ONLINE EXCLUSIVE

Lower Income, Smoking, Cardiopulmonary Comorbidities, and Higher Symptom Burden Influence the Occurrence of Cough in Patients Receiving Chemotherapy

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OBJECTIVES: To identify subgroups of patients with distinct cough occurrence profiles and evaluate for differences among these subgroups.

SAMPLE & SETTING: Outpatients receiving chemotherapy (N = 1,338) completed questionnaires six times over two chemotherapy cycles.

METHODS & VARIABLES: Occurrence of cough was assessed using the Memorial Symptom Assessment Scale. Latent class analysis was used to identify subgroups with distinct cough occurrence profiles. Parametric and nonparametric tests were used to evaluate for differences.

RESULTS: Four distinct cough profiles were identified (None, Decreasing, Increasing, and High). Risk factors associated with membership in the High class included lower annual household income; history of smoking; self-reported diagnoses of lung disease, heart disease, and back pain; and having lung cancer.

IMPLICATIONS FOR NURSING: Clinicians need to assess all patients with cancer for cough and provide targeted interventions.

KEYWORDS cancer; chemotherapy; chest tightness; cough; depression; dyspnea

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Cough is a common and distressing symptom that occurs in 22%–93% of patients with cancer (Chowienczyk et al., 2020; Harle et al., 2019, 2020; Iyer et al., 2014; Lou et al., 2017; Molassiotis et al., 2010; Walling et al., 2015). This broad range in prevalence rates suggests that a large amount of interindividual variability exists in this symptom. However, guidelines for the management of cough published by the American College of Chest Physicians provide recommendations for pharmacologic and nonpharmacologic interventions only for patients with lung cancer (Molassiotis et al., 2017). Of note, all of these interventions are based on level II evidence that indicates uncertainty in the estimates of benefits, risks, and burdens (Molassiotis et al., 2017). Therefore, additional research is needed on the occurrence of and risk factors for cough in patients with heterogenous types of cancer to be able to design targeted assessments and interventions.

Demographic and Clinical Risk Factors

Patients with lung cancer can experience cough from a tumor mass that irritates cough receptors (Li et al., 2021) and/or obstructs the airways (Kvale, 2006) or from secondary causes (e.g., pleural effusion) (Molassiotis et al., 2017). Equally important, risk factors for cough in patients with other types of cancer include older age (McGarvey et al., 2021), past or current history of smoking (McGarvey et al., 2021), cardiopulmonary comorbidities (Christensen et al., 2016; McGarvey et al., 2021), gastrointestinal reflux

(Harle et al., 2019), lung injury or pulmonary toxicity from previous cancer treatments (Li et al., 2021; Long & Suresh, 2020), and/or dysphagia as a result of radiation therapy (Mootassim-Billah et al., 2021). However, studies on demographic and clinical characteristics associated with an increased risk of cough in patients with cancer are extremely limited.

Multiple Dimensions of Cough

Given the paucity of research on cough, no consensus exists on how to assess this symptom (Turner & Birring, 2023). However, similar to other symptoms, multiple dimensions of cough (e.g., occurrence, frequency, severity) and its impact warrant evaluation (Birring & Spinou, 2015; Turner & Birring, 2023). In addition, the American College of Chest Physicians guidelines noted that the affective domain needs to be assessed because an individual's cognitive evaluation of cough and associated response(s) may regulate the cough reflex (Lee et al., 2021). Although no studies have evaluated for affective distress in patients with cancer, patients without cancer with chronic cough reported more negative illness perceptions of the consequences of their cough compared to patients without cough (Hulme et al., 2017).

Co-Occurring Respiratory Symptoms

Several lines of evidence suggest that cough occurs with other respiratory symptoms in patients with cancer. For example, in a study of patients with advanced lung cancer (Lou et al., 2017), cough, difficulty breathing, chest tightness, and shortness of breath were the most common respiratory symptoms. In another study of patients with lung cancer receiving chemotherapy (Wong et al., 2017), cough was clustered with chest tightness, difficulty breathing, and shortness of breath. In addition, in a study of patients with heterogeneous types of cancer that used a network analysis (Kalantari et al., 2022), cough was interrelated with chest tightness, shortness of breath, and difficulty breathing. Finally, in an observational study of records from primary care settings (Chowienczyk et al., 2020), the co-occurrence of cough and dyspnea increased over time in patients with lung cancer when they initially had either single symptom.

Common Cancer-Related Symptoms

Previous research found that patients with chronic cough reported higher levels of anxiety (French et al., 2017; Zhang et al., 2023), depressive symptoms (French et al., 2017; Zhang et al., 2023), sleep disturbance (Lee & Birring, 2010; Zhang et al., 2023), pain (Arinze et al., 2021), fatigue (Arikan et al., 2015; Cheville et al., 2011a, 2011b), and cognitive impairment (Yin et al., 2016). For example, compared to patients with chronic cough who had preexisting anxiety and depression, patients with cough-induced anxiety and depression were more likely to experience more severe coughing for a longer duration (Zhang et al., 2023). These findings suggest that the development and maintenance of cough may derive from interactions with other co-occurring symptoms (French et al., 2017; McGarvey et al., 2006). However, none of the studies cited evaluated for associations between cough and the severity of these other common symptoms in patients with cancer.

Quality of Life

Cough has a negative impact on the physical, psychological, and social well-being of patients with cancer (Harle et al., 2020; Iyer et al., 2014; Lou et al., 2017; Yang et al., 2012). In studies of patients with lung cancer (Iyer et al., 2014; Lou et al., 2017), severe coughing resulted in significant decrements in overall quality of life (QOL). Similarly, in population-based studies conducted in Japan (Kubo et al., 2021) and China (Ma et al., 2009), compared to healthy individuals, participants with chronic cough reported lower scores for both the physical and mental components of the Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12). However, despite its negative impact on QOL, no studies have evaluated the impact of cough on multiple domains of QOL in patients with heterogenous types of cancer.

Latent class analysis (LCA) is a person-centered analytic approach that can be used to identify subgroups (i.e., latent classes) of patients with distinct symptom profiles (Muthén & Muthén, 2000). Given the wide range in occurrence rates for cough among patients with cancer (Harle et al., 2019), the use of LCA may provide insights into modifiable and nonmodifiable risk factors that contribute to its interindividual variability. Therefore, the aims of this study, in a sample of patients receiving outpatient chemotherapy (N = 1,338), were to identify subgroups of patients with distinct cough occurrence profiles; evaluate for differences among the subgroups in demographic and clinical characteristics; evaluate for differences in severity, frequency, and distress of cough; evaluate for differences in the occurrence of other respiratory symptoms; evaluate for differences in the severity of the other common symptoms; and evaluate for differences in QOL outcomes.

Methods

Patients and Settings

This study is part of a larger longitudinal study of the symptom experience of patients receiving outpatient chemotherapy that was conducted prior to the COVID-19 pandemic (Miaskowski et al., 2014). The theory of symptom management provided the overall theoretical framework for the entire study. Specifically, this study examined the relationships between the symptom experience (i.e., cough) and the outcomes concepts (i.e., QOL) as well as the person and health and illness domains (Weiss et al., 2023).

Eligible patients were aged 18 years or older; had a diagnosis of breast, gastrointestinal, gynecologic, or lung cancer; had received chemotherapy within the preceding four weeks; were scheduled to receive at least two additional cycles of chemotherapy; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two comprehensive cancer centers, one Veterans Affairs hospital, and four community-based oncology programs during their first or second cycle of chemotherapy. The major reason for refusal was being overwhelmed with their cancer treatment.

Study Procedures

This study was approved by the Committee on Human Research at the University of California, San Francisco, and by the institutional review boards at each of the study sites. Of the 2,234 patients approached, 1,343 consented to participate (60.1% response rate). Of these 1,343 patients, 1,338 rated the occurrence of cough a total of six times over two chemotherapy cycles (i.e., prior to chemotherapy administration [assessments 1 and 4], about one week after chemotherapy administration [assessments 2 and 5], and about two weeks after chemotherapy administration [assessments 3 and 6]). Patients completed the other measures used in this analysis at enrollment (i.e., prior to their second or third cycle of chemotherapy).

Instruments

Demographic and clinical characteristics: Patients completed a demographic questionnaire, the Karnofsky Performance Status Scale (Karnofsky, 1977), the Self-Administered Comorbidity Questionnaire (Sangha et al., 2003), the Alcohol Use Disorders Identification Test (Bohn et al., 1995), and a smoking history questionnaire. The toxicity of each patient's chemotherapy regimen was rated using the MAX2 score (Extermann et al., 2004). Medical records were reviewed for disease and treatment information.

Cough and other respiratory symptoms: The cough item from the Memorial Symptom Assessment Scale was used to assess for the occurrence of cough at each of the six assessments. Frequency, severity, and distress of cough were evaluated using data from the enrollment assessment. In addition, the occurrence rates for chest tightness, difficulty breathing, and shortness of breath at enrollment were evaluated. Validity and reliability of the Memorial Symptom Assessment Scale are well established (Portenoy et al., 1994).

Other common symptoms: The 20-item Center for Epidemiological Studies–Depression evaluates the major symptoms in the clinical syndrome of depression. A total score can range from 0 to 60, with scores of 16 or greater indicating the need for individuals to seek clinical evaluation for major depression. The Center for Epidemiological Studies–Depression has well-established validity and reliability (Radloff, 1977). Its Cronbach's alpha was 0.89.

The 20 items on the Spielberger State-Trait Anxiety Inventory (STAI-S and STAI-T) were rated from 1 to 4 (Spielberger et al., 1983). The STAI-S measures a person's temporary anxiety response to a specific situation or how anxious or tense a person is "right now" in a specific situation. The STAI-T measures a person's predisposition to anxiety as part of one's personality. Cutoff scores of 31.8 or greater and 32.2 or greater indicate a high level of trait and state anxiety, respectively. Cronbach's alphas for the STAI-T and STAI-S were 0.92 and 0.96, respectively.

The 18-item Lee Fatigue Scale was designed to assess physical fatigue and energy (Lee et al., 1991). Each item was rated on a 0–10 numeric rating scale (NRS). Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items, respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate Lee Fatigue Scale questionnaires, patients were asked to rate each item based on how they felt within 30 minutes of awakening (i.e., morning fatigue and morning energy) and prior to going to bed (i.e., evening fatigue and evening energy). The Lee Fatigue Scale has established cutoff scores for clinically meaningful levels of fatigue (i.e., 3.2 or greater for morning fatigue and 5.6 or greater for evening fatigue) and energy (i.e., 6.2 or less for morning energy and 3.5 or less for evening energy) (Fletcher et al., 2008). Cronbach's alphas were 0.96 for morning fatigue and 0.93 for evening fatigue and 0.95 for morning energy and 0.93 for evening energy.

The 21-item General Sleep Disturbance Scale (GSDS) was designed to assess the quality of sleep in the past week (Lee, 1992). Each item was rated on a NRS ranging from 0 (never) to 7 (every day). The GSDS total score is the sum of the 21 items that can range from 0 (no disturbance) to 147 (extreme sleep disturbance). Higher total scores indicate higher levels of sleep disturbance. A GSDS total score of 43 or greater indicates a significant level of sleep disturbance (Fletcher et al., 2008). Cronbach's alpha for GSDS score was 0.83.

The 16-item Attentional Function Index (AFI) assesses an individual's perceived effectiveness in performing daily activities that are supported by attention and working memory (Cimprich et al., 2011). A higher total mean score on a 0–10 NRS indicates better cognitive function (Cimprich et al., 2011). Total scores are grouped into categories of attentional function (i.e., less than 5 indicates low function, 5–7.5 indicates moderate function, and greater than 7.5 indicates high function) (Cimprich et al., 2005). Its Cronbach's alpha was 0.93.

The occurrence of pain was evaluated using the Brief Pain Inventory (Daut et al., 1983). Patients who responded "yes" to the question about having pain were asked to indicate whether their pain was or was not related to their cancer treatment. Patients were categorized into one of four groups (i.e., no pain, only noncancer pain, only cancer pain, or both cancer and noncancer pain). Patients rated the intensity of their worst pain using a NRS ranging from 0 (none) to 10 (excruciating). In addition, they provided information on pain's level of interference with function.

QOL measures: Disease-specific and generic measures of QOL were used in this study. Disease-specific QOL was evaluated using the Multidimensional QOL Scale–Patient Version (Padilla et al., 1990). This 41-item instrument measures four domains of QOL (i.e., physical, psychological, social, and spiritual well-being) in patients with cancer, as well as a total QOL score.

The SF-12 was the generic measure of QOL that consists of 12 questions about physical and mental health as well as overall health status (Ware et al., 1996). The SF-12 was scored into two components that measure physical (Physical Component Summary [PCS]) and psychological (Mental Component Summary [MCS]) function. These scores can range from 0 to 100. Higher PCS and MCS scores indicate better physical and psychological functioning, respectively.

Data Analysis

Descriptive statistics and frequency distributions were generated for sample characteristics at enrollment using IBM SPSS Statistics, version 29.0. As was done previously (Diaz et al., 2021), unconditional LCA was used to identify distinct cough occurrence profiles that characterized unobserved subgroups of patients (i.e., latent classes) over the six assessments. Before performing the LCA, patients who reported the occurrence of cough for one or fewer of the six assessments were identified and labeled as the None class (n = 842, 62.9%). Then, the LCA was performed on data from the remaining 496 patients using Mplus, version 8.4 (Muthén & Muthén, 1998–2017).

TABLE 1. Latent Profile Solutions and Fit Indices for 1 Through 4 Classes for the Occurrence of Cough

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	–1,718.77	3,449.54	3,474.78	N/A	N/A
2 Class	–1,630.44	3,286.88	3,341.57	0.69	176.65+
3 Class[a]	–1,559.46	3,158.92	3,243.05	0.7	141.97+
4 Class	–1,543.3	3,140.59	3,254.17	0.7	32.32*

* $p < 0.05$; + $p < 0.00005$
[a]The 3-class solution was selected because the BIC for that solution was lower than the BIC for the 2-class solution. In addition, the VLMR was significant for the 3-class solution, indicating that 3 classes fit the data better than 2 classes. The BIC increased for the 4-class compared to the 3-class solution, indicating that the fit of the 4-class solution was worse. Although the VLMR is significant for the 4-class solution, the increase in the BIC is more reliable than the VLMR in identifying the 3-class solution as the best-fitting solution. Therefore, although the VLMR for 4 classes was significant, the increase in the BIC indicates that the 4-class solution has extracted too many classes.
AIC—Akaike information criterion; BIC—Bayesian information criterion; LL—log-likelihood; N/A—not applicable; VLMR—Vuong–Lo–Mendell–Rubin likelihood ratio test for the K versus K-1 model
Note. Baseline entropy and VLMR are N/A for the 1-class solution.

Estimation was carried out with full information maximum likelihood with standard error and a chi-square test that are robust to non-normality and nonindependence of observations ("estimator=MLR"). Model fit was evaluated to identify the solution that best characterized the observed latent class structure with the Bayesian information criterion, Vuong–Lo–Mendell–Rubin likelihood ratio test, entropy, and latent class percentages that were large enough to be reliable (Muthén & Muthén, 1998–2015). Missing data were accommodated for with the use of the expectation–maximization algorithm (Muthén & Shedden, 1999).

Differences among the latent classes in demographic, clinical, and symptom characteristics, as well as QOL outcomes, were evaluated using parametric and nonparametric tests. A p value of less than 0.05 was considered statistically significant. Post hoc contrasts were done using a Bonferroni-corrected p value of less than 0.008 (0.05/6 possible pairwise comparisons).

Results

LCA

The 842 patients (62.9%) who had 1 or fewer occurrences of cough over the six assessments were classified as the None class. For the remaining 496 patients whose data were entered into the LCA, a three-class solution was selected because the three-class solution fit the data better than the two- and four-class solutions (see Table 1 for details).

FIGURE 1. Trajectories of Cough Occurrence for the 4 Latent Classes

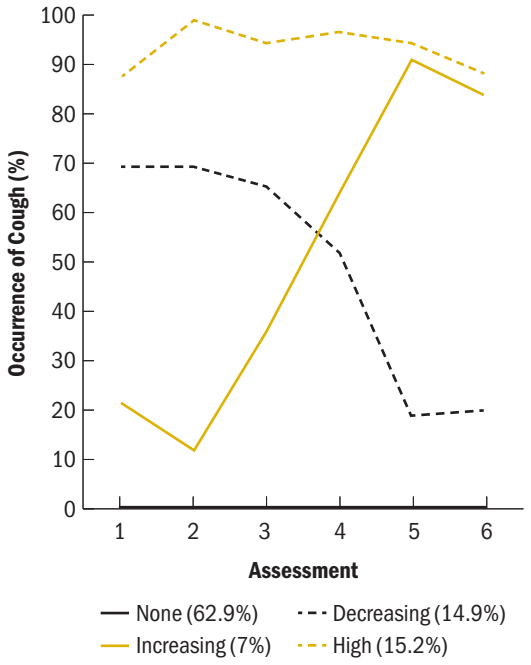

Figure 1 displays the trajectories for the occurrence of cough among the latent classes. For the Decreasing class (14.9%), the occurrence rates for cough decreased slightly from the first to the third assessment; dramatically decreased from the third to the fifth assessment; and then increased slightly from the fifth to the sixth assessment. For the Increasing class (7%), the occurrence rates for cough slightly decreased from the first to the second assessment; dramatically increased from the second to fifth assessments; and then decreased slightly from the fifth to the sixth assessment. For the High class (15.2%), the occurrence rates for cough remained consistently high over the six assessments.

Demographic and Clinical Characteristics

Differences in demographic and clinical characteristics are listed in Table 2. In brief, compared to the None class, the High class was more likely to have a lower annual household income, more likely to self-report diagnoses of heart disease and back pain, and less likely to have gastrointestinal cancer. Compared to the None class, the Decreasing and High classes had a lower Karnofsky Performance Status Scale score and were more likely to have lung metastasis. Compared to the other three classes, the High class had a higher number of comorbidities and higher Self-Administered Comorbidity Questionnaire scores; were more likely to report a past or current history of smoking; were more likely to self-report lung disease; and were more likely to have both lung disease and lung cancer.

Frequency, Severity, and Distress of Cough

For the patients who reported the occurrence of cough, significant differences were found among the classes in its frequency ($p < 0.001$) (see Figure 2A). Post hoc contrasts found that compared to the Decreasing class, the High class reported higher frequency scores. In terms of severity (see Figure 2B), significant differences were found among the classes ($p < 0.001$). Post hoc contrasts found that compared to the Decreasing class, the High class reported higher severity scores. In terms of distress (see Figure 2C), significant differences were found among the classes ($p < 0.001$). Post hoc contrasts found that compared to the Decreasing and Increasing classes, the High class reported higher distress scores.

Other Respiratory Symptoms

Compared to the None class, the Decreasing and High classes reported higher occurrence rates for chest

TABLE 2. Differences in Demographic and Clinical Characteristics Among the Cough Latent Classes

	None (0) (N = 842, 62.9%)		Decreasing (1) (N = 199, 14.9%)		Increasing (2) (N = 93, 7%)		High (3) (N = 204, 15.2%)		
Characteristic	$\bar{X}$	**SD**	$\bar{X}$	**SD**	$\bar{X}$	**SD**	$\bar{X}$	**SD**	**Statistics**
Age (years)	57.3	12.1	55.4	13.4	57.5	12.5	58.3	12.2	F = 1.99, p = 0.113
Education (years)	16.2	3.1	16.2	2.8	16	3.2	16.1	3	F = 0.18, p = 0.91
Body mass index (kg/m^2)	26.1	5.6	26.3	6.1	25.6	5.2	26.8	5.9	F = 1.25, p = 0.292
AUDIT score	3	2.5	2.7	2.2	3.3	2.6	3	2.5	F = 0.79, p = 0.502
Karnofsky Performance Status Scale score	81	12.2	77.9	12.8	81.3	13.3	77.5	12.6	F = 6.57, p < 0.001; 0 > 1 and 3
Number of comorbid conditions	2.3	1.4	2.4	1.4	2.4	1.4	2.9	1.5	F = 9.17, p < 0.001; 0, 1, and 2 < 3
SCQ score	5.2	3	5.6	3.3	5.3	2.9	6.5	3.7	F = 9.02, p < 0.001; 0, 1, and 2 < 3
Time since diagnosis (years)	1.8	3.7	2	3.9	2.1	4.2	2.5	4.5	KW = 8.45, p = 0.038; no significant pw contrasts
Number of prior cancer treatments	1.5	1.5	1.7	1.7	1.5	1.4	1.8	1.5	F = 1.84, p = 0.139
Number of metastatic sites including lymph node involvement[a]	1.2	1.2	1.4	1.3	1.3	1.2	1.3	1.3	F = 1.01, p = 0.389
Number of metastatic sites excluding lymph node involvement	0.8	1	0.8	1.1	0.8	1	0.8	1.1	F = 0.5, p = 0.685
MAX2 score	0.17	0.08	0.17	0.08	0.19	0.09	0.18	0.09	F = 0.99, p = 0.397
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Statistics**
Gender									
Female	642	76	165	83	73	79	160	78	χ^2 = 4.13, p = 0.248
Self-reported ethnicity									χ^2 = 9.02, p = 0.435
Asian or Pacific Islander	103	12	28	14	13	14	21	11	
Black	54	7	15	8	7	8	19	10	
Hispanic, mixed, or other	87	11	28	14	11	12	15	8	
White	587	71	127	64	61	66	145	73	
Married or partnered									
Yes	541	65	126	65	56	62	127	63	χ^2 = 0.85, p = 0.838
Lives alone									
Yes	173	21	41	21	21	23	49	24	χ^2 = 1.28, p = 0.733
Currently employed									
Yes	299	36	69	35	30	32	67	33	χ^2 = 0.87, p = 0.834

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TABLE 2. Differences in Demographic and Clinical Characteristics Among the Cough Latent Classes *(Continued)*

	None (0) (N = 842, 62.9%)		Decreasing (1) (N = 199, 14.9%)		Increasing (2) (N = 93, 7%)		High (3) (N = 204, 15.2%)		
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Statistics**
Annual household income ($)									KW = 12.79, p = 0.005; 0 > 3
Less than 30,000[b]	112	15	40	22	26	31	42	23	
30,000–70,000	163	22	32	18	15	18	42	23	
70,000–100,000	128	17	38	21	8	9	29	16	
Greater than 100,000	351	47	69	39	36	42	67	37	
Childcare responsibilities									
Yes	186	23	48	25	26	29	30	15	$\chi^2 = 9.43$, p = 0.024; 2 > 3
Eldercare responsibilities									
Yes	66	9	7	4	11	13	12	7	$\chi^2 = 8.04$, p = 0.045; 1 < 2
Past or current history of smoking									
Yes	266	32	70	36	30	32	99	50	$\chi^2 = 22.45$, p < 0.001; 0, 1, and 2 < 3
Exercise on a regular basis									
Yes	593	72	138	72	69	76	126	64	$\chi^2 = 5.46$, p = 0.141
Specific comorbid conditions									
Heart disease	41	5	11	6	4	4	21	10	$\chi^2 = 9.35$, p = 0.025; 0 < 3
High blood pressure	251	30	56	28	28	30	70	34	$\chi^2 = 2.1$, p = 0.553
Lung disease	56	7	24	12	7	8	64	31	$\chi^2 = 101.71$, p < 0.001; 0, 1, and 2 < 3
Diabetes	71	8	22	11	12	13	16	8	$\chi^2 = 3.4$, p = 0.334
Ulcer or stomach disease	40	5	9	5	2	2	14	7	$\chi^2 = 3.32$, p = 0.345
Kidney disease	13	2	2	1	–	–	4	2	$\chi^2 = 2.1$, p = 0.551
Liver disease	54	6	14	7	6	7	12	6	$\chi^2 = 0.22$, p = 0.974
Anemia or blood disease	106	13	21	11	10	11	27	13	$\chi^2 = 1$, p = 0.801
Depression	151	18	40	20	16	17	50	25	$\chi^2 = 4.92$, p = 0.178
Osteoarthritis	102	12	21	11	13	14	27	13	$\chi^2 = 0.99$, p = 0.804
Back pain	188	22	60	30	27	29	69	34	$\chi^2 = 14.67$, p = 0.002; 0 < 3
Rheumatoid arthritis	26	3	4	2	3	3	10	5	$\chi^2 = 2.84$, p = 0.417
Cancer diagnosis									$\chi^2 = 89.73$, p < 0.001
Breast cancer	328	39	83	42	42	45	86	42	NS

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TABLE 2. Differences in Demographic and Clinical Characteristics Among the Cough Latent Classes *(Continued)*

	None (0) (N = 842, 62.9%)		Decreasing (1) (N = 199, 14.9%)		Increasing (2) (N = 93, 7%)		High (3) (N = 204, 15.2%)		
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Statistics**
Cancer diagnosis *(continued)*									$\chi^2 = 89.73$, $p < 0.001$
Gastrointestinal cancer	295	35	53	27	20	22	41	20	0 > 3
Gynecologic cancer	155	18	44	22	14	15	20	10	0 and 1 > 3
Lung cancer	64	8	19	10	17	18	57	28	0 < 2 and 3, 1 < 3
Co-occurrence of lung cancer and lung disease									
Yes	34	4	13	7	6	7	45	22	$\chi^2 = 78.93$, $p < 0.001$; 0, 1, and 2 < 3
Prior cancer treatment									$\chi^2 = 16.48$, $p = 0.058$
No prior treatment	208	25	49	25	21	24	47	24	
Only surgery, CTX, or RT	358	44	79	40	41	47	69	35	
Surgery and CTX, or surgery and RT, or CTX and RT	167	20	34	17	13	15	44	22	
Surgery and CTX and RT	88	11	34	17	13	15	36	18	
Metastatic sites									$\chi^2 = 10.69$, $p = 0.298$
No metastasis	282	34	54	27	28	30	63	31	
Only lymph node metastasis	168	20	57	29	20	22	46	23	
Only metastatic disease in other sites	169	20	38	19	23	25	49	24	
Metastatic disease in lymph nodes and other sites	208	25	49	25	22	24	44	22	
Lung metastasis									
Yes	67	12	34	23	10	15	40	29	$\chi^2 = 26.86$, $p < 0.001$; 0 < 1 and 3
CTX regimen									$\chi^2 = 8.62$, $p = 0.503$
Only CTX	589	71	137	70	60	65	133	68	
Only targeted therapy	26	3	7	4	3	3	3	2	
Both CTX and targeted therapy	211	26	51	26	30	32	61	31	
Receipt of targeted therapy									$\chi^2 = 2.59$, $p = 0.459$
Yes	237	29	58	30	33	36	64	33	
Cycle length									KW = 7.44, $p = 0.059$
14-day cycle	372	45	80	41	38	41	68	34	
21-day cycle	407	49	94	48	50	54	120	59	

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TABLE 2. Differences in Demographic and Clinical Characteristics Among the Cough Latent Classes *(Continued)*

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Cycle length *(continued)*									KW = 7.44, p = 0.059
28-day cycle	56	7	22	11	5	5	14	7	
Emetogenicity of the CTX regimen									KW = 7.03, p = 0.071
Minimal/low	155	19	43	22	16	17	45	22	
Moderate	545	65	114	58	48	52	103	51	
High	135	16	40	20	29	31	54	27	
Antiemetic regimen									χ^2 = 7.56, p = 0.579
None	61	8	16	8	6	7	9	5	
Steroid alone or serotonin receptor antagonist alone	161	20	43	22	22	24	39	20	
Serotonin receptor antagonist and steroid	402	49	82	42	40	44	94	48	
NK-1 receptor antagonist and 2 other antiemetics	189	23	54	28	24	26	54	28	

[a] The total number of metastatic sites evaluated was 9.
[b] Reference group
AUDIT—Alcohol Use Disorders Identification Test; CTX—chemotherapy; KW—Kruskal–Wallis; NK-1—neurokinin-1; NS—not significant; pw—pairwise; RT—radiation therapy; SCQ—Self-Administered Comorbidity Questionnaire
Note. Because of rounding, percentages may not total 100.

tightness (see Table 3). Symptom occurrence rates for difficulty breathing and shortness of breath showed a similar pattern (i.e., None < Decreasing < High).

Co-Occurrence of Common Cancer-Related Symptoms

Compared to the None class, the High class reported higher depressive symptoms, state anxiety, and sleep disturbance scores (see Table 3). Compared to the None class, the Decreasing and High classes reported higher trait anxiety and morning fatigue scores and lower AFI scores and were more likely to have both cancer and noncancer pain. Compared to the None class, the Increasing class reported significant decrements in evening energy and was less likely to have only noncancer pain. Compared to the Increasing class, the High class reported a higher level of morning fatigue and was less likely not to have pain.

QOL Scores

For the Multidimensional QOL Scale–Patient Version, compared to the None class, the High class reported lower psychological well-being and total QOL scores (see Figure 3A). Compared to the None and Increasing classes, the High class reported a lower physical well-being score.

For the SF-12, compared to the None class, the High class reported lower physical functioning, general health, vitality, social functioning, and PCS scores (see Figure 3B). Compared to the None class, the Decreasing and High classes reported lower role physical scores.

Discussion

This study is the first to use LCA to identify distinct cough occurrence profiles in patients receiving chemotherapy; evaluate its frequency, severity, and distress; describe the co-occurrence of other common symptoms; and explain its impact on QOL. Of note, across multiple types of cancer, about 40% of these patients reported cough. This finding is consistent with previously reported occurrence rates of between 35.1% and 42.9% in patients undergoing active cancer treatment (Harle et al., 2020;

Molassiotis et al., 2010), but lower than the 62% reported by patients with lung cancer receiving treatment for a severe cough (Harle et al., 2020). This finding underscores the underestimation of this significant symptom that warrants ongoing assessment and treatment.

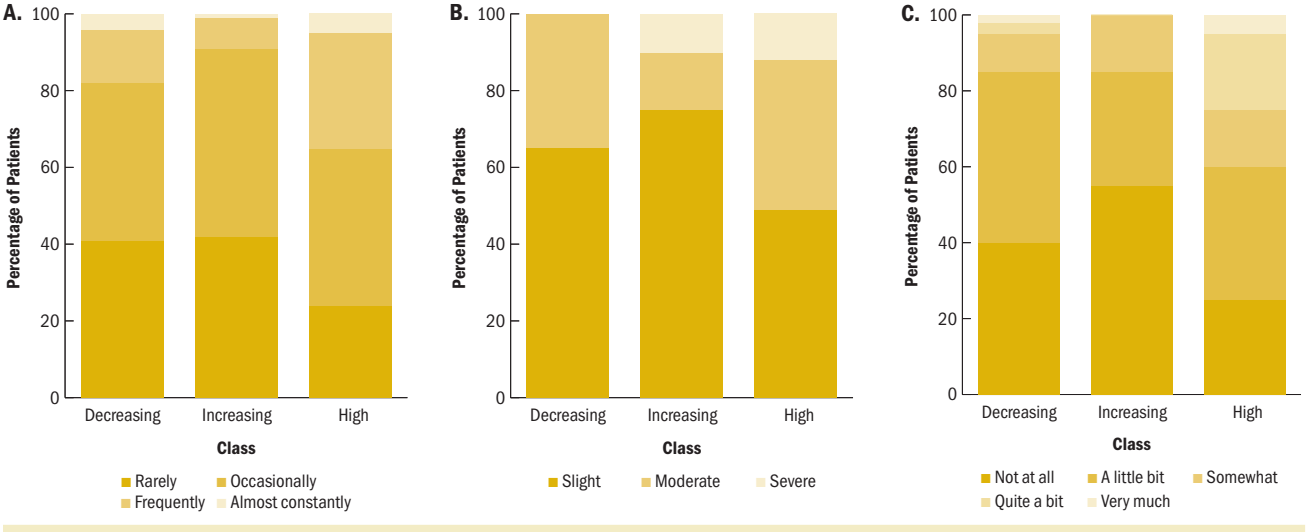
Among the 496 patients who reported cough, 41.1% (n = 204) were in the High class. Compared to the Increasing and Decreasing classes, these patients had persistently high occurrence rates of cough that were more frequent, severe, and distressing. In terms of the Decreasing class (i.e., 40.1% of the patients with cough), possible explanations for their trajectory are that these patients had an acute respiratory infection (Leduc et al., 2017) and/or they received interventions to decrease the symptom. The trajectory of the Increasing class (i.e., 18.8% of the patients with cough) may be related to lack of efficacy of current interventions; increasing pulmonary toxicities associated with chemotherapy or previous treatment(s) (Long & Suresh, 2020); and/or worsening of other chronic cardiopulmonary conditions (Leduc et al., 2017).

To facilitate comparisons of common and distinct risk factors for cough among the latent classes, a summary table was created (see Table 4). The remaining discussion places the authors' findings within the context of the extant literature.

Demographic Characteristics

The only demographic characteristic associated with membership in the High class was having a lower annual income. This finding is consistent with three reviews of the general population (Çolak et al., 2017; Yang et al., 2023; Zhang et al., 2022). Of note, in a U.S. population–based study that spanned from 1959 to 2018 (Gaffney, Himmelstein, et al., 2021), disparities in the occurrence of cough widen over time between the least and most affluent quintiles. These findings provide evidence of respiratory health disparities in individuals with lower incomes. One potential explanation for this association is that patients with lower incomes may have decreased access to health care that results in delays in treatment (Gaffney, Himmelstein, et al., 2021). In addition, these patients may live in areas with higher levels of environmental pollutants that contribute to the development and maintenance of cough (Gaffney, Hawks, et al., 2021). Equally important, certain occupations that are more prevalent among individuals with lower incomes (e.g., industrial cleaner, farmworker) may expose them to carcinogens or respiratory irritants (Menvielle et al., 2010) that heighten their risk of developing lung cancer or respiratory diseases associated with cough (Çolak et al., 2017).

FIGURE 2. Percentages of Patients in the Decreasing, Increasing, and High Classes Who Rated the Frequency (A), Severity (B), and Distress (C) Associated With the Occurrence of Cough



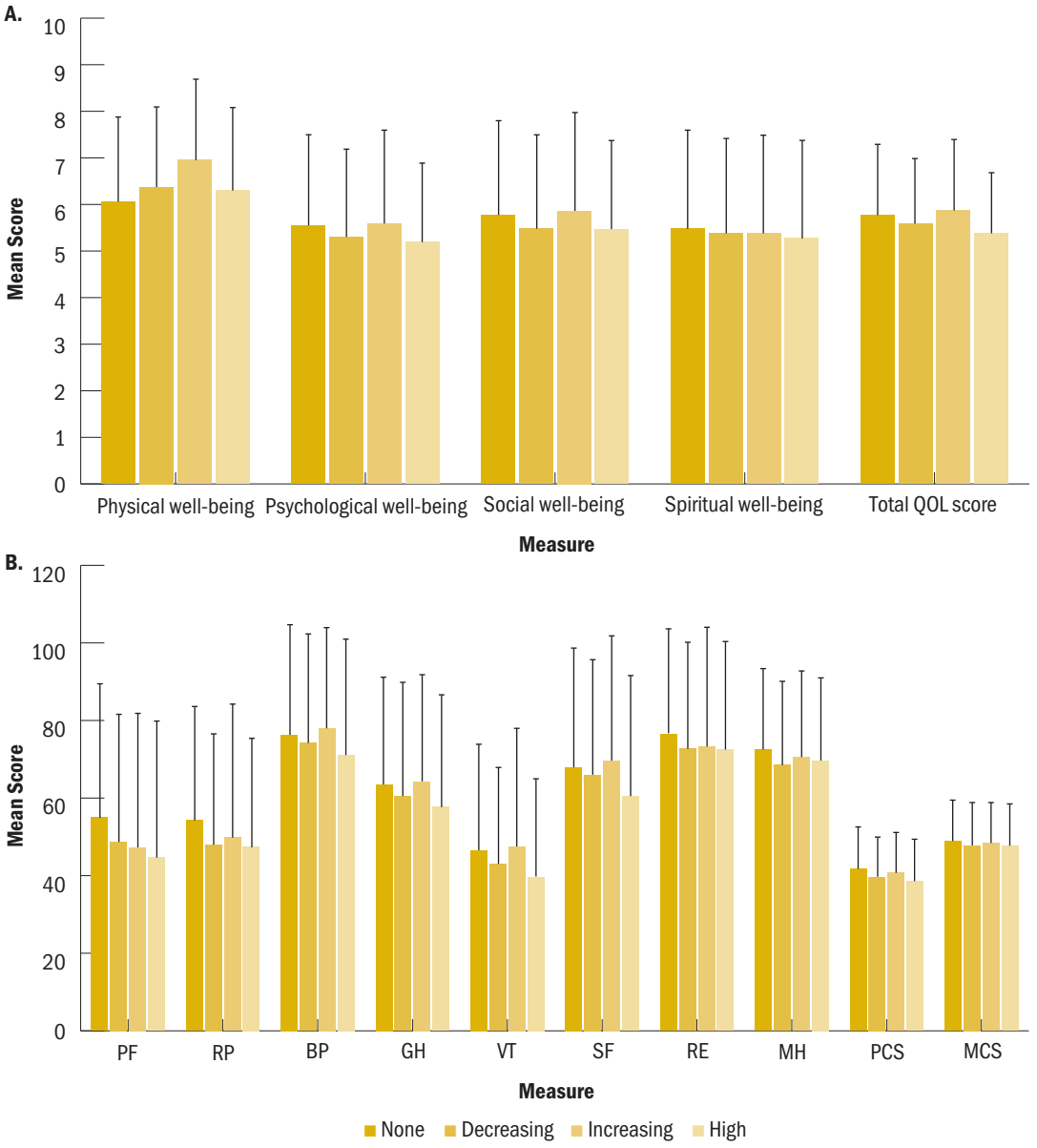
Note. For both frequency (A) and severity (B), significant differences were found among the latent classes ($p < 0.001$) and post hoc contrasts demonstrated that compared to the Decreasing class, the High class reported higher frequency and severity scores. For distress (C), significant differences were found among the classes ($p < 0.001$) and post hoc contrasts demonstrated that compared to the Decreasing and Increasing classes, the High class reported higher distress scores.

TABLE 3. Differences in the Occurrence of Other Respiratory Symptoms and Co-Occurring Symptom Severity Scores at Enrollment Among the Cough Latent Classes

	None (0) (N = 842, 62.9%)		Decreasing (1) (N = 199, 14.9%)		Increasing (2) (N = 93, 7%)		High (3) (N = 204, 15.2%)		
Symptoms	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Statistics**
Occurrence of other respiratory symptoms*									
Chest tightness	106	13	49	25	18	19	64	32	$\chi^2 = 48.52$, $p < 0.001$; 0 < 1 and 3
Difficulty breathing	109	13	52	26	17	18	87	43	$\chi^2 = 98.08$, $p < 0.001$; 0 < 1 < 3
Shortness of breath	167	20	62	32	26	28	102	51	$\chi^2 = 79.95$, $p < 0.001$; 0 < 1 < 3
Co-occurring cancer-related symptom severity[a]									
Symptoms	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**Statistics**
Depressive symptoms (≥ 16)	12.1	9.5	13.8	10.1	12.9	9.7	14.9	9.8	$F = 5.28$, $p = 0.001$; 0 < 3
Trait anxiety (≥ 31.8)	34.4	10.3	37.2	10.5	34.3	11.2	36.7	10.5	$F = 5.61$, $p < 0.001$; 0 < 1 and 3
State anxiety (≥ 32.2)	33.1	12.2	35.2	12.8	33.7	12.4	35.9	12.3	$F = 3.75$, $p = 0.011$; 0 < 3
Morning fatigue (≥ 3.2)	2.9	2.2	3.5	2.4	3	2.5	3.7	2.2	$F = 9.59$, $p < 0.001$; 0 < 1 and 3, 2 < 3
Evening fatigue (≥ 5.6)	5.2	2.2	5.4	2.2	5.3	2.4	5.7	2	$F = 2.58$, $p = 0.053$
Morning energy (≤ 6.2)	4.5	2.3	4.2	2.2	4.4	2.5	4.2	2	$F = 1.49$, $p = 0.214$
Evening energy (≤ 3.5)	3.6	2	3.5	2	3	2	3.7	2	$F = 2.78$, $p = 0.04$; 0 > 2
Sleep disturbance (≥ 43)	51.2	20.2	53.7	20.2	50.9	21.5	57.2	19.1	$F = 5.18$, $p = 0.001$; 0 < 3
Attentional function (< 5 = low, 5–7.5 = moderate, > 7.5 = high)	6.6	1.8	6	1.8	6.3	2	6.1	1.8	$F = 7.76$, $p < 0.001$; 0 > 1 and 3
Symptoms	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**Statistics**
Type of pain									$\chi^2 = 30.02$, $p < 0.001$
No pain	246	30	36	19	35	38	42	21	0 > 1, 1 < 2, 2 > 3
Only noncancer pain	231	28	47	24	14	15	54	27	0 > 2
Only cancer pain	127	15	36	19	15	16	31	16	NS
Both cancer and noncancer pain	223	27	74	38	29	31	73	37	0 < 1 and 3
Symptoms	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**Statistics**
For patients with pain									
Worst pain score	6	2.5	5.8	2.8	6.2	2.7	6.3	2.5	$F = 0.75$, $p = 0.523$
Mean pain interference score	3.1	2.5	3.2	2.5	3.2	2.5	3.2	2.4	$F = 0.24$, $p = 0.866$

* Percentage of patients who reported the occurrence of the symptom
[a] Clinically meaningful cutoff scores
NS—not significant

FIGURE 3. Differences in QOL Scores Among the Cough Latent Classes



BP—bodily pain; GH—general health; MCS—Mental Component Summary; MH—mental health; PCS—Physical Component Summary; PF—physical functioning; QOL—quality of life; RE—role emotional; RP—role physical; SF—social functioning; VT—vitality

Note. Figure 3A shows differences in mean Multidimensional QOL Scale–Patient Version physical, psychological, social, and spiritual well-being domain as well as total QOL scores among the cough latent classes. All values are plotted as means and SDs. For the physical ($p = 0.001$) and psychological ($p = 0.017$) well-being domains, as well as the total QOL ($p = 0.002$) scores, significant differences were found among the classes. For the physical well-being domain, compared to the None and Increasing classes, post hoc contrasts determined that the High class reported a lower score. For the psychological well-being and total QOL scores, compared to the None class, post hoc contrasts determined that the High class reported lower scores.

Note. Figure 3B shows differences in mean Medical Outcomes Study 12-Item Short-Form Health Survey PF, RP, BP, GH, VT, SF, RE, MH, PCS, and MCS scores among the cough latent classes. All values are plotted as means and SDs. For the PF ($p < 0.001$), RP ($p = 0.003$), GH ($p = 0.032$), VT ($p = 0.005$), SF ($p = 0.014$), and PCS ($p = 0.001$) domains, significant differences were found among the latent classes. Compared to the None class, post hoc contrasts demonstrated that the High class reported lower PF, GH, VT, SF, and PCS scores. Compared to the None class, post hoc contrasts demonstrated that the Decreasing and High classes reported lower RP scores.

Clinical Characteristics

Smoking history: Given that smoking is a well-established risk factor for cough (Çolak et al., 2017; Song et al., 2015), it is not unusual that a larger percentage of patients in the High class were past or current smokers. Because individuals with lower incomes have higher smoking rates (Gaffney, Himmelstein, et al., 2021), a synergy may exist between these two risk factors and higher rates and more severe and distressing episodes of cough. Smoking triggers inflammation of the bronchi, with associated increases in mucus production (Strzelak et al., 2018). Coughing is a natural protective mechanism that aids in clearance of irritants, mucus, and foreign particles from the respiratory system (Mukae et al., 2021). Of note, in a study of smokers, the sensitivity of their cough reflex was significantly diminished (Dicpinigaitis, 2003). This deficit resulted in a persistent cough that compensated for impairments in their ability to clear irritants, mucus, or foreign particles. In contrast, quitting smoking led to improvements in the sensitivity of the cough reflex (Dicpinigaitis, Sitkauskiene, et al., 2006). Given that smoking status is a modifiable risk factor, clinicians need to educate patients about the benefits of quitting smoking and prescribe smoking cessation interventions (Pisinger et al., 2008).

Lung and heart disease: Compared to the other three classes, patients in the High class reported a higher number of comorbid conditions and a higher overall comorbidity burden. Specifically, a higher percentage of patients in the High class reported lung disease. This finding is consistent with a population-based study (Johnmary et al., 2020) and a longitudinal study of patients with lung cancer (Harle et al., 2019) that identified chronic obstructive pulmonary disease and/or asthma as independent risk factors for chronic cough.

Consistent with a previous report (Arinze et al., 2022), a higher percentage of patients in the High class reported heart disease. Although specific information on the etiology of heart disease is not available in the current study, pulmonary congestion associated with heart failure can activate vagal nerve endings in the bronchi and lead to cough (Grabczak et al., 2020). In addition, some medications that are used to treat heart disease (e.g., angiotensin-converting enzyme inhibitors [Pinto et al., 2020]) can cause persistent cough.

Back pain: Compared to the None class, patients in the High class were more likely to report back pain. More frequent and more severe coughing may strain the muscles of the upper and lower back and increase pain (Lee et al., 2017). This hypothesis is supported by two population-based studies in Spain (Fuentes-Alonso et al., 2020) and the United States (Chen et al., 2021) that reported that patients with chronic obstructive pulmonary disease or heart failure were at increased risk for chronic back pain compared to patients without cardiopulmonary comorbidity.

Lung cancer: Consistent with a previous study of patients with lung cancer, where more than half reported cough (Harle et al., 2020), a higher percentage of patients in the Increasing and High classes were diagnosed with lung cancer. Lung tumors can physically obstruct, irritate, or inflame the airways and surrounding tissues (Mudambi et al., 2017), stimulating the cough reflex (Mazzone et al., 2003). In addition, in a meta-analysis of patients who received a combination of docetaxel and gemcitabine (Binder et al., 2011), the presence of lung cancer increased the risk of developing drug-induced pulmonary toxicity, characterized by an increase in the occurrence of cough. Of note, more than 22% of the High class had both lung cancer and lung disease. This finding suggests that clinicians need to assess for cough on a routine basis in patients who have both lung cancer and other respiratory conditions.

Co-occurrence of respiratory symptoms: Although the overall occurrence rate for chest tightness in the total sample was 17.8% at enrollment, compared with the None class, these rates were higher in the Decreasing (24.9%) and High (31.7%) classes. A persistent cough may lead to chest tightness by straining the chest muscles (Schattner, 2020). Consistent with previous studies (Chowienczyk et al., 2020; Kalantari et al., 2022; Lou et al., 2017; Wong et al., 2017), almost 50% of the patients in the High class reported difficulty breathing and shortness of breath. This finding is consistent with studies of patients with lung cancer (Lou et al., 2017; Wong et al., 2017), chronic obstructive pulmonary disease (Landt et al., 2020), and asthma (Shen et al., 2013). The lung contains slowly adapting pulmonary stretch receptors, irritant receptors, and C fibers that transmit afferent information through the vagus nerve to the respiratory networks in the medulla oblongata (Shin et al., 2023). These mechanoreceptors are involved in the perception of all four respiratory symptoms (Shin et al., 2023). Potential causes for the co-occurrence of these four respiratory symptoms include perturbations of bronchopulmonary C fibers by lung tumor, lung disease, smoking, and/or toxicities of cancer treatment (Lee, 2009).

TABLE 4. Characteristics Associated With Membership in the Decreasing, Increasing, and High Cough Classes

Characteristic[a]	Decreasing	Increasing	High
Demographic characteristics			
More likely to have a lower annual income			●
Clinical characteristics			
Lower functional status	●		●
Higher number of comorbidities			●
Higher comorbidity burden			●
More likely to have past or current history of smoking			●
More likely to self-report heart disease			●
More likely to self-report lung disease			●
More likely to self-report back pain			●
Less likely to have gastrointestinal cancer			●
Less likely to have gynecologic cancer			●
More likely to have lung cancer		●	●
More likely to have co-occurrence of lung cancer and lung disease			●
More likely to have lung metastasis	●		●
Co-occurrence of respiratory symptoms			
More likely to have chest tightness	●		●
More likely to have difficulty breathing	●		●
More likely to have shortness of breath	●		●
Co-occurring cancer-related symptoms			
Higher depressive symptoms			●
Higher trait anxiety	●		●
Higher state anxiety			●
Higher morning fatigue	●		●
Lower evening energy		●	
Higher sleep disturbance			●
Lower attentional function	●		●
Less likely to have pain	●		
Less likely to have only noncancer pain		●	
More likely to have both cancer and noncancer pain	●		●

Continued on next page

TABLE 4. Characteristics Associated With Membership in the Decreasing, Increasing, and High Cough Classes *(Continued)*

Characteristic[a]	Decreasing	Increasing	High
QOL outcomes			
Multidimensional QOL Scale—Patient Version			
Lower physical well-being			●
Lower psychological well-being			●
Lower total QOL score			●
Medical Outcomes Study 12-Item Short-Form Health Survey			
Lower physical functioning			●
Lower role physical	●		●
Lower general health			●
Lower vitality			●
Lower social functioning			●
Physical Component Summary score			●

[a] Comparisons done with the None group
QOL—quality of life
Note. A circle indicates that the class had this characteristic compared to the None class.

Common Cancer-Related Symptoms

Depressive symptoms and anxiety: Consistent with previous findings (Arinze et al., 2021, 2022; Zhang et al., 2023), patients in the High class reported higher levels of depressive symptoms. Of note, 38.1% of these patients had Center for Epidemiological Studies–Depression scores above the clinically meaningful cutoff score of 16 or greater. This occurrence rate is higher than the 16.4% reported in the general population (Arinze et al., 2022) but lower than the 53% reported by patients with chronic cough (Dicpinigaitis, Tso, & Banauch, 2006).

In terms of trait and state anxiety, the mean scores for all four of the classes were above the clinically meaningful cutoffs for both measures. Specifically, 61.4% and 64.3% of the patients in the High and Decreasing classes, respectively, reported trait anxiety scores of 31.8 or greater. In addition, compared to the None class, 52.3% and 46.9% of the patients in the High and Decreasing classes, respectively, had state anxiety scores of 32.2 or greater. These occurrence rates are higher than the percentages reported by patients with chronic trait (48%) and state (28%) anxiety (McGarvey et al., 2006).

It is reasonable to hypothesize that the overall symptom burden of cough increases patients' risk of developing psychological distress (Arikan et al., 2015; Johnmary et al., 2020). For example, a chronic cough may lead to difficulty speaking, embarrassment, and/or social isolation (French et al., 2017; Molassiotis, Lowe, Ellis, et al., 2011) that has a negative impact on patients' psychological well-being (Harle et al., 2020). Equally important, this psychological distress may increase the occurrence of cough (Ovsyannikov et al., 2019). These reciprocal relationships are supported by findings from a study that demonstrated simultaneous decreases in the severity of cough, anxiety, and depression when effective treatments for chronic cough were prescribed (French et al., 2017).

Morning fatigue and evening energy: Although no differences were found among the classes in evening fatigue scores, morning fatigue scores exceeded clinically meaningful cutoffs in the Decreasing and High classes. In terms of the extant literature, no studies have evaluated for associations between cough and diurnal variations in fatigue severity. However, in qualitative studies of patients with lung cancer (Molassiotis, Lowe, Blackhall, & Lorigan, 2011; Molassiotis, Lowe, Ellis, et al., 2011) and a meta-analysis of patients with COVID-19 (Song et al., 2021), persistent cough was associated with increases in average fatigue severity. Specifically, when cough occurred during the night, it disrupted sleep and led to patients reporting fatigue upon awakening (Molassiotis, Lowe, Blackhall, & Lorigan, 2011; Molassiotis, Lowe, Ellis, et al., 2011; Vena et al., 2006).

In the current study, all the classes had mean morning energy scores that were below the clinically

meaningful cutoff. In addition, compared to the None class, patients in the Increasing class reported clinically meaningful decrements in evening energy. These findings suggest that continuous coughing during the day may decrease patients' energy levels during the day with associated feelings of exhaustion in the evening (Molassiotis, Lowe, Ellis, et al., 2011).

Sleep disturbance: Although all of the classes had clinically meaningful levels of sleep disturbance, compared to the None class, patients in the High class reported higher levels of sleep disturbance. Of note, in qualitative (Molassiotis, Lowe, Blackhall, & Lorigan, 2011; Molassiotis, Lowe, Ellis, et al., 2011) and quantitative (Harle et al., 2020; Lou et al., 2017; Vena et al., 2006) studies of patients with lung cancer, severe coughing was associated with poorer sleep quality and higher levels of sleep disturbance. Although normal sleep suppresses the sensitivity of the cough reflex (Lee & Birring, 2010), patients can experience nocturnal coughing as a result of respiratory infections, drug-induced lung toxicities, chronic respiratory disease, gastroesophageal reflux disease, or heart failure (Singh et al., 2023). These findings suggest that patients who report coughing warrant a thorough evaluation so that targeted interventions can be prescribed.

Cognitive impairment: Although the AFI scores for all of the classes were in the moderate range, 25.7% and 30.4% of patients in the High and Decreasing classes, respectively, had AFI scores of less than 5. These findings are consistent with a study of patients with chronic obstructive pulmonary disease who reported that higher occurrence rates of cough were associated with more severe decrements in cognitive function (Yin et al., 2016). The mechanisms that underlie this association warrant investigation given that a recent editorial suggested that common neurologic disorders (e.g., dementia, Parkinson disease) are associated with changes in cough sensitivity (Al-Biltagi et al., 2022).

Pain: Compared to the None class, patients in the Decreasing and High classes were more likely to have both cancer and noncancer pain. In patients with lung cancer or lung metastasis, cough is associated with chest, pleuritic, and/or rib pain (Harle et al., 2020). In a population-based study (Arinze et al., 2021), the co-occurrence of chronic pain and cough was 4.4%, with the majority of the participants having osteoarthritis (35%) or an unspecified musculoskeletal condition (29%). Of note, chronic pain was an independent risk factor for the development of chronic cough after controlling for smoking status, use of angiotensin-converting enzyme inhibitors, lung cancer, and other cardiopulmonary conditions (Arinze et al., 2021). Although in the current study the specific causes of cancer-related pain were not recorded, across the three classes who reported cough, the occurrence rates for osteoarthritis ranged from 10.6% to 14% and for back pain from 29% to 33.8%.

QOL: Consistent with previous findings in patients with lung cancer (Harle et al., 2020; Iyer et al., 2014; Lou et al., 2017; Yang et al., 2012), compared to the None class, patients in the High class reported worse physical, psychological, and social functioning scores on both the general and disease-specific QOL measures. These decrements in various domains of QOL may be attributed to avoidance of daily activities, embarrassment, challenges with interpersonal relationships, social isolation, and/or psychological distress (Harle et al., 2014, 2019, 2020; Molassiotis, Lowe, Blackhall, & Lorigan, 2011; Molassiotis, Lowe, Ellis, et al., 2011). Of note, patients who received targeted interventions for chronic cough reported improvements in QOL that coincided with decreases in the severity of cough, depression, and anxiety (French et al., 2017).

KNOWLEDGE TRANSLATION

- Across multiple types of cancer, 40% of the patients reported cough. This finding underscores the underestimation of this significant symptom in patients with cancer.
- Risk factors associated with higher rates of cough included current history of smoking; self-reported diagnoses of lung disease, heart disease, and back pain; and more severe symptoms (e.g., anxiety, depression, sleep disturbance).
- Cough co-occurs with other respiratory symptoms (e.g., chest tightness, shortness of breath); cough has a negative impact on patients' physical, psychological, and social well-being.

Limitations

Several limitations warrant consideration. Given that the current sample was relatively homogenous in terms of gender and self-reported race and ethnicity, these findings may not generalize to more diverse patients. Although this study used a valid and reliable measure to assess the subjective experience of cough, future studies need to evaluate for correlations with objective measures of pulmonary function. In addition, detailed information is needed on the patients' specific cardiopulmonary conditions, as well as causes of cancer and noncancer pain. Finally, because information on pharmacologic and nonpharmacologic treatments for cough and other chronic conditions were not available for the current sample, they could

not be used to assist with the interpretation of the study findings.

Implications for Clinical Practice

The findings from the current study underscore the underestimation of the occurrence and severity and significance of cough in patients with cancer. Given its relatively high occurrence rate and negative impact, clinicians need to perform comprehensive assessments of cough, as well as specific comorbidities and pharmacologic interventions that may contribute to its occurrence and severity. In addition, an evaluation of modifiable risk factors (i.e., smoking status, occurrence of back pain, and occurrence and severity of other common symptoms) is warranted to determine the need for adjustments in current treatment regimens and/or additional symptom management interventions. These types of evaluations will decrease the physical and psychological burden associated with chronic cough and lead to improvements in patients' QOL.

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