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REVIEW

Prevalence and risk factors of sleep disturbances among patients with lung cancer: systematic review and meta-analysis

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Abstract

Purpose Patients with lung cancer endure the most sleep problems. Understanding the prevalence and risk factors of sleep disturbances in lung cancer populations is critical in reducing symptom burden and improving their quality of life. This systematic review aimed to determine the prevalence and risk factors of sleep disturbances in patients with lung cancer.

Methods Seven electronic databases were systematically screened for studies on the prevalence or risk factors of sleep disturbances in patients with lung cancer. Subgroup analyses were conducted to investigate significant heterogeneity ($I^2 > 50\%$) across studies.

Results Thirty-seven studies were found eligible. The pooled prevalence was 0.61 (95% CI = [0.54–0.67], $I^2 = 96\%$, $p < 0.00001$). Seven risk factors were subject to meta-analyses. Significant differences were found for old age (OR = 1.23; 95% CI = [1.09–1.39], $p = 0.0006$,$I^2 = 39\%$), a low education level (OR = 1.17; 95%CI = [1.20–2.66], $p = 0.004$, $I^2 = 42\%$), fatigue (OR = 1.98; 95%CI = [1.23–3.18], $p = 0.005$, $I^2 = 31\%$), pain (OR = 2.63; 95% CI = [1.35–5.14], $p = 0.005$, $I^2 = 91\%$), tumor stage of III or IV (OR = 2.05; 95%CI = [1.54–2.72], $p < 0.00001$, $I^2 = 42\%$), anxiety (OR = 1.62; 95%CI = [1.22–2.14], $p = 0.0008$, $I^2 = 78\%$), and depression (OR = 4.02; 95% CI = [1.39–11.61], $p = 0.01$, $I^2 = 87\%$). After the included studies were withdrawn one after the other, pain (OR = 3.13; 95% CI = [2.06–4.75], $p < 0.00001$, $I^2 = 34\%$) and depression (OR = 5.47; 95% CI = [2.65–11.30], $p < 0.00001$) showed a substantial decrease of heterogeneity. Meanwhile, the heterogeneity of anxiety symptoms remained unchanged.

Conclusion Results showed that sleep disturbances were experienced in more than 60% of patients with lung cancer. The comparatively high prevalence of sleep disturbances in this population emphasizes the need to adopt measures to reduce them. Significant associations were found between sleep disturbances and various factors, including age, education level, fatigue, pain, cancer stage, anxiety, and depression. Among these factors, depression emerged as the most significant. Future research should concentrate on identifying high-risk individuals and tailored interdisciplinary interventions based on these risk factors.

Keywords Systematic review · Meta-analysis · Sleep disturbances · Prevalence · Risk factors · Lung cancer

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Introduction

Lung cancer is one of the most common malignancies. Lung cancer has the highest mortality rate (18.0%) and the second highest incidence (11.4%) among all cancers worldwide, as stated in the Global Cancer Statistics 2020 [1]. In recent years, the promotion and application of lung cancer treatments have improved the survival rate of patients with lung cancer [2]. However, this situation also means that the various symptoms accompanying the disease and treatment, such as sleep disturbances, have a persistent and far-reaching influence on patients [3]. Despite significant progress in lung cancer supportive care, their symptom burden remains substantial [4]. Sleep disturbances is one of the most annoying among lung cancer symptoms and symptom clusters[5].

In general, sleep disturbances include disorders that initiate and maintain sleep and abnormal events during sleep, such as difficulty falling asleep, sleep apnea, restless legs syndrome, insomnia, and daytime sleepiness [6, 7]. Compared with other cancers, patients with lung cancer have endured the most sleep problems [8, 9]. Different from other cancers, respiratory symptoms such as cough and dyspnea are common in patients with lung cancer. In addition, chronic obstructive pulmonary disease affects over 50% of patients diagnosed with primary lung cancer [10]. Getting a good sleep is difficult when patients have trouble breathing. Yet sleep disturbances has been found to be prevalent in this group, with reported rates ranging from 32 to 96% in various studies [11, 12], and such a wide range was due to different regions with different assessment tools used. Even though some use the same tool, their cut-off scores are still separate [13–15]. Reviewing and summarizing the overall prevalence of sleep disturbances in this population is necessary to further guide clinical practice and related research.

Sleep disturbances have many adverse effects on physical and mental health in patients with lung cancer, such as increased pain, more fatigue, and psychological distress [16]. They increase symptom burden and impair health-related quality of life among this population [15, 17]. Besides, studies have pointed out that sleep disturbances influence first-line progression-free survival and overall survival among patients with advanced lung cancer [17]. Known risk factors of sleep disturbances in the different cancer groups include high body mass index, pain, fatigue, anxiety and depression, nausea and vomiting, and shortness of breath [18, 19]. However, most previous studies focused on breast cancer patients whose disease features and treatments differ from those of lung cancer. Furthermore, several risk factors of sleep disturbances remain ambiguous in studies of patients with lung cancer, such as one study showed old age was a risk factor, while the other study have not reported [20, 21]. Therefore, to enhance the quality of life and alleviate the symptom burden in patients with lung cancer, it is crucial to comprehend the risk factors associated with sleep disturbances.

This study aimed to comprehensively review the prevalence and risk factors of sleep disturbances in patients with lung cancer, identify the gaps and strengths in the existing research, and provide directions for subsequent studies.

Methods

A systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[22]. And registered in the PROSPERO under No. CRD42023433918.

Literature search strategy

A comprehensive search was conducted in PubMed, EMBASE, Web of Science, CNKI, SinoMed, Wanfang Database, and VIP Database for studies on the prevalence of sleep disturbances and risk factors in patients with lung cancer up to December 31, 2022. The search terms were derived from the PECO framework, including population: patients with lung cancer, exposure: sleep disturbances, outcome: risk factors, and prevalence numbers. No control group was included. The search was conducted using both subject terms and free terms. The relevant search terms are

Table 1. Search strategy

	P: Population	E: Exposure	O: Outcome	
	Lung cancer patients	Sleep disturbances	prevalence numbers and risk factors	
MeSH terms	Lung neoplasms	Sleep–wake disorders	Epidemiology Prevalence Morbidity Probability	Risk factors Etiology Causality
Free terms	Lung neoplasms Lung cancer Pulmonary cancer Pulmonary neoplasm	Sleep disorder Sleep disturbances Sleep–wake disorders Short sleeper syndrome	Epidemiology Prevalence Morbidity Probability	Epidemiologic factors Influence factors Related factors Epidemiologic determinant

listed in Table 1.. Manual searches were also conducted to find additional pertinent publications in the citation lists of included studies.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) subjects were patients diagnosed with lung cancer aged ≥ 18 years; (2) a structured scale was used to assess the extent of patients' sleep disturbances; (3) data related to the prevalence or risk factors for sleep disturbances must be reported; (4) types include cross-sectional studies, case–control studies, and cohort studies; and (5) languages were English, Chinese, or other languages for which English versions could be retrieved.

The following were exclusion criteria: (1) animal trials; (2) literature for which data could not be extracted or transformed after attempting to contact the author; (3) literature of low quality [Agency for Healthcare Research and Quality (AHRQ) score ≤ 5; Newcastle–Ottawa Scale (NOS) of Quality scores < 3]; (4) full text was not available; (5) conference abstracts; and (6) scientific and technological achievements;

Data extraction and validity assessment

Before screening and removing duplicates, all studies were imported into the Endnote X9 application (Clarivate Analytics, London, UK). All article titles and abstracts were reviewed for relevance to the predetermined selection criteria by two researchers (Y.H. and C.Y.T.). The included articles were then screened after full-text reading. The data were extracted independently into a sheet that had a prespecified set of variables (general information from reports, including author names; year of publication and nation; patient characteristics, such as sample size, mean age, and disease characteristics; study design; prevalence of sleep disturbances; assessment tool; reported risk factors and any other relevant findings). The entire review team agreed to settle any disputes between the investigators.

Two researchers (Y.H. and W.H.C.) independently evaluated the quality of the research included. The NOS was used to assess case–control studies and cohort studies. It comprised three primary sections: selection, comparability, exposure, and outcome. NOS used the semi-quantitative "star" technique of rating literature quality; the maximum possible rating was 9, with each star representing one point. A low-quality study was defined as a score of less than 5, and a high-quality study was described as a score of ≥ 5. To evaluate cross-sectional studies, we used the American Agency for Healthcare Research and Quality (AHRQ) recommended criteria for evaluating observational studies [6]. These criteria included 11 items answerable by "yes," "no," or "unclear." The " yes " answer to each entry was scored 1, and "no" was scored 0. Item 5 was the reverse scoring item, with a total of 11 points. Great than or equal to 8 scores were granted for high quality, 6–7 for medium quality, and ≤ 5 for poor quality.

Statistical analysis

This meta-analysis used Review Manager 5.4 (Cochrane Collaboration, London, UK). Microsoft Excel calculated the pooled prevalence and standard error (SE). For risk factor meta-analysis, the best-corrected value was selected for merging when multiple values were provided for the study. Given the high prevalence of sleep disturbances in patients with lung cancer, the RR and HR values were still equal to OR values. Log [odds ratio] and SE was used for all effect measures of risk factors.

Heterogeneity was determined by the Q test, and the level of heterogeneity was assessed using the I^2 value. Multiple relevant studies were regarded as homogenous if $p \geq 0.1$ and I^2 was less than 50%; in this case, the fixed-effects model was used to determine the combined volume. Inversely, p less than 0.1 and $I^2 \geq 50\%$ indicated that multiple similar studies were heterogeneous, sensitivity analysis and subgroup analysis were used to explore the sources of heterogeneity, and random-effects model or descriptive analysis was used if they could not be solved. When ≥ 10 studies were included, funnel plots were drawn to analyze publication bias. Finally, sensitivity analysis was used to test the stability of the results.

Results

Study selection

The initial review identified 6395 relevant papers, including 3159 in Chinese and 3236 in English. A total of 2543 duplicate papers were excluded by Endnote X9 software, and 3852 were obtained. Finally, 37 studies were included in this meta-analysis, including 22 published in Chinese [11, 14, 15, 20, 23–40] and 15 published in English [10, 12, 13, 17, 21, 41–50], with a total of 4849 patients (Fig. 1).

Study characteristics

Sample sizes of included studies ranged from 29 to 473. Among the studies, 32 were cross-sectional, and five were longitudinal (Table 2). Nine studies were conducted in high-income countries and the remainder in middle-income countries. In assessing sleep disturbances, 29 studies used the PSQI, six used the Athens Insomnia Scale (AIS), and the remaining used other scales such as the Self-Rating Scale of Sleep and General Sleep Disturbance Scale. Meanwhile, four studies used the Epworth Sleepiness Scale to assess daytime sleepiness.

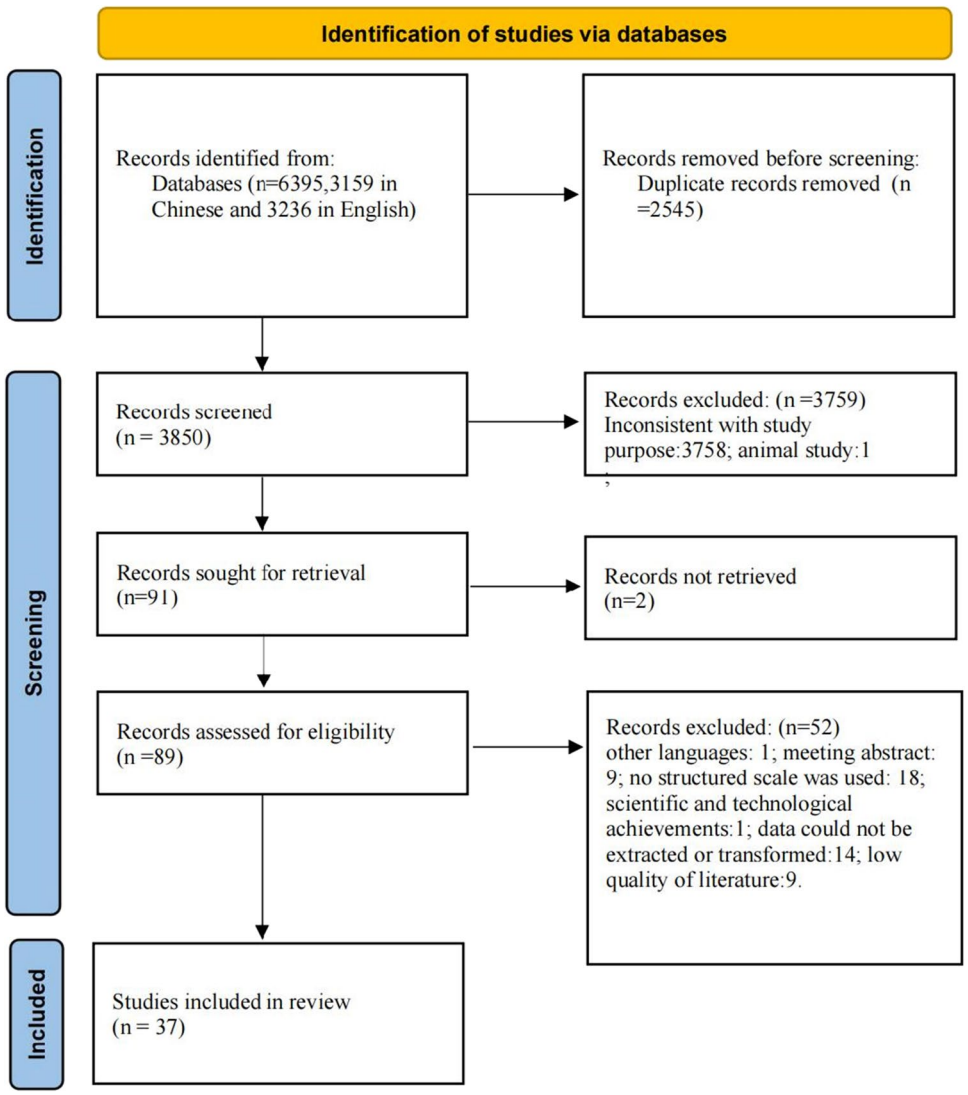

Fig. 1 Flow chart

Quality assessment

The total quality assessment scores for the five longitudinal studies were 5, indicating that all were of moderate quality (Table 3). AHRQ was used to evaluate the quality of 32 articles (Table 4), and the overall score was between 6 and 10. Among them, three studies were of high quality, and 29 were of medium quality, with a score of ≤ 7. Low-quality studies were excluded from this meta-analysis.

Syntheses of results

Prevalence of sleep disturbances in patients with lung cancer

The prevalence of sleep disturbances in patients with lung cancer ranged from 0.32 (95% CI = [0.23–0.41]) to 0.96 (95% CI = [0.90–1.00]) (Table 5), and the pooled prevalence was 0.61 (95% CI = [0.54–0.67], $I^2 = 96\%$, $p < 0.00001$(Fig. 2); 33 studies including 28 cross-sectional studies and five longitudinal studies). The results of subgroup analyses are presented in Table 6. Any of the subgroup analyses did not clarify the reasons for the high heterogeneity.

Risk factors for the development of sleep disturbances in patients with lung cancer

A total of seventeen studies documented 33 risk factors associated with the development of sleep disturbances in patients with lung cancer. The risk factors were identified in at least two studies as follows.: old age, low education level, tumor stage III or IV, pain, fatigue, anxiety, and depression (Table 7). Meta-analyses were executed for the risk factors represented in more than one article.

Table 2 Characteristics of all included studies

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Su 2022 [14]	China	Cross-sectional	63% (126/200)	200	58.60 ± 6.92	Radical resection of LC or received chemotherapy ≥ 1 cycle	AIS > 4	Tumor stage, pain, anxiety, and depression	Gender, times of chemotherapy	6; medium
Chen 2022 [23]	China	Cross-sectional	49% (50/102)	102	NR	NR	PSQI > 7	Tumor stage III or IV, distant metastasis, low serum 25 (OH) D_3 expression	/	6; medium
Tan 2021 [15]	China	Cross-sectional	63% (252/400)	400	NR	Radical resection of LC or received chemotherapy ≥ 1 cycle	AIS > 6	Tumor stage, pain, anxiety, and depression	Gender, times of chemotherapy	6; medium
Liu 2021 [30]	China	Cross-sectional	78.57% (110/140)	140	NR	Primary LC; Tumor stage was III or IV; Receiving chemotherapy	PSQI > 5	NR	/	7; medium
Lin 2021 [29]	China	Cross-sectional	NR	154	NR	Primary bronchogenic carcinoma; Without surgical treatment and the time from the end of the last chemotherapy > 14 d	PSQI ≥ 7	Anxiety, times of chemotherapy, adverse reactions of chemotherapy, Acceptance-resignation coping mode	Occupation, education level, payment method, family monthly income; comorbid chronic diseases; depression	7; medium
Li 2021 [26]	China	Cross-sectional	NR	150	62.33 ± 7.49	Newly diagnosed LC and hospitalized	PSQI ≥ 7	IES-R total score and intrusion dimension	Avoidance and hyperarousal dimension	7; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Zhang 2020 [40]	China	Cross-sectional	40.5% (64/158)	158	NR	Newly diagnosed LC	AIS > 6	Tumor stage, pain, anxiety, and depression	Gender, education level, payment method, religious affiliation or not, age, pathological type	6; medium
Liu 2020 [31]	China	Cross-sectional	89% (421/473)	473	63.60 ± 9.4	Admitted for treatment of primary LC	PSQI > 7	NR	/	6; medium
Lian 2020 [27]	China	Cross-sectional	NR	106	Not reported	Hospitalized patients with LC	PSQI Cut-off unknown	Smoking history, tumor stage, economic status, and KPS score	Gender, residence, marital status, educational level, history of alcohol consumption	6; medium
An 2020 [11]	China	Cross-sectional	After chemotherapy 31.81% (35/110)	110	NR	Primary bronchogenic carcinoma without metastasis agreed to chemotherapy	SRSS ≥ 30	Surgical resection and education level	pathological type, Chemotherapy cycle	7; medium
Liu 2019 [32]	China	Prospective observational	Before chemotherapy:59.7% (37/62) After the first chemotherapy: 69.4% (43/62) After second chemotherapy: 79% (49/62)	62	57.59 ± 9.0	Stage IIIB/IV non-small cell LC; prepared for chemotherapy	PSQI ≥ 5	NR	/	5; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Zhang 2019 [39]	China	Cross-sectional	37.5% (84/224)	224	57.25 ± 9.96	Diagnosed LC; Initial admission for antineoplastic therapy	AIS > 6	NR	/	6; medium
Chen 2018 [24]	China	Cross-sectional	47.83% (44/92)	92	62.39 ± 5.6	Diagnosed LC	AIS > 6	NR	/	6; medium
Zhang 2018 [38]	China	Cross-sectional	63.29% (100/158)	158	NR	Primary bronchogenic carcinoma received chemotherapy ≥ 1 cycle	PSQI > 7	NR	/	6; medium
Wei 2016 [36]	China	Prospective Observational	Before radiotherapy: 33.3% (19/57) 2 weeks radiotherapy: 36.8% (21/57) Radiotherapy 4 weeks: 39.1% (23/57) Completion of radiotherapy: 52.6% (30/57)	57	59.22 ± 8.08	LC, Receiving thoracic radiotherapy	PSQI > 7	Before radiotherapy: anxiety, pain, fatigue, and cough Radiotherapy for 2 weeks: advanced age, depression, anorexia, dyspnea, and constipation Radiotherapy for 4 weeks: concurrent chemotherapy, fatigue, anorexia, dry mouth, CD3 +, CD3 + CD4 + At the end of radiotherapy: anxiety, fatigue, dry mouth, IL-6	Before radiotherapy: Depression, constipation; Radiotherapy for 2 weeks: anxiety, pain, diabetes, chemotherapy history, fatigue, weight loss, cough; Radiotherapy for 4 weeks: cough, anxiety, depression; At the end of radiotherapy: depression	5; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Gu 2016 [20]	China	Cross-sectional	89% (89/100)	100	66.28 ± 7.40	Diagnosed LC; Received chemotherapy for more than 2 weeks	PSQI Cut-off unknown	Age, education level, payment method, tumor stage, and presence or absence of complications	//	7; medium
Wei 2015 [37]	China	Cross-sectional	68. 4% (106 /155)	155	59. 6 ± 8. 6	Diagnosed LC; Received chemotherapy	PSQI > 7	NR	/	6; medium
Wang 2015 [35]	China	Cross-sectional	68% (68/100)	100	NR	Diagnosed LC; Received thoracotomy under general anesthesia	PSQI > 7	NR	/	7; medium
Lin 2015 [28]	China	Cross-sectional	55.14% (59/107)	107	55.63 ± 6.7	Diagnosed LC; Received chemotherapy ≥ 1 cycle	PSQI > 7	NR	/	6; medium
Sha 2012 [33]	China	Cross-sectional	46.1% (70/152)	152	57.09	ICU stay time ≥ 7 days, LC undergoing thoracotomy under general anesthesia	PSQI > 7	Unfamiliar environment, physical discomfort, and pain caused by diseases	Nocturnal therapeutic care, nurse's footsteps, cough, dyspnea, foreign body sensation from intubation, excessive daytime sleep, worry about condition, emotional boredom, missing loved ones	7; medium
Teng 2011 [34]	China	Cross-sectional	59.4% (57/96)	96	69.2 ± 8.9	Age > 60 years old; Diagnosed LC	PSQI ≥ 8	NR	/	7; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Li 2011 [25]	China	Cross-sectional	45.9% (45/98)	98	31–88; mean 58.8	Hospitalized primary bronchogenic carcinoma	PSQI > 7	Marital status and KPS score	NR	9; high
Chen 2008 [44]	Taiwan, China	Cross-sectional	52% (60/115)	115	59.4 ± 10.7	Diagnosed with stage III or IV LC; planning to receive chemotherapy	PSQI > 5	NR	/	7; medium
Dean 2013 [45]	USA	Cross-sectional	80% (28/35)	35	63.5 ± 9.7	Diagnosis of SCLC or NSC LC received chemotherapy ≥ 1 cycle	PSQI > 5	NR	/	7; medium
Dean 2015 [10]	USA	Prospective observational	baseline:76% DS: 21% baseline, 33% at pre-second chemotherapy, and 35% at pre-third chemotherapy (10/29)	29	66.6 ± 9.5	Diagnosis of inoperable NSCLC; scheduled to receive chemotherapy	PSQI > 5 daytime sleepiness: ESS > 10	NR	/	5; medium
Halle 2017 [21]	Norway	Prospective observational	60.9% at baseline, 68.5% at Month 1, 55.4% at Month 5, 51.3% at Month 9, and 49.7% at Month 12	264	65.8 (± 8.5)	Scheduled for surgery for primary LC	GSDS total sum score ≥ 43	NR	/	5; medium
Lou 2017 [48]	China	Cross-sectional	62.5% (80/128)	128	60.60 ± 9.82	advanced LC (stage III or IV)	PSQI > 5	NR	/	6; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Papadopoulos 2019 [41]	Greece	Cross-sectional	58.2% (69/119)	119	64	Diagnosed LC; received chemotherapy ≥ 1 cycle	PSQI > 5	anxiety and stress symptoms and positive coping practices	Gender, age, pain, Charlson Comorbidity Index, cancer stage, use of concomitant medications, history of brain metastases, sleep hygiene practices, recent surgery or radiation therapy, dyspnea, chemotherapy type, cough, depression, negative coping, comfort/support seeking coping, social support	9; high
Belloumi 2020 [42]	Tunisia	prospective study	Before chemotherapy: 15.6% (10/64) After chemotherapy 45.3% (29/64)	64	62:9 ± 8:18	NSCLC with histological proof; stage III or IV; chemotherapy course	PSQI > 5	therapeutic management delays (Mean delay to histological confirmation; Mean delay to treatment onset)	Chemotherapy complications, depressive humor, anxious humor	5; medium
Mercadante 2021 [13]	Italy	Cross-sectional secondary analysis	83.2% (151/182)	182	69.9 ± 10.8	Diagnosed LC	AIS ≥ 6	drowsiness, HADS-A, HADS-D, and time from diagnosis	Poor karnofsky level, nausea	7; medium

Table 2 (continued)

Study	Country	Design	Prevalence of sleep disturbances	Sample size (N)	Age (mean years ± SD)	Inclusion criteria	Sleep outcome; Cut-off	Risk factors for sleep disturbances	Other factors included in multivariate analysis	Quality assessment score
Takemura 2021 [49]	Hong Kong, China	Cross-sectional	49.4% (81/164)	164	61.16 ± 8.80	Diagnosed with stage IIIB or IV NSCLC	PSQI > 5	Timed up and go (TUGT)	NR	7; medium
He 2022 [17]	China	Cross-sectional	48.9% (48/98)	98	57	Diagnosed advanced LC (stage III/IV); untreated before the evaluation	PSQI > 7	NR	/	6; medium
Lee 2022 [47]	Korea	Cross-sectional	Poor sleep quality:45% (31/69) DS:10% (7/69) clinical insomnia: 4%	69	68.0 ± 9.8	Diagnosed LC	PSQI > 5 ESS > 10 ISI > 14	NR	/	6; medium
Vena 2006 [50]	USA	Cross-sectional	Poor sleep quality: 88%(38/43) DS:44%(19/44)	43	62.70 ± 9.87	Primary diagnosis of stage IIIB or IV NSCLC or extensive SCLC	PSQI ≥ 5 ESS > 10	NR	/	6; medium
Gooneratne 2007 [46]	USA	Cross-sectional	56.6% (43/76)	76	73.6 ± 6.7	At least 5 years post-diagnosis of LC	PSQI > 5	NR	/	6; medium
Le Guen 2007 [12]	France	Cross-sectional	Poor sleep quality: 96%(28/29) DS:42%(12/29)	29	59 ± 12	Newly diagnosed LC	PSQI ≥ 5 ESS ≥ 10	NR	/	6; medium
Chang 2017 [43]	Taiwan	Cross-sectional	NR	40	66.92 ± 11.01	Diagnosed LC; not received related treatment	PSQI > 8	the diurnal cortisol slope and BFI score	HADS-A, HADS-D, salivary melatonin, diurnal melatonin, salivary cortisol	9; high

AIS: Athens Insomnia Scale; *PSQI*: Pittsburgh Sleep Quality Index; *SRSS*: Self-Rating Scale of Sleep; *ESS*: Epworth Sleepiness Scale; *GSDS*: General Sleep Disturbance Scale; *BFI*: Brief Fatigue Inventory; *IES-R*: Impact of Event Scale-Revised; *HADS-A*: Hospital anxiety and depression scale-Anxiety; *HADS-D*: Hospital anxiety and depression scale-Depression; *NR*: Not Reported; *LC*: lung cancer; *SCLC*: small cell lung cancer; *NSCLC*: non-small cell lung cancer; *DS*: daytime sleepiness

Table 3 NOS assessment for longitudinal studies

Author(year)	Selection				Comparability	Exposure			**Quality/ score**
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
Belloumi 2020 [42]	1	0	1	0	0	1	1	1	Medium /5
Liu 2019 [32]	1	0	1	0	0	1	1	1	Medium /5
Halle 2017 [21]	1	0	1	0	0	1	1	1	Medium /5
Wei 2016 [36]	1	0	1	0	0	1	1	1	Medium /5
Dean 2015 [10]	1	0	1	0	0	1	1	1	Medium /5

Notes: Q1. Whether case determination is appropriate; Q2. Representativeness of cases; Q3. Control selection; Q4. Determination of control; Q5. Consider the comparability of cases and controls when designing and making a statistical analysis; Q6. Determination of the exposure factors; Q7. The same methods were used to determine the exposure factors in the cases and controls; Q8. No response rates

Meta-analysis of demographic factors

Age and educational level were the demographic factors considered in this meta-analysis (Fig. 3). Two studies [20, 36] reported the relationship between age and sleep disturbances in patients with lung cancer. According to their findings, old age was a significant risk factor associated with sleep disturbances based on the combined effect size (OR = 1.23; 95% CI = [1.09–1.39]; $p = 0.0006$; $I^2 = 39\%$). Two studies [11, 20] have reported a correlation between educational level and sleep disturbances in patients with lung cancer. The combined findings of the studies indicate that individuals with low educational backgrounds are at a greater risk of experiencing sleep disturbances (OR = 1.17; 95% CI = [1.20–2.66]; $p = 0.004$; $I^2 = 42\%$). Marital status, payment methods of medical expenses, and smoking history were covered by only one study each. Therefore, these results could not be synthesized, and only descriptive analysis was performed.

Meta-analysis of clinical factors

The clinical factors included in this study were fatigue, pain, and tumor stage (Fig. 4). Two studies [36, 43] reported the relationship between fatigue and sleep disturbances in patients with lung cancer. Based on the synthesized results, it was determined that fatigue is a risk factor for sleep disturbances, as the combined effect size was statistically significant (OR = 1.98, 95% CI = [1.23–3.18], $p = 0.005$; $I^2 = 31\%$). Five different research studies [14, 15, 33, 36, 40] have shown a high level of heterogeneity between pain and sleep disturbances ($p < 0.05$, $I^2 = 91\%$). The heterogeneity was found to originate from the study conducted by Sha et cl. [33], as revealed by sensitivity analysis. However, after excluding this study, the combined results of the remaining studies confirmed that pain was indeed a risk factor for sleep disturbances (OR = 3.13, 95% CI = [2.06–4.75], $p < 0.00001$, $I^2 = 34\%$). Four studies [14, 15, 23, 40] reported the relationship between tumor stage and sleep disturbances. The combined effect size's statistical significance was observed in synthesizing their findings. Sleep disturbances were more likely to occur in individuals diagnosed with tumor stage III or IV (OR = 2.05, 95% CI = [1.54–2.72], $p < 0.00001$, $I^2 = 42\%$). Although two studies [25, 27] reported that a KPS score ≤ 70 was a risk factor for sleep disturbances, only a standardized regression coefficient and p-value could be acquired. Their effect size could not be combined, so descriptive analysis was performed. Cycles of chemotherapy, adverse reactions of chemotherapy, surgery, complications, the physical discomfort caused by disease, unfamiliar surroundings, stress symptoms, therapeutic management delays, drowsiness, time from diagnosis, cough, anorexia, dyspnea, constipation, physical performance, the diurnal cortisol slope, low serum 25 (OH) D_3 expression, IL-6, CD3 + and CD3 + CD4 + were studied in a single study. Their effect sizes could not be combined, so descriptive analysis only examined them.

Meta-analysis of psychological factors

The psychological factors of interest included anxiety, depression, psychological stress, and positive coping practices. Seven studies [13–15, 29, 36, 40, 41] demonstrated the correlation between anxiety and sleep disturbances. The combined effect size's statistical significance was observed in synthesizing their findings. Anxiety was identified as a risk factor for sleep disturbances (OR = 1.62, 95% CI = [1.22–2.14,] $p = 0.0008$, $I^2 = 78\%$) (Fig. 5). Depression was studied in five articles [13–15, 40, 41]. Following a comprehensive analysis, individuals who suffered from depression had a 4.02 times higher likelihood of developing sleep disturbances (OR = 4.02, 95% CI = [1.39–11.61], p = 0.01, I 2 = 87%) than those who did not have depression. Subgroup analysis revealed an improvement in heterogeneity ($I^2 = 29\%$, $p = 0.24$) after withdrawing the study by Papadopoulos et cl. [41], and the pooled OR increased to 5.47

Table 4 AHRQ assessment for cross-sectional studies

List of items	Chen 2022 [23]	Su 2022 [14]	Tan 2021 [15]	Liu 2021 [30]	Lin 2021 [29]	Li 2021 [45]	Zhang 2020 [40]	Liu 2020 [31]	Lian 2020 [27]	An 2020 [11]	Zhang 2019 [39]	Zhang 2018 [38]
1. Define the source of information (survey, record review);	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Indicate time period used for identifying patients;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Indicate whether or not subjects were consecutive if not population-based;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants;	No	No	No	No	No	No	No	No	No	No	No	No
6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements);	Yes	No	No	No	No	No	No	No	No	No	No	No
7. Explain any patient exclusions from analysis;	No	No	No	No	No	No	No	No	No	No	Yes	No
8. Describe how confounding was assessed and/or controlled;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No
9. If applicable, explain how missing data were handled in the analysis;	No	No	No	No	No	No	No	No	No	No	No	No
10. Summarize patient response rates and completeness of data collection;	No	No	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes
11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	No	No	No	No	No	No	No	No	No	No	No	No
Score	7	6	6	7	7	7	6	6	6	7	6	6
List of items	Chen 2018 [24]	Gu 2016 [20]	Wei 2015 [37]	Lin 2015 [28]	Wang 2015 [35]	Sha 2012 [33]	Li 2011 [25]	Teng 2011 [34]	Vena 2006 [50]	Chen 2008 [44]	Le Guen 2007 [12]	Gooneratne 2007 [46]
1. Define the source of information (survey, record review);	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 4 (continued)

2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Indicate time period used for identifying patients;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
4. Indicate whether or not subjects were consecutive if not population-based;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants;	No	No	No	No	No	No	No	No	No	No	No	No
6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements);	Yes	No	No	No	Yes	No	No	Yes	No	No	Yes	No
7. Explain any patient exclusions from analysis;	No	No	No	No	No	No	Yes	No	Yes	No	No	Yes
8. Describe how confounding was assessed and/or controlled;	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	No	Yes
9. If applicable, explain how missing data were handled in the analysis;	No	No	No	No	No	No	No	No	No	No	No	No
10. Summarize patient response rates and completeness of data collection;	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	No	No	No	No	No	No	Yes	No	No	No	No	No
Score	6	7	6	6	7	7	9	7	6	7	6	6
List of items	Dean 2013 [45]	Lou 2017 [48]	Chang 2017 [43]	Papadopoulos 2019 [41]		Mercadante 2021 [13]		Takemura 2021 [49]		He 2022 [17]		Lee 2022 [47]
1. Define the source of information (survey, record review);	Yes	Yes	Yes	Yes		Yes		Yes		Yes		Yes
2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications;	Yes	Yes	Yes	Yes		Yes		Yes		Yes		Yes
3. Indicate time period used for identifying patients;	No	Yes	Yes	Yes		Yes		Yes		Yes		Yes

Table 4 (continued)

4. Indicate whether or not subjects were consecutive if not population-based;	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear
5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants;	No	No	No	No	No	No	No	No
6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements);	No	No	Yes	No	Yes	Yes	Yes	Yes
7. Explain any patient exclusions from analysis;	Yes	No	Yes	Yes	No	No	No	Yes
8. Describe how confounding was assessed and/or controlled;	No	Yes	Yes	Yes	Yes	Yes	Yes	No
9. If applicable, explain how missing data were handled in the analysis;	Yes	No	No	Yes	No	No	No	No
10. Summarize patient response rates and completeness of data collection;	Yes	No	Yes	Yes	No	Yes	No	No
11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	No	No	No	No	No	No	No	No
Score	7	6	9	9	7	7	6	6

Table 5 Prevalence numbers of sleep disturbances in lung cancer

Study	Country	Design	Prevalence of sleep disorders	Standard error (SE)	Sample size (N)	Age (mean years ± SD)	Sleep outcome; Cut-off	Quality assessment score
Su 2022 [14]	China	Cross-sectional	63% (126/200)	0.0341	200	58.60 ± 6.92	AIS > 4	6; medium
Chen 2022 [23]	China	Cross-sectional	49% (50/102)	0.0495	102	Not mention	PSQI > 7	6; medium
Tan 2021 [15]	China	Cross-sectional	63% (252/400)	0.0241	400	Not reported	AIS > 6	6; medium
Liu 2021 [30]	China	Cross-sectional	78.57% (110/140)	0.0347	140	Not reported	PSQI > 5	7; medium
Zhang 2020 [40]	China	Cross-sectional	40.5% (64/158)	0.0391	158	Not reported	AIS > 6	6; medium
Liu 2020 [31]	China	Cross-sectional	89% (421/473)	0.0144	473	63.60 ± 9.4	PSQI > 7	6; medium
An 2020 [11]	China	Cross-sectional	31.81% (35/110)	0.0444	110	Not reported	SRSS ≥ 30	7; medium
Liu 2019 [32]	China	Prospective observational	79% (49/62)	0.0517	62	57.59 ± 9.0	PSQI ≥ 5	5; medium
Zhang 2019 [39]	China	Cross-sectional	37.5% (84/224)	0.0323	224	57.25 ± 9.96	AIS > 6	6; medium
Chen 2018 [24]	China	Cross-sectional	47.83% (44/92)	0.0521	92	62.39 ± 5.6	AIS > 6	6; medium
Zhang 2018 [38]	China	Cross-sectional	63.29% (100/158)	0.0383	158	Not reported	PSQI > 7	6; medium
Wei 2016 [36]	China	Prospective Observational	52.6% (30/57)	0.0661	57	59.22 ± 8.08	PSQI > 7	5; medium
Gu 2016 [20]	China	Cross-sectional	89% (89/100)	0.0313	100	66.28 ± 7.40	PSQI Cut-off unknown	7; medium
Wei 2015 [37]	China	Cross-sectional	68. 4% (106 /155)	0.0373	155	59. 6 ± 8. 6	PSQI > 7	6; medium
Wang 2015 [35]	China	Cross-sectional	68% (68/100)	0.0466	100	Not reported	PSQI > 7	7; medium
Lin 2015 [28]	China	Cross-sectional	55.14% (59/107)	0.0484	107	55.63 ± 6.7	PSQI > 7	6; medium
Sha 2012 [33]	China	Cross-sectional	46.1% (70/152)	0.0404	152	57.09	PSQI > 7	7; medium
Teng 2011 [34]	China	Cross-sectional	59.4%(57/96)	0.0501	96	69.2 ± 8.9	PSQI ≥ 8	7; medium
Li 2011 [25]	China	Cross-sectional	45.9% (45/98)	0.0503	98	31–88; mean 58.8	PSQI > 7	9; high
Chen 2008 [44]	Taiwan	Cross-sectional	52%	0.0466	115	59.4 ± 10.7	PSQI > 5	7; medium
Dean 2013 [45]	USA	Cross-sectional	80% (28/35)	0.0676	35	63.5 ± 9.7	PSQI > 5	7; medium
Dean 2015 [10]	USA	Prospective observational	35% (10/29)	0.0883	29	66.6 ± 9.5	PSQI > 5	5; medium
Halle 2017 [21]	Norway	Prospective observational	68.5%	0.0286	264	65.8 (± 8.5)	GSDS total score ≥ 43	5; medium
Lou 2017 [48]	China	Cross-sectional	62.5% (80/128)	0.0428	128	60.60 ± 9.82	PSQI > 5	6; medium

Table 5 (continued)

Study	Country	Design	Prevalence of sleep disorders	Standard error (SE)	Sample size (N)	Age (mean years ± SD)	Sleep outcome; Cut-off	Quality assessment score
Papadopoulos 2019 [41]	Greece	Cross-sectional	58.2% (69/119)	0.0452	119	64	PSQI > 5	9; high
Belloumi 2020 [42]	Tunisia	prospective study	45.3% (29/64)	0.0622	64	62:9 ± 8:18	PSQI > 5	5; medium
Mercadante 2021 [13]	Italy	Cross-sectional	83.2% (151/182)	0.0279	182	69.9 ± 10.8	AIS ≥ 6	7; medium
Takemura 2021 [49]	Hong Kong	Cross-sectional	49.4% (81/164)	0.039	164	61.16 ± 8.80	PSQI > 5	7; medium
He 2022 [17]	China	Cross-sectional	48.9% (48/98)	0.0505	98	57	PSQI > 7	6; medium
Lee 2022 [47]	Korea	Cross-sectional	45% (31/69)	0.0599	69	68.0 ± 9.8	PSQI > 5	6; medium
Vena 2006 [50]	USA	Cross-sectional	88%(38/43)	0.0489	43	62.70 ± 9.87	PSQI ≥ 5	6; medium
Gooneratne 2007 [46]	USA	Cross-sectional	56.6% (43/76)	0.0569	76	73.6 ± 6.7	PSQI > 5	6; medium
Le Guen 2007 [12]	France	Cross-sectional	96%(28/29)	0.0339	29	59 ± 12	PSQI ≥ 5	6; medium

AIS: Athens Insomnia Scale; *PSQI*: Pittsburgh Sleep Quality Index; *SRSS*: Self-Rating Scale of Sleep; *GSDS*: General Sleep Disturbance Scale

(95% CI = [2.65–11.30], $p < 0.00001$) (Fig. 5). Psychological stress [26], acceptance-resignation coping mode [29], and positive coping practices [41] were discussed in only one study each, so only descriptive analysis was performed on these factors.

Discussion

This systematic review and meta-analysis aimed to investigate the prevalence of sleep disturbances among patients with lung cancer and identify the risk factors that contribute to sleep disturbances in this population. Finally, our study included a total of 37 studies, which comprised 33 prevalence numbers, as well as 33 risk factors that were found to be responsible for sleep disturbances. The vast majority of the included studies used PSQI or AIS to assess sleep disturbances. Prevalence rates varied across the studies, ranging from 0.32 to 0.96, but the combined estimate was 0.61. Nonetheless, there was significant heterogeneity among the studies. Even after subgroup analyses, we still obtained minimal changes. Among the 33 risk factors, 7 (age, education level, fatigue, pain, tumor stage, anxiety, and depression) were suitable for a meta-analysis. The pooled results showed that these seven risk factors were significantly associated with the odds of developing sleep disturbances.

Compared to other types of cancer, individuals with lung cancer are more likely to experience sleep disturbances [51]. Our synthesis results further reinforced the possibility of this argument and revealed a higher pooled prevalence for lung cancer compared with breast cancer [52], head-neck cancer[53], and mixed cancer [6]. Subgroup analysis confirmed the stability of our result, but the final results still had substantial heterogeneity ($I^2 = 96\%$). Several possible reasons account for these discrepancies. First, most of the included studies were cross-sectional and thus did not adequately assess sleep disturbances at different stages of treatment and may have overestimated or underestimated the existing prevalence. Second, the cause of heterogeneity might be the measurement tools. Although most studies in this study used PSQI or AIS, their cut-off scores varied in different studies. Different cut-off scores may lead to difference in the prevalence of sleep disturbances. Previous studies have used receiver operator characteristic (ROC) analysis in cancer populations to validate that a PSQI score greater than 7 has the best sensitivity and specificity[54]. However, it has not yet been validated in the lung cancer population, and more works need to be done to establish a cut point that is valid in this population. Various demographic or clinical characteristics of the subjects might also cause heterogeneity. Considering that more than half of patients with lung cancer might have sleep disturbances, future studies should further investigate different types of sleep disturbances, cancer stages, treatment regimens, and treatment stages further to clarify the prevalence of sleep disturbances in these patients.

Among the demographic factors, the results of the meta-analysis suggested that elderly patients with lung cancer were likely to develop sleep disturbances. According to

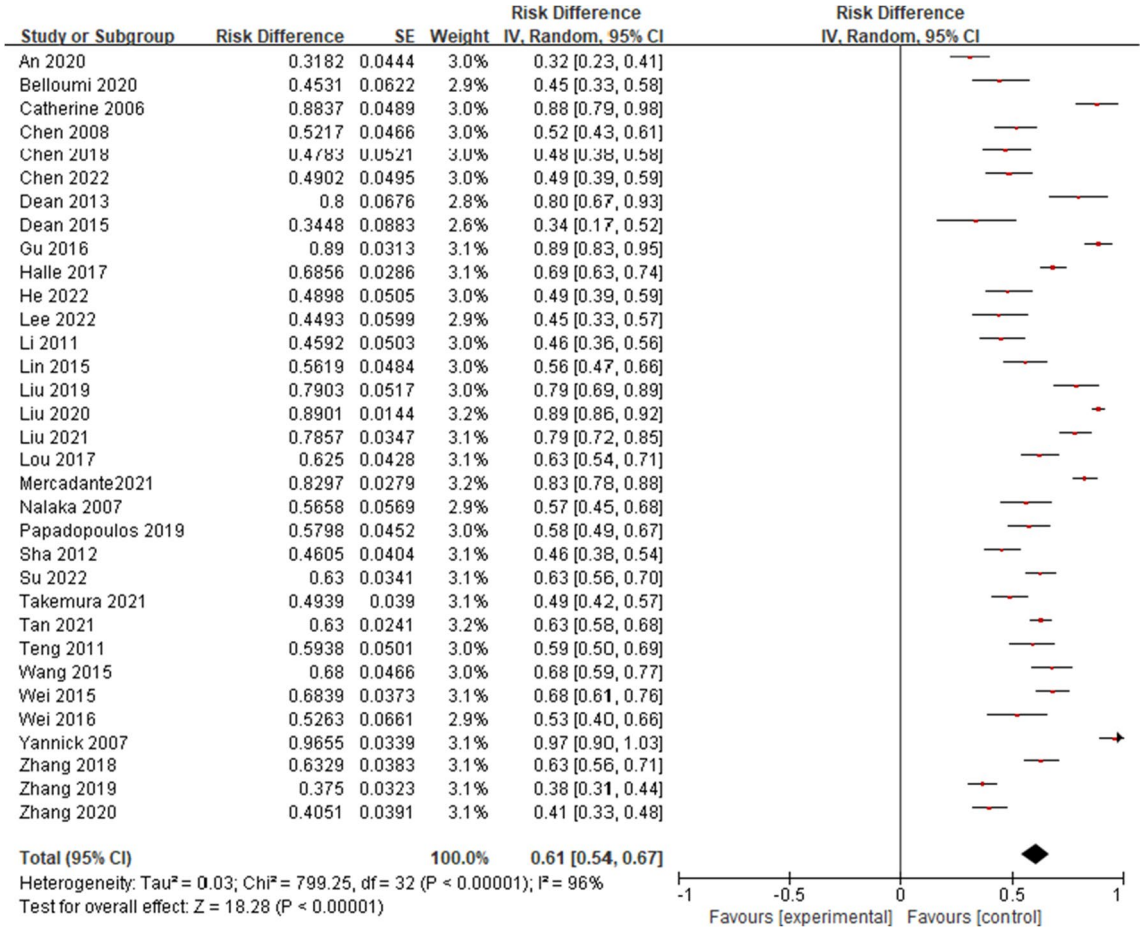

Fig. 2 Forest plot of all sleep disturbances prevalence rates

Table 6 Overview of the subgroup analyses for the prevalence of sleep disturbances in lung cancer

Subgroup	No. of studies	Prevalence [95% CI]	I^2 (%)	*p* value
All studies	33	0.61 [0.54–0.67]	96	$P<0.00001$
Different countries or regions				
Mainland	21	0.59 [0.51, 0.68]	97	$P<0.00001$
Other countries or regions	12	0.65 [0.53, 0.76]	95	$P<0.00001$
Study quality				
High	2	0.52 [0.40, 0.64]	69	$P<0.00001$
Medium	31	0.61 [0.55, 0.68]	96	$P<0.00001$
Study object				
Surgical patients	4	0.56 [0.41, 0.70]	94	$P<0.00001$
Patients receiving chemotherapy	11	0.62 [0.51, 0.73]	94	$P<0.00001$
Study design				
Cross-sectional study	28	0.61 [0.54, 0.69]	96	$P<0.00001$
Longitudinal study	5	0.57 [0.43, 0.71]	88	$P<0.00001$
Measurement tool				
AIS	6	0.56 [0.42, 0.70]	97	$P<0.00001$
PSQI	25	0.63 [0.55, 0.70]	95	$P<0.00001$

AIS: Athens Insomnia Scale; *PSQI*: Pittsburgh Sleep Quality Index

Table 7 Included studies for risk factor meta-analysis

Risk factor	Study	Country	Design	Sample size (N)	Age (mean years ± SD)	Sleep outcome; Cut-off	Log [odds ratio]	Standard error (SE)
Age	Gu 2016 [20]	China	Cross-sectional	100	66.28 ± 7.40	PSQI Cut-off unknown	0.942	0.577
	Wei 2016 [36]	China	Prospective Observational	57	59.22 ± 8.08	PSQI > 7	0.201	0.0611
Education	An 2020 [11]	China	Cross-sectional	110	Not reported	SRSS ≥ 30	1.2709	0.5631
	Gu 2016 [20]	China	Cross-sectional	100	66.28 ± 7.40	PSQI Cut-off unknown	0.477	0.2185
KPS	Lian 2020 [27]	China	Cross-sectional	106	Not reported	PSQI Cut-off unknown	-0.345	/
	Li 2011 [25]	China	Cross-sectional	98	31–88; mean 58.8	PSQI > 7	-0.355	/
Fatigue	Chang 2017 [43]	Taiwan	Cross-sectional	40	66.92 ± 11.01	PSQI > 8	0.57	0.26
	Wei 2016 [36]	China	Prospective Observational	57	59.22 ± 8.08	PSQI > 7	1.451	0.686
Pain	Sha 2012 [33]	China	Cross-sectional	152	57.09	PSQI > 7	0.167	0.167
	Su 2022 [14]	China	Cross-sectional	200	58.60 ± 6.92	AIS > 4	0.839	0.3458
	Tan 2021 [15]	China	Cross-sectional	400	Not reported	AIS > 6	1.1343	0.1445
	Wei 2016 [36]	China	Prospective Observational	57	59.22 ± 8.08	PSQI > 7	3.3491	1.1336
	Zhang 2020 [40]	China	Cross-sectional	158	Not reported	AIS > 6	1.1641	0.427
Tumor stage	Chen 2022 [23]	China	Cross-sectional	102	Not mention	PSQI > 7	0.6622	0.2453
	Su 2022 [14]	China	Cross-sectional	200	58.60 ± 6.92	AIS > 4	0.4941	0.2119
	Tan 2021 [15]	China	Cross-sectional	400	Not reported	AIS > 6	1.4024	0.4675
	Zhang 2020 [40]	China	Cross-sectional	158	Not reported	AIS > 6	1.3948	0.4933
Depression	Tan 2021 [15]	China	Cross-sectional	400	Not reported	AIS > 6	2.2244	0.846
	Su 2022 [14]	China	Cross-sectional	200	58.60 ± 6.92	AIS > 4	1.0508	0.3744
	Zhang 2020 [40]	China	Cross-sectional	158	Not reported	AIS > 6	2.2799	0.9076
	Papadopoulos 2019 [41]	Greece	Cross-sectional	119	64	PSQI > 5	0.0583	0.0349
	Mercadante 2021 [13]	Italy	Cross-sectional	182	69.9 ± 10.8	AIS ≥ 6	2.21	0.6123
Anxiety	Tan 2021 [15]	China	Cross-sectional	400	Not reported	AIS > 6	1.9899	0.7058
	Su 2022 [14]	China	Cross-sectional	200	58.60 ± 6.92	AIS > 4	1.249	0.48
	Zhang 2020 [40]	China	Cross-sectional	158	Not reported	AIS > 6	2.0134	1.0142
	Papadopoulos 2019 [41]	Greece	Cross-sectional	119	64	PSQI > 5	0.157	0.075
	Mercadante 2021 [13]	Italy	Cross-sectional	182	69.9 ± 10.8	AIS ≥ 6	1.98	0.5459
	Wei 2016 [36]	China	Prospective Observational	57	59.22 ± 8.08	PSQI > 7	0.145	0.0659
	Lin 2021 [29]	China	Cross-sectional	154	Not reported	PSQI ≥ 7	0.349	0.106

AIS: Athens Insomnia Scale; *PSQI*: Pittsburgh Sleep Quality Index; *SRSS*: Self-Rating Scale of Sleep

lung cancer's demographic characteristics, lung cancer incidence is high among people over 60 years old [55], and the elderly population is prone to sleep disturbances such as early waking because of their physiological

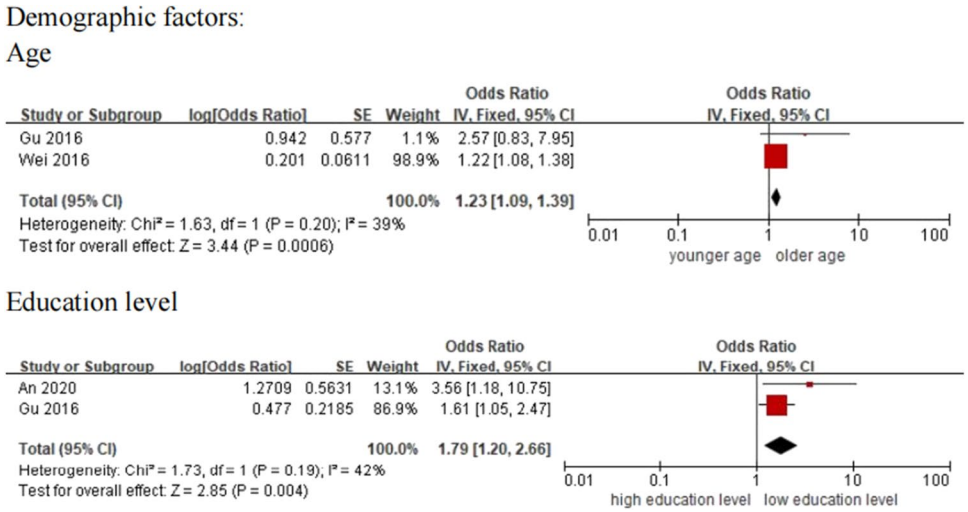

Fig. 3 Forest plot of demographic risk factors

characteristics [56]. However, it has also been reported that young patients with lung cancer are more likely to experience sleep problems [21]. The symptoms experienced by elderly and young patients with cancer are different [21]. In terms of the age factor, only two articles were included in this systematic review, and the influence of age on the sleep disturbances of patients with lung cancer must be further demonstrated in the future. In addition, the present review suggested that a low education level was a risk factor for sleep disturbances in patients with lung cancer. Compared with people with high education levels, those with low education levels have increased pressure from economic, life, and other aspects and relatively poor cognition of disease and treatment, eventually affecting their sleep [57].

For clinical factors, tumor stages III and IV were significant sleep disturbances risk factors. In terms of the disease, more than 50% of patients with lung cancer are diagnosed at an advanced stage [54]. Meanwhile, patients with advanced lung cancer need complex treatment regimens, and the side effects of treatment combined with the discomfort caused by the disease burden them with many symptoms [58]. Fatigue was also a risk factor for sleep disturbances. Fatigue and sleep disturbances often appear as symptom clusters and might have an interactive relationship between them [59]. Researchers have demonstrated their possible common underlying mechanism, the inflammatory markers, in breast cancer populations [60]. Continued fundamental research and interdisciplinary collaboration are needed in lung cancer population study to prevent or treat fatigue and sleep disturbances early. Patients with lung cancer may benefit from routine multidisciplinary assessments of these symptoms. Finally, this systematic review found that pain was also one of the risk factors for sleep disturbances in patients. Pain has a high incidence in these patients. Surgery, chemotherapy, and radiotherapy may lead to pain after cancer treatment, and lung cancer is one of the most common cancers causing pain [61]. Lack of sleep can both cause and result in pain [62]. Inadequate pain control and management may worsen physical and psychological symptoms in patients, negatively impact their rehabilitation, and diminish their daily quality of life. Respiratory symptoms (e.g., dyspnea, cough) and comorbidities such as chronic obstructive pulmonary disease are important factors that should be considered in influencing sleep disturbances in patients with lung cancer. However, the relationship between respiratory symptoms and sleep disturbances has not been fully evaluated. Thus, this should be a critical direction for future research. For psychological factors, this meta-analysis suggested that anxiety and depression were risk factors for sleep disturbances in individuals with lung cancer. Researchers assessed the prevalence of anxiety and depression in 222 patients with lung cancer and reported values of 34.2% and 58.1%, respectively [63]. Their results showed that insomnia was the common factor of depression and anxiety [63]. Anxiety and depression could exist simultaneously, could be influenced independently by sleep disturbances, and could affect each other. Certain neuro-immunologic interactions may be the common factor causing mood disorders and sleep/wake disturbances [41]. The cytokine-induced sickness behavior has been hypothesized as a shared underlying feature of symptom clusters in cancer patients [45]. The relationship between anxiety, depression, and sleep disturbances requires further clarification through prospective research to establish a causal link between them to provide fresh viewpoints on interventions as well as improve patient outcomes[64].

Nowadays, researchers have used omics methods to find that sleep disturbances have common genes with other symptoms in symptom science, and these genes are related to classical pathways such as immunity, inflammation, and cell signaling[65]. In the future, omics methods can be used to understand the biological mechanism of the development of symptoms, such as sleep disturbances, to achieve precise interventions.

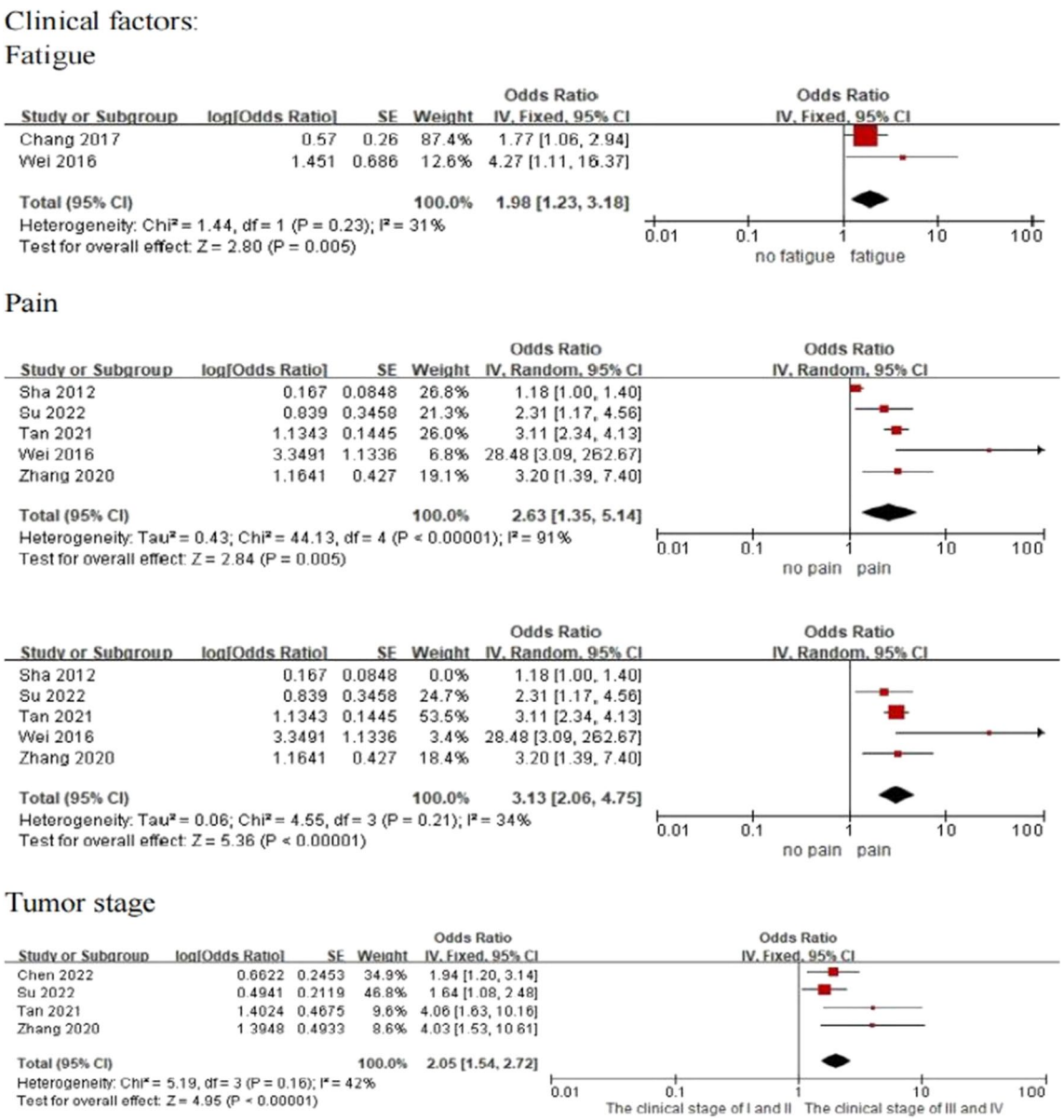

Fig. 4 Forest plot of clinical risk factors

Limitations

The evidence-based strength of the 37 studies included in the analysis is low due to their primarily cross-sectional nature. Additionally, the limited number of studies analyzed for each risk factor made it difficult to create a funnel plot in all cases, which may have resulted in publication bias. Secondly, the inclusion criteria for the studies limited the comprehensiveness of the analysis, as only English and Chinese language articles were included, and studies of mixed tumor types that may have included sub group analyses for lung cancer were excluded. Future studies are needed to evaluate sleep disturbances in patients with lung cancer comprehensively. Thirdly, different studies used different sleep disturbances assessment tools, assessment time, and follow-up time, resulting in a high heterogeneity of results. In addition, the results of pooled prevalence showed publication bias (Fig. 6). Additional high-quality studies on sleep disturbances in patients with lung cancer are needed.

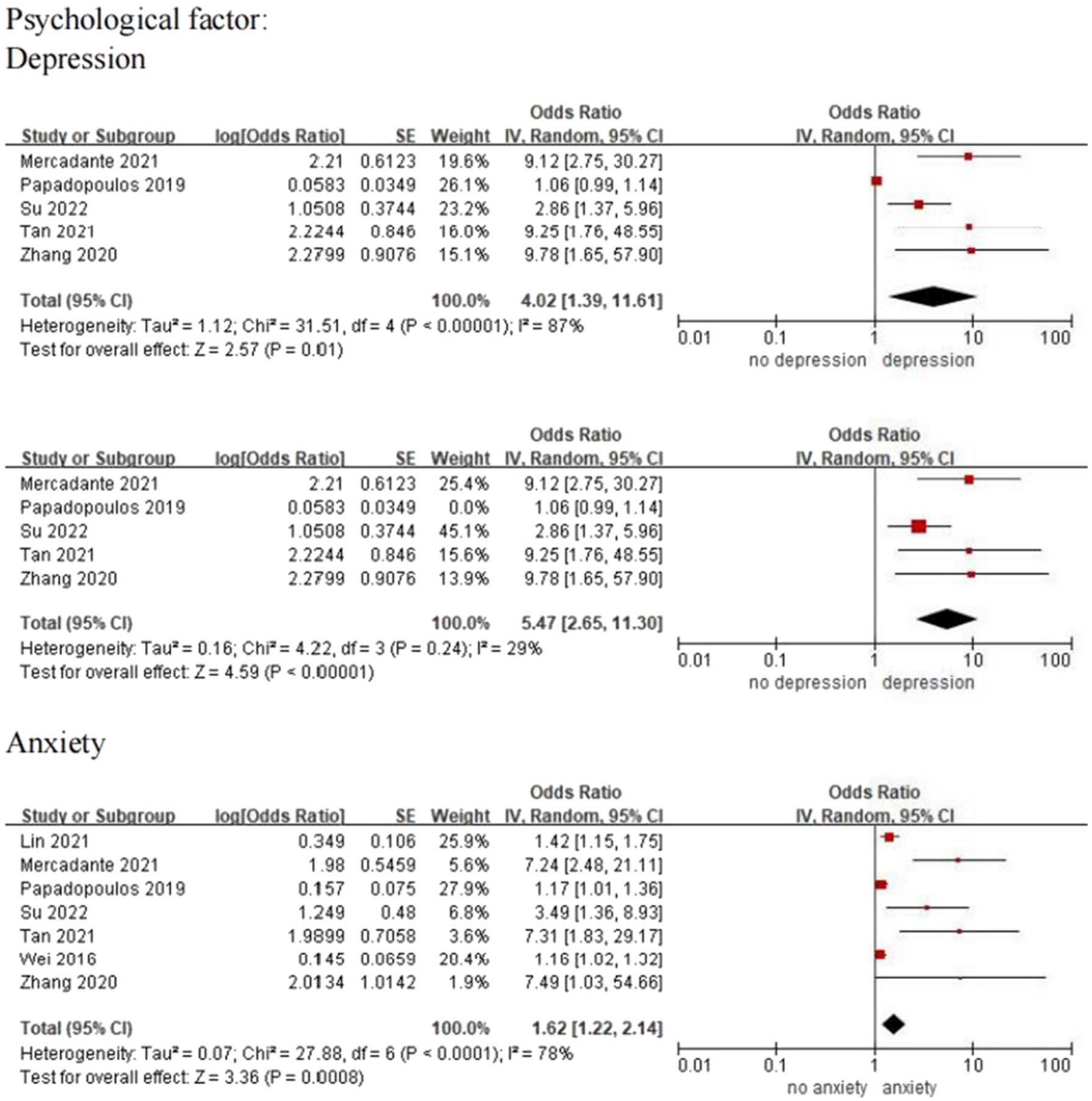

Fig. 5 Forest plot of psychological risk factors

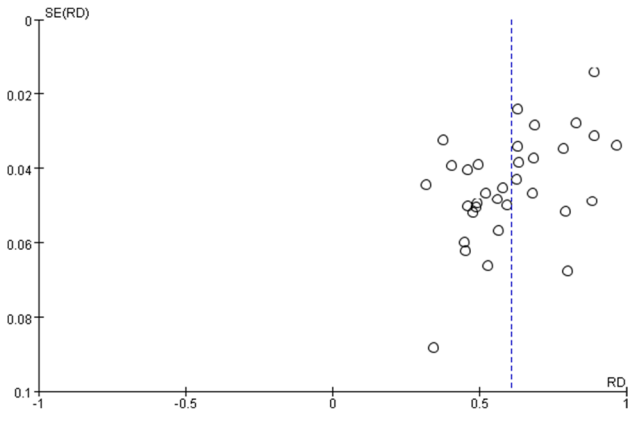

Fig. 6 Funnel plot of comparison: The overall prevalence of sleep disturbances in lung cancer patients

Conclusion

To the best of our knowledge, this work was the first systematic review and meta-analysis to report the prevalence and risk factors of sleep disturbances in patients with lung cancer. Results showed that more than 60% of patients with lung cancer experienced sleep disturbances, which was higher than that for the general population and other diseases. The comparatively high prevalence of sleep disturbances in this population emphasizes the need to adopt measures to reduce them. Sleep disturbances in patients with lung cancer deserve more attention. Significant risk factors for developing sleep disturbances include age, education level, fatigue, pain, cancer stage, anxiety, and depression, with depressive symptoms being the most

prominent among them. The influence of coping style on sleep disturbances remains uncertain. As sleep is a complex physiological process that is affected by physical, psychological, cognitive, behavioral, social, and other aspects, more multidisciplinary efforts should be made to fully identify, evaluate, and manage sleep disturbances in patients with lung cancer to ease symptom burden better and improve their quality of life.

Author contribution Conceptualization: Ying Hu, Yao Wang; Methodology: Ying Hu, Yao Wang; Literature Research: Ying Hu, Cai Yun Tang, Wen Hui Cao; Writing- Original draft preparation: Ying Hu, Cai Yun Tang, Wen Hui Cao; Writing- Reviewing and Editing: Lily Dongxia Xiao, Yao Wang; Supervision: Lily Dongxia Xiao, Yao Wang; Funding acquisition: Yao Wang.

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Data availability All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval Not applicable (not a clinical trial).

Consent to participate Not applicable (not a clinical trial).

Consent for publication All the coauthors have seen and approved the manuscript.

Competing interests The authors declare no competing interests.

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