

## Appendix 1 The questionnaire for clinicians on severe lung cancer

### *Investigation of severe lung cancer*

Our team proposed the concept of advanced and severe lung cancer in 2012. After continuous improvement, it was officially published in the *Chinese Journal of Oncology* in 2017. In 2019, the team proposed the “Diagnosis and Treatment Strategies for Advanced Severe Lung Cancer” in the *Chinese Journal of Practical Internal Medicine*. Furthermore, it published the “International Consensus on Severe Lung Cancer (First Edition) in the *Journal of Translational Research in Lung Cancer* in 2021. To understand your colleagues’ understanding of the concept of severe lung cancer, we conducted this survey. To fully protect your privacy, the survey will be completed anonymously. We also declare that the data collected in this survey will only be used for academic research and will only be handled by professional researchers related to this topic. Furthermore, the statistical analysis will not involve any specific individual or unit; your answers will be confidential. Thank you again for your support and cooperation!

### **National Clinical Research Center for Respiratory Disease China Respiratory Oncology Collaboration**

1. Your work unit level is [multiple choice]

- Grade-one hospital
- Grade-two hospital
- Tertiary hospital

2. What is the level of your work unit? [Multiple choice]

- Class a
- Class b
- Class c

3. What department do you work in? [Multiple choice]

- Respiratory
- Thoracic surgery
- Oncology
- Radiotherapy department
- Intervention division
- Others \_\_\_\_\_ \*

4. What is your professional title? [Multiple choice] \*

- No Title
- Junior professional title
- Intermediate title
- Senior title

5. Your work unit is located in: [fill in the blanks] \*

6. Do you see or treat lung cancer at work? [Multiple choice] \*

- Consultation but no treatment
- Consultation and treatment
- No consultation but treatment
- No consultation or treatment

7. What stage of lung cancer patients have you encountered or treated? [Multiple Choice Questions] \*

- Early
- Locally advanced
- Advanced

8. In your newly diagnosed lung cancer patients, are there often patients with PS 2–4? [Multiple choice] \*

- Seldom (30%)
- Sometimes (50%)
- Frequently (80%)

9. What are the main factors that cause newly diagnosed lung cancer patients to have PS 2–4? [Multiple Choice Questions] \*

- Comorbidities (COPD, ILD, hypertension, diabetes, heart failure, stroke, etc.)
- Cancer-related symptoms (pulmonary embolism, brain metastasis, bone metastasis, etc.)
- Other: \_\_\_\_\_ \*

10. Are treated lung cancer patients prone to PS 2–4? [Multiple choice] \*

- Seldom (30%)
- Sometimes (50%)
- Frequently (80%)

11. What are the main factors leading to PS 2–4 for lung cancer patients undergoing treatment? [Multiple Choice Questions] \*

- Comorbidities (COPD, ILD, hypertension, diabetes, heart failure, stroke, etc.)
- Tumor complications (pulmonary embolism, brain metastasis, bone metastasis, etc.)
- Treatment-related adverse reactions (such as hepatitis, pneumonia, surgical complications, radiotherapy-related complications, etc.)
- Other: \_\_\_\_\_ \*

12. Among the lung cancer patients you have treated, how many are prone to recurring PS of 2–4 (more than twice)? [Multiple choice] \*

- Seldom (30%)
- Sometimes (50%)
- Frequently (80%)

13. End stage lung cancer refers to patients whose PS is 2–4, for whom only palliative care relieve symptoms. Do you agree with this view? [Multiple choice] \*

- Agree
- Somewhat agree
- Not sure

14. What is your understanding of end stage and advanced lung cancer? [Multiple choice] \*

- End stage lung cancer is advanced lung cancer
- End stage lung cancer is the critical stage of advanced lung cancer
- End stage lung cancer is the critical stage of lung cancer and is not entirely related to the stage of lung cancer
- Not sure

15. Severe lung cancer is a disease in which the patient has a PS (performance status) score between 2 and 4 in certain stages due to various acute or chronic comorbidities, the tumor itself, and treatment-related AEs but also has a high probability of achieving survival benefit and/or improvement in the PS score after supportive care and antitumor treatment based on dynamic and precise testing (PMID: 34295668). Do you agree with the above point of view? [Multiple choice] \*

- Agree
- Somewhat agree
- Not sure

16. What is your understanding of severe lung cancer and end stage lung cancer? [Multiple choice] \*

- Severe lung cancer is end stage lung cancer
- Severe lung cancer is not necessarily end stage lung cancer
- Severe lung cancer and end stage lung cancer are two completely different concepts
- Not sure

17. The most significant difference between severe lung cancer and end stage lung cancer is that severe lung cancer has clinical therapeutic value (survival benefit and/or PS score improvement from various treatments). Do you agree with this point of view? [Multiple choice] \*

- Agree
- Somewhat agree
- Not sure

18. In clinical work, do you think it is necessary to distinguish patients with end stage lung cancer from those with severe lung cancer? [Multiple choice] \*

- Very necessary
- Necessary
- Not necessary
- It does not matter

19. What is your treatment strategy for patients with severe lung cancer caused by pulmonary complications (such as COPD, interstitial lung, tuberculosis)? [Multiple choice] \*

- Tumor treatment only
- Treatment of comorbidities only
- Same treatment for the cancer and lung
- Palliative care

20. What is your confidence in dealing with severe lung cancer? [Multiple choice] \*

- Not at all sure
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- Master

21. Which of following treatment strategies for severe lung cancer do you recognize?: [Multiple Choice Questions] \*

- Same treatment for the cancer and lung
- Select the treatment method according to the PS score
- Upgrade and downgrade of antitumor drugs
- Dynamic and accurate detection (identify treatment targets or avoid high-risk treatment groups)
- Combination of antitumor therapy, synergistic effect, and detoxification

## Appendix 2 ECOG Performance Status Scale

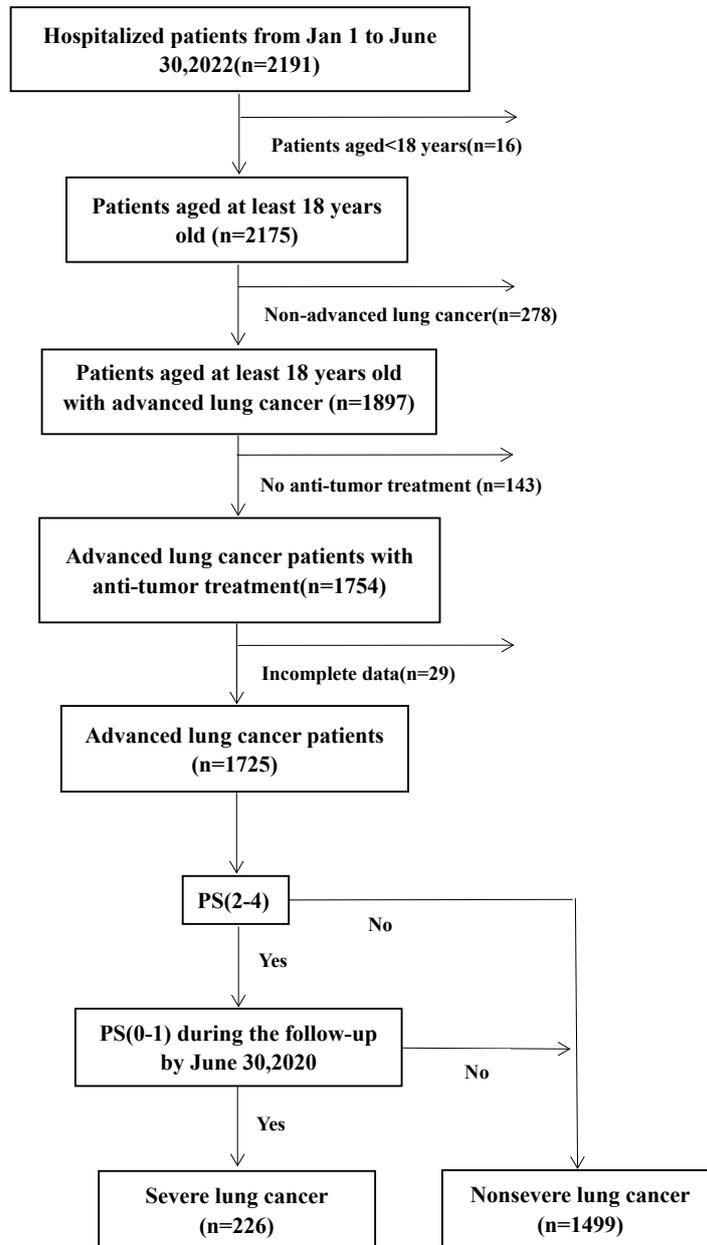
Grade	ECOG Performance Status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry an any self-care; totally confined to bed or chair
5	Dead

Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982 Dec;5(6):649-55. PMID: 7165009.

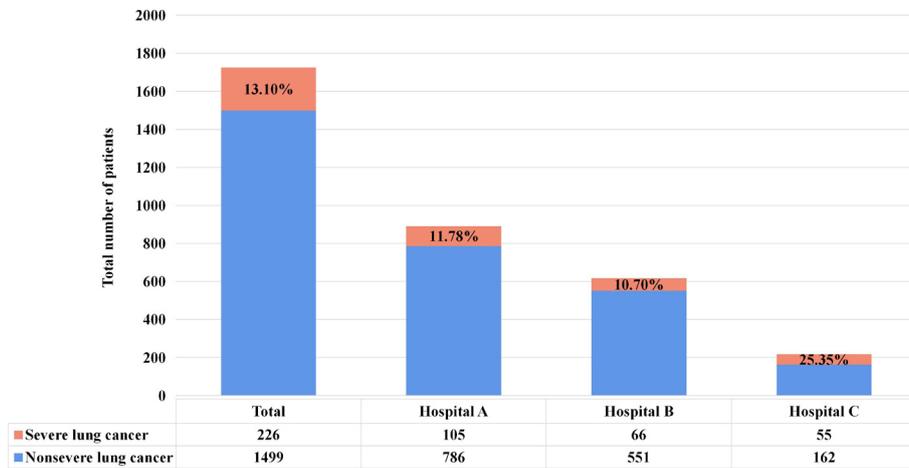
**Table S1** Clinical characteristics of fatal cases with severe lung cancer from different causes (n=95)

Category and subcategory	Cancer-related symptoms (n=55)	Treatment-related AEs (n=40)	Total	P value
Age (y), n (%)				<0.001
≥65	19 (35.6)	26 (65.0)	45 (47.4)	
<65	36 (65.4)	14 (36.0)	50 (52.6)	
Gender, n (%)				0.90
Male	42 (76.4)	31 (77.5)	73 (76.8)	
Female	13 (23.6)	9 (22.5)	22 (23.2)	
Pathological classification, n (%)				0.30
Nonsquamous NSCLC	40 (72.7)	25 (62.5)	65 (68.4)	
Squamous cell carcinomas	10 (18.2)	7 (17.5)	17 (17.9)	
Small cell lung cancer	5 (9.1)	8 (20.0)	13 (13.7)	
Neoplasm staging, n (%)				0.58
IIIB and IIIC	9 (16.4)	5 (12.5)	14 (14.7)	
IV	46 (83.6)	35 (87.5)	81 (85.3)	
Genetic mutations, n (%)				0.13
No	30 (54.5)	30 (72.0)	60 (63.2)	
Yes	25 (45.5)	10 (25.0)	35 (36.8)	
Operation history, n (%)				0.99
No	47 (85.5)	34 (85.0)	81 (85.3)	
Yes	8 (15.5)	6 (15.0)	14 (14.7)	
Comorbidities, n (%)				0.48
No	46 (83.6)	30 (75.0)	76 (80.0)	
Yes	9 (16.4)	10 (25.0)	19 (20.0)	
History of other tumors, n (%)				0.95
No	54 (98.2)	38 (95.0)	92 (96.8)	
Yes	1 (1.8)	2 (5.0)	3 (3.2)	

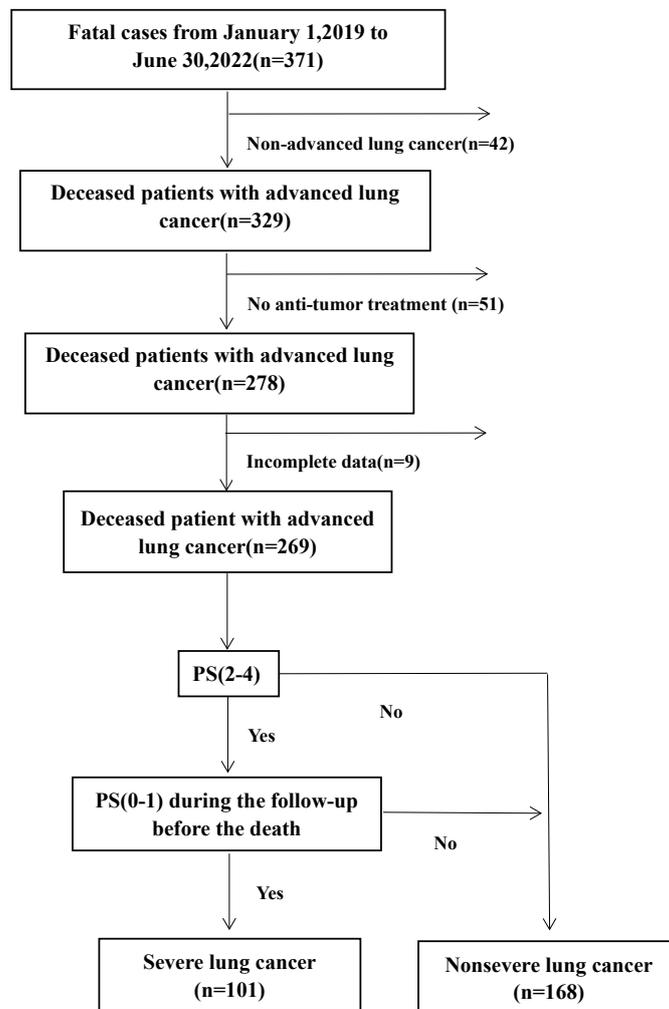
NSCLC, non-small cell lung cancer.



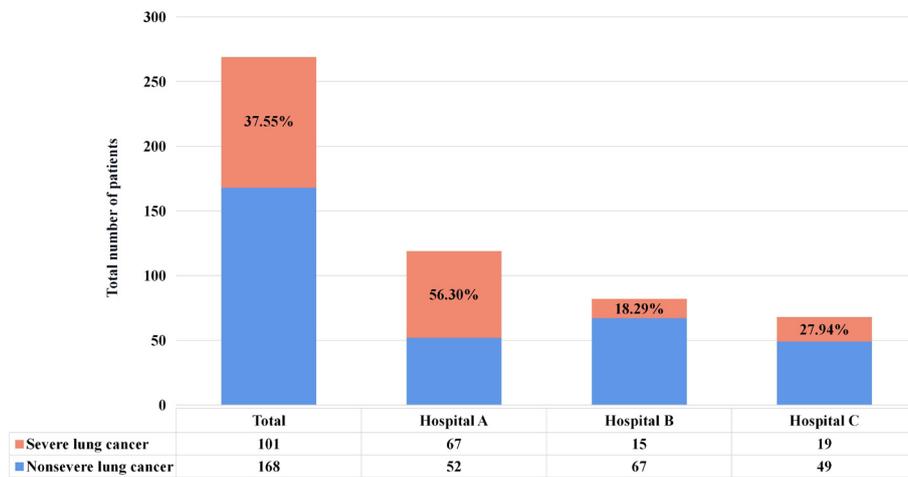
**Figure S1** Flowchart of the enrolled patients with advanced lung cancer in the cross-sectional study. PS, performance status.



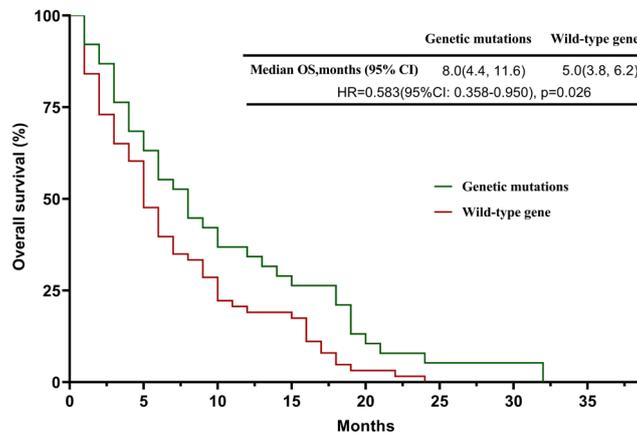
**Figure S2** The incident of severe lung cancer from 3 participating institutes in the cross-sectional study.



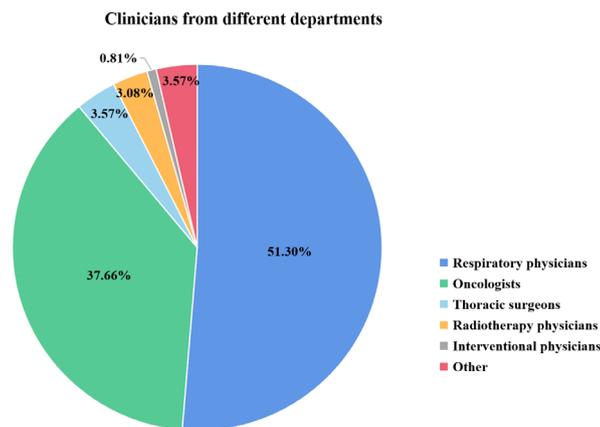
**Figure S3** Enrollment flowchart of the fatal cases of advanced lung cancer. PS, performance status.



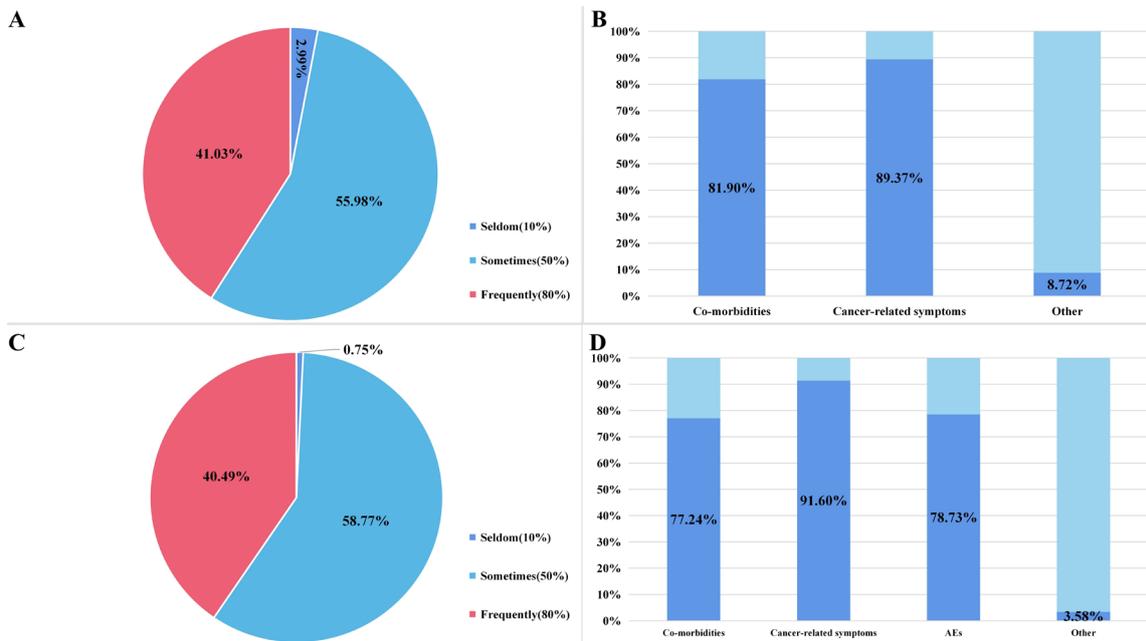
**Figure S4** The incident of severe lung cancer from 3 participating institutes in fatal cases.



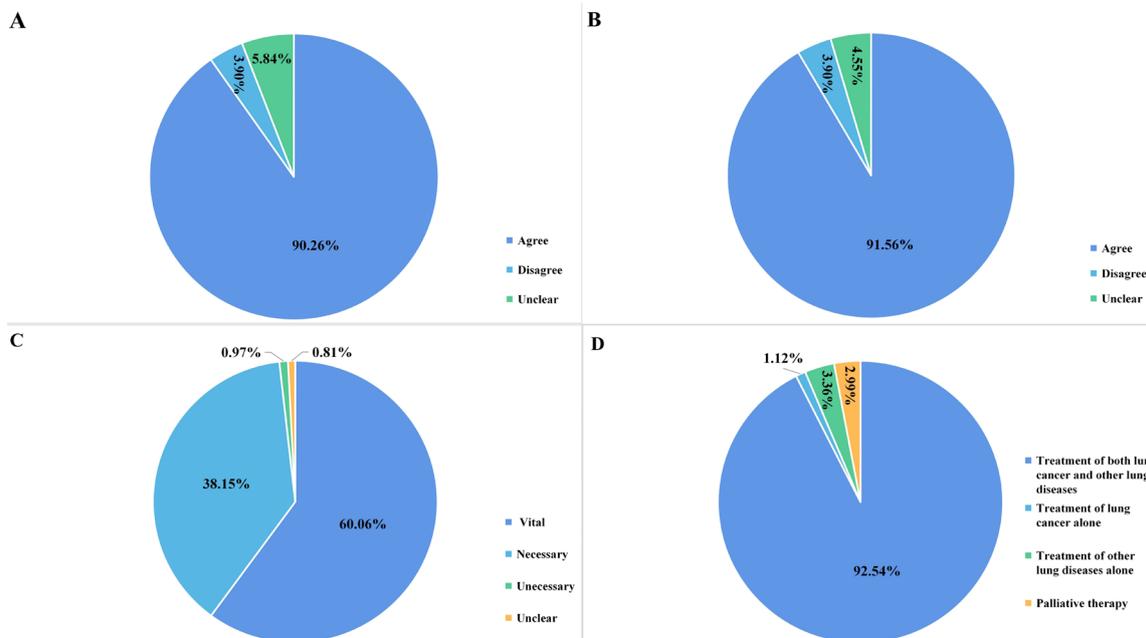
**Figure S5** Survival curves between patients with genetic mutations and those with wild-type genes in fatal cases of severe lung cancer. OS, overall survival; CI, confidence interval.



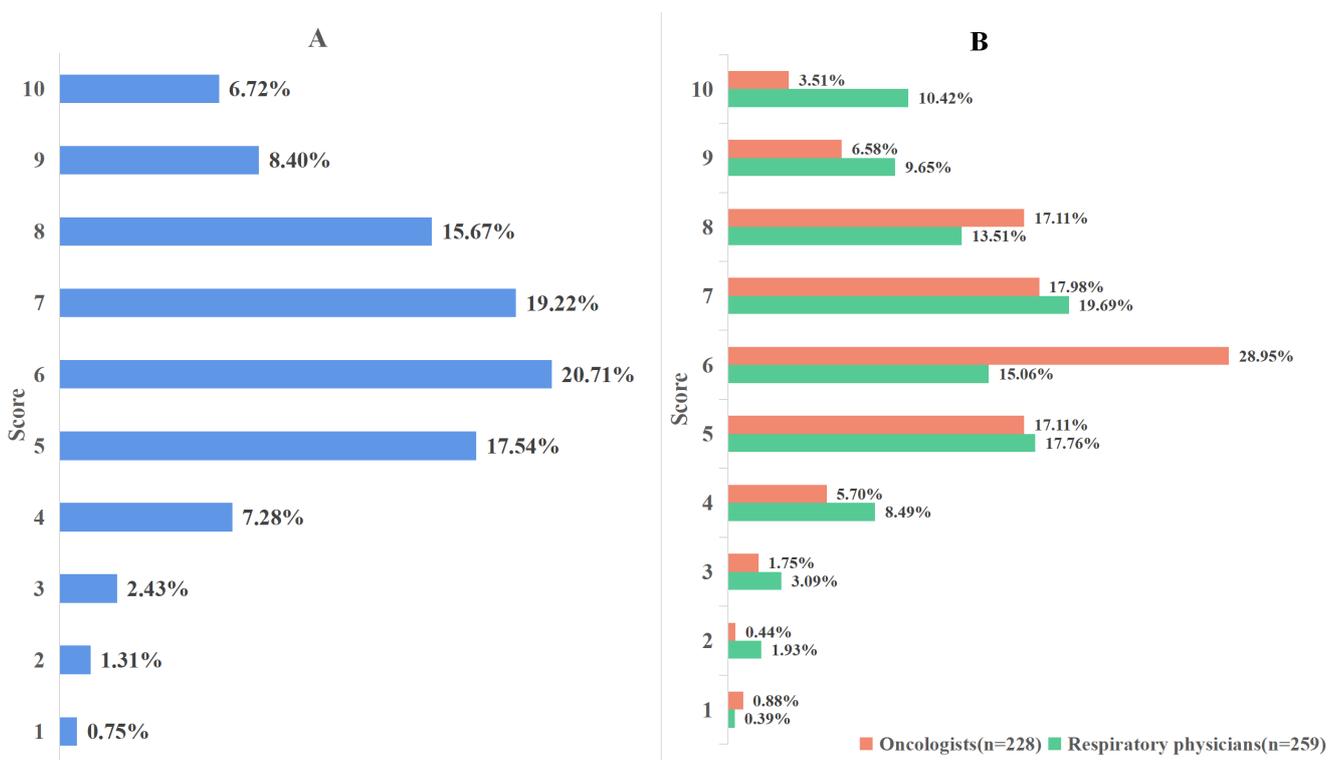
**Figure S6** Department distribution of the 616 clinicians who participated in the questionnaire.



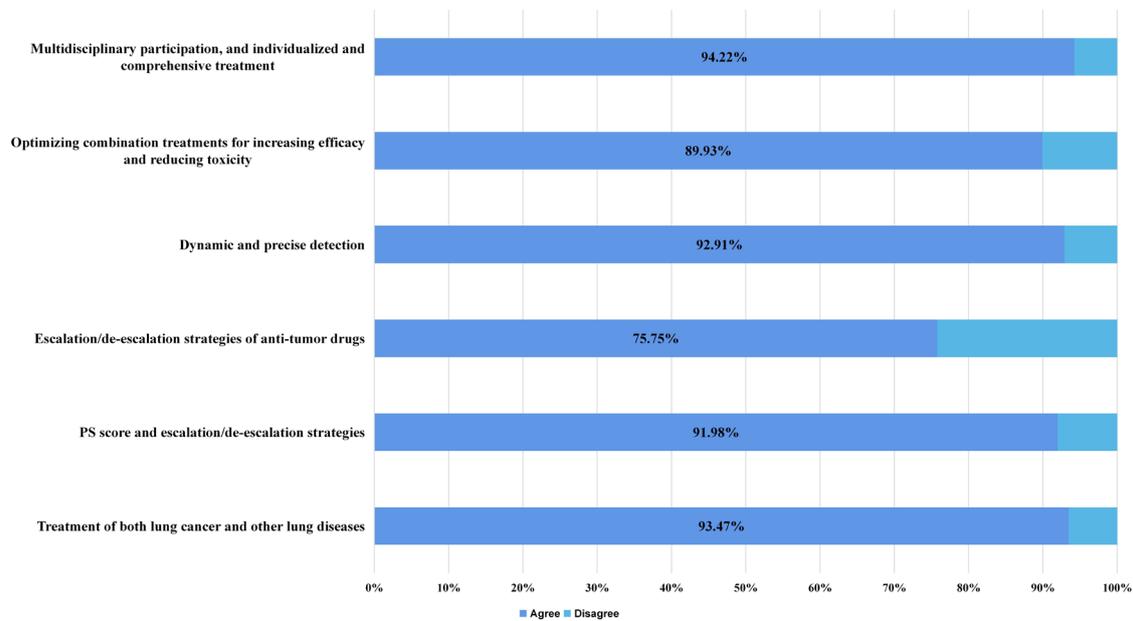
**Figure S7** Panel A shows the frequency at which 616 clinicians diagnosed and treated newly diagnosed lung cancer patients with poor PS scores in clinic. Panel B shows the opinion of 616 clinicians on the causes of poor PS scores in newly diagnosed lung cancer patients. Panel C shows the frequency at which 616 clinicians diagnosed and treated patients with lung cancer and poor PS scores who underwent antitumor therapy in clinic. Panel D shows the opinion of 616 clinicians on the causes of poor PS scores in lung cancer patients who had antitumor treatment in clinic. PS, performance status.



**Figure S8** Panel A shows clinicians' acceptance of the concept of severe lung cancer. Panel B shows clinicians' approval of the therapeutic value of the severe lung cancer concept. Panel C shows clinicians' support of the necessity of distinguishing severe lung cancer from end stage lung cancer. Panel D shows clinicians' support of the necessity to treat both lung cancer and comorbidities.



**Figure S9** Panel A shows clinicians' self-assessment of their ability to manage patients with severe lung cancer. Panel B shows the self-assessment of respiratory clinicians' and oncologists' ability to manage patients with severe lung cancer.



**Figure S10** Clinician support rate for each treatment strategy recommended in the international consensus for severe lung cancer.