Appendix 1

Search strategy

1 COPD

(((((((((((((((((((((Chronic Obstructive Pulmonary Diseases[MeSH Terms]) OR (Asthma Chronic Obstructive Pulmonary Disease Overlap Syndrome[Title/Abstract])) OR (Asthma-COPD Overlap Syndrome[Title/Abstract])) OR (Asthma COPD Overlap Syndrome[Title/Abstract])) OR (Asthma-COPD Overlap Syndromes[Title/Abstract])) OR (Overlap Syndrome, Asthma-COPD[Title/Abstract])) OR (Airflow Obstruction, Chronic[Title/Abstract])) OR (Airflow Obstructions, Chronic[Title/Abstract])) OR (Chronic Airflow Obstructions[Title/Abstract])) OR (Chronic Airflow Obstruction[Title/Abstract])) OR (COAD[Title/Abstract])) OR (COPD[Title/Abstract])) OR (Chronic Obstructive Airway Disease[Title/Abstract])) OR (Chronic Obstructive Lung Disease[Title/Abstract])) OR (Chronic Obstructive Pulmonary Diseases[Title/Abstract])) OR (Chronic Airflow Obstructions[Title/Abstract])) OR (Chronic Airflow Obstruction[Title/Abstract])) OR (COPD, Severe Early-Onset[Title/Abstract])) OR (Lung Diseases, Obstructive[Title/Abstract])) OR (Lung Disease, Obstructive[Title/Abstract])) OR (Obstructive Lung Disease[Title/Abstract])) OR (Obstructive Lung Diseases[Title/Abstract])) OR (Obstructive Pulmonary Diseases[Title/Abstract])) OR (Obstructive Pulmonary Disease[Title/Abstract])) OR (Pulmonary Disease, Obstructive[Title/Abstract])) OR (Pulmonary Diseases, Obstructive[Title/Abstract])

2 Emphysema

((((((((((((((((((((((Pulmonary Emphysema[MeSH Terms]) OR (Emphysemas, Pulmonary[Title/Abstract])) OR (Pulmonary Emphysemas[Title/Abstract])) OR (Emphysema, Pulmonary[Title/Abstract])) OR (Focal Emphysema[Title/Abstract])) OR (Emphysema, Focal[Title/Abstract])) OR (Emphysemas, Focal[Title/Abstract])) OR (Focal Emphysemas[Title/Abstract])) OR (Panacinar Emphysema[Title/Abstract])) OR (Emphysema, Panacinar[Title/Abstract])) OR (Emphysemas, Panacinar[Title/Abstract])) OR (Panacinar Emphysemas[Title/Abstract])) OR (Panlobular Emphysema[Title/Abstract])) OR (Emphysema, Panlobular[Title/Abstract])) OR (Emphysemas, Panlobular[Title/Abstract])) OR (Panlobular Emphysemas[Title/Abstract])) OR (Centriacinar Emphysema[Title/Abstract])) OR (Centriacinar Emphysemas[Title/Abstract])) OR (Emphysema, Centriacinar[Title/Abstract])) OR (Emphysemas, Centriacinar[Title/Abstract])) OR (Centrilobular Emphysema[Title/Abstract])) OR (Centrilobular Emphysemas[Title/Abstract])) OR (Emphysema, Centrilobular[Title/Abstract])) OR (Emphysemas, Centrilobular[Title/Abstract])) OR (Emphysema, Subcutaneous[Title/Abstract])

3 Solitary Pulmonary Nodule

((((((((((((((Solitary Pulmonary Nodule[MeSH Terms]) OR (Pulmonary Nodule, Solitary[Title/Abstract])) OR (Solitary Lung Nodule[Title/Abstract])) OR (Lung Nodule, Solitary[Title/Abstract])) OR (Nodule, Solitary Lung[Title/Abstract])) OR (Solitary Lung Nodules[Title/Abstract])) OR (Solitary Pulmonary Nodules[Title/Abstract])) OR (Nodule, Solitary Pulmonary[Title/Abstract])) OR (Nodules, Solitary Pulmonary[Title/Abstract])) OR (Pulmonary Nodules, Solitary[Title/Abstract])) OR (Pulmonary Coin Lesion[Title/Abstract])) OR (Lesion, Pulmonary Coin[Title/Abstract])) OR (Coin Lesions, Pulmonary[Title/Abstract])) OR (Pulmonary Coin Lesions[Title/Abstract])) OR (Coin Lesion, Pulmonary[Title/Abstract]))

4 Lung Neoplasm

((((((((((((((Lung Neoplasm[MeSH Terms]) OR (Pulmonary Neoplasms[Title/Abstract])) OR (Neoplasms, Lung[Title/Abstract])) OR (Lung Neoplasm[Title/Abstract])) OR (Neoplasm, Lung[Title/Abstract])) OR (Neoplasms, Pulmonary[Title/Abstract])) OR (Neoplasm, Pulmonary[Title/Abstract])) OR (Pulmonary Neoplasm[Title/Abstract])) OR (Cancer, Lung[Title/Abstract])) OR (Cancers, Lung[Title/Abstract])) OR (Lung Cancers[Title/Abstract])) OR (Pulmonary Cancer[Title/Abstract])) OR (Cancer, Pulmonary[Title/Abstract])) OR (Cancers, Pulmonary[Title/Abstract])) OR (Pulmonary Cancers[Title/Abstract])) OR (Cancer of the Lung[Title/Abstract])) OR (Cancer of Lung[Title/Abstract])

(#1 OR #2) AND (#3 OR #4)

Table S1 Population source and CT scan parameters

Study/year	Country	Population source	CT scan parameters
Kishi et al. 2002 (24)	USA	Mayo Clinic, Rochester	CT parameter: GE (High Speed Advantage);
			Scanning technique: Low dose CT;
			Thickness of slices: 5 mm;
			Respiratory phase: Inspiratory scan
			Reconstruction method: Edge-enhancing
Wilson et al. 2011 (33)	USA	The Pittsburgh Lung Screening Study	CT parameter: GE (multidetector);
			Scanning technique: Low dose CT;
			Thickness of slices: NS;
			Reconstruction method: High spatial frequency;
			Respiratory phase: Inspiratory scan
Schwartz et al. 2016 (25)	USA	Karmanos Cancer Center (KCC) and Henry Ford Health System (HFHS)	CT parameter: NS; Scanning technique: Low dose CT; Thickness of slices: NS; Reconstruction method: NS; Respiratory phase: Inspiratory and expiratory scan
Chubachi et al. 2017 (26)	Japan	the Keio COPD Comorbidity Research	CT parameter: Toshiba (64 detectors, Aquilion 64), GE (256 detectors, Revolution CT) or Toshiba (320 detectors, Aquilion One Genesis); GE (64 detectors), LightSpeed VCT, and Discovery CT 750 HD;
			Scanning parameter: Standard dose CT;
			Thickness of slices: 1.0–1.25 mm;
			Reconstruction method: Chest and FC 50;
			Respiratory phase: Inspiratory and expiratory scan
Gagnat et al. 2017 (27)	Norway	the GenKOLS (Genetic COPD)	CT parameter: GE (8 slices, LightSpeed Ultra)
			Scanning technique: Standard dose CT;
			Thickness of slices: 1 mm;
			Reconstruction method: NS;
			Respiratory phase: Inspiratory scan
Carr. et al. 2018 (28)	USA	COPD Gene study	CT parameter: NS;
			Scanning technique: NS;
			Thickness of slices: 0.75 mm;
			Reconstruction method: B35 F;
			Respiratory phase: NS

Table S1 (*continued*)

Table S1 (*continued*)

Study/year	Country	Population source	CT scan parameters
Mouronte-Roibás *et al.* 2018 (29)	USA	the Vigo University Hospital from January 2014 to September 2016	CT parameter: GE (64 detectors), Lightspeed VCT, or Siemens (6 detectors, Somatom Emotion);
			Scanning technique: NS;
			Thickness of slices: NS;
			Reconstruction method: NS;
			Respiratory phase: NS
Nishio *et al.* 2019 (30)	Japan	The Institutional Review Board of Kyoto University Hospital	CT parameter: Toshiba (320 or 64 detectors, Aquilion ONE or Aquilion 64);
			Scanning technique: Standard dose CT;
			Thickness of slices: 0.5 or 1.0 mm;
			Reconstruction method: NS;
			Respiratory phase: NS
Husebø *et al.* 2019 (31)	Norway	the Bergen COPD Cohort Study	CT parameter: NS;
			Thickness of slices: NS;
			Reconstruction method: NS;
			Respiratory phase: NS
			Scanning technique: NS;
Gonzalez *et al.* 2019 (34)	Spain	International Early Lung Cancer Action Program (I-ELCAP)	CT parameter: Healthcare (Somatom Sensation 64, Somatom Definition); Siemens (64 detectors Somatom Plus 4)
			Scanning technique: Low dose CT;
			Thickness of slices: 1.0 mm;
			Reconstruction method: B60;
			Respiratory phase: Inspiratory scan
Yong *et al.* 2019 (35)	USA	The National Lung Screening Trial(NLST)	CT parameter: NS
			Scanning technique: Low dose CT;
			Thickness of slices: 1.0 mm;
			Reconstruction method: Soft tissue;
			Respiratory phase: Not specified;
Peters *et al.* 2023 (32)	Germany	Hospital(not specific) based	CT parameter: Definition AS64, Siemens, Siemens Medical Solutions;
			Scanning technique: Low dose CT;
			Thickness of slices: 1.0 mm;
			Reconstruction method: I40f;
			Respiratory phase: Inspiratory scan

Note: COPD, chronic obstructive pulmonary disease; CT, computed tomography; NS, not specified.

The results of the publication bias assessments using Begg's test and Egger's test did not indicate significant publication bias. Specifically, Begg's test yielded a p-value of 0.350 (p > 0.05), and Egger's test produced a p-value of 0.241 (p > 0.05).

Begg's Test

```
adj. Kendall's Score (P-Q) =     13
       Std. Dev. of Score =   12.85
        Number of Studies =     11
                    z =   1.01
              Pr > |z| =  0.312
                    z =   0.93 (continuity corrected)
              Pr > |z| =  0.350 (continuity corrected)
```

Egger's test

```
-------------------------------------------------------------------------
   Std_Eff |  Coefficient    Std. err.   t   P>|t|     [95% conf. interval]
-------------------------------------------------------------------------
     slop |   .628923     .207012    3.04  0.014    .1606294   1.097217
     Bias |   .9739846   .7756641    1.26  0.241    .7806894   2.728659
-------------------------------------------------------------------------
```


Meta-analysis estimates, given named study is omitted
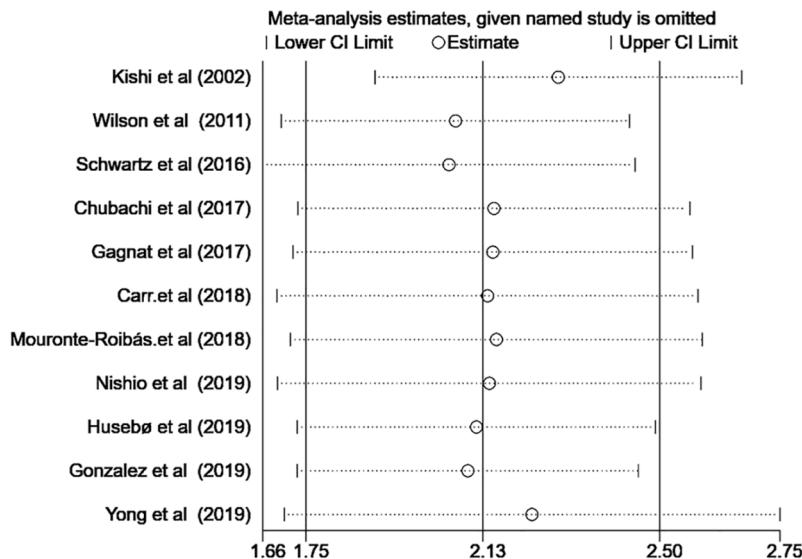
Figure S1 An examination of how the overall relationship between lung cancer and emphysema (a dichotomous variable evaluated either visually or quantitatively) is affected by sensitivity analysis.
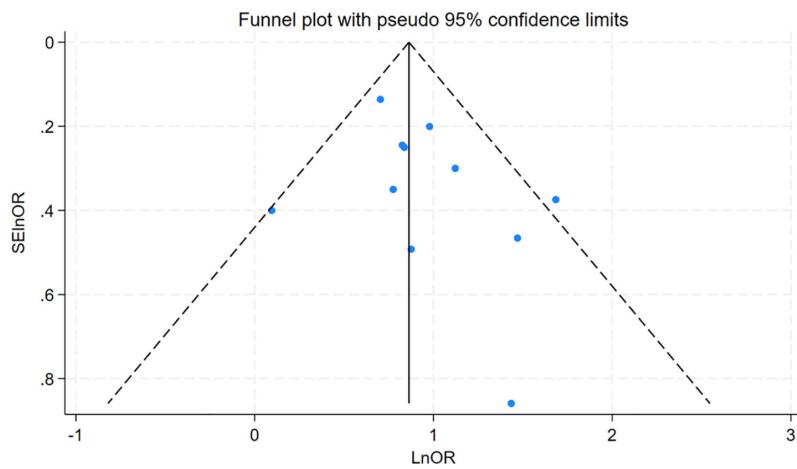
Figure S2 A funnel plot was utilized to assess publication bias regarding the relationship between emphysema, evaluated either visually or quantitatively, and lung cancer. Ln = natural logarithm; OR = odds ratio; SE = standard error.
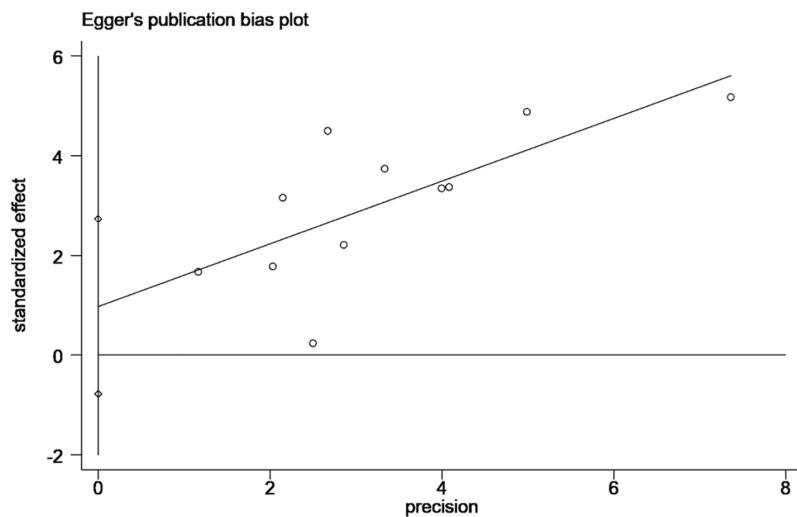
Figure S3 Egger's plot illustrating publication bias concerning the link between lung cancer and emphysema.
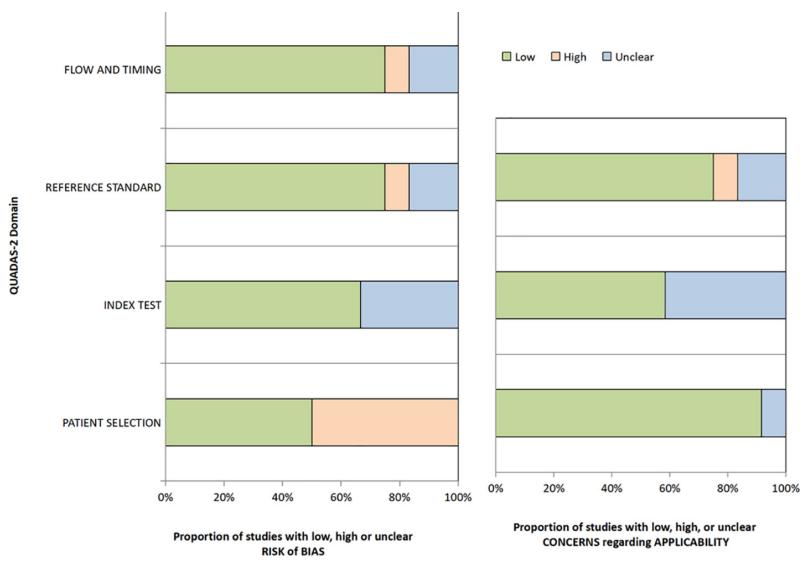
Figure S4 Summary of QUADAS-2 assessments of included studies. QUADAS, Quality Assessment of Diagnostic Accuracy Studies.

Sources of Heterogeneity

Study			%
ID		ES (95% CI)	Weight

HB

Study	ES (95% CI)	Weight
Kishi et al (2002)	1.10 (0.50, 2.40)	5.55
Schwartz et al (2016)	2.66 (1.80, 3.95)	15.69
Chubachi et al (2017)	4.20 (1.00, 29.00)	1.35
Mouronte-Roibás.et al (2018)	2.17 (1.09, 4.30)	6.96
Nishio et al (2019)	2.28 (1.43, 3.72)	12.05
Subtotal (I-squared = 9.8%, p = 0.351)	2.24 (1.69, 2.97)	41.60

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PB

Study	ES (95% CI)	Weight
Wilson et al (2011)	3.07 (1.45, 4.70)	8.92
Gagnat et al (2017)	2.40 (0.90, 6.20)	3.84
Carr.et al (2018)	2.31 (1.41, 3.76)	11.70
Husebø et al (2019)	4.35 (1.74, 10.80)	4.25
Gonzalez et al (2019)	5.39 (2.59, 11.24)	6.22
Yong et al (2019)	2.02 (1.55, 2.64)	23.48
Subtotal (I-squared = 41.8%, p = 0.127)	2.74 (2.01, 3.73)	58.40

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	ES (95% CI)	Weight
Overall (I-squared = 24.2%, p = 0.213)	2.45 (2.01, 2.99)	100.00

NOTE: Weights are from random effects analysis

.0345   1   29

Study ID	ES (95% CI)	% Weight
America		
Kishi et al (2002)	1.10 (0.50, 2.40)	5.55
Wilson et al (2011)	3.07 (1.45, 4.70)	8.92
Schwartz et al (2016)	2.66 (1.80, 3.95)	15.69
Carr.et al (2018)	2.31 (1.41, 3.76)	11.70
Mouronte-Roibás.et al (2018)	2.17 (1.09, 4.30)	6.96
Yong et al (2019)	2.02 (1.55, 2.64)	23.48
Subtotal (I-squared = 10.2%, p = 0.351)	2.21 (1.82, 2.69)	72.29
.		
Aisa		
Chubachi et al (2017)	4.20 (1.00, 29.00)	1.35
Nishio et al (2019)	2.28 (1.43, 3.72)	12.05
Subtotal (I-squared = 0.0%, p = 0.495)	2.39 (1.51, 3.79)	13.40
.		
Europe		
Gagnat et al (2017)	2.40 (0.90, 6.20)	3.84
Husebø et al (2019)	4.35 (1.74, 10.80)	4.25
Gonzalez et al (2019)	5.39 (2.59, 11.24)	6.22
Subtotal (I-squared = 0.0%, p = 0.420)	4.10 (2.51, 6.71)	14.31
.		
Overall (I-squared = 24.2%, p = 0.213)	2.45 (2.01, 2.99)	100.00

NOTE: Weights are from random effects analysis

.0345   1   29

Study		
ID	ES (95% CI)	% Weight
Retrospective study		
Kishi et al (2002)	1.10 (0.50, 2.40)	5.55
Schwartz et al (2016)	2.66 (1.80, 3.95)	15.69
Mouronte-Roibás.et al (2018)	2.17 (1.09, 4.30)	6.96
Nishio et al (2019)	2.28 (1.43, 3.72)	12.05
Yong et al (2019)	2.02 (1.55, 2.64)	23.48
Subtotal (I-squared = 4.5%, p = 0.381)	2.13 (1.75, 2.59)	63.73
.		
Prospective study		
Wilson et al (2011)	3.07 (1.45, 4.70)	8.92
Chubachi et al (2017)	4.20 (1.00, 29.00)	1.35
Gagnat et al (2017)	2.40 (0.90, 6.20)	3.84
Carr.et al (2018)	2.31 (1.41, 3.76)	11.70
Husebø et al (2019)	4.35 (1.74, 10.80)	4.25
Gonzalez et al (2019)	5.39 (2.59, 11.24)	6.22
Subtotal (I-squared = 0.0%, p = 0.481)	3.10 (2.31, 4.17)	36.27
.		
Overall (I-squared = 24.2%, p = 0.213)	2.45 (2.01, 2.99)	100.00

NOTE: Weights are from random effects analysis

.0345   1   29