

The Burden of Cough and Phlegm in People with COPD: A COPD PPRN Study

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BACKGROUND

- Chronic obstructive pulmonary disease (COPD) affects 15–25 million individuals in the US and is the 4th leading cause of death and 2nd leading cause of disability in the US.¹
- In the US, COPD is a direct cause of >140,000 deaths annually with costs >\$50 billion, >700,000 hospitalizations and 1.5 million emergency room department visits.¹
- Cough and phlegm are common symptoms reported by the majority of people with COPD.²⁻⁴
- Most treatment for cough and phlegm are directed at bronchodilation and inflammation with few treatments addressing directly either cough or phlegm.⁵
- Limited information has been published addressing the patient reported burden of cough or phlegm on functional status, role fulfillment abilities and impact on mood.
- We used patient self-reported data the COPD Foundation's Patient-Powered Research Network (COPD PPRN) to highlight the frequency, severity and life factors associated with cough and phlegm in a large group of individuals reporting physician diagnosis of COPD.

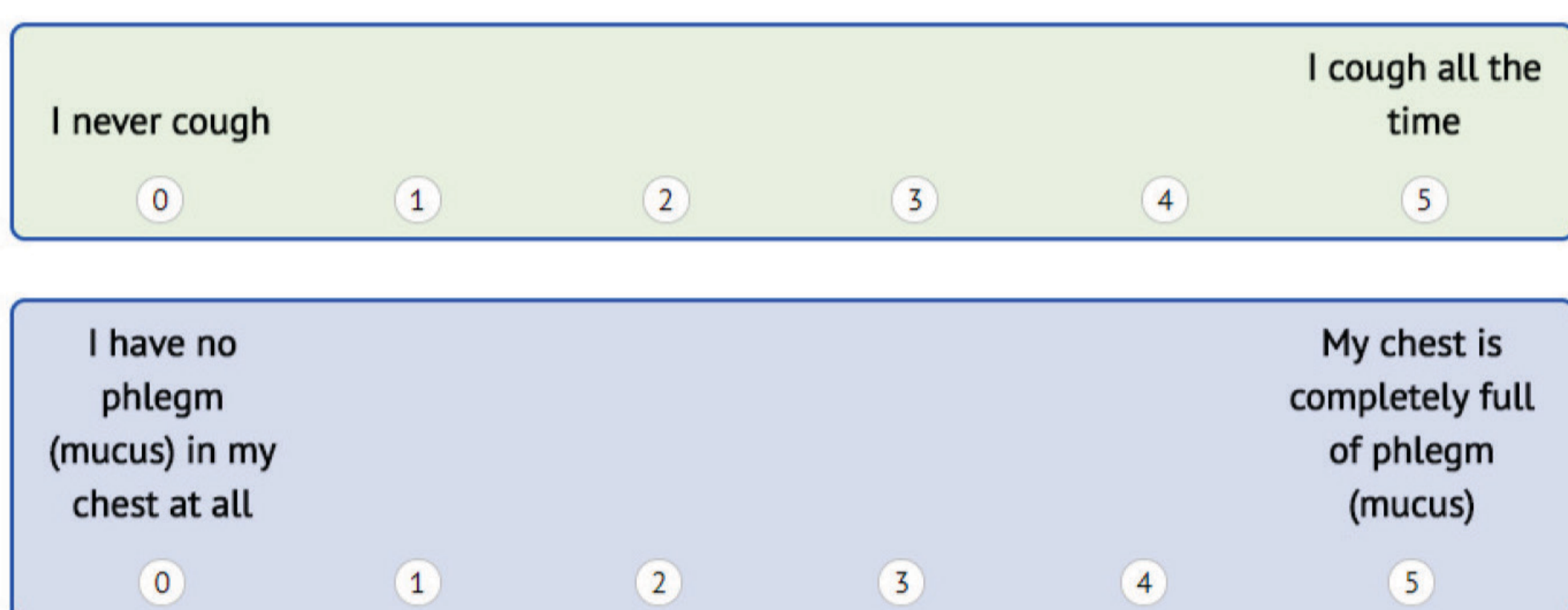
OBJECTIVE

- To present the patient perspective on the burden of cough and phlegm occurring in COPD.

METHODS

- Data were patient reported using the online COPD Foundation's Patient-Powered Research Network (COPD PPRN). For individuals with self-reported COPD demographic, COPD disease related (COPD Assessment Test [CAT], exacerbations and FEV₁), and functional status and quality of life data were collected following completion of eConsent.
- The frequency of cough and phlegm were assessed using questions 1 (cough) and 2 (phlegm) of the COPD Assessment Test (CAT).⁶ (Figure 1) Frequency/ severity were summarized as low (scores of 0-1), moderate (scores of 2-3) and high (scores 4-5) based on the 5 level CAT responses.

Figure 1. Cough and Phlegm as measure by CAT



- Levels of cough and phlegm frequency were compared by gender, age groups, and self-reported exacerbation rates in the previous 12 months.
- Further analyses compared levels of cough and phlegm with the 7 domains of the PROMIS-29 including: anxiety, depression, fatigue, sleep, pain, social role functioning and physical role functioning.⁷
- The PROMIS-29 domain scores were weighted and standardized to place the average person's score at 50 (scale 0 to 100) with deviations from 50 suggesting burden or improvement compared to the "average" US person.⁸
- Descriptive statistics are reported as mean (SD) for continuous variables, and frequencies (%) for categorical variables (demographic and clinical characteristics, and total CAT scores) and then as stratified by levels of cough and phlegm. Values between the groups were compared using Chi-squared test (for categorical variables) and t-test/ANOVA (for continuous variables) respectively. The weighted standardized PROMIS 29 scores were also stratified by levels of cough and phlegm.

RESULTS

- Overall, 5,314 individuals with self-reported physician diagnosed COPD were included in the analyses. 60.4% were women with an average age of 64.4 (SD=11.5). 51.2% were married and 42.2% had caregivers. Both men and women were very likely to have ever smoked and many were current smokers; 88.2% ever smokers, 17.8% of those were current smokers.

Table 1. Demographic characteristics of group (N = 5,314)

	Phlegm Levels		Cough Levels	
	No or low (0,1) N=1712*	Moderate/High (2-5) N=3596*	No or low (0,1) N=1712*	Moderate/High (2-5) N=3596*
Age†				
Mean (SD)	65.2 (11.3)	64.0 (11.5)	65.8 (11.1)	63.8 (11.5)
Median [Q1-Q3]	67 [59-73]	65 [57-72]	67 [60-73]	65 [57-72]
Race, n (%)***				
White	1584 (95.9)	3241 (95.0)	1333 (95.8)	3489 (95.1)
Black	72 (7.1)	218 (10.0)	51 (5.9)	245 (10.5)
Asian	9 (0.9)	18 (0.9)	10 (1.2)	18 (0.8)
Gender, n (%)				
Female	1095 (64.2)	2101 (58.6)	854 (59.8)	2345 (60.6)
Male	610 (35.8)	1487 (41.1)	574 (40.2)	1523 (39.4)
Ethnicity, n (%)				
Hispanic	48 (2.9)	94 (2.7)	34 (2.4)	107 (2.8)
BMI, mean (SD)	28.0 (7.1)	28.5 (7.7)	27.4 (6.7)	28.7 (7.8)
Never smokers, n (%)	233 (13.6)	390 (10.9)	154 (10.8)	472 (12.2)
Current smoker, n (%)	111 (6.5)	711 (19.8)	81 (5.7)	738 (19.0)
Pack/year among ever smokers	N=1432	N=3093	N=1232	N=3293
Mean (SD)	45.5 (28.0)	45.6 (28.4)	47.9 (28.6) ‡	44.7 (28.2) ‡
Median [Q1-Q3]	42 [25.5-62]	41 [24.5-63]	44 [27.9-66]	40 [24-61.5]
mMRC, n (%) †, ††				
0	231 (13.7)	221 (6.2)	208 (14.7)	244 (6.3)
1	595 (35.2)	939 (26.2)	489 (34.5)	1048 (27.2)
2	476 (28.1)	1167 (32.6)	374 (26.4)	1268 (32.9)
3	265 (15.7)	733 (20.5)	229 (16.1)	768 (19.9)
4	125 (7.4)	521 (14.6)	119 (8.4)	525 (13.6)
Exacerbations in the past 1 yr †††				
0	606 (36.0)	591 (16.7)	520 (37.1)	677 (17.7)
1	474 (28.2)	695 (19.6)	388 (27.7)	781 (20.4)
2	256 (15.2)	702 (19.8)	209 (14.9)	750 (19.6)
3	163 (9.7)	598 (16.9)	131 (9.4)	633 (16.5)
4+	185 (11.0)	961 (27.1)	153 (10.9)	993 (25.9)

*and ** Do not add up to 5314 due to missing data. *** Do not add to 100% due to overlap in races; †p<0.0001; ††max number of antibiotic/prednisone/ER visit/ hospital

mMRC++:
0: "I only get breathless with strenuous exercise"
1: "I get short of breath when hurrying on the level or walking up a slight hill"
2: "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"
3: "I stop for breath after walking about 100 yards or after a few minutes on the level"
4: "I am too breathless to leave the house" or "I am breathless when dressing or undressing"

- The distribution of both cough and phlegm are similar with over 45% of individuals reporting moderate frequencies of either cough or phlegm and slightly over 20% reporting high frequencies. (Table 2) The percent of individuals with self-reported frequent exacerbations (>2) increase significantly with increasing frequencies of both cough becoming twice as great for those with high levels of cough or phlegm compared to those with low levels. The CAT score is >10 for about two third of those with low levels of cough and phlegm but over 94% of those with moderate to high levels. The levels of cough and phlegm and total CAT score are co-linear and highly associated. (Table 3)

Table 2. Frequency of cough and phlegm levels by disease characteristics (N= 5,314)

Cough Levels	Low (0,1) N = 1712	Moderate (2,3) N = 2492	High (4,5) N = 1110
Overall frequency *	32.2%	46.9%	20.9%
>2 exacerbations/yr* +	35.2%	56.2%	73.9%
CAT>10 * +	68.3%	94.3%	99.6%
Phlegm Levels	Low (0,1) N = 1429	Moderate (2,3) N = 2620	High (4,5) N = 1259
Overall frequency *	26.9%	49.3%	23.7%
>2 exacerbations/yr* +	35.9%	59.4%	73.6%
CAT>10 * +	69.7%	96.6%	99.6%

* Percent frequency by row + Levels varied significantly--p <.001

Table 3. Cross tabulation of levels of cough and phlegm frequencies (N = 5,314)

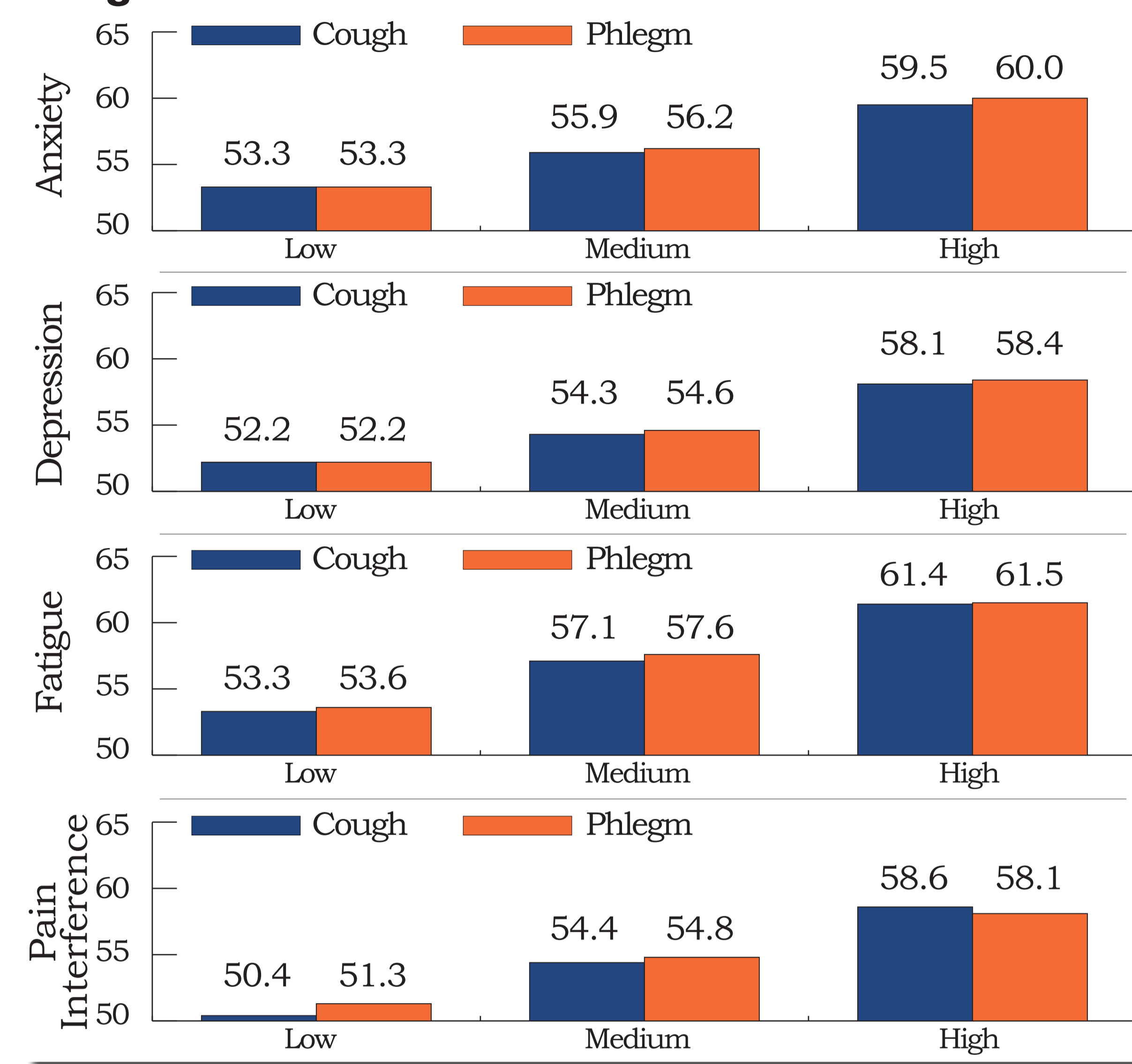
	Cough Levels			Phlegm Levels		
	Low (0,1)	Moderate (2,3)	High (4,5)	Low (0,1)	Moderate (2,3)	High (4,5)
Cough	----	----	----			
Low				78.2%	19.5%	2.3%
Mod				20.6%	65.4%	14.0%
High				3.8%	39.7%	56.5%
Phlegm				----	----	----
Low	65.6%	31.6%	2.8%			
Mod	11.2%	68.7%	20.1%			
High	2.9%	33.0%	64.1%			

- The burden of cough and phlegm may be seen in the association of the levels of cough and phlegm frequency and the standardized scores on the domains of the PROMIS-29. Figure 2 demonstrates the increase in the burden of depression, anxiety, fatigue and pain as both cough and phlegm frequency increases. Depression scores increase from 52.2 to 58.1 with increasing frequency of cough. Interestingly, increasing cough and phlegm frequency but no effect of levels was seen on reported sleep disturbance.

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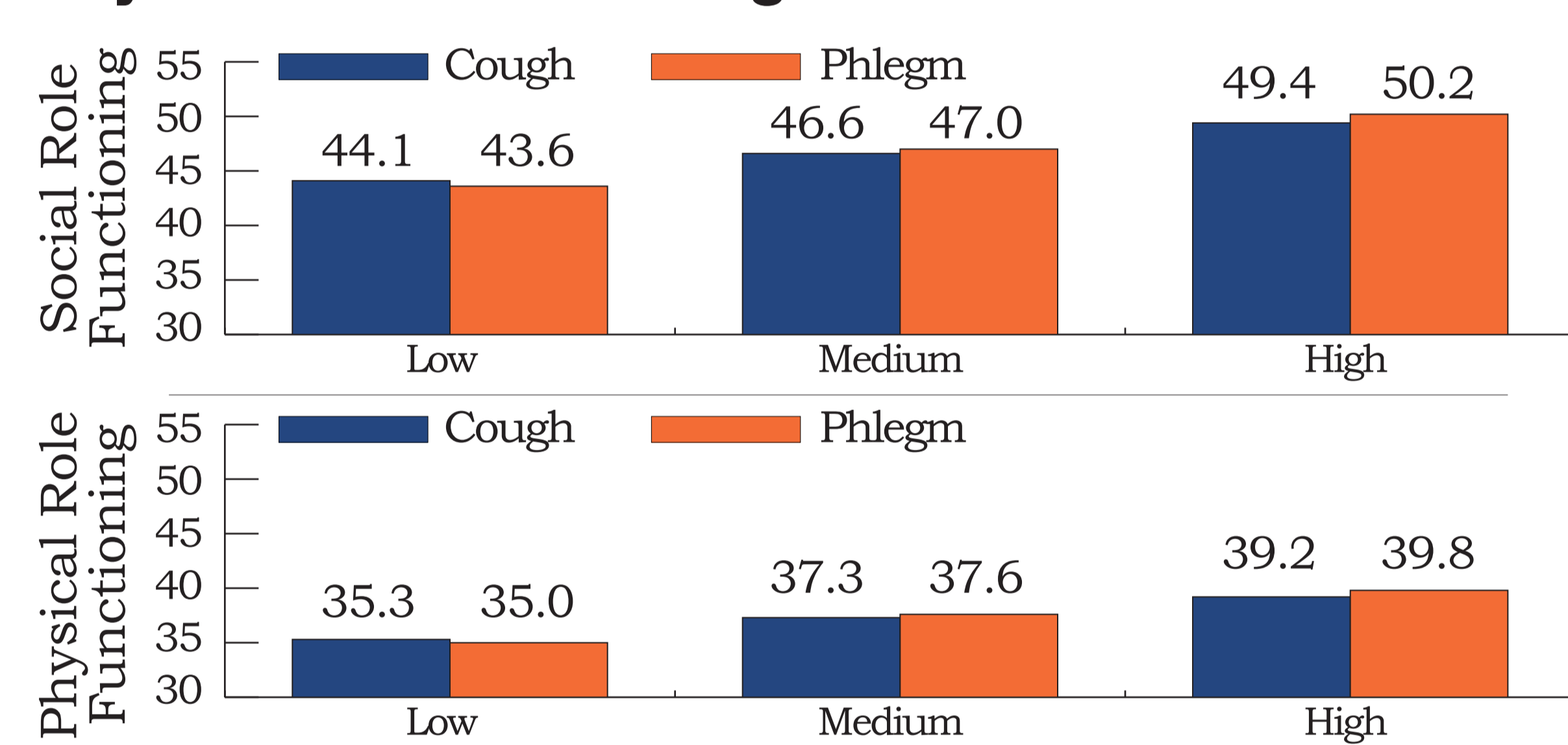
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Figure 2. Impact of Cough and Phlegm on Mood, Fatigue and Pain



- For social and physical role functioning, lower scores --below the average score of "50" for age matched individuals show declines in ability to meet the patient's expectation of these role functions. However, the impact of increasing frequency of both cough and phlegm appear to have a paradoxical impact. (Figure 3) Further evaluation is warranted.

Figure 3. Impact of Cough and Phlegm on Social and Physical Role Functioning



DISCUSSION

- Others have also reported on the frequency and potential impact of cough and phlegm as a marker of COPD phenotypes, especially chronic bronchitis^{2,3,9} and as risk factors for exacerbations and death.¹⁰ Miravittles and Ribera² outlined the impact of COPD on many symptoms but did not look at the specific impact of COPD cough or phlegm. Narrowing the focus to cough and phlegm specifically is important since currently few pharmacotherapies directly address either cough or phlegm.⁵ The results of our study confirms that about two thirds of COPD patients have moderate to high cough and phlegm burden. Increasing levels of cough and phlegm are associated with increasing levels of adverse impact on rates of exacerbations, mood, pain, and fatigue. The association with levels of physical and social role function require further study.
- The observed high impact of increasing levels of cough and phlegm illustrate the need to renew the search for therapies designed specifically to directly reduce cough or phlegm burden in people with COPD.
- Our work is limited by the potential selection bias of our online registry and the self-reported nature of the information including self-reported COPD diagnoses. However, using self-reported data regarding seldom addressed outcomes such as patient perceived impact on anxiety, depression, pain, fatigue and role functioning as well as frequency of cough and phlegm production is also the strength of this work.

CONCLUSIONS

- In people with COPD, cough and phlegm are associated with greater likelihood of having "frequent exacerbations", higher CAT scores and increasing magnitude of depression, anxiety, fatigue and pain but not sleep disturbance. While these may be direct effects of cough and phlegm, increasing frequency of cough and phlegm may also be a marker of increasing COPD severity. Further work in this area is required with exploration of new treatments specifically aimed at cough and phlegm.

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