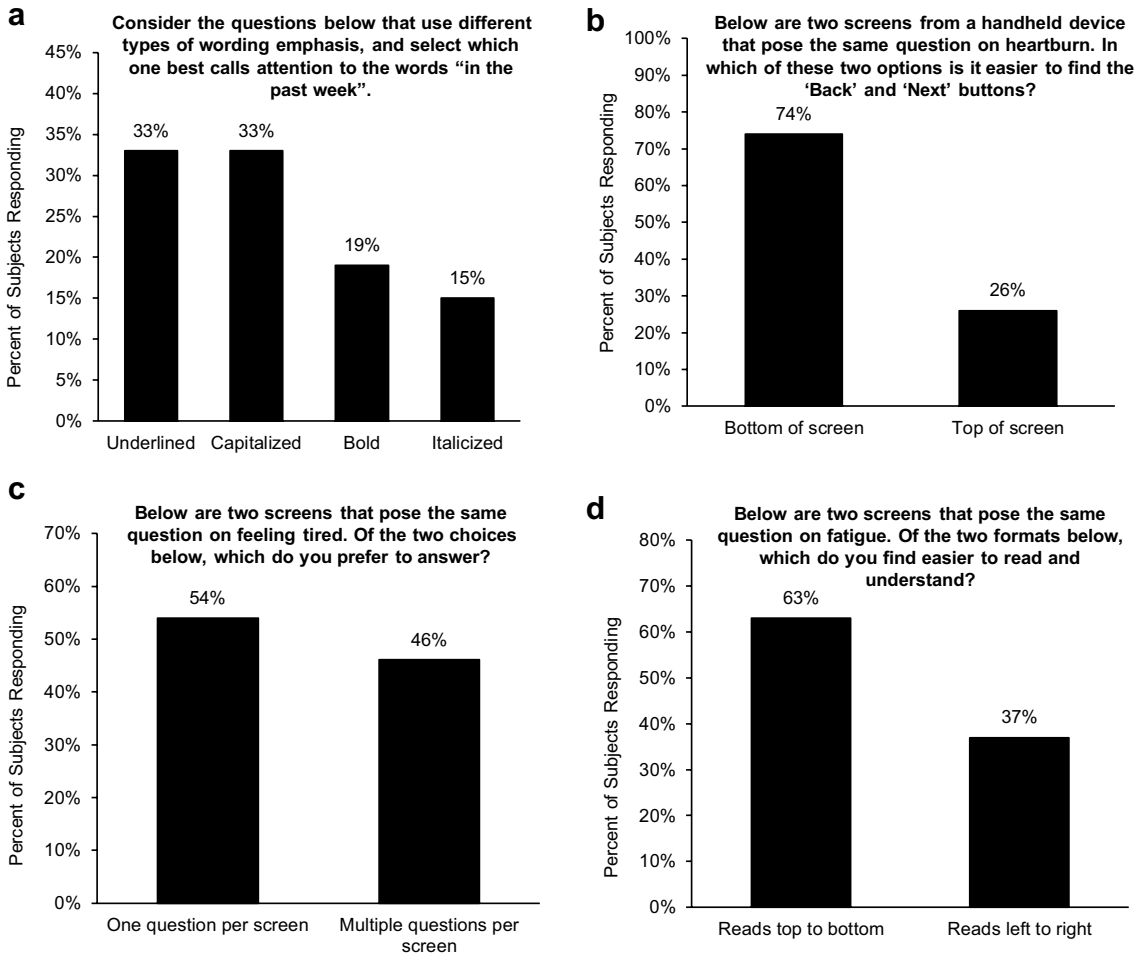

Fig. 2 See electronic supplementary material for response options/screen shots for each question. **a** Subject responses on the best way to emphasize key words in a question ($N=100$). **b** In those subjects with a preference, subject responses to their preferred location of 'Back' and 'Next' buttons ($N=77$). **c** Subject responses on their preference on number of questions per screen ($N=76$). **d** In those subjects with a preference, subject responses to what question and answer format is easier to read and understand ($N=54$)

study compliance rate alone, their study compliance rate plus either the target or average compliance rate of the study, or their study compliance rate and a sad face if their compliance was lower than expected. For each screen, subjects showed a significant difference in whether they would find them motivating or not ($\chi^2_4=63.1$, $\chi^2_4=72.5$, $\chi^2_4=53.2$, $\chi^2_4=23.3$, all $p<0.001$). The most motivating screen (i.e., reported to 'motivate a lot' or 'motivate a little') was a screen showing words of encouragement and their compliance rate plus their compliance compared with the study target compliance (79%). This was closely followed by words of encouragement and their compliance rate alone (76%), and words of encouragement and their compliance rate plus their compliance compared with the average compliance of all participants in the study (72%). In contrast, only 49% of subjects reported that they would be motivated to complete their diary each day by seeing a screen with a graphic of a sad face if their compliance was lower than expected (Fig. 3e).

4 Discussion

Understanding symptoms from the patients' perspective is imperative for managing and tracking COPD progression, as objective measures alone do not portray the full impact of COPD on patients' health-related quality of life. Furthermore, as outlined in the FDA's Patient-Focused Drug Development initiative, ensuring that patients' experiences and preferences are incorporated into drug evaluation is important for advancing approaches to collect patient input, establishing best practices, and minimizing patient burden [19]. Our results show that most subjects with COPD prefer to report their disease symptoms using an electronic method, supporting recent trends and recommendations for using technology for PRO data collection in both clinical trials and clinical practice [20–22]. In addition, subjects with COPD showed specific preferences for how ePRO questionnaires should be designed and

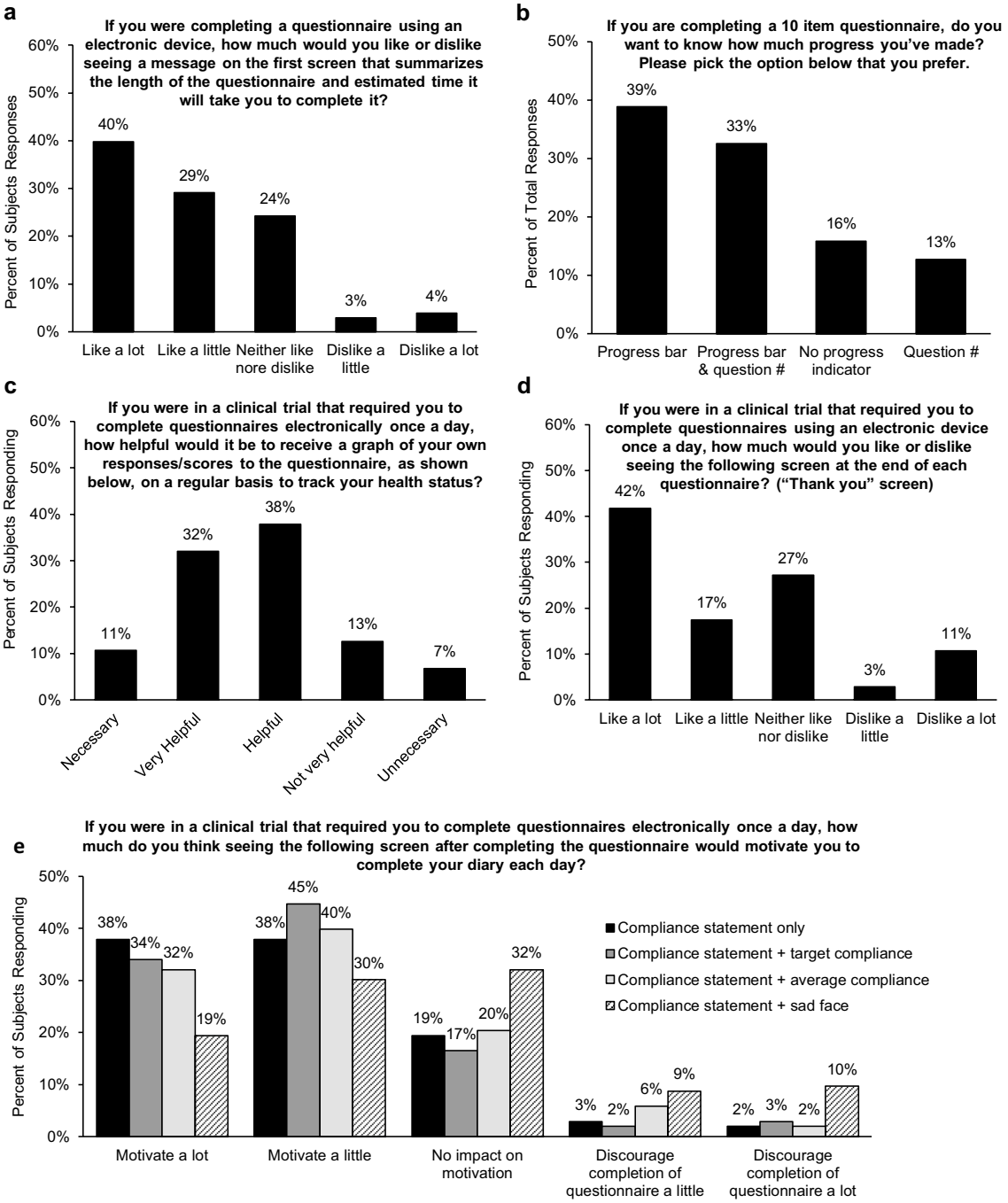

Fig. 3 See electronic supplementary material for response options/screen shots for each question. **a** Subject responses to whether they would like to see a screen that summarizes the length of the questionnaire and estimated time to complete ($N=103$). **b** Subject responses to whether they would want to see an indicator to track their progress when completing questionnaires ($N=96$). **c** Subject responses to whether they would find it helpful to see a graph of their own responses in order to track health status ($N=103$). **d** Subject responses to whether they would like a 'thank you' screen at the end of a questionnaire ($N=103$). **e** Subject responses to how motivated they would be by screens that display compliance metrics ($N=103$)

what types of features they should include, such as audible alarms and screens showing completion progress and compliance rates. These patient preferences should guide the design of ePRO instruments for use by COPD patients, with the goal of reducing patient burden and increasing engagement and compliance.

ePRO has many advantages over paper, such as higher compliance, increased accuracy, reduced site burden and

reduced cost [11–15, 23]. Our data showing that ePRO is also preferred over paper in subjects with COPD is an additional advantage. This preference is in line with studies showing preference for ePRO across therapeutic areas, such as oncology, headache, arthritis, pain, gastrointestinal disorders, and respiratory disorders [24–30]. Furthermore, this preference was shown in subjects with COPD despite less than half of subjects having a computer at home or owning a smartphone, suggesting that regular use of electronic devices is not a prerequisite for preferring to report symptoms electronically. Our data therefore suggests that ePRO should be considered for use in COPD patients not only because of the numerous advantages of ePRO over paper in metrics of compliance, accuracy, and reduced burden, but also because COPD patients prefer it.

The most highly preferred method for reporting disease symptoms was on a smartphone provided by a physician. This was preferred over other electronic options, notably, an app on your smartphone. Reporting disease symptoms on ones' personal device (i.e., smartphone) is considered to be a "Bring Your Own Device" (BYOD) solution [31]. BYOD has advantages like reducing the cost of buying study devices and reducing patient burden of carrying/managing a separate study device. However, concerns over data privacy and security, operational issues (i.e., unforeseen software updates, space limitations), equivalency, and indeterminate regulatory support limit its use. Our data suggests that patient preference should also be considered when deciding to use a BYOD solution.

When migrating an instrument from paper to an electronic mode of administration, the format should be preserved as much as possible in order to retain original intent and content [18]. However, electronic devices are inherently different than paper (e.g., size, functionality), requiring certain modifications of the design and display during this migration. For example, 'Back' and 'Next' buttons are added to allow the user to navigate through screens, and screen size can limit the number of questions per screen. Subjects with COPD found it easier to find 'Back' and 'Next' buttons when they were at the bottom rather than at the top of the screen. Subjects with COPD did not show a significant preference for number of questions per screen (one or multiple), but found questions easier to read and understand when they read top to bottom rather than left to right. We recommend that these preferences be incorporated into ePRO design of future COPD clinical trials in order to create simple and easy to use ePRO assessments. Creating ePRO with optimal usability can ultimately help reduce patient burden and increase engagement and compliance.

A key advantage of using ePRO is the ability to use the technology to add valuable features that are not possible on paper. Many of these features can help with compliance and in managing disease symptoms, and were liked by subjects with COPD in this study. For example, most subjects found audible alarms necessary or helpful to remind them to take medication or report symptoms, and most subjects thought that screens showing feedback on their compliance rate would help motivate them to complete a daily diary. It would be interesting to determine whether feedback on compliance would increase compliance rates in future studies. Using ePRO can also restrict the window of availability of assessments to encourage consistent and routine reporting. Subjects with COPD preferred to report disease symptoms at night or in the morning versus midday. Incorporating these above preferences into clinical practice or research may have the potential to benefit COPD treatment adherence. For example, electronic alarms have been found to increase medication adherence in chronic disease care [32, 33]. In addition, most COPD subjects found it helpful or necessary to receive a graph of their own responses on a regular basis in order to track their health status. This feature could further benefit COPD care, as active self-management has been found to improve health status in COPD patients [34], and has the potential to facilitate early detection and treatment of COPD exacerbations [17].

The following limitations should be considered when interpreting study results. The sample size is relatively small, which may warrant additional studies using larger sample sizes. For example, further stratification of responses between sub-groups (i.e., technology experience) using regression analyses in studies with larger sample sizes may provide further information on the specificity of these ePRO preferences. In addition, 50% of the population reported having participated in a clinical trial, which is higher than we would expect from the general population. Although we did not find a significant difference in how participants prefer to report disease symptoms between those who have participated in a clinical trial versus those who have not, additional studies with larger sample sizes may confirm the generalizability of our results to the wider COPD population. Furthermore, although our study is important for establishing patient preferences within the COPD population, patient preferences across other indications were not assessed. Although we would expect patient preferences to be generally similar across indications, further research is required to generalize these results to a wider population.

5 Conclusion

COPD is a chronic and pervasive disease that requires collection of PRO data in order to characterize the full impact of the disease on patient health status, particularly in the context of evaluating efficacy endpoints in clinical trials. Careful consideration of patient preferences should be

incorporated into ePRO design to create optimal usability and engagement. Our results show that subjects with COPD prefer to report their disease symptoms electronically versus on paper, and that subjects have specific preferences for the design and display of electronic assessments. These results should be considered when designing PRO assessments for use in COPD treatment management or research, with the ultimate goal of reducing patient burden, increasing patient compliance, and improving COPD health care.

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Author Contributions Author KMD analyzed the data and wrote the manuscript. Authors ND, LK, and ST contributed to data analysis. Authors BW and CJE performed participant interviews and edited the manuscript. Author SMD contributed to study design and edited the manuscript.

Data Availability Statement The datasets generated during and/or analyzed during the current study are not publicly available because all data are proprietary to eResearch Technology (ERT), but are available from the corresponding author on reasonable request.

Compliance with Ethical Standards

Ethical Approval All procedures performed involving human participants were in accordance with the ethical standards of the national research committee (Copernicus Group IRB) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Conflict of Interest Authors KMD, ND, LK, STG, and SMD are employees of eResearch Technology (ERT), which funded this research, and authors CE and BW are employees of Endpoint Outcomes, which performs services for ERT.

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