Original Research

Health Status Progression Measured Using Weekly Telemonitoring of COPD Assessment Test Scores Over 1 Year and Its Association with COPD Exacerbations

Paul Jones, MD, PhD[1a] Toru Soutome, BPharm[2a,b] Taizo Matsuki, PhD[2a] Masahiro Shinoda, MD, PhD[3] Osamu Hataji, MD, PhD[4] Motohiko Miura, MD, PhD[5] Masaharu Kinoshita, MD[6] Akira Mizoo, MD[7] Kazunori Tobino, MD[8] Takanobu Nishi, MSc[2] Takeo Ishii, MD, PhD[2b] Yoko Shibata, MD, PhD[9]

[a]*Contributed equally*

[b]*At the time of the study*

[1]GSK, Brentford, Middlesex, United Kingdom

[2]Japan Medical & Development, GSK K.K, Tokyo, Japan

[3]Tokyo Shinagawa Hospital, Tokyo, Japan

[4]Matsusaka Municipal Hospital, Matsusaka, Mie, Japan

[5]Tohoku Rosai Hospital, Miyagi, Japan

[6]Nagata Hospital, Fukuoka, Japan

[7]Japan Community Healthcare Organization Tokyo Shinjuku Medical Center, Tokyo, Japan

[8]Iizuka Hospital, Fukuoka, Japan

[9]Fukushima Medical University, Fukushima, Japan

***Address correspondence to*:**
Paul Jones, MD, PhD
GSK
980 Great West Road
Brentford, Middlesex
TW8 9GS, United Kingdom
Phone: +44 (771) 340-1434
Email: paul.8.jones@gsk.com

***Running Head*: CAT Score Progression Link to Exacerbation Risk**

***Keywords*:** patient-reported outcome; telemonitoring; CAT score; exacerbations; COPD

***Abbreviations*:** ACO, Asthma-COPD Overlap; CAT, COPD Assessment Test; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ER, emergency room; EXACT,

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Exacerbation of Chronic Pulmonary Disease Tool; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HR, hazard ratio; ICS, inhaled corticosteroid; IQR, interquartile range; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; PRO, patient-reported outcome; SD, standard deviation.

***Funding Support*:** This study was funded by GSK (Study 212648/HO-19-19947).
The funders of the study had a role in study design, data analysis, data interpretation, and writing of the report. The corresponding author had full access to all the data and the final responsibility to submit for publication.

Date of Acceptance: February 23, 2024 | ***Publication Online Date:*** February 27, 2024

Citation: Jones P, Soutome T, Matsuki T, et al. Health status progression measured using weekly telemonitoring of COPD Assessment Test scores over 1 year and its association with COPD exacerbations. *Chronic Obstr Pulm Dis.* 2024; Published online February 27, 2024. https://doi.org/10.15326/jcopdf.2023.0415

This article has an online supplement.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Abstract (250/250 words)

Background: A previous longitudinal study of chronic obstructive pulmonary disease (COPD) Assessment Test (CAT) score changes suggested patients fall into three patterns: stable, improving and worsening. This study assessed the evolution of CAT scores over time and its relationship to exacerbations.

Methods: In total, 84 participants used a telemedicine platform to complete CAT weekly for 52 weeks. Completion rates, annualized change in CAT score and learning effects were measured, as well as CAT changes of >4 units during look-back periods of 4 and 8 weeks. In a subgroup of participants with least 25% completion rate (adherent group, n=68 [81%]), the relationship between change in CAT score and exacerbations at any time during the study was examined post hoc.

Results: Linear regression showed that 50%, 22% and 28% of the adherent subgroup had CAT scores indicating worsening, stable and improving health status, respectively. In the adherent subgroup, 70% (n=7/10) of participants who had an exacerbation during the study had worsening CAT score, versus 47% (n=27/58) without an exacerbation. The hazard ratio association between CAT score increase and moderate exacerbation was 1.13 (95% confidence interval: 1.03-1.24).

Most participants experienced at least one CAT score change of >4 units, and 7% showed an initial learning effect with a median of 2 weeks.

Conclusions: Measuring trends in CAT score may allow future studies to group patients into three defined categories of change over time and quantify CAT change trajectories to assess treatment response and potentially predict medium-term outcomes within individual patients.

Funding: GSK (212648/HO-19-19947).

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Introduction

The use of diary cards administered via paper or electronically to measure patient-reported outcomes (PRO) in chronic obstructive pulmonary disease (COPD) have been validated,[1] though patients often prefer an electronic format.[2] The COPD Assessment Test (CAT) was developed to provide a quick, easy-to-use tool to assess health status that is applicable worldwide.[3] Its reliability and validity are established,[4] and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy report recommends it as a comprehensive health status questionnaire developed to be applicable worldwide.[5] Its main advantages are coverage of important clinical aspects of COPD and short time required for completion.[6] Along with the Exacerbation of Chronic Pulmonary Disease Tool (EXACT) exacerbation diary, the CAT was found to be more responsive than other measures during recovery from severe exacerbation.[7] In this context, it should be noted that the EXACT is a daily diary specifically designed to detect and quantify episodic events like exacerbations.[8,9] Whereas the CAT is a disease-specific health status measure designed to quantify impairment of health status due to any cause.[3]

Increasing CAT scores are associated with worsening health status. Among patients with a history of exacerbations, CAT scores predict risk of further exacerbations in the following 6 months.[10] The link between exacerbations and evolution of CAT scores over time were further demonstrated in a study in Switzerland, which found a positive association between evolution of CAT over time and incidence of exacerbations.[11] Change over time in CAT score may also provide a responsive outcome measure in clinical studies. In a recent trial, patients randomized to telemedicine showed a lower rate of worsening in CAT score compared with those receiving standard care.[12]

While use of weekly CAT has been reported previously, replication of these findings in Japan is needed, as Japanese patients typically report low scores on the CAT and St

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

George's Respiratory Questionnaire,[13] and reporting of exacerbations is less frequent in Japan compared with the rest of the world.[14,15] The feasibility and acceptability of using telemedicine to support standard care of patients with COPD or asthma-COPD overlap (ACO) in Japan has recently been explored.[16]

This study used the same platform and aimed to assess the evolution of CAT scores over time and its relationship with exacerbations among patients with COPD.

Methods

Study design

Full details of the study design, patient population, telemedicine platform, and preliminary data analysis have been published elsewhere.[16] Briefly, this was a 52-week multicenter, prospective, single-arm, cohort study assessing the feasibility and acceptability of the use of a telemedicine platform (GSK study: jRCT1080224832) for COPD management. In this study, we used the same platform to examine changes in weekly CAT score.

Patient population

Japanese participants aged 40 years or older with an established clinical history of COPD or ACO, according to the American Thoracic Society/European Respiratory Society[17] and Japanese Respiratory Society COPD and ACO[18] guidelines, and who could provide informed consent and participate were enrolled in the study. Participants were selected from six sites where the telemedicine YaDoc platform (YaDoc; Integrity Healthcare Co. Ltd, Tokyo, Japan) was implemented.[16] Participants must have undergone lung function testing within the previous 12 months and be receiving maintenance inhaled therapy with a long-acting muscarinic antagonist (LAMA) and/or long-acting β_2-agonist (LABA). LAMA/LABA or inhaled corticosteroid (ICS) combinations were permitted but use of triple therapy

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

(ICS/LAMA/LABA) or biological therapy was not. Participants receiving triple therapy were excluded with the aim of recruiting a study population that was typical of patients with COPD in Japan, rather than restrict participation to specific subgroups of patients such as those with frequent exacerbations, or those with ACO, who may not be typical of the broader COPD population in this country. Full inclusion and exclusion criteria are presented in **Supplementary Table 1**.

Outcomes

The primary objective of this analysis was to evaluate the evolution of CAT scores over time. The secondary objective was to assess the relationship between longitudinal changes in CAT and exacerbations of COPD and was hypothesis-generating. Exacerbations were identified via healthcare records and included those identified by a physician as COPD exacerbations, those requiring courses of systemic steroids or antibiotics, or requiring hospitalization or emergency room (ER) visit for a COPD exacerbation. Evolution of the CAT score over 52 weeks was assessed for the total population and, in a post hoc analysis, for a subgroup of participants who completed at least 25% of the 52 weekly CAT entries. Below this threshold was considered not sufficient to gain a reliable insight into health status. The proportion of participants with CAT score changes of more than 4 units (i.e., at least twice the minimum clinically important difference) over look-back periods of 4 and 8 weeks was investigated, as well as the association between the evolution of the CAT score and COPD exacerbations. An analysis of the initial learning effect on CAT scores was also performed.

Data collection and analysis

Participants were trained to use the telemedicine platform YaDoc at study entry (new user) or at initiation (existing user) by a physician or facility staff member. Participants used

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

the YaDoc smartphone application to complete electronic PROs, including weekly questions from the CAT.[19]

To evaluate change of the CAT score over 52 weeks, each participant was categorized into one of three groups using linear regression of change over time: improved (negative slope with upper limit of 95% confidence interval [CI] of slope estimate below 0), worsened (positive slope with lower limit of 95% CI of slope estimate above 0), and stable health status (all other cases) based on CAT change over time. This evaluation was performed for the total population and, in a post hoc analysis, for a subgroup of participants who achieved at least 25% compliance in completion of the CAT.

Group-based trajectory modeling was used to identify clusters of individuals who followed similar patterns of evolution of the CAT during the study period,[20] and clusters were characterized by patient demographics. This analysis was performed based on changes from baseline in weekly CAT score (using median changes for participants with multiple records in a single analysis week) and the analysis week used for convergence. Group trajectories were estimated assuming the distribution of the evolution of CAT scores followed a censored normal distribution, with upper and lower censoring points of 40 and −40, respectively. The optimal number of clusters (2, 3, or 4) was determined based on Bayesian Information Criteria.

The association between the evolution of the CAT score and COPD exacerbations was evaluated using the Andersen–Gill formulation of the Cox proportional hazards model with covariates of time-dependent CAT scores, age, sex and percent predicted forced expiratory volume in 1 second (FEV_1) for moderate exacerbations (requiring corticosteroids and/or antibiotics) and severe exacerbations (requiring hospitalization or ER visit).[21] Moderate and severe exacerbations were assessed separately as a sensitivity analysis. No

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

formal analyses assessing differences between groups based on combined CAT score and exacerbation profile were performed.

A test for the presence of an initial learning effect for completion of the CAT was performed using a second order regression model in comparison with a linear model. A learning effect was assumed if the second order model produced a significant improvement in goodness of fit compared with linear regression. This method of comparing goodness of fit across models has been used to assess a learning effect in COPD focused studies.[11]

Results

Study population

Overall, 72 of the 84 (86%) participants enrolled completed the study, and the median weekly CAT completion rate was 83%.[16] Baseline demographics and clinical characteristics are shown in **Table 1** and have been published previously.[16] Most participants were male (n=74; 88%) and the mean (standard deviation [SD]) age was 68.7 (9.17) years. Approximately a fifth (22.6%) of participants were current smokers, with the remainder former smokers. The population was considered representative of a population with mild COPD: overall the mean (SD) percent predicted FEV_1 was 72.9% (22.0). The mean (SD) predicted FEV_1 for the Improved, Stable and Worsened groups was 72.0% (18.6), 71.3 (20.0), and 70.6 (23.5) respectively. Overall, 40% of participants were classified as GOLD grade 1 (FEV_1 ≥80% predicted),[5] including 37%, 40% and 38% of participants in the Improved, Stable and Worsened groups, respectively. In addition, 50 (60%) participants overall, including 53%, 60% and 65% of participants in the Improved, Stable and Worsened groups, respectively, were considered to be at low risk of exacerbations (GOLD Group A).[5]

Of the 84 participants enrolled in the study, 68 (81%) had ≥25% adherence in terms of CAT score completion and were included in the ≥25% adherent subgroup. Baseline

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

demographics and clinical characteristics for this subgroup, categorized by CAT score evolution group, are shown in **Table 1.**

CAT score evolution

The evolution of CAT scores over time for both the overall population and the ≥25% compliance subgroup showed substantial variation between individual participants. Data from participants selected as representative examples of the three patterns of evolution are shown in **Figure 1**. Individual CAT score trajectories are shown in **Supplementary Figure 1**. Linear regression at an individual patient level showed that 42% of participants had CAT scores indicating worsening health status, 35% had scores showing little change, and 23% had scores indicating improving health status.

In the ≥25% adherence subgroup, 50%, 22% and 28% of participants had CAT scores indicating worsened, stable or improved health status, respectively (**Table 2**). The median (interquartile [IQR]) slope for CAT score change per year in the ≥25% adherence subpopulation over the study period was 0.6 (-1.0–3.8) units/year. Participants with CAT scores indicating improvement had a numerically shorter mean duration of COPD, and higher initial mean modified Medical Research Council (mMRC) and CAT scores than participants in the stable or worsened groups

(**Table 1**).

Over the course of the study, 62 (74%) participants experienced a change in CAT score of

>4 units over look-back periods of 4 and 8 weeks. Most of these changes (n=60 [81%]) were within

a 4-week period (**Table 3**).

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Association between CAT score changes and exacerbation risk

Among participants in the ≥25% adherent subpopulation who had an exacerbation at some point during the study period (n=10), CAT score indicated a worsened health status for 7 (70%) participants compared with 27 of 58 (47%) participants who did not (**Table 2**). The median (IQR) slope for CAT change per year over the study period was 2.7 (0.5–5.7) units/year for participants with exacerbations and 0.2 (-1.1–3.0) units/year for those without exacerbations.

The risk of an exacerbation increased per unit increase in CAT score over 1 year for both total exacerbations and moderate exacerbations (hazard ratio [HR]: 1.13 [95% CI: 1.03, 1.24]) and severe exacerbations (HR: 1.22 [95% CI: 1.05, 1.41]) (**Table 4**).

Learning effect to complete the CAT

Six (7%) participants showed evidence of a learning effect across the first few measurements at the start of the study, which can be seen for individual participants in **Figure 1**. The effect was observable in both directions and seemed to be unrelated to the CAT slopes after that initial period. The median learning time was 13.3 days (IQR 8.9–64.8).

Trajectory analysis

The trajectory analysis identified three clusters of participants (**Figure 2**) which fit the pattern of the CAT score evolution groups, with clusters representing improved, worsened and unchanged (stable) health status. Participants in the cluster showing improvement had numerically fewer moderate/severe exacerbations in the previous 12 months, and higher initial CAT scores. Percent predicted FEV_1 and forced vital capacity (FVC) were all higher in the improved cluster compared with those in the worsened cluster (**Table 5**).

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Discussion

This study shows that the CAT may detect trends in health status using weekly scores collected over 1 year and help define patient's disease trajectory as worsening, stable, or improving. This may support a previous finding of a link between progression of CAT score and patient health status in a telemedicine setting.[11] A significant positive association was observed between worsening CAT scores over time and the occurrence of both moderate and severe COPD exacerbations, with a 13% increased risk of moderate exacerbations, and a 22% increased risk of severe exacerbations observed for each unit increase in CAT score over 1 year. These findings may indicate that the use of CAT via a smartphone app allows regular telemonitoring of COPD-related health status, enabling patients and/or physicians to identify a pattern of worsening during routine COPD management. This could provide an opportunity for earlier treatment of symptoms, improving patient outcomes.[22]

The significant positive association between CAT score worsening and exacerbation occurrence may be due to the fact that exacerbations worsen the CAT score for several days,[23] and worsen health status for several weeks following the acute event.[24] It is also known that higher CAT scores are a risk factor for exacerbations.[10,25] Visual observation of the CAT slopes did not demonstrate a change in CAT before or after an exacerbation, however we did not perform formal statistical comparisons between the CAT slope before and after an exacerbation, as the low number of events limited this analysis.

Using a change of >4 units over a look-back period of 4 weeks, we observed acute changes in 74% of participants, but this approach may miss exacerbations, since a previous study showed a

4-unit recovery following an exacerbation after approximately 8 days and a mean change in CAT score of approximately 5 units between the stable state and an exacerbation.[23] Furthermore, our findings suggest that changes of >4 units can occur in an individual over a

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

period of up to a month, even in the absence of an acute exacerbation. This is important, because most studies measure CAT change between two timepoints, for example, beginning and end; however, this study shows that there are between-measurement changes that are clinically significant in magnitude, but may be due to normal day-to-day variation coupled with measurement error. Trends based on weekly measurements should provide greater precision in estimates of change over time because they use a larger number of measurements, which may increase the CAT's sensitivity to identify worsening or improving health status.

When using this type of methodology, adherence and the possibility of a learning effect should be considered. We used a cut-off of ≥25% adherence of regular data collection for this analysis to ensure that we had sufficient data to reliably estimate the slope of change over time, and 81% of participants were able to achieve this. The learning effect was not observed frequently, and the median time was approximately 2 weeks but, in the context of a clinical study, a decision to ignore the first 4 weeks (if using weekly measurements) could be pre-specified. After any initial learning effect, the slope of change over time in this cohort study appeared to be largely linear. This contrasts with findings, often seen in pharmaceutical trials, where a rapid initial benefit may occur at the start of treatment, followed by stability or worsening.[26,27] However, a non-linear initial response should not be an obstacle to the use of CAT diaries, since appropriate methods can be used to take these initial effects into account.

The use of telemedicine to collect multiple CAT measurements may have significant application in future studies of COPD because of the precision permitted by multiple measurements and the ability to categorize patients into three defined groups using pre-set criteria. Identification of patients exhibiting deteriorating health status versus those who are stable or improving is clinically important due to the heterogeneity seen in COPD symptoms and response to treatment. The slope of the CAT score over time has already been shown to

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

be affected in a disease management system.[12] The methodology may also have application to predict medium-term outcomes; future research could explore whether a 4-6 week recording period may predict deterioration assessed using a composite outcome measure such as the CID.[28]

A strength of this study is that it extends observations from a study in Switzerland to participants in Japan. The participants recruited to this study had better lung function than those in the Swiss study[11] (predicted FEV_1 73% vs 38%), but a similar pattern of results was seen in both studies, suggesting that weekly CAT measurement may be effectively implemented in different healthcare settings and is not affected by COPD severity.

There are also limitations to this methodology; participants and physicians included in this study were selected from only six sites employing the YaDoc platform. However, these sites covered a diverse area and rural/urban locations in Japan. Some participants who are not accustomed to using mobile phone applications, may have been less willing to participate, so the study population may be early adopters of the technology. Finally, while the trajectory analysis identified three clear patient clusters, the composition of these clusters may have been affected by a small learning effect in some participants, as well as by participants with particularly high or low baseline scores. The relatively small sample size in each individual cluster, as well as the overall sample size, should also be considered when making conclusions. However, the sample size was larger than that of the Swiss study,[11] and large enough to identify health status patterns among the ≥25% adherent subgroup with some confidence. The low number of exacerbations is a weakness, but the relationship between CAT change and exacerbations was not the primary hypothesis under test and the exacerbation analysis should be considered a hypothesis generating.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Conclusion

The study shows that measurement of trends in CAT score over time, obtained using weekly scores collected via telemedicine, may provide insights into medium-term COPD trajectories by identifying a pattern of worsening and alerting patients and/or physicians. This will be important for future studies where identification of patients exhibiting deteriorating health status versus those whose status is stable or improving will provide insights into response to treatment. Prospective treatment trials are required to confirm these findings. Future studies could also examine CAT items separately for non-respiratory versus respiratory items, as well as to examine what drives fluctuations in CAT scores.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Acknowledgments

We thank the participants and physicians/facility staff in Japan who participated in this study. The data included in this manuscript have previously been presented at the European Respiratory Society International Congress 2022.

Takeo Ishii, Paul Jones, Taizo Matsuki, Yoko Shibata, and Takanobu Nishi contributed to the conception and design of the study. Masahiro Shinoda, Osamu Hataji, Motohiko Miura, Masaharu Kinoshita, Akira Mizoo and Kazunori Tobino contributed to the acquisition of data. Toru Soutome, Takeo Ishii, Paul Jones, Taizo Matsuki, Yoko Shibata and Takanobu Nishi contributed to the data analysis and interpretation.

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Ethical considerations

The study was conducted in accordance with applicable local regulations, and the principles stated in the Declaration of Helsinki. All study documents were reviewed and approved by institutional review boards and/or independent ethics committee(s) at all investigational sites.[16] All participants provided written, informed consent. YaDoc data was extracted and deidentified in accordance with the Personal Information Protection Act of Japan.

Data availability

Anonymized individual participant data and study documents can be requested for further research from https://www.gsk-studyregister.com/en/

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Declaration of Interest

Masahiro Shinoda, Osamu Hataji, Motohiko Miura, Masaharu Kinoshita, Akira Mizoo and Kazunori Tobino report having received grants from the GSK group of companies for the conduct of this study. Yoko Shibata reports having received personal fees from the GSK group of companies during the conduct of the study, and lecture fees from AstraZeneca, Novartis and Boehringer Ingelheim. Takanobu Nishi is an employee of GSK. Taizo Matsuki is an employee of GSK and holds stocks/shares. Takeo Ishii and Toru Soutome are former employees of GSK. Paul Jones is an Emeritus Professor of Respiratory Medicine at St George's, University of London, and a former full-time employee of GSK at the time of protocol development and contributed to study design and protocol on behalf of GSK. He is a part-time consultant at GSK and holds stocks/shares.

Editorial support in the form of preparation of the first draft based on input from all authors, and collation and incorporation of author feedback to develop subsequent drafts, was provided by Christopher Heath, PhD, at Fishawack Indicia Ltd, UK, part of Avalere Health, and was funded by GSK.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

References

1. Nishimura K, Kusunose M, Sanda R, Tsuji Y, Hasegawa Y, Oga T. Comparison between electronic and paper versions of patient-reported outcome measures in subjects with chronic obstructive pulmonary disease: an observational study with a cross-over administration. *BMJ open.* 2019;9(12):e032767.
2. Dumais KM, Dias N, Khurana L, et al. Preferences for use and design of electronic patient-reported outcomes in patients with chronic obstructive pulmonary disease. *The Patient-Patient-Centered Outcomes Research.* 2019;12(6):621-629.
3. Jones P, Harding G, Berry P, Wiklund I, Chen W, Leidy NK. Development and first validation of the COPD Assessment Test. *European Respiratory Journal.* 2009;34(3):648-654.
4. Gupta N, Pinto LM, Morogan A, Bourbeau J. The COPD assessment test: a systematic review. *European Respiratory Journal.* 2014;44(4):873-884.
5. Global IfCOPD. Global strategy for prevention, diagnosis and management of COPD; 2023. Available from: https://goldcopd.org/2023-gold-report-2/. Accessed 13 January, 2023.
6. Lari SM, Attaran D, Tohidi M. Improving communication between the physician and the COPD patient: an evaluation of the utility of the COPD assessment test in primary care. *Patient related outcome measures.* 2014;5:145.
7. Nishimura K, Nakamura S, Kusunose M, et al. Comparison of patient-reported outcomes during acute exacerbations of chronic obstructive pulmonary disease. *BMJ Open Respiratory Research.* 2018;5(1):e000305.
8. Jones PW, Chen W-H, Wilcox TK, Sethi S, Leidy NK, group E-Ps. Characterizing and quantifying the symptomatic features of COPD exacerbations. *Chest.* 2011;139(6):1388-1394.
9. Leidy NK, Wilcox TK, Jones PW, Roberts L, Powers JH, Sethi S. Standardizing measurement of chronic obstructive pulmonary disease exacerbations: reliability and validity of a patient-reported diary. *American Journal of Respiratory and Critical Care Medicine.* 2011;183(3):323-329.
10. Lee S-D, Huang M-S, Kang J, et al. The COPD assessment test (CAT) assists prediction of COPD exacerbations in high-risk patients. *Respiratory medicine.* 2014;108(4):600-608.
11. Rassouli F, Baty F, Stolz D, et al. Longitudinal change of COPD assessment test (CAT) in a telehealthcare cohort is associated with exacerbation risk. *International Journal of Chronic Obstructive Pulmonary Disease.* 2017;12:3103.
12. Rassouli F, Germann A, Baty F, et al. Telehealth mitigates COPD disease progression compared to standard of care: a randomized controlled crossover trial. *Journal of internal medicine.* 2021;289(3):404-410.
13. Kato M, Tomii K, Hashimoto K, et al. The IMPACT study–single inhaler triple therapy (FF/UMEC/VI) versus FF/VI and UMEC/VI in patients with COPD: efficacy and safety in a Japanese population. *International Journal of Chronic Obstructive Pulmonary Disease.* 2019;14:2849.
14. Betsuyaku T, Kato M, Fujimoto K, et al. A randomized trial of symptom-based management in Japanese patients with COPD. *Int J Chron Obstruct Pulmon Dis.* 2018;13:2409-2423. doi:10.2147/COPD.S152723.
15. Ishii T, Nishimura M, Akimoto A, James MH, Jones P. Understanding low COPD exacerbation rates in Japan: a review and comparison with other countries. *Int J Chron Obstruct Pulmon Dis.* 2018;13:3459-3471. doi:10.2147/copd.s165187.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

16. Shinoda M, Hataji O, Miura M, et al. A Telemedicine Approach for Monitoring COPD: A Prospective Feasibility and Acceptability Cohort Study. *Int J Chron Obstruct Pulmon Dis.* 2022;17:2931-2944. doi:10.2147/copd.s375049.
17. Celli BR, MacNee W, Agusti A, et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *European Respiratory Journal.* 2004;23(6):932-946.
18. Yanagisawa S, Ichinose M. Definition and diagnosis of asthma–COPD overlap (ACO). *Allergology International.* 2018;67(2):172-178.
19. Integrity Healthcare Co.Ltd. the YaDoc telemonitoring platform (Japanese); 2022. Available from: https://www.yadoc.jp/about/feature. Accessed 16 May, 2019.
20. Jones BL, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. *Sociological methods & research.* 2007;35(4):542-571.
21. Global Initiative for Chronic Obstructive Pulmonary Disease. Global strategy for prevention, diagnosis and management of COPD; 2023. Available from: https://goldcopd.org/2023-gold-report-2/. Accessed 13 January, 2023.
22. Donner CF, ZuWallack R, Nici L. The Role of telemedicine in extending and enhancing medical management of the patient with Chronic Obstructive Pulmonary Disease. *Medicina.* 2021;57(7):726.
23. Mackay AJ, Donaldson GC, Patel AR, Jones PW, Hurst JR, Wedzicha JA. Usefulness of the chronic obstructive pulmonary disease assessment test to evaluate severity of COPD exacerbations. *American journal of respiratory and critical care medicine.* 2012;185(11):1218-1224.
24. Spencer S, Jones PW. Time course of recovery of health status following an infective exacerbation of chronic bronchitis. *Thorax.* 2003;58(7):589-593.
25. Thomashow B, Stiegler M, Criner GJ, et al. Higher COPD Assessment Test score associated with greater exacerbations risk: a post hoc analysis of the IMPACT trial. *Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation.* 2022;9(1):68.
26. Lipson DA, Barnacle H, Birk R, et al. FULFIL trial: once-daily triple therapy for patients with chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine.* 2017;196(4):438-446.
27. Jones PW, Gelhorn H, Wilson H, et al. Socioeconomic status as a determinant of health status treatment response in COPD trials. *Chronic Obstructive Pulmonary Diseases.* 2017;4(2):150.
28. Naya IP, Tombs L, Muellerova H, Compton C, Jones PW. Long-term outcomes following first short-term clinically important deterioration in COPD. *Respiratory research.* 2018;19(1):1-10.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Table 1. Baseline demographics and clinical characteristics by CAT score evolution group and overall.

	≥25% compliance subpopulation			Total population
Variable	**Group: Improved (n=19)**	**Group: Stable (n=15)**	**Group: Worsened (n=34)**	**Total[a] (N=84)**
Age, mean (SD), years	68.8 (8.76)	65.9 (8.65)	69.0 (9.62)	68.7 (9.17)
Male, n (%)	18 (95)	13 (87)	29 (85)	74 (88)
Smoking history, n (%)				
Past	16 (84)	12 (80)	26 (76)	65 (77)
Current	3 (16)	3 (20)	8 (24)	19 (23)
COPD type, n (%)				
Chronic bronchitis	3 (16)	6 (40)	5 (15)	20 (24)
Emphysema	16 (84)	9 (60)	29 (85)	64 (76)
Duration of COPD, years				
Mean (SD),	2.4 (2.43)	3.5 (4.42)	4.4 (3.46)	3.5 (3.57)
Median	1.0	2.0	4.5	3.0
Respiratory comorbidity, n (%)				
Asthma	1 (5)	3 (20)	3 (9)	10 (12)
Pulmonary arterial hypertension	0 (0)	1 (7)	0 (0)	2 (2)
mMRC score, mean (SD)	1.1 (1.22)	0.4 (0.51)	0.6 (0.77)	0.6 (0.85)
CAT score, mean (SD)	10.5 (8.83)	6.5 (5.53)	7.9 (5.79)	8.3 (6.57)
% predicted FEV_1, mean (SD)	72.0 (18.6)	71.3 (20.0)	70.6 (23.5)	72.9 (22.0)
Number of exacerbations in the last 12 months (hospitalization or ER visit), n (%)				
0	18 (95)	13 (87)	31 (91)	77 (92)
1	1 (5)	2 (13)	2 (6)	6 (7)
2	0	0	1 (3)	1 (1)
GOLD grade, n (%)				
Grade 1	7 (37)	6 (40)	13 (38)	33 (40)
Grade 2	10 (53)	6 (40)	15 (44)	38 (46)
Grade 3	2 (11)	3 (20)	6 (18)	11 (13)
Grade 4	0	0	0	1 (1)
GOLD group, n (%)				
Group A	10 (53)	9 (60)	22 (65)	50 (60)
Group B	8 (42)	4 (27)	9 (26)	26 (31)
Group C	0	2 (13)	0	3 (4)
Group D	1 (5)	0	3 (9)	4 (5)

[a]Published previously.[16]

CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; ER, emergency room; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council; SD, standard deviation.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Table 2. Change in CAT score from baseline in participants with and without exacerbations over the study period, for the ≥25% compliance subgroup and total population.

	≥25% compliance subpopulation (n=68)			Total population (n=84)		
	Overall (n=68)	**With exacerbation (n=10)**	**Without exacerbation (n=58)**	**Overall (n=83)**	**With exacerbation (n=11)**	**Without exacerbation (n=72)**
Evolution of CAT score[a], n (%)						
Improved	19 (28)	2 (20)	17 (29)	19 (23)	2 (18)	17 (24)
Stable	15 (22)	1 (10)	14 (24)	29 (35)	2 (18)	27 (38)
Worsened	34 (50)	7 (70)	27 (47)	35 (42)	7 (64)	28 (39)
CAT change per year[b]						
Median (IQR)	0.6 (-0.97, 3.76)	2.7 (0.52, 5.71)	0.2 (-1.09, 3.02)	0.2 (-1.15, 4.39)	2.8 (0.52, 5.84)	0.1 (-1.21, 3.37)

[a]Evaluated using a linear regression by participant and categorized by the slope estimate (beta): improved if the lower limit of the 95% CI of beta was <0, worsened if the upper limit of the 95% CI of beta was >0, or stable in all other cases; [b]Calculated by participants as 365.25 * slope estimate/duration (days)

CAT, COPD Assessment Test; CI, confidence interval; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SD, standard deviation.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Table 3. Number of participants with acute changes in CAT score over the study period.

Participants with acute CAT changes[a], n (%)	Total population (n=84)
During the study	
N	62
Within any 1-month period	60 (97)
Within any 2-month period	62 (100)
0–3 months after study start	
N	56
Within any 1-month period	54 (96)
Within any 2-month period	56 (100)
3–6 months after study start	
N	44
Within any 1-month period	38 (86)
Within any 2-month period	44 (100)
6–12 months after study start	
N	43
Within any 1-month period	38 (88)
Within any 2-month period	43 (100)

[a]Acute CAT change is defined as an increase of CAT of >4 during a 1- or 2-month look-back period.

CAT, COPD Assessment Test.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Table 4. Association between CAT score increase over the study period and COPD exacerbation risk in the total population.

	Unadjusted hazard ratio (95% CI)	Adjusted hazard ratio[a] (95% CI)
Physician-defined exacerbation	1.15 (1.06, 1,26)	1.13 (1.03, 1.24)
Moderate exacerbation (requiring use of systemic steroid or antibiotics)	1.15 (1.06, 1.26)	1.13 (1.03, 1.24)
Severe exacerbation (requiring hospitalization or ER visit)	1.27 (1.10, 1.46)	1.22 (1.05, 1.41)

N=84. [a]Cox proportional hazard model with covariates of time-dependent CAT scores, age, sex and % predicted FEV_1 was used to estimate the hazard ratio and the risk of exacerbations per unit increase in CAT.

CAT, COPD Assessment Test, CI, confidence interval; COPD, chronic obstructive pulmonary disease; ER, emergency room; FEV_1, forced expiratory volume in 1 second.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Table 5. Baseline demographic and clinical characteristics by cluster (trajectory analysis).

	Improved (N=8)	Stable (N=50)	Worsened (N=25)
Sex, n (%)			
Male	8 (100)	44 (88)	21 (84)
Age (years)[a]			
Mean	70.9	68.3	68.6
SD	5.87	8.34	11.68
Age group (years)[a], n (%)			
40–64	1 (13)	13 (26)	8 (32)
65–74	5 (63)	25 (50)	10 (40)
≥75	2 (25)	12 (24)	7 (28)
GOLD Grade, n (%)[b]			
Grade 1	3 (38)	18 (37)	12 (48)
Grade 2	2 (25)	24 (49)	11 (44)
Grade 3	3 (38)	6 (12)	2 (8)
Grade 4	0	1 (2)	0
GOLD Group, n (%)			
Group A	1 (13)	32 (64)	17 (68)
Group B	7 (88)	12 (24)	7 (28)
Group C	0	3 (6)	0
Group D	0	3 (6)	0
COPD Type, n (%)			
Chronic bronchitis	3 (38)	12 (24)	5 (20)
Emphysema	5 (63)	38 (76)	20 (80)
Duration of COPD (years)			
Mean	3.250	3.640	3.360
SD	2.5495	3.9526	3.1607
FEV_1 (L)[a]			
Mean	1.994	2.001	2.118
SD	0.7454	0.6825	0.8583
% predicted FEV_1 (%)[b]			
Mean	68.20	71.57	77.18
SD	26.612	21.637	21.939

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

FVC (L)[b]			
Mean	3.589	3.334	3.347
SD	0.5859	0.7776	0.9996
Charlson Comorbidity Index, n (%)			
0	5 (63)	35 (70)	17 (68)
1	2 (25)	8 (16)	5 (20)
2	1 (13)	6 (12)	3 (12)
3	0	1 (2)	0
4	0	0	0
5 or more	0	0	0
Initial CAT Score			
Mean	17.9	7.1	7.4
SD	9.42	5.17	5.72
Initial mMRC Score			
Mean	1.5	0.5	0.6
SD	1.41	0.71	0.77

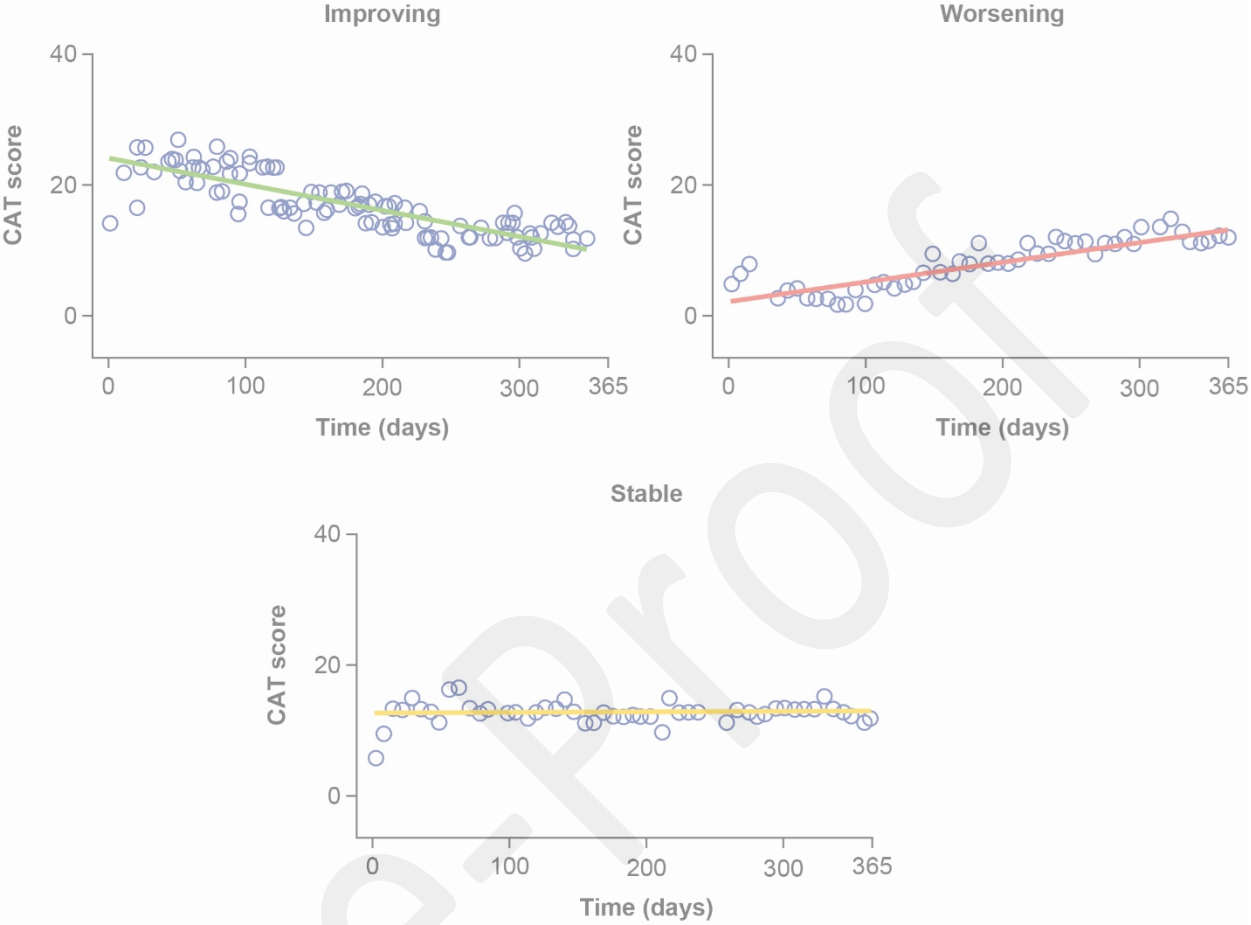
[a]Age is imputed when full date of birth is not provided.

[b]n=49 for Cluster 2.

CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; ER, emergency room; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; L, liters; mMRC, modified Medical Research Council; SD, standard deviation.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

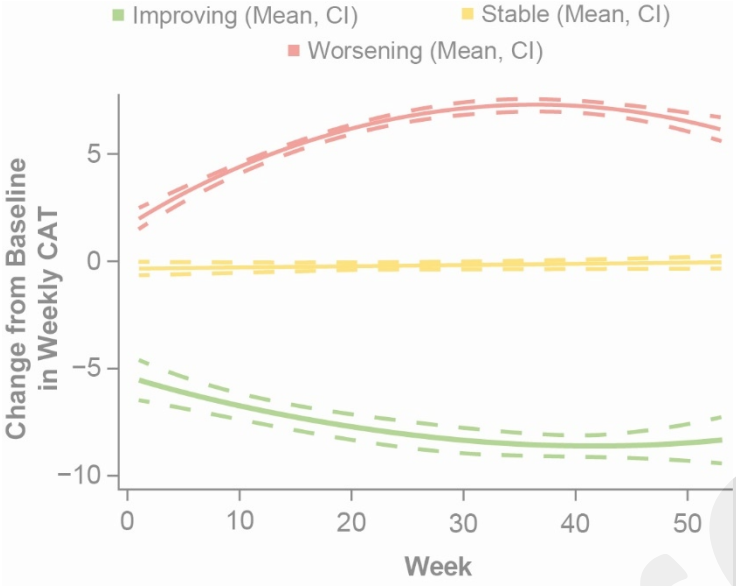
Figure 1. Examples of improving, worsening and stable CAT score slopes for three individual participants over the study period in the ≥25% compliance subpopulation. CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease.



Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Figure 2. Trajectory analysis of CAT score progression (three cluster pattern).

CAT, COPD Assessment Test; CI, confidence interval; COPD, chronic obstructive pulmonary disease.



Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Online Supplement

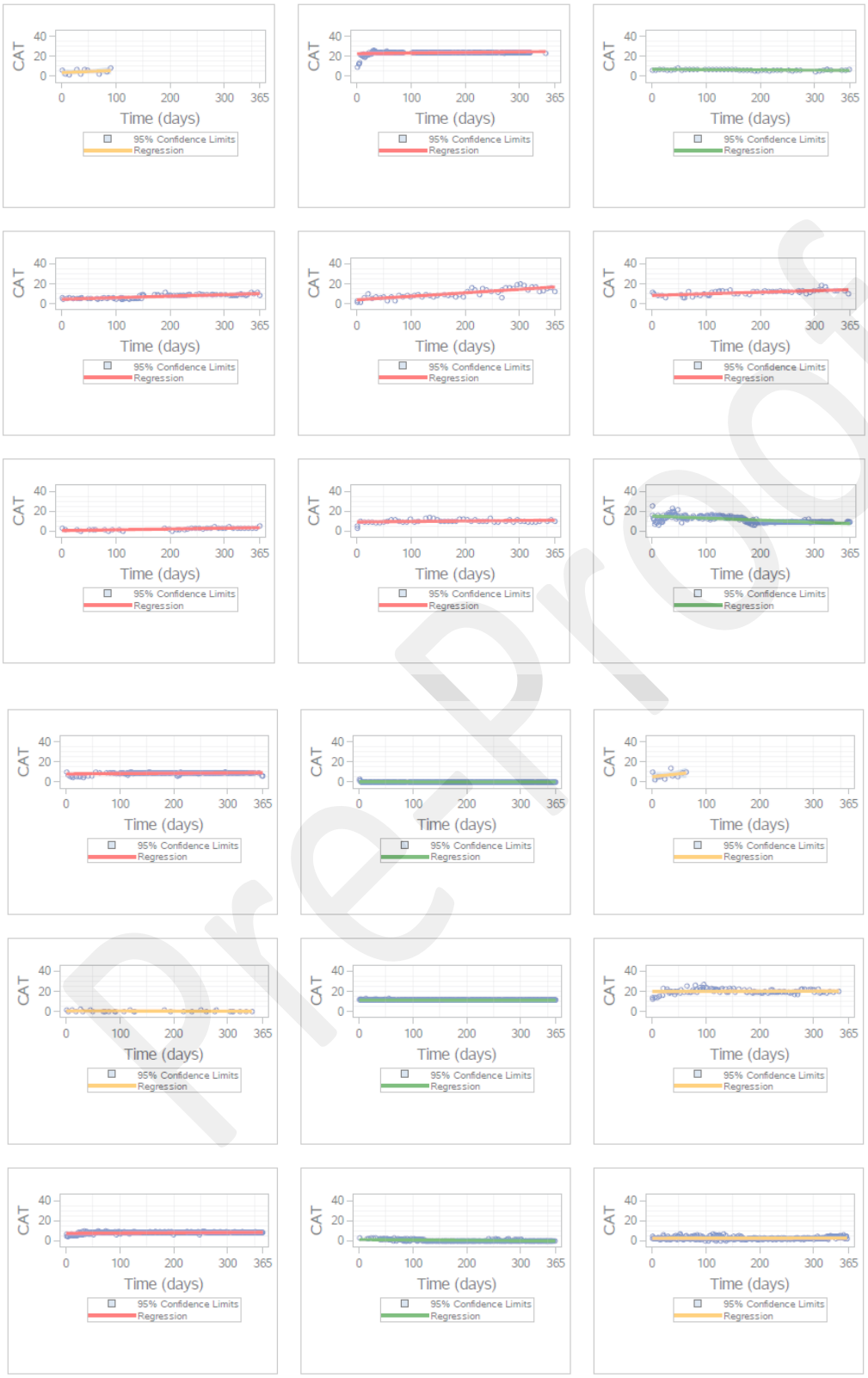
Supplementary Table 1. Full study inclusion and exclusion criteria

Inclusion criteria
Capable of giving signed informed consent, including compliance with the requirements and restrictions required for the study
≥40 years of age inclusive at the time of inclusion in the study
An established clinical history of COPD in accordance with the definition by the American Thoracic Society/European Respiratory Society and Japanese Respiratory Society COPD and ACO guidelines.
Treated with inhaled LAMA and/or LABA as maintenance medication at the screening visit. LAMA/ LABA or ICS combinations will be allowed but inhaled triple therapy (e.g., ICS/LAMA/LABA) will not be allowed at baseline visit. Other short-acting bronchodilators, roflumilast, systemic steroids, or antibiotics medications are permitted.
Lung function test in the 12 months prior to study.
Exclusion criteria
Unable or unwilling to use the required telemonitoring device/ system.
Treated with ICS/LAMA/LABA triple combination at screening visit or during past 3 months before screening visit even open or closed combinations.
Treated with biologicals during past 6 months before screening visit such as omalizumab or mepolizumab.
Pregnant or lactating or are planning on becoming pregnant during the study.
Concurrently participating in another clinical trial, in which the participant has been or will be exposed to an investigational or a non-investigational vaccine/ product (pharmaceutical product).

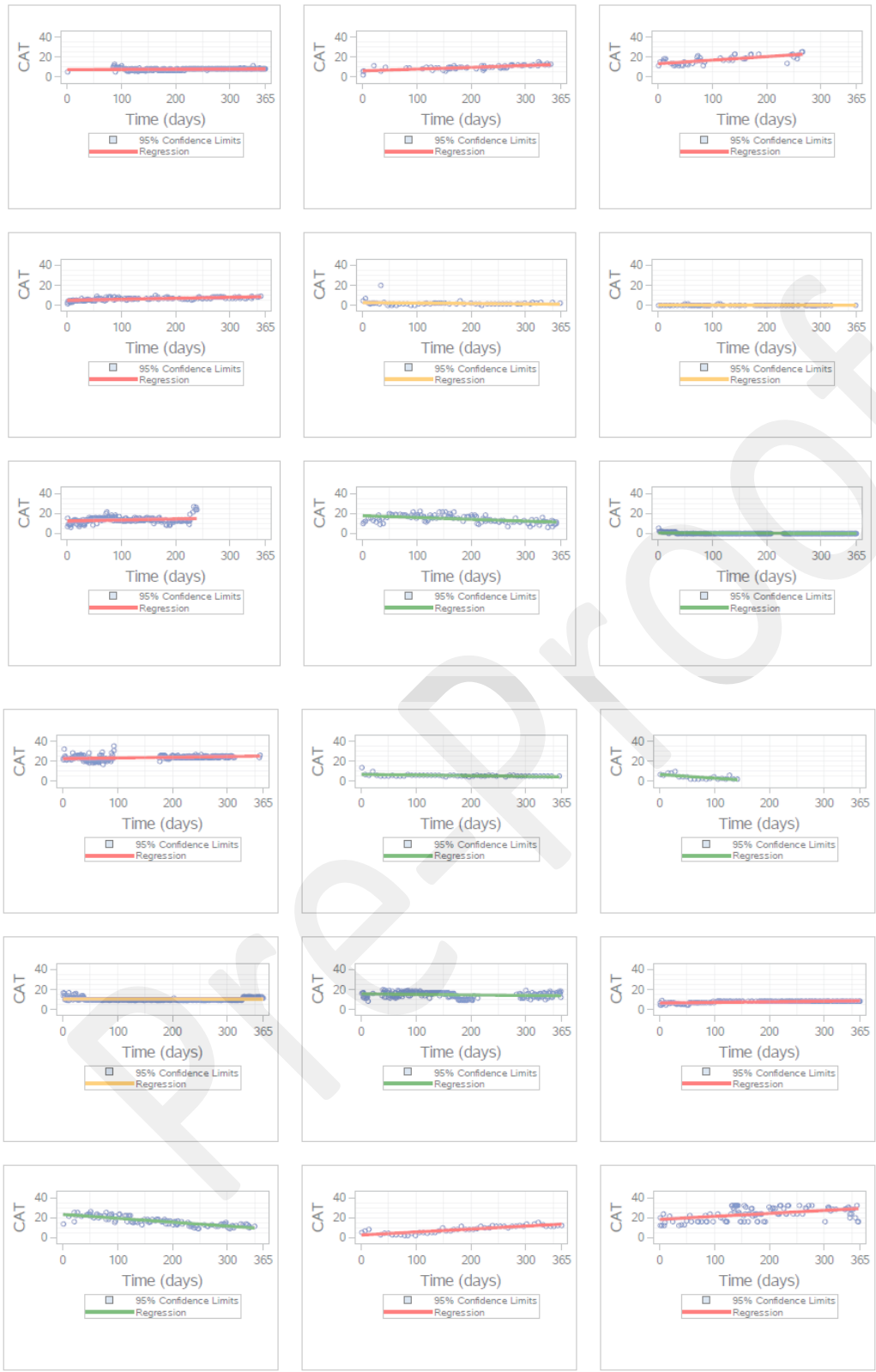
ACO, Asthma-COPD Overlap; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist.

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Supplementary Figure 1. Individual CAT Score Plot



Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415



Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415

Published online February 27, 2024 https://doi.org/10.15326/jcopdf.2023.0415