

Korean Journal of Adult Nursing Vol. 36 No. 4, 271-297, November 2024

### **ORIGINAL ARTICLE**

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# Symptom Clusters among Lung Cancer Patients: A Scoping Review



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Purpose: Lung cancer (LC) is the leading cause of cancer-related death globally, and understanding symptom clusters (SCs) among LC patients could improve symptom management. This scoping review provides a comprehensive summary of the most common SCs and their compositions identified in studies specifically investigating SCs of LC patients. Methods: A scoping review was conducted following the Joanna Briggs Institute methodology. The study included LC patients as participants, SCs as the concept, and studies with distinct aim to investigate LC SCs as the context. We searched studies from inception to September 2022 in PubMed, Embase, PsycINFO, CINAHL, and the Cochrane Library databases using the terms: "lung cancer," "cancer survivors," and "symptom cluster." Results: Of 41 reviewed reports, 188 SCs were identified. Both a priori and de novo method were used to identify LC SCs, with exploratory factor analysis being the most commonly used statistical method in the de novo approach. The three most frequent SCs were respiratory, gastrointestinal (GI), and psychological SCs. The most common respiratory SC included cough + dyspnea. Nausea + vomiting was the most prevalent cluster membership among GI SCs. Sad + feeling irritable + feeling nervous + worrying was the most common cluster membership among psychological SCs. Conclusion: Respiratory, GI, and psychological SCs were common among LC patients, and addressing these clusters could improve symptom management strategies. Further research on SCs across the lung cancer trajectory is essential to enhance our understanding about SCs and facilitate effective symptom management throughout the disease course.

Key Words: Cancer survivors; Lung neoplasms; Review; Syndrome

## INTRODUCTION

Globally, lung cancer is the leading cause of cancer-related death, accounting for an estimated 2 million cases and 1.8 million deaths reported in 2011 [1]. Lung cancer patients often experience a high symptom burden, both emotional and physical, due to the disease itself and treatments such as chemotherapy [2], or surgery [3]. These symptoms significantly impact their quality of life [4]. Commonly reported symptoms among lung cancer patients include cough (87%), breathlessness (61%), and chest pain (58%) [5]. Additionally, fatigue and weight loss are frequently seen in those with advanced stages of the disease [6]. Given the complex and diverse nature of these symptoms, it is crucial to investigate the symptom experiences of lung cancer patients to enhance symptom management and overall patient care.

Symptom Clusters (SCs) are groups of two or more related symptoms that occur together and may or may not share same etiology [7]. These symptoms are not random groupings of symptoms but are usually interconnected, and their interaction can lead to a compounded effect on patient outcomes [8,9]. The symptoms within a cluster interact and have a progressively strong effect on patient outcomes compared to individual symptoms; thus, SCs are crucial for clinical practice [10]. Effective symptom management can be achieved by considering SCs to better understand the patients' symptom experience.

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Received: Jul 11, 2024 / Revised: Oct 22, 2024 / Accepted: Nov 8, 2024

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A comprehensive review of reports on SCs among lung cancer patients could enhance our understanding of lung cancer-related SCs and symptom management strategies. Although previous reviews have explored SCs in this patient group, their scope has been limited. A narrative literature review of SCs among lung cancer patients included only five reports [11]. In contrast, a recent scoping review on the SCs of lung cancer patients encompassed 53 articles covering 48 studies. However, this review employed a broad definition of SC, including reports that measured multiple co-occurring symptoms, regardless of whether the study's primary aim was to investigate symptom clusters. This approach may have limited the depth of the findings [12]. Symptoms were grouped into a limited number of broader symptom categories, encompassing a wide range of different symptom expressions. While this approach provides a comprehensive overview, narrowing down symptoms into broader but limited number of symptom categories did not sufficiently differentiate each symptom, thus not adequately reflecting their unique characteristics in SC analysis. So far, no scoping review has summarized common SCs and, the specific symptom memberships by reviewing studies with distinct aim to investigate SCs. Additionally, there has no detailed examination of the analytic methods used to identify SCs in lung cancer patients.

The current scoping review aimed to provide a comprehensive understanding of SCs among lung cancer patients by exploring the methods used to identify SCs, the most common SCs, and their compositions in studies specifically focused on SCs.

## METHODS

### 1. Study Design

The design of the study was a scoping review, which was performed in accordance with the Joanna Briggs Institute (JBI) methodology [13].

#### 1) Research questions

 How are SCs identified among lung cancer patients in the studies which had distinct aim to investigate SCs?
 What common SCs exist in lung cancer patients in the studies which had distinct aim to investigate SCs? 3) What are the compositions of common SCs identified among lung cancer patients in the studies which had distinct aim to investigate SCs?

#### 2) Eligibility criteria

The inclusion criteria were as follows: (i) participants

were adults diagnosed with lung cancer at any stage, (ii) concept was SCs of lung cancer patients, and (iii) context as original reports with any type of design with distinct aim to investigate LC SCs. There were no restrictions regarding the type or phase of treatment, the time points for assessment, or the type of symptom assessments used, whether symptoms were measured by severity, occurrence, or distress. All types of study designs were included in this scoping review, except for review articles because the sources of the reviews had already been identified either through the database searches or from the manual search of the reference lists of the included reports.

#### 3) Search strategy, evidence screening and selection

The PubMed, Embase, PsycINFO, CINAHL, and Cochrane Library databases were searched from inception to September 2022. The search strategies were developed with the assistance of a librarian and included terms such as "lung cancer", "symptom cluster", and "cancer survivor" (Supplementary Table 1). The search was limited to reports published in English. Initially, 1138 reports were identified. The search was mostly updated on 31 November 2023, at which point the total number of reports reached 1743. These reports were then exported to EndNote X20, where duplicates were removed.

To select eligible reports, two authors (AJ and CYY) independently screened the titles and abstracts of all reports retrieved from the databases. They compared their screened results and selected reports by consulting a third reviewer. From the databases, a total of 1,743 reports were identified and screened based on their titles and abstracts, resulting in 60 articles being chosen for full-text screening. After applying eligibility criteria-such as the absence of a symptom cluster description, review paper, report paper, studies on other cancers, or papers in languages other than English-26 reports were excluded. Consequently, 34 reports were initially selected for the current study. A manual search of the reference lists in the selected reports identified 7 additional reports for inclusion. Ultimately, 41 reports were included in this review, as detailed in a PRISMA-ScR flow diagram [14] (Figure 1).

#### 4) Data extraction

Two authors (AJ and CYY) independently extracted the following data by using the data extraction instrument suggested by the JBI scoping review methodology: study setting, study design, sample size, instrument used for symptom assessment, analytic technique used to identify SCs, the identified SCs, and symptom membership in each SC.



Figure 1. PRISMA flow diagram for report selection.

Some reports presented SC results from the same study (report ID #3 [A3] and 4 [A4], report ID #6 [A6] and 7 [A7], report ID #15 [A15] and 16 [A16], report ID #31 [A31] and 38 [A38]). Identical SC results obtained from the same study, using the same data and analysis methodology, were considered duplicates and thus treated as a single result from a single study with separate reports in the current review (report ID #3 [A3] and 4 [A4]). In the cases where reports employed different analytic techniques on the same study data and achieved different SC results, each result was considered as a separate result derived from a single study (report ID #6 [A6] and 7 [A7]). Distinct results from the same study data with different analyses, based on different compositions of symptom items, were considered separate results i.e. separate reports within a single study (report ID #15 [A15] and 16 [A16]). For results based on the same study data and the same analysis but utilizing different dimensions of symptoms, such as severity or occurrence, and achieving different results, each result was counted separately (report ID #31 [A31] and 38 [A38]). For SCs identified from longitudinal data ('report ID #2 [A2], 4 [A4], 5 [A5], 6 [A6], 7 [A7], 12 [A12], 16 [A16], 17 [A17], 20 [A20], 21 [A21], 24 [A24], 31 [A31], and 36 [A36]), the results from each time point were considered separately. For the reports identifying multiple results by analyzing multiple symptom dimensions or collecting data at multiple time points, an  $\alpha$  bet letter was added to the report ID # to distinguish the SC result of each dimension or time point (e.g., report ID #5a, 5b, 5c, 5d; report ID #18a, 18b; report ID #20a, 20b, 20c, 20d, 20e, 20f, report ID #21a, 21b, 21c, 24a, 24b; report ID #31a, 31b, 31c, 31d, 31e, 31f; report ID #38a, 38b, which analyzed SCs based on symptom occurrence and severity at different time points using longitudinal data).

### 5) Data analysis and presentation

In accordance with the JBI methodology [13], the data about the lung cancer patients (participants) and symp-

tom cluster (concept) were extracted. The general characteristics of the reports, such as study design and sample size, along with specific information about the lung cancer patient, including treatment received, were detailed. The instruments to measure symptoms, the methodologies employed to identify SCs, and the identified SCs were summarized and categorized. Symptoms that were measured based on symptom occurrence, severity, or distress and identified as SCs were organized accordingly. For identified SCs labeled as "no name," cluster membership was reviewed and categorized into a specific SC if more than half of the symptoms belonged to that SC. The SCs were listed, and frequently reported common SCs were identified. To clarify SC membership, specific cluster memberships of common symptom SCs are summarized in the tables.

## RESULTS

#### 1. How SCs were Identified among Lung Cancer Patients

#### 1) General characteristics of the included reports

A total of 10,829 participants were included, with individual reports ranging from 10 to 2,405 patients. Approximately 55% of the participants were male. The mean age of the participants ranged from 52 to 72 years. The study employed various designs, including cross-sectional, longitudinal, interventional and qualitative approaches. Nearly half of the reports applied a cross-sectional design (49%) [A1,A8-11,A13-15,A18,A22,A23,A28-30, A32-35,A38, A41]; and 32% adopted a longitudinal design [A2,A4-7, A12,A16,A17,A20,A21,A24,A31,A36]. Chemotherapy was the most frequently reported treatment modality for lung cancer, cited in 32% of the studies [A8,A9,A14,A17-19, A21, A23, A24, A31, A35, A38, A41]. Additionally, approximately 7% of the patients underwent radiotherapy [A2-4]. The earliest report of SCs among lung cancer patients was published in 1997. The reports were conducted in eleven countries: the U.S., the U.K., China, Thailand, Hong Kong, Sweden, Korea, Taiwan, Brazil, Japan, and Vietnam. Notably, 27% of the reports were conducted in the United States [A1,A6,A7,A9,A10,A12,A13,A30-32,A38] (Table 1).

#### 2) Measurements of symptoms and results

The measurement instruments used for symptoms and results are summarized in Supplementary Table 2. A total of 13 reports (32%) used the M.D. Anderson Symptoms Inventory (MDASI) [15], which was developed for a brief measure of the severity and impact of cancer-related symptoms [A5,A8,A14,A17,A20-A22,A24,A28,A34-A36,A41]. Four reports (10%) employed the Memorial Symptom Assessment Scale (MSAS) [A18,A29,A31,A38], and another four reports (10%) used European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [A11,A15,A16,A23]. Three reports (7%) applied the Lung Cancer Symptoms Scale (LCSS) [A1,A6,A7], and another three (7%) used the Symptom Distress Scale (SDS) [A9,A15,A32]. An additional three reports (7%) utilized the Visual Analogue Scale (VAS) [A2-4]. Two reports employed the Numeric Rating Scale (NRS) [A37,A39], and two used the Physical Symptom Experience Tool (PSET) [A12,A13]. Reports also mentioned the use of the Short-Form 36 Health Status Survey (SF-36) [A10], Short-From 12 Health Status Survey (SF-12) [A30], ESAS [A19], and FACT [A27]. Symptoms were measured across two different dimensions in four reports where participants were receiving chemotherapy. Dimensions such as symptom occurrence and severity [A20, A31,A38] or symptom distress and severity [A18] were assessed using either the either MDASI-LC or MSAS. Commonly measured symptoms were identified among the various measurements used.

There are reports of the same instruments being used with different variations. To identify commonly measured symptoms, measurement instruments were categorized into 11 instruments that were specific to lung cancer symptoms.

SCs identified by occurrence and severity dimension shared congruent names and corresponding numerical patterns, whereas the actual composition of symptom membership diverged [A20,A31,A38]. This study identified five symptom clusters based on symptom distress or severity. Among these, two SCs shared identical names with similar composition of symptom memberships, while the remaining three were distinct SCs [A18].

A total of 17 reports identified SCs assessed them at multiple time points, ranging from three to seven [A2-7, A12,A16,A17,A20,A21,A24,A26,A27,A31,A36,A37] (Supplementary Table 2). Most of the designated time points were related to treatment, i.e., chemotherapy [A17, A21,A24,A31,A36], radiation therapy [A2,A3,A4], either chemotherapy or radiation therapy [A26,A27], surgery [A5,A20,A37], or any form of treatment [A16]. Three reports assessed symptoms at time points related to cancer diagnosis [A6,A7,A12]. Following baseline data collection, symptoms assessments were subsequently conducted from 6 days to 5 years.

# 3) Analytical methods for symptom cluster identification

SCs were identified through either an a priori method,

Report ID #	Author, Year	Country	Study design	Participants (n)	Male (%)	Mean age	Treatment
1	Brown et al., 2011	USA	Cross-sectional	196	0.0	65.4	Surgery, CTx, RTx
2	Chan et al., 2005	Hong Kong	Longitudinal	27	85.0	63.1	RTx
3	Chan et al., 2011	Hong Kong	Quasi-experimental	140	82.9	63.5	RTx
4	Chan et al., 2013	Hong Kong	Longitudinal	140	82.9	63.5	RTx
5	Chen et al., 2023	China	Longitudinal	200	55.0	69.4	Surgery
6	Cheville et al., 2011a	USA	Longitudinal	2,405	530	67.4	Not specified
7	Cheville et al., 2011b	USA	Longitudinal	2,405	53.0	67.4	Not specified
8	Choi and Ryu, 2018	Korea	Cross-sectional	178	57.9	54.0	CTx
9	Fodeh et al., 2013	USA	Cross-sectional	51	26.0	59.6	CTx
10	Fox and Lyon, 2006	USA	Cross-sectional	13	260	56.9	Not specified
11	Franceschini et al., 2013	Brazil	Cross-sectional	50	68.0	61.3	Not specified
12	Gift et al., 2003	USA	Longitudinal	112	52.0	72.0	Surgery, CTx, RTx
13	Gift et al., 2004	USA	Cross-sectional	220	59.0	72.0	Not specified
14	Hamada et al., 2016	Japan	Cross-sectional	60	36.0	64.3	CTx
15	Henoch et al., 2009	Sweden	Cross-sectional	400	52.0	64.5	Not specified
16	Henoch and Lövgren, 2014	Sweden	Longitudinal	400	52.0	64.5	CTx and RTx
17	Ju et al., 2023	China	Longitudinal	175	81.7	63.6	CTx
18	Khamboon et al., 2015	Thailand	Cross-sectional	300	55.7	61.4	CTx
19	Khamboon and Pakanta, 2021	Thailand	Quasi-experimental	80	57.5	60.4	CTx
20	Li et al., 2021a	China	Longitudinal	217	53.0	59.8	Surgery
21	Li et al., 2021b	China	Longitudinal	144	75.7	62.7	CTx
22	Lin et al., 2013	China	Cross-sectional	145	68.3	59.0	Surgery
23	Liu et al., 2021	China	Cross-sectional	127	63.5	39~80	CTx
24	Ma et al., 2022	China	Longitudinal	180	62.2	52.2	CTx
25	Maguire et al., 2014	UK	Qualitative	10	40.0	63.2	Not specified
26	Molassiotis et al., 2011	UK	Qualitative	17	70.6	66.7	CTx and RTx
27	Molassiotis et al., 2021	Vietnam	RCT	156	74.4	56.8	CTx and RTx
28	Oh et al., 2019	Korea	Cross-sectional	46	84.8	$\leq 65 \text{ (n=23)}$ $\geq 66 \text{ (n=23)}$	Not specified
29	Pudtong et al., 2014	Thailand	Cross-sectional	165	66.1	62.4	Not specified
30	Reyes-Gibby et al., 2013	USA	Cross-sectional	599	52.8	61.0	Not specified
31	Russell et al., 2019	USA	Longitudinal	145	43.4	64.0	CTx
32	Sarna and Brecht, 1997	USA	Cross-sectional	60	0.0	58.3	Not specified
33	Takemura et al., 2023	Hong Kong	Cross sectional	161	47.2	61.2	Not specified
34	Wang et al., 2008	Taiwan	Cross-sectional	108	63.5	67.5	Not specified
35	Wang and Fu, 2014	China	Cross-sectional	183	63.9	58.3	CTx
36	Wang et al., 2014	Taiwan	Longitudinal	57	42.1	62.3	Gefitinib
37	Wang et al., 2023	China	RCT	100	50.0	Int.: 57.3 Cont.: 58.4	Surgery
38	Wong et al., 2017	USA	Cross-sectional	145	43.4	64.0	CTx
39	Yorke et al., 2015	UK	RCT	101	46.5	67.6	Not specified
40	Yorke et al., 2022	UK	RCT	263	50.0	69.0	Not specified
41	Zhang et al., 2022	China	Cross-sectional	148	85.8	$\leq 65 \ (60.8\%)$ $\geq 66 \ (39.2\%)$	CTx

Table 1. General Characteristics of the Included Reports

Cont.=Control; CTx=chemotherapy; Int.=Intervention; RCT=randomized controlled trial; RTx=radiotherapy

#### Table 2. Respiratory Symptom Clusters

n	Symptom cluster membership	Report ID #	Times
2	Cough + dyspnea - Cough + breathing - Cough + dyspnea	9 15, 16	3
	Cough + expectoration	20c, 20d, 20f	3
	Chest tightness + SOB	20c	1
3	Cough + dyspnea + fatigue - Cough + dyspnea + fatigue - Cough + breathlessness + fatigue	6, 7 26, 39, 40	5
	Cough + SOB + expectoration	5a, 21b, 24a, 24b	4
	Cough + difficulty breathing + SOB + chest tightness	31b, 38a	2
	Cough + dyspnea + insomnia - Cough + SOB + difficulty sleeping - Cough + breathing + insomnia	18a 32	2
	Expectoration + hemoptysis + chest tightness	20b	1
	Chest tightness + SOB + fatigue	20d	1
	Cough + expectoration + hemoptysis	21a	1
	Cough + expectoration + chest tightness	23	1
	Cough + shortness of breath + dry mouth	41	1
4	Cough + SOB + expectoration + chest tightness	17, 20a, 21c	3
	Chest tightness + SOB + distress + pain	20f	1
	Cough + difficulty breathing + SOB +dry mouth + swelling of arms or legs	31a	1
	Cough + difficulty breathing+ SOB + dry mouth+ chest tightness	31e	1
	Cough + difficulty breathing + chest tightness + swelling of arms or legs	38b	1
5	Cough + shortness of breath + expectoration + chest tightness + pain	5b, 5c, 5d	3
6	Cough + shortness of breath + sore throat+ constipation + dry mouth + drowsy	8	1
	Cough + chest tightness + expectoration + fatigue + pain + distress	20e	1
	Cough + difficulty breathing + SOB + chest tightness + weight loss + dizziness + pain	31c	1
7	Cough + difficulty breathing + SOB + chest tightness + dizziness + pain + feeling drowsy + lack of energy	31d	1
8	Cough + difficulty breathing + SOB + chest tightness + dry mouth + pain + difficulty concentrating + feeling drowsy + lack of energy	31f	1

Note. For report IDs # 6, 7, 9, 17 & 40, symptom clusters were categorized based on symptoms comprising the symptom cluster because no names were identified for the symptom clusters.; n=number of symptoms; SOB=shortness of breath.

where predefined SC membership was applied based on empirical evidence, or a de novo method applying a quantitative statistical analysis technique [16]. Two reports used a qualitative analytical approach [A25,A26]. Over half of the reports (56%) employed a de novo approach to identify SCs.

A priori analysis was used in 16 reports (39%) [A1-A4, A7,A9,A12,A16,A19,A22,A27,A30,A36,A37,A39,A40].

Gift et al. (2003) initially employed a priori analysis to identify a SC and evaluated the SC's internal consistency with Cronbach's  $\alpha$ . Most of the reports that adopted an a priori approach were published between 2003 and 2015 [A1-4,A7,A9,A12,A16,A22,A30, A36,A39], except for those that were part of intervention studies [A19,A27,A37,A40].

Among the de novo approach reports, Explanatory Factor Analysis (EFA) was the most commonly used stat-

istical method (n=11) [A5,A6,A8,A14,A20,A21,A24,A31,A35, A38,A41]. Only a few reports specified the rotation method used: varimax [A6,A8,A35], promax [A14], orthogonal [A20], geomin [A31], oblique [A38], and maximal variation rotation [A41]. Principal Component Analysis (PCA) with varimax rotation was the second most frequently employed analytic technique for SC analysis (n=4) [A15,A18, A29,A32]. Two reports applied correlational analysis [A10,A33], and another two reports applied both factor analysis and hierarchical cluster analysis to identify SCs [A23,A34]. Studies employed the de novo approach were published between 2003 and 2023. There was a single report employing Latent Class Growth Analysis (LCGA) published in 2023, which aimed to explore longitudinal trajectories to identify subgroups of symptom clusters [A17].

### 2. Symptom Clusters Identified in Lung Cancer Patients

A total of 188 SCs were identified in lung cancer patients. Among the SC studies with a priori approach, the respiratory SC was the primary focus of investigation. Dyspnea and cough were the main component of two SC memberships [A9,A16], while three SC memberships with fatigue [A1,A7,A39,A40], and four SC memberships addressed fatigue and pain [A37]. Dyspnea was also associated with fatigue and anxiety [A2-4,A26].

Overall, the three most common SCs identified among lung cancer patients, regardless of the analytic approach, were respiratory SCs (21%), gastrointestinal (GI) SCs (22%), and psychological SCs (14%). The remaining categories, no-name (12%) and other SCs (31%), are presented in Supplementary Table 3 and 4. In the SC studies with a de novo approach (n=164), one of the most frequently identified SCs was related to respiratory SC named as lung cancerspecific SC (n=18) and respiratory SC (n=15). Additionally, there were studies without specific names but associated with the respiratory SC because of the membership (n=3). GI SCs were identified almost as frequently as respiratory SCs, with categories including gastrointestinal SC, referred to as nutritional SC (n=15), gastrointestinal SC (n=14), digestive SC (n=3), anorexia SC (n=3), and SCs with no name (n=2). Overall, both GI SCs and respiratory SCs accounted for over 20% of the reports using the de novo approach. Psychological SCs were identified 25 times with the de novo approach and included names such as psychological SC (n=18), mental SC (n=4), emotional SC (n=4). One SC named "pain" and another with no name were categorized as psychological SCs considering their memberships.

## 3. Compositions of Common SCs Identified among Lung Cancer Patients

#### 1) Respiratory symptom cluster

A total of 39% of the reports included in the review identified respiratory SCs (40 times in 23 types), which were originally referred to as respiratory/respiratory function/respiratory distress/respiratory tract/pulmonary/ lung cancer-related/lung cancer-specific SCs. The number of symptoms per cluster ranged from 2 to 8 symptoms (Table 2). Considering that dyspnea corresponds with breathing symptoms, shortness of breath (SOB) or difficulty breathing, three different cases of dyspnea were considered "dyspnea" for this review. For example, one report reported cough + difficulty breathing + shortness of breath as a SC [A31]; these findings were considered cough + dyspnea. Cough + dyspnea was identified as a single cluster 3 times (report ID #9 [A9], 15 [A15], 16 [A16]), and it was accompanied by fatigue (report ID #6 [A6], 7 [A7], 26 [A26], 39 [A39], 40 [A40]), expectoration (report ID #5a [A5], 21b [A21], 24a, 24b [A24]), chest tightness (report ID #31b [A31], 38a [A38]), or insomnia (report ID #18a [A18], 32 [A32]). Additionally, cough + dyspnea also clustered with chest tightness + expectoration (report ID #17 [A17], 20a [A20], 21c [A21]) and chest tightness + expectoration + pain (report ID #5b, 5c, 5d [A5]) (Table 2).

#### 2) Gastrointestinal symptom clusters

GI SCs were identified in 37% of the reports (41 times, across 26 types) and were initially categorized under various names including nutritional, digestive function, digestive impairment, anorexia-related, fatigue-anorexia, epithelial-GI, treatment-related GI and other, GI distress, and GI SCs. These SCs consisted of 2 to 13 symptoms (Table 3). Nausea + vomiting was the most frequently identified SC (report ID #20b, 20e [A20], 21b, 21c [A21], 34 [A34], 35 [A35], 36 [A36], 41 [A41]. This cluster, Nausea + vomiting, also appeared in combination with constipation + lack of appetite (report ID #24a, 24b [A24]) and with lack of appetite + weight loss + fatigue + altered sense of taste + weakness (report ID #12a, 12b, 12c [A12], 13 [A13]). Additionally, nausea + vomiting also clustered with hair loss (report ID #18a [A18]), dizziness (report ID #18b [A18], numbness and dry mouth (report ID #28 [A28]), and appetite loss/anorexia + hypodipsia (report ID #23 [A23]). A unique cluster featuring of lack of appetite + increasing appetite + weight gain was identified in one report (report ID #31a, 31c [A31]), while lack of appetite + increasing appetite + weight gain + weight loss was identified in two reports (report ID #31b, 31e [A31], 38a, 38b [A38]) (Table 3).

 Table 3. Gastrointestinal Symptom Clusters

n	Symptom cluster membership	Report ID #	Times
2	Nausea + vomiting - Nausea + emesis - Nausea + vomiting	20b, 20e 21b, 21c, 34, 35, 36, 41	8
	Nausea + appetite	32	1
3	Lack of appetite + constipation + weight loss	5с	1
	Lack of appetite + increase appetite + weight gain	31a, 31c	2
	Dry mouth + change in the way food tastes + lack of appetite	18a	1
	Nausea + vomiting + hair loss	18a	1
	Nausea + vomiting + dizziness	18b	1
	Lack of appetite + weight loss + dry mouth	20e	1
	Nausea + lack of appetite + change in food taste	29	1
	Increased appetite + weight gain + weight loss	31f	1
4	Lack of appetite + increase appetite + weight loss + weight gain	31b, 31e, 38a, 38b	4
	Nausea + vomiting + lack of appetite + constipation	24a, 24b	2
	Dry mouth + change in the way food tastes + lack of appetite + lack of energy	18b	1
	Lack of appetite + weight loss + dry mouth + disturbed sleep	20b	1
	Nausea + vomiting + numbness + dry mouth	28	1
	Appetite loss + anorexia + nausea + vomiting + hypodipsia	23	1
	Loss of appetite + nausea + bowel problem + fatigue	16	1
	Increased appetite + sweats + lack of appetite + weight gain	31d	1
5	Dry mouth + altered sense of taste + drowsiness + fatigue/tiredness + lack of appetite	14	1
	Lack of appetite + dry mouth + numbness + weight loss + disturbed remembering	20f	1
	Lack of appetite + constipation + weight loss + nausea + emesis	5b	1
	Loss of appetite + nausea + bowel problems + pain + fatigue	16	1
6	Lack of appetite + dry mouth + numbness + weight loss + disturbed remembering + sadness	20c	1
7	Nausea + vomiting + lack of appetite + weight loss + fatigue + altered taste + weakness	12a, 12b, 12c, 13	4
8	Constipation + nausea + sweats + lack of appetite+ weight loss + changes in skin + I do not look like myself + change in the way food tastes	31d	1
9	Abdominal cramps + constipation + nausea + sweats + lack of appetite + weight loss + changes in skin + I do not look like myself + change in the way food tastes	31a	1
13	Abdominal cramps + sweats + lack of appetite + changes in skin + I do not look like myself+ change in the way food tastes + mouth sores + hair loss + feeling drowsy + feeling bloated + weight gain + dizziness+ problems with sexual interest or activity	31c	1
	Abdominal cramps + constipation + sweats + lack of appetite + weight loss + changes in skin + I do not look like myself + change in the way food tastes + mouth sores+ hair loss + feeling bloated + dizziness + problems with sexual interest or activity	31f	1

Note. For report IDs #12, 13 & 28, symptom clusters (SCs) were categorized based on symptoms comprising the symptom cluster (SC) because no names were identified for the SCs. For report ID #14, the SC was categorized based on the symptoms comprising the SC because it was named as a "fatigue-anorexia" cluster in the original report. For report ID #16, the SC was categorized based on symptoms comprising the SC because it was named as a "pain cluster" in the original report.; n=number of symptoms.

#### 3) Psychological symptom clusters

A total of 27% of the reports identified psychological SCs (26 times, 20 types), which were initially named psychological, psychological-somatic, global mental function, special mental function, mood, and emotional SCs. The "pain cluster" mentioned in the report ID #14 [A14] refers to a SC consisting of anxiety, sadness, and pain, and is thus classified as a psychological SC. The number of symptoms per cluster varied from 2 to 8 (Table 4). Sad + distress formed two membership SCs (report ID #24a [A24], 35 [A35]). Additionally, sad + distress were also clustered with memory disturbance in report ID #5a, 5b, 5c, 5d [A5]. Four symptoms-sad + feeling irritable + feeling nervous + worrying-were identified a total of 7 times across two reports. These symptoms were observed twice as a single cluster in report ID #31e [A31], and 38b [A38], and addi-

tionally, five more times in combination with other symptoms in report ID #31a, 31b, 31c, 31d [A31], and 38a [A38] (Table 4).

### DISCUSSION

This scoping review provided a comprehensive overview of symptom clusters that were identified in studies of lung cancer patients. The three common symptom clusters among lung cancer patients were identified as respiratory SCs, GI SCs, and psychological SCs.

### 1. How SCs were Identified among Lung Cancer Patients

Various instruments were utilized to measure symptoms in the reports, with several symptoms commonly

#### Table 4. Psychological Symptom Clusters

n	Symptom cluster membership	Report ID #	Times
2	Sad + distress	24a, 35	2
	Distress+ fatigue	20b	1
	Sadness + short of breath	20e	1
	Fatigue + sadness	20f	1
3	Sad + distress + memory disturbance - Sad + distress + memory disturbance - Sadness + distress + difficulty remembering	5a, 5b, 5c 5d 21b	5
	Anxiety + sadness + pain	14	1
	Fatigue + distress + sadness	20a	1
	Distress + lack of appetite + sadness	21a	1
	Sleep disturbance + distress + sadness	21c	1
4	Sad + feeling irritable + feeling nervous + worrying	31e, 38b	2
	Worry + depression + concentration + insomnia	16	1
5	Sad + distressed + remembering things + fatigue + numbness or tingling	8	1
	Feeling nervous + feeling sad + worrying + vomiting + nausea	31f	1
6	Sadness + distress + drowsiness + pain + fatigue + numbness	24b	1
	Impaired concentration + irritability + depression + weight loss + difficulty remembering + SOB	14	1
	Feeling irritable + feeling nervous + feeling sad + worrying + vomiting + nausea	31c	1
7	Sad + feeling bloated + feeling irritable + feeling nervous + worrying + difficulty in concentration + problem with sexual interest	31b, 38a	2
	Feeling sad + feeling bloated + feeling irritable + feeling nervous + worrying + weight loss + difficulty sleeping	31d	1
8	Feeling sad + feeling bloated + feeling irritable + feeling nervous + worrying + weight loss + difficulty concentrating + difficulty breathing	31a	1

Note. For report ID #14, symptom clusters (SCs) were categorized based on the symptoms comprising the SC because they were named as a "pain cluster" or no name was identified for the SCs.; n=number of symptoms.

measured across them. There were two different conceptual approaches to symptom cluster research: a priori and de novo. In the current review, reports adopting the a priori approach were published earlier, between 2003 and 2015. Since then, there has been a shift toward the de novo approach, which employs statistical analysis techniques. Reports using the de novo approach have been published up to 2023, with the most recent report employing LCGA to identify subgroups of symptoms and longitudinal trajectories among homogenous patients, reflecting the lasted research trends.

The current review is consistent with the previous review, indicating that the majority of reports examining symptom clusters de novo, and there are statistical analytic methods such as factor analysis and cluster analysis in order to determine the number of symptom clusters and their symptom memberships [16]. Dong et al. (2014) reported relatively consistent results using PCA and HCA [17], although outcomes differed when using EFA. Two reports with de novo approach included in the current review applied multiple analytic techniques to identify lung cancer symptom clusters (LC SCs.) The findings from different analytic techniques, namely cluster analysis and HCA, and factor analysis combined with HCA, yielded consistent results. Approximately one-third of the studies employed longitudinal design. Regarding the stability of SC findings, the current study's results partially align with those of the Dong et al., which supported instability, and partially with the findings of Rha et al. in 2019 and 2020, both of which suggested a relative stability of SCs. This includes recent studies reporting on stability of SCs [18,19].

Another analytic approach to SC research is the identification of subgroups of patients who experience various levels of symptom burden within specific SCs. This method has been highlighted in prior studies, and one report in our review used latent class analysis [20]. The current review sheds light on the conceptual approaches employed in symptom cluster reports and emphasizes the need for further research to identify subgroups of patients who are vulnerable to higher symptom burden and poorer outcome [16].

## 2. Common SCs and Its Composition Identified in Lung Cancer Patients

#### 1) Respiratory symptom clusters

Cough + dyspnea was the most frequently identified respiratory cluster membership. The finding aligns with the results of a previous narrative review of SCs among lung cancer patients [11]. Cough + dyspnea was identified as single cluster, and also clustered with fatigue. The current study results are consistent with the previous scoping review that fatigue is a frequently reported symptom throughout the entire course of the lung cancer [11]. This finding underscores the importance of early screening of cancer-related fatigue, as it significantly impacts patients' quality of life [21]. The current review also identified that cough + dyspnea was associated with other co-occurring respiratory or related symptoms, such as expectoration, chest tightness, difficulty sleeping, chest tightness + expectoration, and pain + expectoration + chest tightness. These complex symptom interactions highlight the need for a comprehensive approach to symptom management, as respiratory symptoms often exacerbate other physical and emotional burdens [22].

It is understood that cough + dyspnea could be considered a common SC among those with respiratory SC, which could include additional respiratory or related symptoms. The close relationships between respiratory symptoms and other conditions such as fatigue, insomnia, or pain well depict complex symptom issues among lung cancer patients.

#### 2) Gastrointestinal symptom clusters

Nausea + vomiting was the most frequently identified GI SC. These findings are consistent with previous reviews of symptom clusters [17,23,24]. Similarly, this result corresponds to a previous review of symptom clusters in head and neck cancer in which approximately half of the studies identified nausea + vomiting as GI cluster memberships [25]. Although the participants in this review were receiving various treatments, the majority were undergoing chemotherapy, which is widely known to induce nausea and vomiting [26]. This may explain why these symptoms were frequently identified as part of the SCs. Consequently, future studies should consider investigating SCs based on different treatment modalities to better understand variations among patient groups. Additionally, this review also identified additional GI symptoms that could occur with nausea and vomiting, including lack of appetite and constipation, appetite loss/anorexia + hypodipsia, as well as non-GI symptoms such as hair loss, dizziness, numbness and dry mouth. Variations in patient characteristics, treatment types, symptom measurement, and the analysis method of symptoms may have contributed to the heterogeneity in the findings.

#### 3) Psychological symptom clusters

The third common cluster identified was a psychological SC. The predominant symptoms in the psychological SC were sad + distress. These findings are consistent with previous findings on SCs among head and neck cancer patients, in which approximately 38% of the reports identified sadness + distress as a psychological cluster membership [25]. Notably, sad + distress also clustered with other symptoms, and three clusters associated with memory disturbance were identified four times. The four symptoms, i.e., sad + feeling irritable + feeling nervous + worrying, were identified as a single cluster, and these findings correspond with those of other studies of SCs in patients receiving chemotherapy [27]. Another systematic review of SCs among breast cancer patients reported that psychological SCs were similar but differed because they included anxiety and depression in addition to sadness, irritability, nervousness and worry [28]. Considering the repeated clustering of sad + feeling irritable + feeling nervous+ worrying in psychological SCs, it is essential to comprehensively assess psychological symptoms in lung cancer patients.

### 3. Implications for Nursing Practice and Research

This review comprehensively identified common SCs and their memberships in lung cancer patients, which provides foundational information to nursing practice and research. Understanding common SCs and their membership can facilitate approaches to symptom management. Future studies should develop and evaluate interventions for symptom management that focus on the most frequently identified SCs and their memberships, such as cough + dyspnea, nausea + vomiting, and sad + distress. The association between respiratory symptoms and fatigue, insomnia, or pain indicates a need to investigate the underlying mechanisms shared by the symptoms involved in these SCs.

### 4. Limitations

This review has some limitations. This scoping review included reports from 11 countries without restrictions on the countries included, limiting the reports to those published in English may have resulted in the omission of some relevant studies. Contradictory symptoms such as weight gain and weight loss, or lack of appetite and increasing appetite were reported in the same SCs based on the findings of the reports, which logically cannot occur simultaneously. This may indicate a measurement issue that could lead to misinterpretation of concurrent symp-

tom experiences. Caution is needed when interpreting these results. There are only a few studies that have verified the association between influencing factors or the causal relationship of influencing factors to SCs, which require further investigation. Through this study, various analysis methods used to identify lung cancer-related symptom clusters were analyzed, and the results were summarized and presented. However, suggesting the most appropriate method for symptom cluster analysis was beyond the scope given the nature of a scoping review. The limited number of existing longitudinal studies with various treatments and time points restricted our understanding of changes in SCs. Although this scoping review has provided a comprehensive summary of current knowledge, future studies could leverage big data analyses from healthcare records to gain deeper insights into symptom cluster dynamics and influencing factors in larger, more diverse lung cancer populations. Longitudinal exploration of SCs will help understand the progression of SCs across the cancer trajectory.

## CONCLUSION

This scoping review summarized SCs among patients with lung cancer. The most frequently observed SCs were respiratory, GI and psychological. Cough + dyspnea, nausea + vomiting, and sadness + feeling irritable + feeling nervous + worrying were representative symptoms of common SCs. These SCs among lung cancer patients should be specifically addressed in oncology nursing practice. Further studies on SCs throughout the lung cancer trajectory could enhance understanding of SCs and improve symptom across the course of the disease.

#### **CONFLICTS OF INTEREST**

The authors declared no conflict of interest.

#### AUTHORSHIP

Study conception and/or design acquisition - CYY, AJ, and LJ; analysis - CYY, AJ, and LJ; interpretation of the data - CYY, AJ, and LJ; and drafting or critical revision of the manuscript for important intellectual content - CYY, AJ, and LJ.

#### ACKNOWLEDGEMENT

This study received no external funding. Yun Young Choi received a scholarship from the Brian Korea 21 FOUR Project funded by the National Research Foundation of Korea, Yonsei University, College of Nursing. Jotsna Akter received a scholarship from the United Board for Christian Higher Education in Asia.

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### Supplementary Table 1. Search Terms

## a. CINAHL

	Syntax	
S1	(MH "Lung Neoplasms+") OR (MH "Carcinoma, Non-Small-Cell Lung")	52,936
S2	TI (neoplasms OR cancer OR cancers OR tumor OR leukemi* OR leukaemi* OR lymphoma*OR myeloma*) OR AB (neoplasms OR cancer OR cancers OR tumor OR leukemi* OR leukaemi* OR lymphoma*OR myeloma*)	657,049
S3	S1 OR S2	657,049
S4	TI ("symptom cluster*" OR "cluster symptoms" OR "multiple symptoms" OR "symptom constellations" OR "symptom combination*" OR "concurrent symptoms") OR AB ("symptom cluster*" OR "cluster symptoms" OR "multiple symptoms" OR "symptom constellations" OR "symptom combination*" OR "concurrent symptoms")	2,363
S5	(MH "Patients+") OR TI (patient*) OR AB (patient*) OR (MH "Cancer Survivors") OR TI ("cancer survivor*") OR AB ("cancer survivor*")	2,326,795
S6	S3 AND S4 AND S5	680
S7	((MH "Patients+") OR TI (patient*) OR AB (patient*) OR (MH "Cancer Survivors") OR TI ("cancer survivor*") OR AB ("cancer survivor*")) AND (S3 AND S4 AND S5)) AND (S3 AND S4 AND S5) Limiters - Published Date: up to-20231131; Human; Language: English	642

# b. Cochrane Library

	Syntax	
1	MeSH descriptor: [Lung Neoplasms] explode all trees	10,583
2	lung neoplasms OR 'lung cancer OR 'lung cancers OR 'lung tumor	34,422
3	#1 OR #2	34,657
4	symptom cluster OR cluster symptoms OR multiple symptoms OR 'symptom constellations OR symptom combination OR 'concurrent symptoms	30,350
5	Patients	1,120,373
6	MeSH descriptor: [Patients] explode all trees	3,808
7	MeSH descriptor: [Cancer Survivors] explode all trees	827
8	cancer survivors OR cancer survivor OR cancer survivorship	7,201
9	#5 OR #6 OR #7 OR #8	1,124,652
10	#3 AND #4 AND #9	1,183
11	#3 AND #4 AND #9 English up to 2023-11-31	827

## c. Embase

	Syntax							
1	lung cancer'/exp	492,124						
2	lung neoplasms':ab,ti OR 'lung cancer':ab,ti OR 'lung cancers':ab,ti OR 'lung tumor':ab,ti	320,546						
3	#1 OR #2	270,569						
4	symptom cluster*':ab,ti OR 'cluster symptoms':ab,ti OR 'multiple symptoms':ab,ti OR 'symptom constellations':ab,ti OR 'symptom combination*':ab,ti OR 'concurrent symptoms':ab,ti	6,845						
5	patient'/exp OR patient*:ab,ti OR 'cancer survivor'/exp OR 'cancer survivors':ab,ti OR 'cancer survivor':ab,ti OR 'cancer survivorship':ab,ti	12,448,481						
6	#3 AND #4 AND #5 AND [english] up to 2023-11-31	103						

### Supplementary Table 1. Search Terms (Continued)

### d. PsycINFO

	Syntax	
S1	ab ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor") OR ti ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor")	2,903
S2	ab ("symptom cluster*' OR 'cluster symptoms' OR 'multiple symptoms' OR 'symptom constellations' OR 'symptom combination*' OR 'concurrent symptoms') OR ti ('bulimia and symptoms')	48,116
S3	mainsubject ("cancer survivors" OR "patients") OR ab ('patient*' OR 'cancer survivor' OR 'cancer survivors' OR 'cancer survivors' OR 'cancer survivors' OR 'cancer survivors' OR 'cancer survivorship')	777,282
S4	S1 AND S2 AND S3 ((ab ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor") OR ti ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor"))) AND (ab ("symptom cluster*' OR 'cluster symptoms' OR 'multiple symptoms' OR 'symptom constellations' OR 'symptom combination*' OR 'concurrent symptoms') OR ti ('bulimia and symptoms')) AND (mainsubject ("cancer survivors" OR "patients") OR ab ('patient*' OR 'cancer survivor' OR 'cancer survivors' OR 'cancer survivorship') OR ti ('patient*' OR 'cancer survivor' OR 'cancer survivors' OR 'cancer survivorship'))	83
S5	S1 AND S2 AND S3 Filters: English ((ab ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor") OR ti ("lung neoplasms" OR "lung cancer" OR "lung cancers" OR "lung tumor"))) AND (ab ("symptom cluster*' OR 'cluster symptoms' OR 'multiple symptoms' OR 'symptom constellations' OR 'symptom combination*' OR 'concurrent symptoms') OR ti ('bulimia and symptoms')) AND (mainsubject ("cancer survivors" OR "patients") OR ab ('patient*' OR 'cancer survivor' OR 'cancer survivors' OR 'cancer survivorship') OR ti ('patient*' OR 'cancer survivor' OR 'cancer survivors' OR 'cancer survivorship'))[english] up to 2023-11-31	79

#### e. PubMed

	Syntax	
1	"Lung Neoplasms"[Mesh]	278,052
2	"lung neoplasms"[All Fields] OR "lung cancer"[All Fields] OR "lung cancers"[All Fields] OR "lung tumor"[All Fields]	220,022
3	Search #1 OR #2"	261,253
4	"symptom cluster*"[tiab] OR "cluster symptoms"[tiab] OR "multiple symptoms"[tiab] OR "symptom constellations"[tiab] OR "symptom combination*"[tiab] OR "concurrent symptoms"[tiab]	4,927
5	"patients"[All Fields] OR "patient*"[All Fields] OR "cancer survivors"[All Fields] OR "cancer survivor*"[All Fields]	8,605,443
6	("Lung Neoplasms" [MeSH Terms] OR ("Lung Neoplasms" [Title/Abstract] OR "lung cancer" [Title/Abstract] OR "lung cancers" [Title/Abstract] OR "lung tumor" [Title/Abstract])) AND ("symptom cluster*" [Title/Abstract] OR "cluster symptoms" [Title/Abstract] OR "multiple symptoms" [Title/Abstract] OR "symptom constellations" [Title/Abstract] OR "symptom combination*" [Title/Abstract] OR "concurrent symptoms" [Title/Abstract] OR "lung tumor" [MeSH Terms] OR	93
7	(("Lung Neoplasms"[MeSH Terms] OR ("Lung Neoplasms"[Title/Abstract] OR "lung cancer"[Title/Abstract] OR "lung cancers"[Title/Abstract] OR "lung tumor"[Title/Abstract])) AND ("symptom cluster*"[Title/Abstract] OR "cluster symptoms"[Title/Abstract] OR "multiple symptoms"[Title/Abstract] OR "symptom constellations"[Title/Abstract] OR "symptom combination*"[Title/Abstract] OR "concurrent symptoms"[Title/Abstract]) AND ("patients"[MeSH Terms] OR "patient*"[Title/Abstract] OR ("cancer survivors"[MeSH Terms] OR "cancer survivor*"[Title/Abstract])))) AND (english[Filter]) up to 2023	92

Report	Author,	Chatiatian lan alamia	MC	Symptom clusters (original names)		Re-catego	orized	as
ID #	year	Statistical analysis	MS	Symptom clusters (original names)	RSC	GI SC	PSC	Other
1	Brown et al., 2011	A priori	LCSS, CES-D	No name: fatigue, SOB, cough, pain, and anorexia	-	-	-	•
2	Chan et al., 2005	A priori	VAS	No name: breathlessness, fatigue, and anxiety	-	-	-	•
3	Chan et al., 2011	A priori	VAS	No name: breathlessness, fatigue, and anxiety	-	-	-	•
4	Chan et al., 2013	A priori	VAS	No name: breathlessness, fatigue, and anxiety	-	-	-	•
5a	Chen et al., 2023	De novo: EFA	MDASI-LC (T0)	Respiratory function SC: expectoration, cough, SOB Global mental function SC: fatigue, disturbed sleep, lack of appetite Special mental function SC: distress, memory disturbance, sadness	• •	- - -	-	-
5b	Chen et al., 2023	Same as above	MDASI-LC (T1)	Respiratory function SC: pain, expectoration, chest tightness, cough, SOB Global mental function SC: fatigue, disturbed sleep, drowsiness Special mental function SC: distress, memory disturbance, sadness Digestive function SC: lack of appetite, constipation, weight loss, nausea, emesis Sensory function SC: dry mouth, numbness		-	-	-
5c	Chen et al., 2023	Same as above	MDASI-LC (T2)	Respiratory function SC: pain, expectoration, chest tightness, cough, SOB Global mental function SC: fatigue, disturbed sleep, drowsiness Special mental function SC: distress, memory disturbance, sadness Digestive function SC: lack of appetite, constipation, weight loss	• • •	- - -	- - -	-
5d	Chen et al., 2023	Same as above	MDASI-LC (T3)	Respiratory function SC: pain, expectoration, chest tightness, cough, SOB Special mental function SC: distress, memory disturbance, sadness Global mental function SC: fatigue, disturbed sleep	-	- - -	-	-
6	Cheville et al., 2011a	De novo: EFA with varimax rotation	LCSS, LASA	No name: fatigue, dyspnea, and cough	•	-	-	-
7	Cheville et al., 2011b	A priori	LCSS, LASA	No name: fatigue, SOB, and cough	•	-	-	-
8	Choi and Ryu, 2018	De novo: EFA, principal axis factoring with	MDASI-LC	Treatment-related SC: nausea, vomiting, disturbed sleep, pain, lack of appetite Lung cancer-related SC: sore throat, SOB, cough, constipation, dry	-	-	-	•
		varimax rotation		mouth, drowsy Psychological SC: distressed, sad, remembering things, fatigue, numbness or tingling	-	-	•	-
9	Fodeh et al., 2013	A priori	SDS	No name: breathing, cough	-	-	-	-
10	Fox and Lyon, 2006	De novo: correlation analysis	SF-36	No name: depression, fatigue	-	-	-	•
11	Franceschini et al., 2013	De novo: cluster analysis and HCA	EORTC QLQ-C30	No name: fatigue, dyspnea, insomnia, pain	-	-	-	•
12a	Gift et al., 2003	A priori	PSET (T0)	No name: fatigue, weakness, weight loss, appetite loss, nausea, vomiting, altered taste	-	•	-	-
12b	Gift et al., 2003	Same as above	PSET (T1)	Same as above	-	•	-	-
12c	Gift et al., 2003	Same as above	PSET (T2)	Same as above	-	•	-	-
13	Gift et al., 2004	De novo: factors analysis	PSET	No name: nausea, fatigue, weakness, appetite loss, weight loss, altered taste, vomiting	-	-	-	-

### Supplementary Table 2. Results of Symptom Cluster Reports (N=41)

Report	Author,	Chatiatiaal an alaasia	MC	Computer shortens (mininglaness)	I	Re-catego	orized	as
ID #	year	Statistical analysis	MS	Symptom clusters (original names)	RSC	GI SC	PSC	Other
14	Hamada et al., 2016	De novo: EFA with promax rotation	MDASI-J, advanced NSCLC symptom scale	No name: impaired concentration, irritability, depression, weight loss, difficulty remembering, SOB Fatigue/anorexia cluster: dry mouth, altered sense of taste, drowsiness, fatigue/tiredness, lack of appetite Pain cluster: anxiety, sadness, pain No name: sleep disturbance, nausea, cough Numbness cluster: Numbness, leg weakness, distress		-	• - • -	- - -
15	Henoch et al., 2009	De novo: PCA with varimax rotation	SDS, EORTC QLQ-C30, EORTC LC13	Pain cluster: bowel issues, nausea, pain, appetite loss, fatigue Mood cluster: outlook, mood, concentration, insomnia Respiratory cluster: coughing, dyspnea	-	- - -	- - -	•
16	Henoch and Lövgren, 2014	A priori	EORTC QLQ C-30, EORTC QLQ LC13	Pain cluster: bowel problems, nausea, pain, loss of appetite, and fatigue Mood cluster: worry, depression, concentration, and insomnia Respiratory cluster: coughing and dyspnea	-	-	-	- -
17	Ju et al., 2023	De novo: latent class growth analysis	MDASI-LC	No name: difficulty remembering, numbness, hemoptysis, weight loss No name: cough, expectoration, chest tightness, SOB No name: nausea, sleep disturbance, drowsiness, vomiting No name: pain, distress, dry mouth, sadness, constipation No name: fatigue, lack of appetite	-	- - -	- - - -	
18a	Khamboon et al., 2015	De novo: PCA with varimax rotation	MSAS (severity)	Emotional-elimination discomfort cluster: feeling irritable, feeling drowsy, feeling bloated, dizziness, problems with urination, constipation, changes in skin Anorexia-related SC: dry mouth, change in the way food tastes, lack of appetite Treatment-related GI and other cluster: nausea, vomiting, hair loss Neurological and body image SC: numbness/tingling in hands/ feet, "I don't look like myself", pain, worrying, weight loss Respiratory and sleep disturbance SC: SOB, cough, difficulty sleeping	-	-	-	•
18b	Khamboon et al., 2015	Same as above	MSAS (distress)	Emotional, elimination and respiratory SC: feeling irritable, feeling bloated, problems with urination, constipation, SOB, worrying Body image SC: "I don't look like myself", hair loss, itching, changes in skin Anorexia-related SC: dry mouth, change in the way food tastes, lack of appetite, lack of energy Treatment-related GI and other SC: nausea, vomiting, dizziness Treatment-related neurological and other SC: numbness/tingling in hands/feet, weight loss, difficulty sleeping	-	-	-	-
19	Khamboon and Pakanta, 2021	A priori	ESAS	No name: Fatigue, loss of appetite, and anxiety	-	-	-	•
20a	Li et al., 2021a	De novo: EFA with orthogonal rotation	MDASI-LC (occurrence, T1)	Lung cancer-specific SC: expectoration, cough, chest tightness, SOB Sleep disturbance SC: fatigue, distress, sadness Psychological SC: lack of appetite, disturbed sleep Neurological SC: disturbed remembering, dry mouth	-	- - -	-	-
20b	Li et al., 2021a	Same as above	MDASI-LC (occurrence, T2)	Nutritional SC: lack of appetite, weight loss, dry mouth, disturbed sleep GI SC: Emesis, nausea Sleep disturbance SC: drowsiness, sadness, SOB Psychological SC: distress, fatigue Lung cancer-specific SC: expectoration, haemoptysis, chest tightness	- - -	-	- - -	-
20c	Li et al., 2021a	Same as above	MDASI-LC (occurrence, T3)	Nutritional specific SC: lack of appetite, dry mouth, numbness, weight loss, disturbed remembering, sadness, Lung cancer specific SC: chest tightness, SOB Respiratory SC: cough, expectoration Sleep disturbance SC: disturbed sleep, constipation Neurological SC: constipation, haemoptysis, pain	-	-	- - -	-

Report	Author,	Statistical analyzis	MC	Sumptom dustars (original names)	F	Re-catego	orized	as
ID #	year	Statistical analysis	IVI5	Symptom crusters (original names)	RSC	GI SC	PSC	Other
20d	Li et al., 2021a	Same as above	MDASI-LC (severity, T1)	Respiratory SC: expectoration, cough Lung cancer-specific SC: chest tightness, SOB, fatigue Sleep disturbance SC: lack of appetite, disturbed sleep Neurological SC: dry mouth, sadness, disturbed remembering	-	- - -	- - -	-
20e	Li et al., 2021a	Same as above	MDASI-LC (severity, T2)	Lung cancer-specific SC: fatigue, pain, expectoration, distress, chest tightness, cough GI SC: emesis, nausea Nutritional SC: lack of appetite, weight loss, dry mouth Psychological SC: sadness, SOB Sleep disturbance SC: disturbed sleep, drowsiness Neurological SC: haemoptysis, disturbed remembering		-		-
20f	Li et al., 2021a	Same as above	MDASI-LC (severity, T3)	Nutritional SC: lack of appetite, weight loss, dry mouth, disturbed remembering, numbness Lung cancer-specific SC: chest tightness, SOB, distress, pain Psychological SC: fatigue, sadness Respiratory SC: expectoration, cough Sleep disturbance SC: drowsiness, disturbed sleep Neurological SC: haemoptysis, constipation	-		-	
21a	Li et al., 2021b	De novo: EFA	MDASI-LC (T1)	Psychological SC: distress, lack of appetite, sadness Somatic SC: fatigue, SOB, drowsiness, chest tightness Perceptual SC: pain, dry mouth, numbness, weight loss Lung cancer specific SC: cough, expectoration, hemoptysis	- -	- - -	- - -	
21b	Li et al., 2021b	Same as above	MDASI-LC (T2)	Psychological SC: distress, difficulty remembering, sadness Chemotherapy SC: fatigue, lack of appetite, drowsiness, constipation Perceptual SC: pain, dry mouth, numbness, weight loss Lung cancer-specific SC: SOB, cough, expectoration GI SC: nausea, vomiting	- - -	- - -	-	• •
21c	Li et al., 2021b	Same as above	MDASI-LC (T3)	Chemotherapy SC: fatigue, lack of appetite, drowsiness, constipation Psychological SC: sleep disturbance, distress, sadness Lung cancer-specific SC: SOB, cough, expectoration, chest tightness GI SC: nausea, vomiting Perceptual SC: numbness, weight loss	-		-	-
22	Lin et al., 2013	A priori	MDASI	No name: pain, fatigue, disturbed sleep, and distress	-	-	-	•
23	Liu et al., 2021	De novo: Factor analysis and HCA	EORTC QLQ-C30	GI SC: appetite loss, anorexia, nausea and vomiting, hypodipsia Fatigue-insomnia-emotion: appetite loss, anorexia, nausea and vomiting, hypodipsia Respiratory: cough and expectoration, chest tightness	-	-	- -	•
24a	Ma et al., 2022	De novo: EFA	MDASI-LC (T1)	Gastrointestinal SC: cough and expectoration, chest tightness Respiratory tract SC: cough, expectoration, SOB Psychological SC: sadness, distress Somatic SC: drowsiness, pain, fatigue, numbness	- - -	- - -	- - -	- - -
24b	Ma et al., 2022	Same as above	MDASI-LC (T2)	Gastrointestinal SC: nausea, vomiting, constipation, lack of appetite Respiratory tract SC: cough, expectoration, SOB Psychological-somatic SC: sadness, distress, drowsiness, pain, fatigue, numbness	-	- -	-	- - -
25	Maguire et al., 2014	Qualitative	Interview	No name: fatigue, pain, cough, and breathlessness	-	-	-	•
26	Molassiotis et al., 2011	Qualitative	Semistructure d interviews	Respiratory distress SC: breathlessness, cough, and fatigue	•	-	-	-
27	Molassiotis et al., 2021	A priori	FACT-F, DASS21-A, CDS	No name: dyspnea, fatigue, and anxiety	-	-	-	•
28	Oh et al., 2019	De novo: HCA	MDASI-K	No name: nausea, vomiting, numbness, dry mouth No name: lack of appetite, disturbed sleep, fatigue, sadness, difficulty remembering, distress, SOB, drowsiness, pain	-	-	-	-

Report	Author,	Ctatistical analysis	tical analysis MS Symptom clusters (original names)	F	Re-categorized as			
ID #	year	Statistical analysis		Symptom clusters (original names)	RSC	GI SC	PSC	Other
29	Pudtong et al., 2014	De novo: PCA with varimax rotation	MSAS	Body image SC: "I don't look like myself", weight loss, irritability, difficulty swallowing, hair loss Neuropsychological SC: drowsiness, sadness, difficult in concentration, nervous, numbness/tingling, dry mouth Sleep alteration SC: sleeping difficulty, problem of urination, coughing Digestive impairment SC: nausea, lack of appetite, change in food taste Dermatologic and dizziness SC: itching, change in skin, dizziness Bowel-emotional dysfunction SC: constipation, worrying, feeling bloated Pain related discomfort SC: pain, SOB, lack of energy				•
30	Reyes-Gibby et al., 2013	A priori	Anxiety and fatigue: SF-12, pain: an 11-point numeric scale	No name: high symptom burden (pain, depressed mood, fatigue) No name: low symptom burden No name: higher pain, lower depressed mood, and fatigue No name: higher fatigue, lower depressed mood and pain No name: higher depressed mood and fatigue and lower pain		- - -	- - -	
31a	Russell et al., 2019	De novo: EFA with geomin rotation	MSAS (occurrence, T1)	<ul> <li>Sickness behavior SC: lack of energy, problems with sexual interest or activity, hair loss, dizziness, feeling drowsy, swelling of arms or legs</li> <li>Lung cancer-specific SC: cough, difficulty breathing, SOB, dry mouth, swelling of arms or legs</li> <li>Psychological SC: difficulty concentrating, difficulty breathing, feeling bloated, feeling irritable, feeling nervous, feeling sad, worrying, weight loss</li> <li>Nutritional SC: increased appetite, lack of appetite, weight gain</li> <li>Epithelial/GI SC: abdominal cramps, constipation, nausea, sweats, lack of appetite, weight loss, changes in skin, I do not look like myself, change in the way food tastes</li> </ul>	-		-	-
31b	Russell et al., 2019	Same as above	MSAS (occurrence, T2)	Sickness behavior SC: lack of energy, abdominal cramps, constipation, difficult concentrating, nausea, sweats, vomiting, cough, feeling drowsy Lung cancer-specific SC: cough, difficulty breathing, SOB, chest tightness Psychological SC: difficulty concentrating, feeling bloated, feeling irritable, feeling nervous, feeling sad, worrying, problems with sexual interest or activity Nutritional SC: increased appetite, lack of appetite, weight gain, weight loss Epithelial SC: changes in skin, hair loss, "I do not look like myself", mouth sores	-	-	-	•
31c	Russell et al., 2019	Same as above	MSAS (occurrence, T3)	Sickness behavior SC: lack of energy, difficult concentrating, cough, feeling drowsy Lung cancer-specific SC: cough, difficulty breathing, SOB, chest tightness, weight loss, dizziness, pain Psychological SC: irritable, feeling nervous, feeling sad, worrying, vomiting, nausea Nutritional SC: increased appetite, lack of appetite, weight gain Epithelial/GI SC: abdominal cramps, sweats, lack of appetite, changes in skin, I do not look like myself, change in the way food tastes, mouth sores, hair loss, feeling drowsy, feeling bloated, weight gain, dizziness, problems with sexual interest or activity	-		-	•
31d	Russell et al., 2019	Same as above	MSAS (severity, T1)	Lung cancer-specific SC: cough, difficulty breathing, SOB, chest tightness, dizziness, pain, feeling drowsy, lack of energy Psychological SC: feeling bloated, feeling irritable, feeling nervous, feeling sad, worrying, weight loss, difficulty sleeping Nutritional SC: increased appetite, sweats, lack of appetite, weight gain Epithelial/GI SC: constipation, nausea, sweats, lack of appetite, weight loss, changes in skin, I do not look like myself, change in the way food tastes	-	-	-	-

Report	Author, year	Statistical analysis	MS	Symptom clusters (original names)	Re-categorized as			as
ID #					RSC	GI SC	PSC	Other
31e	Russell et al., 2019	Same as above	MSAS (severity, T2)	Sickness behavior SC: lack of energy, problems with sexual interest or activity, dizziness, dry mouth, abdominal cramps, constipation, difficult concentrating, nausea, sweats, vomiting, feeling bloated, drowsy, feeling nervous, feeling sad, worrying, pain, swelling of arms or legs Lung cancer-specific SC: cough, difficulty breathing, SOB, dry mouth, chest tightness Psychological SC: feeling irritable, feeling nervous, feeling sad, worrying Nutritional SC: increased appetite, lack of appetite, weight gain, weight loss Epithelial SC: changes in skin, "I do not look like myself", mouth	-	-	-	-
31f	Russell et al.,	Same as above	MSAS	sores, swelling of arms and legs Sickness behavior SC: dizziness, difficult concentrating, feeling	-	-	-	-
	2019		(severity, T3)	irritable, feeling nervous, chest tightness Lung cancer-specific SC: cough, difficulty breathing, SOB, dry mouth, chest tightness, pain, difficulty concentrating, feeling drowsy, lack of energy	•	-	-	-
				vomiting, nausea Nutritional SC: increased appetite, weight gain, weight loss Epithelial/GI SC: abdominal cramps, constipation, sweats, lack of appetite, weight loss, changes in skin, I do not like myself. change in the way food tastes, mouth sores, hair loss, feeling bloated, dizziness, problems with sexual interest or activity	-	•	-	-
32	Sarna and Brecht, 1997	De novo: PCA with varimax rotation	SDS	Gastrointestinal distress: nausea frequency, nausea severity, appetite Respiratory distress: insomnia, breathing, cough	-	•	-	-
				Malaise: fatigue, concentration Malaise SC: fatigue, concentration Emotional and physical suffering SC: pain frequency, pain severity, bowel, appearance, outlook	- -	- -	- -	
33	Takemura et al., 2023	De novo: correlational analysis variance inflation factor	PSQI, BFI, HADS	No name: sleep disturbances, fatigue, anxiety, and depression	-	-	-	•
34	Wang et al., 2008	De novo: EFA and HCA	MDASI-T	General SC: fatigue, sleep disturbance, pain, drowsiness, lack of appetite, SOB, numbness, difficulty remembering, dry mouth, distress, and sadness GI SC: nausea and vomiting	-	-	-	-
35	Wang and Fu, 2014	De novo: EFA, principal axis factoring with varimax rotation	MDASI-C	GI SC: nausea and vomiting Emotional SC: distressed, sad Fatigue-related: feeling fatigued, disturbed sleep, pain	- -	-	-	- -
36	Wang et al., 2014	A priori	MDASI-T	General SC: distress, sadness, fatigue, sleepiness, dry mouth, lack of appetite, difficulty remembering, drowsiness, SOB, numbness, and pain GI SC: nausea and vomiting	-	-	-	•
37	Wang et al., 2023	A priori	NRS, CS, FACIT-F, Borg scale score, CASQ	No name: SOB, cough, pain, fatigue	-	-	-	•
38a	Wong et al., 2017	De novo: EFA with oblique rotation	MSAS (occurrence)	Sickness behavior SC: abdominal cramps, constipation, difficulty concentrating, feeling drowsy, lack of energy, nausea, sweats, vomiting Lung cancer-specific SC: chest tightness, cough, difficulty breathing, SOB Psychological SC: difficulty concentrating, feeling bloated, feeling irritable, feeling nervous, feeling sad, problems with sexual interest or activity, worrying Nutritional SC: increased appetite lack of appetite weight gain	-	-	-	-
				weight loss Epithelial SC: change in skin, hair loss, "I do not look like myself", mouth sores	-	-	-	

Report ID #	Author, year	Statistical analysis	MS	Symptom clusters (original names)	Re-categorized as			
					RSC	GI SC	PSC	Other
38b	Wong et al., 2017	Same as above	MSAS (severity)	Sickness behavior SC: abdominal cramps, constipation, difficulty concentrating, feeling drowsy, lack of energy, nausea, sweats, vomiting, feeling bloated, feeling nervous, feeling sad, problems with sexual interest or activity, worrying, dizziness, dry mouth, pain, swelling of arms or legs	-	-	-	•
				Lung cancer-specific SC: chest tightness, cough, difficulty breathing, SQB, swelling of arms or legs		-	-	-
				Psychological SC: feeling irritable, feeling nervous, feeling sad, worrying	-	-	•	-
				Nutritional SC: increased appetite, lack of appetite, weight gain, weight loss	-		-	-
				Epithelial SC: changes in skin, "I do not look like myself", swelling of arms or legs	-	-	-	•
39	Yorke et al., 2015	A priori	NRS, D-12, MCLC, FACIT-F	Respiratory SC: breathlessness-cough-fatigue	•	-	-	-
40	Yorke et al., 2022	A priori	D-12, MCLC FACIT-F	No name: breathlessness, cough, and fatigue	•	-	-	-
41	Zhang et al., 2022	De novo: EFA using PAF with	MDASI-LC	General cluster SC: fatigue, distress, appetite loss, sadness, drowsiness	-	-	-	•
		the maximal variance rotation		Immunotherapy-related SC: Difficulty remembering, constipation, sore throat, disturbed sleep	-	-	-	•
				Pulmonary SC: GL cluster: courshing, dry mouth, SOB		-	-	-
				Neural cluster: pain and numbness	-	-	-	

BFI=Brief Fatigue Inventory; CASQ=Cancer Appetite and Symptom Questionnaire; CDS=Cancer Dyspnea Scale; CES-D=Center for Epidemiologic Studies-Depression Scale; CS=Cough Score; D-12=Dyspnea-12; DASS21-A=Anxiety Subscale of Depression Anxiety Stress Scales 21; EFA=Exploratory Factor Analysis; EORTC LC13=Lung Cancer-specific EORTC; EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; ESAS=Edmonton Symptom Assessment System; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-G=Functional Assessment of Cancer Therapy-General; FACT-L=Functional Assessment of Cancer Therapy-Lung; FSQOLS=Fox Simple QOL Scale; GI=Gastrointestinal; HADS=Hospital Anxiety and Depression Scale; HCA=Hierarchical cluster analysis; LASA=Linear Analog Self-Assessment; LCSS=Lung Cancer Symptom Scale; MCLC=Manchester Cough in Lung Cancer Scale; MDASI-C=Chinese Version of the M. D. Anderson Symptom Inventory; MDASI-J=Japanese version of the M. D. Anderson Symptom Inventory; MDASI-K=Korean version of the M.D. Anderson Symptom Inventory; MDASI-LC=Lung Cancer Module of the M.D. Anderson Symptom Inventory; MDASI-T=Taiwanese Version of the M.D. Anderson Symptom Inventory; MDASI-LC=Lung Cancer Module of the M.D. Anderson Symptom Inventory; MDASI-T=Taiwanese Version of the M.D. Anderson Symptom Inventory; MS=easurements of symptoms (dimension or time of measurement); MSAS=Memorial Symptom Assessment Scale; NRS=Number Rating Scale; PAF=principal axis factoring; PCA=principal component analysis; PSC=psychological symptom cluster; PSET=Physical Symptom Experience Tool; PSQI=Pittsburgh Sleep Quality Index; RSC=respiratory symptom cluster; SC=symptom cluster; SD=Symptom Distress Scale; SF-12=12-item Short Form Health Survey; SF-36=Short-Form 36 Health Status Survey; SOB=shortness of breath; T0=time 0; T1=time 1; T2=time 2; T

Report ID #	Author, year	Symptom clusters
1	Brown et al., 2011	Fatigue, shortness of breath, cough, pain, and anorexia
2	Chan et al., 2005	Breathlessness, fatigue, and anxiety
3*	Chan et al., 2011	Breathlessness, fatigue, and anxiety
4*	Chan et al., 2013	Breathlessness, fatigue, and anxiety
10	Fox and Lyon, 2006	Depression and fatigue
11	Franceschini et al., 2013	Fatigue, dyspnea, insomnia, pain
14	Hamada et al., 2016	Sleep disturbance, nausea, cough
17	Ju et al., 2023	Difficulty remembering, numbness, hemoptysis, weight loss Nausea, sleep disturbance, drowsiness, vomiting Pain, distress, dry mouth, sadness, constipation Fatigue, lack of appetite
19	Khamboon and Pakanta, 2021	Fatigue, loss of appetite, and anxiety.
22	Lin et al., 2013	Pain, fatigue, disturbed sleep and distress.
25	Maguire et al., 2014	Fatigue, pain, cough, and breathlessness
27	Molassiotis et al., 2021	Dyspnea, fatigue, and anxiety
28	Oh et al., 2019	Lack of appetite, disturbed sleep, fatigue, sadness, difficulty remembering, distress, SOB, drowsiness, pain
30	Reyes-Gibby et al., 2013	High symptom burden (pain, depressed mood, fatigue) Low symptom burden Higher pain, lower depressed mood, and fatigue Higher fatigue, lower depressed mood and pain Higher depressed mood and fatigue and lower pain
33	Takemura et al., 2023	Sleep disturbances, fatigue, anxiety, and depression
37	Wang et al., 2023	Shortness of breath, cough, pain, fatigue

### Supplementary Table 3. No Name Symptom Clusters

\*Same study and same result.

Report ID#	Author, year	Symptom cluster: Symptom cluster membership
5a	Chen et al., 2023	Global mental function SC: Fatigue, disturbed sleep, lack of appetite
5b	Chen et al., 2023	Global mental function SC: Fatigue, disturbed sleep, drowsiness Sensory function SC: Dry mouth, numbness
5c	Chen et al., 2023	Global mental function SC: Fatigue, disturbed sleep, drowsiness
5d	Chen et al., 2023	Global mental function SC: Fatigue, disturbed sleep
8	Choi and Ryu, 2018	Treatment related SC: Nausea, vomiting, disturbed sleep, pain, lack of appetite
14	Hamada et al., 2016	Numbness cluster: Numbness, leg weakness, distress
15	Henoch et al., 2009	Pain cluster: Bowel issues, nausea, pain, appetite loss, fatigue Mood cluster: Outlook, mood, concentration, insomnia
18a	Khamboon et al., 2015	Emotional-elimination discomfort SC: Feeling irritable, feeling drowsy, feeling bloated, dizziness, problems with urination, constipation, changes in skin. Neurological and body image SC: Numbness/tingling in hands/feet, "I don't look like myself", pain, worrying, weight loss
18b	Khamboon et al., 2015	Emotional, elimination and respiratory: Feeling irritable, feeling bloated, problems with urination, constipation, SOB, worrying Body image: "I don't look like myself", hair loss, itching, changes in skin. Treatment-related neurological and other SC: Numbness/tingling in hands/feet, weight loss, difficulty sleeping
20a	Li et al., 2021a	Sleep disturbance SC: Lack of appetite, disturbed sleep Neurological SC: Disturbed remembering, dry mouth
20b	Li et al., 2021a	Sleep disturbance SC: Drowsiness, sadness, SOB
20c	Li et al., 2021a	Sleep disturbance SC: Disturbed sleep, constipation Neurological SC: Constipation, hemoptysis, pain
20d	Li et al., 2021a	Sleep disturbance SC: Lack of appetite, disturbed sleep Neurological SC: Dry mouth, sadness, disturbed remembering
20e	Li et al., 2021a	Sleep disturbance SC: Disturbed sleep, drowsiness Neurological SC: Hemoptysis, disturbed remembering
20f	Li et al., 2021a	Sleep disturbance SC: Drowsiness, disturbed sleep Neurological SC: Hemoptysis, constipation
21a	Li et al., 2021b	Somatic SC: Fatigue, SOB, drowsiness, chest tightness Perceptual SC: Pain, dry mouth, numbness, weight loss
21b	Li et al., 2021b	Chemotherapy SC: Fatigue, lack of appetite, drowsiness, constipation Perceptual SC: Pain, dry mouth, numbness, weight loss
21c	Li et al., 2021b	Chemotherapy SC: Fatigue, lack of appetite, drowsiness, constipation Perceptual SC: Numbness, weight loss
23	Liu et al., 2021	Fatigue-insomnia-emotion: Fatigue, insomnia, depression
24	Ma et al., 2022	Somatic SC: Drowsiness, pain, fatigue, numbness
29	Pudtong et al., 2014	<ul> <li>Body image SC: "I don't look like myself", weight loss, irritability, difficulty swallowing, hair loss.</li> <li>Neuropsychological SC: Drowsiness, sadness, difficult in concentration, nervous, numbness/tingling, dry mouth</li> <li>Sleep alteration SC: Sleeping difficulty, problem of urination, coughing.</li> <li>Dermatologic and dizziness SC: Itching, change in skin, dizziness.</li> <li>Bowel-emotional dysfunction SC: Constipation, worrying, feeling bloated.</li> <li>Pain related discomfort SC: Pain, shortness of breath, lack of energy</li> </ul>

### Supplementary Table 4. Other Symptom Clusters

R	eport ID#	Author, year	Symptom cluster: Symptom cluster membership
	31a	Russell et al., 2019	Sickness behavior SC: Lack of energy, problems with sexual interest or activity, hair loss, dizziness, feeling drowsy, swelling of arms or legs
	31b	Russell et al., 2019	Sickness behavior SC: Lack of energy, abdominal cramps, constipation, difficult concentrating, nausea, sweats, vomiting, cough, feeling drowsy. Epithelial SC: Changes in skin, hair loss, "I do not look like myself", mouth sores
	31c	Russell et al., 2019	Sickness behavior SC: Lack of energy, difficult concentrating, cough, feeling drowsy
	31e	Russell et al., 2019	Sickness behavior SC: Lack of energy, problems with sexual interest or activity, dizziness, dry mouth, abdominal cramps, constipation, difficult concentrating, nausea, sweats, vomiting, feeling bloated, drowsy, feeling nervous, feeling sad, worrying, pain, swelling of arms or legs. Epithelial SC: Changes in skin, "I do not look like myself", mouth sores, swelling of arms and legs
	31f	Russell et al., 2019	Sickness behavior SC: Dizziness, difficult concentrating, feeling irritable, feeling nervous, chest tightness.
	32	Sarna and Brecht, 1997	Malaise SC: fatigue, concentration Emotional and physical suffering: Pain frequency, pain severity, bowel, appearance, outlook
	34	Wang et al., 2008	General SC: Fatigue, sleep disturbance, pain, drowsiness, lack of appetite, shortness of breath, numbness, difficulty remembering, dry mouth, distress, and sadness.
	35	Wang and Fu, 2014	Fatigue-related SC: Feeling fatigued, disturbed sleep, pain
	36	Wang et al., 2014	General SC: Distress, sadness, fatigue, sleepiness, dry mouth, lack of appetite, difficulty remembering, drowsiness, SOB, numbness, and pain.
	38a	Wong et al., 2017	Sickness behavior SC: Abdominal cramps, constipation, difficulty concentrating, feeling drowsy, lack of energy, nausea, sweats, vomiting Epithelial SC: change in skin, hair loss, "I do not look like myself", mouth sores
	38b	Wong et al., 2017	Sickness behavior SC: Abdominal cramps, constipation, difficulty concentrating, feeling drowsy, lack of energy, nausea, sweats, vomiting, feeling bloated, feeling nervous, feeling sad, problems with sexual interest or activity, worrying, dizziness, dry mouth, pain, swelling of arms or legs Epithelial SC: Changes in skin, "I do not look like myself", swelling of arms or legs
	41	Zhang et al., 2022	General cluster: Fatigue, distress, appetite loss, sadness, drowsiness Immunotherapy-related cluster: Difficulty remembering, constipation, sore throat, disturbed sleep. Neural SC: Pain and numbness

### Appendix 1. List of Reports Included in the Scoping Review

- A1. Brown JK, Cooley ME, Chernecky C, Sarna L. A symptom cluster and sentinel symptom experienced by women with lung cancer. Oncology Nursing Forum. 2011;38(6):E425-35. https://doi.org/10.1188/11
- A2. Chan CW, Richardson A, Richardson J. A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer. European Journal of Oncology Nursing. 2005;9(4):325-33. https://doi.org/10.1016/j.ejon.2005.02.003
- A3. Chan CW, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy: results of a psychoeducational randomized controlled trial. Journal of Pain and Symptom Management. 2011;41(2):347-57. https://doi.org/10.1016/j.jpainsymman
- A4. Chan CW, Richardson A, Richardson J. An investigation of a symptom cluster in Chinese patients with lung cancer receiving radiotherapy. Contemporary Nurse. 2013;45(2):164-73. https://doi.org/10.5172/conu.2013.45.2.164
- A5. Chen K, Yang D, Li F, Gao L, Tian Y, Xu B, et al. Changes in the symptom clusters of elderly patients with lung cancer over the course of postoperative rehabilitation and their correlation with frailty and quality of life: a longitudinal study. European Journal Oncology Nursing. 2023;67:102388. https://doi.org/10.1016/j.ejon.2023.102388
- A6. Cheville AL, Novotny PJ, Sloan JA, Basford JR, Wampfler JA, Garces YI, et al. Fatigue, dyspnea, and cough comprise a persistent symptom cluster up to five years after diagnosis with lung cancer. Journal of Pain and Symptom Management. 2011;42(2):202-12.
  - https://doi.org/10.1016/j.jpainsymman.2010.10.257
- A7. Cheville AL, Novotny PJ, Sloan JA, Basford JR, Wampfler JA, Garces YI, et al. The value of a symptom cluster of fatigue, dyspnea, and cough in predicting clinical outcomes in lung cancer survivors. Journal of Pain and Symptom Management. 2011;42(2):213-21.

https://doi.org/10.1016/j.jpainsymman.2010.11.005

- A8. Choi S, Ryu E. Effects of symptom clusters and depression on the quality of life in patients with advanced lung cancer. European Journal of Cancer Care. 2018;27(1):e12508. https://doi.org/10.1111/ecc.12508
- A9. Fodeh SJ, Lazenby M, Bai M, Ercolano E, Murphy T, McCorkle R. Functional impairments as symptoms in the symptom cluster analysis of patients newly diagnosed with advanced cancer. Journal of Pain and Symptom Management. 2013;46 (4):500-10.

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