Supplementary Information

Towards and Assessment of Perceived COPD Exacerbation Triggers: Initial Development and Validation of a Questionnaire Measure

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Appendix S1-EXPANDED METHODS

Participants

Patients were recruited through respiratory specialty clinics and online postings to self-help groups to complete either questionnaires online or as paper-and-pencil surveys, which were returned in prepaid envelopes. Inclusion criteria were a physician diagnosis of COPD, age ≥40

years, and being able the ability to read and understand English. Hospitalized participants were excluded to avoid confounds by treatment-induced symptomatology and experiences. The study was approved by the Institutional Review Boards at Southern Methodist University and Baylor Healthcare System and informed consent was obtained from all participants. Participants received a compensation of $10.

Measures

COPD Exacerbation Trigger Inventory (CETI)

The initial research version of the CETI consisted of 53 items that included a variety of potential exacerbation triggers, including infections, illness, physical activities, moods, weather, allergens, irritants, and behaviors. This list of triggers was developed based on collaboration with health care professionals who regularly treat patients with COPD and on existing literature. An initial pool of items was developed by the investigators and then reviewed by a physician who treats COPD and a pulmonary rehabilitation specialist. Participants rated on a 5-point scale (0-4: never, rarely, sometimes, most of the time, always) how often each trigger is involved when they experience a drastic worsening of their COPD. They were instructed to base their responses on their personal experience rather than what they believe should be triggers for the typical patient. In addition, patients were asked to list up to six of their strongest triggers of COPD exacerbations and indicate on a 5-point scale (0-4: not at all, slightly, moderately, very much, completely) how well they felt they could control or avoid that particular trigger. This portion of the survey is a semi-structured format that provides quantitative data regarding perceived trigger controllability.

Demographic Information

The following information was collected about participants' demographic characteristics: age, gender, height, weight, marital status, race, ethnicity, education, current occupation and income.

Medical History

Participants' self-report was used to gather information about their medical history, including diagnosis of COPD, presence of other comorbid conditions, smoking history, COPD medications, oxygen use, number of exacerbations in the past year, number of times in the past year an exacerbation caused them to seek medical attention, number of times in the past year an exacerbation lead to a change in their medication regimen, and number of lifetime emergency visits for their disease. Comorbidities included a history or current diagnosis in the following four categories: heart disease, lung cancer, asthma, and other respiratory disorder.

COPD Assessment Test (CAT)

The CAT is an 8-item questionnaire that assesses the overall health status of patients with COPD and is designed for everyday clinical use by health professionals [e1]. The measure demonstrates excellent internal consistency (α=.88), very good test-retest reliability (r_{tt}= 0.8) and is sensitive to changes in overall health. Higher scores on the CAT are indicative of greater impairment.

Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item questionnaire that separates into two subscales assessing anxious and depressed mood in the past week[e2]. It has been demonstrated to have good internal

consistency (α=.67-.93) across a variety of research settings and populations and also demonstrates sensitivity and specificity in identifying clinical cases[e3]. To reduce patient burden and maximize return from our postal survey, the HADS was only administered to participants who completed the online survey. Twenty participants returned sufficient HADS data.

Procedure

All participants were asked to complete a questionnaire packet that included the CETI and other measures as described above. Those that completed the paper version of the questionnaire packet were provided written information regarding study participation and confidentiality and asked to return the completed packet in a sealed envelope. Participants who completed the survey online were provided a link to the Qualtrics based survey which provided informed consent information online at the beginning of the survey.

Data Analysis

Principle component analysis with Varimax rotation was used to explore the structure of the CETI, with extraction of five to seven factors to explore plausible solutions guided by prior knowledge of potential triggers factors from the literature (airway infections, weather/climate, air pollution, psychological factors) [e4-e7] [Table S1]. Exploratory factor analysis included examination of scree plots and eigenvalues for 5-7 factor solutions, using mean substitution for missing values on CETI items. After item pool reduction, subscale scores were calculated by averaging items. Internal consistencies of the subscales were estimated using item-intercorrelations, item-total correlations, and Cronbach's α. Spearman's rho correlations were

used to investigate the relation between CETI subscales. Hierarchical multiple linear regression analyses were used to investigate whether the resulting trigger scales predicted overall health status, number of exacerbations in the past year, healthcare utilization, and medication changes over and above demographics, COPD severity (oxygen use), duration, and comorbidities.

Partial correlations were calculated to examine the relation between the CETI subscales and standardized HADS anxiety and depression subscales, controlling for oxygen use as an indicator of disease severity [e8-e10]. Hierarchical multiple linear regression analyses were used to investigate whether past or current heart disease, lung cancer, asthma, or other respiratory condition predicted CETI subscales and trigger controllability over and above demographics, COPD severity (oxygen use), and COPD duration.

Appendix S2-ADDITIONAL RESULTS

Associations of CETI subscales with anxiety and depression

Results indicated that none of the CETI subscales were significantly correlated with anxiety or depression scores, after controlling for disease severity (Table S2). However, patients who reported a greater number of psychological triggers also tended to have higher anxiety scores.

Associations between Comorbidities and CETI Subscales

Hierarchical multiple regression analyses examining the impact of COPD comorbidities found that past or current comorbidities accounted for a significant amount of variance in the

CETI psychological subscale (Table S3). Together, comorbidities accounted for 6.8% of the variance in the psychological subscale beyond that accounted for by covariates (age, gender, race, education, COPD duration, and oxygen use). Individuals with current or past heart disease or lung cancer were more likely to endorse psychological exacerbation triggers of their COPD.

Although comorbidities as a whole did not significantly predict any of the other CETI subscales, history or current lung cancer emerged as a significant predictor of exercise related triggers. Those with a history of or current lung cancer were more likely to endorse exercise-related exacerbation triggers (Table S3).

Association between Trigger Controllability and Quality of Life

Trigger controllability accounted for 4.0% of the variance in the CAT scores beyond covariates, $F(1,105)=6.24$, $p=.014$, for R^2 change (total $R^2=0.32$, $F(8,105)=6.28$, $p<.001$). Greater controllability was associated with higher quality of life, $t=-2.50$, $\beta=-0.21$, $p=.014$. Higher quality of life was also associated with higher age, $t=-3.12$, $\beta=-0.26$, $p=.002$; having a higher educational attainment, $t=-2.16$, $\beta=-0.18$, $p=.033$; and not receiving oxygen therapy, $t=4.51$, $\beta=0.38$, $p<.001$.

Appendix S3-ADDITIONAL DISCUSSION

The finding of insignificant correlations between the HADS and CETI subscales adds to the validity of the CETI by demonstrating that participant ratings of triggers do not appear to be based solely on mood states such as anxiety and depression. Two correlations exhibited a trend

towards significance: those between the HADS anxiety score and the Psychological and Exercise subscales. It is possible that participants with higher baseline anxiety levels tend to also interpret psychological factors as more threatening to their health, as well as the physiological arousal that accompanies physical activity. Research on patients with COPD and panic disorder demonstrates higher levels of anxiety and greater perception of severe consequences of the disease compared to those without panic of similar disease severity[e11]. However, such results should be interpreted with caution as the number of participants who completed the HADS was small.

Insignificant associations between comorbidities and CETI subscales suggest robustness of the measure across different subpopulations and add to the validity of the measure. Those with other comorbid disorders may be more likely to experience distress or negative mood, which could lead to physiological changes that promote increased risk for exacerbations. Alternatively, those with a history of heart disease or lung cancer may have greater past experiences and therefore greater awareness of physiological changes in response to stress or negative emotional states, making them more likely to report psychological triggers

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Appendix S4 - COPD Trigger Exacerbation Inventory (CETI)

Patients with COPD sometimes experience episodes when their disease becomes drastically worse with much stronger symptoms than on average days. Such episodes are called exacerbations and there are many different causes for COPD exacerbations. Causes can vary considerably from one person to the other.

Instructions: **Please indicate for each of the listed causes below how often they have been involved when you had experienced drastic worsening of your COPD. In doing so, please base your answers on your own personal experience, not on what you think should lead to COPD exacerbations for the typical patient.**

The following things can trigger my COPD exacerbations alone or in part:

Please make sure you have circled one answer for each trigger

		Never	Rarely	Sometimes	Most of the time	Always
1.	Having a cold	0	1	2	3	4
2.	Cigarette smoke	0	1	2	3	4
3.	Running	0	1	2	3	4
4.	Being angry	0	1	2	3	4
5.	Exhaust fumes	0	1	2	3	4
6.	Certain intensive odours	0	1	2	3	4
7.	Feeling tense	0	1	2	3	4
8.	Climbing flights of stairs	0	1	2	3	4
9.	Depressed mood	0	1	2	3	4
10.	Smell of paint	0	1	2	3	4
11.	Sport activities	0	1	2	3	4
12.	Perfumes	0	1	2	3	4
13.	Arguments with people	0	1	2	3	4
14.	Flu	0	1	2	3	4
15.	Sinus problems	0	1	2	3	4
16.	Being excited	0	1	2	3	4
17.	Intense worries	0	1	2	3	4
18.	Feeling unhappy	0	1	2	3	4
19.	Overexertion	0	1	2	3	4
20.	Viruses	0	1	2	3	4
21.	Sprays	0	1	2	3	4
22.	Humid air	0	1	2	3	4
23.	Dry air	0	1	2	3	4
24.	Hot climate	0	1	2	3	4
25.	Weather changes	0	1	2	3	4

Please make sure you have circled <u>one</u> answer for <u>each</u> trigger

		Never	Rarely	Sometimes	Most of the time	Always
26.	Cold air	0	1	2	3	4
27.	Damp rooms	0	1	2	3	4
28.	Brisk walking	0	1	2	3	4
29.	Sore throat	0	1	2	3	4
30.	Wood fire	0	1	2	3	4
31.	Chest infections	0	1	2	3	4
32.	Muggy air	0	1	2	3	4
33.	Walking uphill	0	1	2	3	4

<u>Instructions:</u> **Please list below up to six of the strongest triggers of your COPD exacerbations.**
Next, indicate to what extent you are able to control or avoid each of these exacerbation triggers in your daily life:

Triggers	I can control this trigger...				
	Not at all	Slightly	Moderately	Very much	Completely
1.Trigger #1: _____	0	1	2	3	4
2.Trigger #2: _____	0	1	2	3	4
3.Trigger #3:_____	0	1	2	3	4
4.Trigger #4:_____	0	1	2	3	4
5.Trigger #5:_____	0	1	2	3	4
6.Trigger #6:_____	0	1	2	3	4

Appendix S5: Item Key for COPD Exacerbation Trigger Inventory

For each subscale, sum up the following items:

Psychological Triggers: Being Angry, Feeling Tense, Depressed Mood, Arguments with People, Being Excited, Intense Worries, Feeling Unhappy

Weather/Climate Triggers: Humid Air, Dry Air, Hot Climate, Weather Changes, Cold Air, Damp Rooms, Muggy Air

Air Pollution/Irritant Triggers: Cigarette Smoke, Exhaust Fumes, Certain Intensive Odours, Smell of Paint, Perfumes, Sprays, Wood Fire

Physical Activity Triggers: Running, Climbing Flight of Stairs, Overexertion, Sport Activities, Brisk Walking, Walking Uphill

Infection/Illness Triggers: Having a Cold, Flu, Sinus Problems, Viruses, Sore Throat, Chest Infection

Table S1.

CETI 33-Item Factor Loadings and Communalities (N = 192)

Rotated Component Matrix[a]

	Component					Communality
	1	2	3	4	5	
having a cold	.10	.06	.17	.19	**.79**	.71
cigarette smoke	.07	**.70**	.29	.05	.09	.60
running	.14	.20	**.79**	-.05	.15	.71
Being angry	**.64**	.26	.24	.13	.12	.56
exhaust fumes	.26	**.70**	.25	.21	.13	.68
certain intensive odours	.25	**.75**	.07	.27	.22	.75
feeling tense	**.80**	.16	.15	.28	.14	.79
climbing flights of stairs	.20	.18	**.80**	.22	.11	.78
depressed mood	**.80**	.16	.06	.18	.20	.73
smell of paint	.17	**.79**	.09	.26	.18	.76
sport activities	.19	.11	**.73**	.12	.24	.66
perfumes	.09	**.70**	.16	.21	.21	.61
arguments with people	**.78**	.18	.22	.13	.11	.72
flu	.13	.28	.30	.08	**.76**	.77
sinus problems	.32	.15	.23	.29	**.60**	.62
being excited	**.66**	.18	.23	.32	.07	.63

intense worries	**.87**	.08	.16	.20	.19	.87
feeling unhappy	**.85**	.07	.09	.18	.11	.77
overexertion	.22	.21	**.77**	.25	.15	.77
viruses	.15	.19	.18	.12	**.81**	.75
sprays	.11	**.69**	.18	.41	.21	.73
humid air	.24	.23	.24	**.74**	.24	.77
dry air	.26	.17	.08	**.67**	.14	.57
hot climate	.32	.27	.29	**.67**	.09	.71
weather changes	.25	.23	.15	**.72**	.30	.75
cold air	.11	.16	.13	**.59**	.13	.42
damp rooms	.26	.36	.14	**.59**	.28	.63
brisk walking	.09	.06	**.76**	.27	.17	.70
sore throat	.21	.33	-.08	.23	**.66**	.64
wood fire	.15	**.75**	.10	.16	.13	.63
chest infections	.11	.16	.22	.24	**.78**	.75
muggy air	.24	.32	.31	**.66**	.17	.71
walking uphill	.19	.26	**.78**	.26	.13	.79

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 5 iterations.

b. Component 1: Psychological; 2: Irritants; 3: Exercise; 4: Weather/Climate; 5: Infection

Table S2

HADS and CETI Subscales Partial Correlations (n=20)

	HADS Anxiety	HADS Depression
Psychological	0.44†	-0.20
Weather/Climate	0.34	0.17
Irritants	0.10	0.08
Exercise	0.39†	0.03
Infection	0.25	-0.03

Partial correlation controlling for oxygen use and using standardized HADS scores that control for gender differences

† $p<.10$, two-tailed

Table S3.
Explained Variance in CETI Subscales by Comorbidities [a]

Criterion	R^2 Change[b]	P	Comorbidity Predictors[c]	T[d]	p	R^2 for Total Model
Psychological	0.068	0.037	Heart Disease	2.17	0.032	0.213
			Lung Cancer	2.19	0.031	
Weather/Climate	0.11	0.786	None	-	-	0.181
Infection	0.003	0.980	None	-	-	0.156
Exercise	0.037	0.245	Lung Cancer	2.05	0.043	0.180
Irritants	0.012	0.767	None	-	-	0.194
Trigger Controllability	0.008	0.931	None	-	-	0.060

[a] Results from hierarchical multiple linear regressions analysis after controlling for age, gender, race, and education in Step 1, COPD duration and oxygen use in Step 2, and comorbidities (heart disease, asthma, lung cancer, other respiratory disorder) in Step 3.

[b] Change in R^2 for the four comorbidities entered in Step 3.

[c] Only predictors that are significant ($p < .05$) or marginal ($p < .10$) are reported.

[d] t-test results for beta weights; positive values indicate a positive association between comorbidities (as predictors) and dependent variable.