Supplementary

Appendix 1

1. Strategy for PubMed (n=672):

#1 "Lung Neoplasms"[MeSH Terms] OR "Carcinoma, Non-Small-Cell Lung"[MeSH Terms] OR "lung neoplasm*"[Title/Abstract] OR "neoplasms, lung"[Title/Abstract] OR "neoplasms, pulmonary"[Title/Abstract] "neoplasm, pulmonary"[Title/Abstract] OR "neoplasm, lung"[Title/Abstract] OR "pulmonary neoplasm*"[Title/Abstract] OR "lung cancer*"[Title/Abstract] OR "cancer, lung"[Title/Abstract] OR "cancers, lung"[Title/Abstract] OR "lung tumo*"[Title/Abstract] OR "lung carcinoma*"[Title/Abstract] OR "Pulmonary Neoplasm*"[Title/Abstract] OR "pulmonary cancer*"[Title/Abstract] OR "pulmonary tumo*"[Title/Abstract] OR "pulmonary carcinoma*"[Title/Abstract] OR "cancer of the lung"[Title/Abstract] OR "cancer of lung"[Title/Abstract] OR "cancer, pulmonary"[Title/Abstract] OR "cancers, pulmonary"[Title/Abstract]

#2 (Adenocarcinoma, Bronchiolo-Alveolar[MeSH Terms]) OR ((((((((((((((((((((((((((Adenocarcinoma, Bronchiolo Alveolar[Title/Abstract]) OR (Adenocarcinomas, Bronchiolo-Alveolar[Title/Abstract])) OR (Bronchiolo-Alveolar Adenocarcinoma[Title/Abstract])) OR (Bronchiolo-Alveolar Adenocarcinomas[Title/Abstract])) OR (Adenocarcinoma, Alveolar[Title/Abstract])) OR (Adenocarcinomas, Alveolar[Title/Abstract])) OR (Alveolar Adenocarcinoma[Title/Abstract])) OR (Alveolar Adenocarcinomas[Title/Abstract])) OR (Carcinoma, Alveolar[Title/Abstract])) OR (Alveolar Carcinoma[Title/Abstract])) OR (Alveolar Carcinomas[Title/Abstract])) OR (Carcinomas, Alveolar[Title/Abstract])) OR (Carcinoma, Bronchiolo-Alveolar[Title/Abstract])) OR (Bronchiolo-Alveolar Carcinoma[Title/Abstract])) OR (Bronchiolo-Alveolar Carcinomas[Title/Abstract])) OR (Carcinoma, Bronchiolo Alveolar[Title/Abstract])) OR (Carcinomas, Bronchiolo-Alveolar[Title/Abstract])) OR (Alveolar Cell Carcinoma[Title/Abstract])) OR (Alveolar Cell Carcinomas[Title/Abstract])) OR (Carcinoma, Alveolar Cell[Title/Abstract])) OR (Carcinomas, Alveolar Cell[Title/Abstract])) OR (Carcinoma, Bronchiolar[Title/Abstract])) OR (Bronchiolar Carcinoma[Title/Abstract])) OR (Bronchiolar Carcinomas[Title/Abstract])) OR (Carcinomas, Bronchiolar[Title/Abstract])) OR (Carcinoma, Bronchioloalveolar[Title/Abstract])) OR (Bronchioloalveolar Carcinoma[Title/Abstract])) OR (Bronchioloalveolar Carcinomas[Title/Abstract])) OR (Carcinomas, Bronchioloalveolar[Title/Abstract]))

#3 "Adenocarcinoma of Lung"[MeSH Terms] OR "lung adenocarcinomas"[Title/Abstract] OR "lung adenocarcinoma"[Title/Abstract] OR "adenocarcinoma lung"[Title/Abstract] OR "adenocarcinomas lung"[Title/Abstract] OR ("LUAD"[Title/Abstract])

#4 ("Solitary Pulmonary Nodule"[Mesh]) 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])) OR "ground-glass nodule*"[Title/Abstract] OR "solid nodule*"[Title/Abstract] OR "subsolid nodule*"[Title/Abstract] OR "part-solid nodule*"[Title/Abstract] OR "non-solid nodule*"[Title/Abstract] OR ("groundglass opacities"[Title/Abstract]) OR ("ground-glass"[Title/Abstract]) OR ("GGO"[Title/Abstract]) OR ("GGN"[Title/Abstract]) OR ("SPN"[Title/Abstract] OR "pGGN"[Title/Abstract]) OR ("PSN"[Title/Abstract]) OR ("SSN"[Title/Abstract]) OR ("mGGN"[Title/Abstract]) OR ("NSN"[Title/Abstract])

#5 "multiple pulmonary nodules"[MeSH Terms] OR "multiple pulmonary nodule"[Title/Abstract] OR "pulmonary nodule multiple"[Title/Abstract] OR "pulmonary nodules multiple"[Title/Abstract]

#6 #1or#2or#3or#4or#5

#7 "Artificial Intelligence"[Mesh] OR "Machine Learning"[Mesh] OR "Deep Learning"[Mesh] OR "artificial intelligence"[Title/Abstract] OR "Machine learning model" [Title/Abstract] OR "Machine learning algorithms" [Title/Abstract] OR "Algorithms" [Title/Abstract] OR "Machine Learning"[Title/Abstract] OR "Deep Learning"[Title/Abstract] OR "machine intelligence"[Title/Abstract] OR "Computational Approach" [Title/Abstract] OR "computer intelligence"[Title/Abstract] OR "Computer Reasoning"[Title/Abstract] OR "Computer Vision System*"[Title/Abstract] OR "Automated-computer aided" [Title/Abstract]OR "Knowledge Representation" [Title/Abstract] OR "Knowledge Acquisition"[Title/Abstract] OR "Expert system*"[Title/Abstract] OR "Neural Network*"[Title/Abstract] OR "Convolutional

neural network" [Title/Abstract] OR "CNN"[Title/Abstract] OR "Artificial neuronal network" [Title/Abstract] OR "AI" [Title/Abstract]
#8 "Tomography, X-Ray Computed"[MeSH Terms] OR "tomography scanners, x-ray computed"[Title/Abstract] OR "computed tomography"[Title/Abstract] OR "computer assisted tomography"[Title/Abstract] OR "CT"[Title/Abstract]
#9 "Invasive"[Title/Abstract] OR "invasiveness"[Title/Abstract] OR "risk"[Title/Abstract] OR "Risk Stratification"[Title/Abstract] OR "Risk assessment"[Title/Abstract] OR "risk management"[Title/Abstract] OR "subtype classification"[Title/Abstract] OR "histological assessment"[Title/Abstract]
#10 #6AND#7AND#8AND#9

2. Strategy for Embase (n=1,327):
#1 ('lung cancer'/exp 'lung tumor'/exp 'lung nodule'/exp OR 'Multiple Pulmonary Nodules'/exp OR 'Adenocarcinoma of Lung'/exp OR 'Adenocarcinoma, Bronchiolo-Alveolar'/exp OR 'Carcinoma, Non-Small-Cell Lung'/exp OR 'Carcinoma, Bronchogenic'/exp OR 'Bronchial Neoplasms'/exp OR 'Lung Neoplasms'/exp OR 'Bronchiolo-Alveolar Carcinomas':ti,ab,kw OR 'Adenocarcinomas, Lung':ti,ab,kw OR 'Carcinoma, Alveolar':ti,ab,kw OR 'Bronchiolo-Alveolar Carcinoma':ti,ab,kw OR 'Carcinomas, Bronchial':ti,ab,kw OR 'Carcinomas, Alveolar':ti,ab,kw OR 'Pulmonary Nodules, Multiple':ti,ab,kw OR 'Non-Small-Cell Lung Carcinoma':ti,ab,kw OR 'Cancer, Pulmonary':ti,ab,kw OR 'Bronchiolar Carcinomas':ti,ab,kw OR 'Carcinomas, Bronchiolar':ti,ab,kw OR 'Lung Carcinomas, Non-Small-Cell':ti,ab,kw OR 'Nonsmall Cell Lung Cancer':ti,ab,kw OR 'Alveolar Carcinomas':ti,ab,kw OR 'Neoplasm, Bronchial':ti,ab,kw OR 'Adenocarcinomas, Alveolar':ti,ab,kw OR 'Carcinoma, Bronchiolo-Alveolar':ti,ab,kw OR 'Carcinoma, Bronchiolar':ti,ab,kw OR 'Lung Cancers':ti,ab,kw OR 'Alveolar Adenocarcinomas':ti,ab,kw OR 'Alveolar Cell Carcinoma':ti,ab,kw OR 'Bronchiolo-Alveolar Adenocarcinoma':ti,ab,kw OR 'Cancer, Lung':ti,ab,kw OR 'Carcinomas, Bronchogenic':ti,ab,kw OR 'Bronchiolar Carcinoma':ti,ab,kw OR 'Neoplasms, Pulmonary':ti,ab,kw OR 'Non-Small Cell Lung Cancer':ti,ab,kw OR 'Carcinoma, Bronchioloalveolar':ti,ab,kw OR 'Carcinoma, Non-Small Cell Lung':ti,ab,kw OR 'Alveolar Adenocarcinoma':ti,ab,kw OR 'Adenocarcinoma, Alveolar':ti,ab,kw OR 'Bronchial Carcinoma':ti,ab,kw OR 'Pulmonary Nodule, Multiple':ti,ab,kw OR 'Carcinoma, Bronchial':ti,ab,kw OR 'Carcinomas, Non-Small-Cell Lung':ti,ab,kw OR 'Carcinomas, Bronchiolo-Alveolar':ti,ab,kw OR 'Neoplasm, Pulmonary':ti,ab,kw OR 'Non-Small-Cell Lung Carcinomas':ti,ab,kw OR 'Neoplasms, Bronchial':ti,ab,kw OR 'Bronchioloalveolar Carcinoma':ti,ab,kw OR 'Bronchogenic Carcinomas':ti,ab,kw OR 'Carcinoma, Non Small Cell Lung':ti,ab,kw OR 'Alveolar Cell Carcinomas':ti,ab,kw OR 'Lung Neoplasm':ti,ab,kw OR 'Cancers, Pulmonary':ti,ab,kw OR 'Bronchogenic Carcinoma':ti,ab,kw OR 'Pulmonary Cancers':ti,ab,kw OR 'Adenocarcinoma, Bronchiolo Alveolar':ti,ab,kw OR 'Lung Adenocarcinoma':ti,ab,kw OR 'Non Small Cell Lung Carcinoma':ti,ab,kw OR 'Multiple Pulmonary Nodule':ti,ab,kw OR 'Lung Cancer':ti,ab,kw OR 'Cancer of Lung':ti,ab,kw OR 'Lung Adenocarcinomas':ti,ab,kw OR 'Neoplasm, Lung':ti,ab,kw OR 'Adenocarcinomas, Bronchiolo-Alveolar':ti,ab,kw OR 'Bronchial Neoplasm':ti,ab,kw OR 'Adenocarcinoma, Lung':ti,ab,kw OR 'Pulmonary Neoplasms':ti,ab,kw OR 'Carcinomas, Bronchioloalveolar':ti,ab,kw OR 'Bronchiolo-Alveolar Adenocarcinomas':ti,ab,kw OR 'Lung Carcinoma, Non-Small-Cell':ti,ab,kw OR 'Carcinoma, Bronchiolo Alveolar':ti,ab,kw OR 'Cancer of the Lung':ti,ab,kw OR 'Pulmonary Cancer':ti,ab,kw OR 'Neoplasms, Lung':ti,ab,kw OR 'Pulmonary Neoplasm':ti,ab,kw OR 'Alveolar Carcinoma':ti,ab,kw OR 'Carcinomas, Alveolar Cell':ti,ab,kw OR 'Cancers, Lung':ti,ab,kw OR 'Bronchial Carcinomas':ti,ab,kw OR 'Bronchioloalveolar Carcinomas':ti,ab,kw OR 'Carcinoma, Alveolar Cell':ti,ab,kw OR 'GGO':ti,ab,kw OR 'pGGN':ti,ab,kw OR 'PSN':ti,ab,kw OR 'GGN':ti,ab,kw OR 'mGGN':ti,ab,kw OR 'SSN':ti,ab,kw OR 'SPN':ti,ab,kw OR 'NSN':ti,ab,kw OR 'LUAD':ti,ab,kw)
#2 ('Artificial Intelligence'/exp OR 'Neural Networks, Computer'/exp OR 'Knowledge Bases'/exp OR 'Robotics'/exp OR 'Unsupervised Machine Learning'/exp OR 'Fuzzy Logic'/exp OR 'Natural Language Processing'/exp OR 'Deep Learning'/exp OR 'Expert Systems'/exp OR 'Supervised Machine Learning'/exp OR 'Computer Heuristics'/exp OR 'Machine Learning'/exp OR 'Vision System, Computer':ti,ab,kw OR 'Machine Learning, Unsupervised':ti,ab,kw OR 'Semi supervised Learning':ti,ab,kw OR 'Computer Vision Systems':ti,ab,kw OR 'Knowledge Representations':ti,ab,kw OR 'Machine Learning, Supervised':ti,ab,kw OR 'Remote Operation':ti,ab,kw OR 'Systems, Computer Vision':ti,ab,kw OR 'Network Models, Neural':ti,ab,kw OR 'Intelligence, Artificial':ti,ab,kw OR 'Computational Neural Network':ti,ab,kw OR 'Network, Computer Neural':ti,ab,kw OR 'Networks, Computational Neural':ti,ab,kw OR 'Soft Robotics':ti,ab,kw

OR 'Neural Network Models':ti,ab,kw OR 'Computer Vision System':ti,ab,kw OR 'Perceptrons':ti,ab,kw OR 'Soft Robotic':ti,ab,kw OR 'System, Computer Vision':ti,ab,kw OR 'Models, Neural Network':ti,ab,kw OR 'Neural Network Model':ti,ab,kw OR 'Networks, Computer Neural':ti,ab,kw OR 'Learning, Unsupervised Machine':ti,ab,kw OR 'Connectionist Model':ti,ab,kw OR 'Intelligence, Computational':ti,ab,kw OR 'Expert System':ti,ab,kw OR 'Intelligence, Machine':ti,ab,kw OR 'Learning, Hierarchical':ti,ab,kw OR 'Neural Networks, Computational':ti,ab,kw OR 'Operation, Remote':ti,ab,kw OR 'Learning, Transfer':ti,ab,kw OR 'Robotic, Soft':ti,ab,kw OR 'Transfer Learning':ti,ab,kw OR 'Learning, Active Machine':ti,ab,kw OR 'Telerobotics':ti,ab,kw OR 'Network, Neural':ti,ab,kw OR 'Systems, Expert':ti,ab,kw OR 'Model, Neural Network':ti,ab,kw OR 'Models, Connectionist':ti,ab,kw OR 'Perceptron':ti,ab,kw OR 'Knowledge Bases':ti,ab,kw OR 'Computational Intelligence':ti,ab,kw OR 'Network, Computational Neural':ti,ab,kw OR 'Learning from Labeled Data':ti,ab,kw OR 'Reasoning, Computer':ti,ab,kw OR 'Knowledge Representation':ti,ab,kw OR 'Logic, Fuzzy':ti,ab,kw OR 'Heuristics, Computer':ti,ab,kw OR 'Neural Network, Computer':ti,ab,kw OR 'Neural Network':ti,ab,kw OR 'Bases, Knowledge':ti,ab,kw OR 'Learning, Inductive Machine':ti,ab,kw OR 'Operations, Remote':ti,ab,kw OR 'Learning, Deep':ti,ab,kw OR 'Learning, Supervised Machine':ti,ab,kw OR 'Machine Learning, Inductive':ti,ab,kw OR 'Model, Connectionist':ti,ab,kw OR 'Hierarchical Learning':ti,ab,kw OR 'Learning, Machine':ti,ab,kw OR 'Networks, Neural':ti,ab,kw OR 'Connectionist Models':ti,ab,kw OR 'Semi-supervised Learning':ti,ab,kw OR 'System, Expert':ti,ab,kw OR 'Natural Language Processings':ti,ab,kw OR 'Computer Reasoning':ti,ab,kw OR 'Computer Neural Network':ti,ab,kw OR 'Neural Network, Computational':ti,ab,kw OR 'Heuristic, Computer':ti,ab,kw OR 'Machine Learning with a Teacher':ti,ab,kw OR 'Knowledgebase':ti,ab,kw OR 'Language Processing, Natural':ti,ab,kw OR 'Knowledge Base':ti,ab,kw OR 'Knowledge Acquisition':ti,ab,kw OR 'Base, Knowledge':ti,ab,kw OR 'Computational Neural Networks':ti,ab,kw OR 'Representation, Knowledge':ti,ab,kw OR 'Vision Systems, Computer':ti,ab,kw OR 'Learning, Semi-supervised':ti,ab,kw OR 'Processings, Natural Language':ti,ab,kw OR 'Acquisition, Knowledge':ti,ab,kw OR 'Neural Networks':ti,ab,kw OR 'Machine Intelligence':ti,ab,kw OR 'Machine Learning, Active':ti,ab,kw OR 'Active Machine Learning':ti,ab,kw OR 'Knowledgebases':ti,ab,kw OR 'Robotics, Soft':ti,ab,kw OR 'Network Model, Neural':ti,ab,kw OR 'Inductive Machine Learning':ti,ab,kw OR 'Computer Heuristic':ti,ab,kw OR 'Remote Operations':ti,ab,kw OR 'Computer Neural Networks':ti,ab,kw OR 'Language Processings, Natural':ti,ab,kw OR 'Processing, Natural Language':ti,ab,kw OR 'AI':ti,ab,kw OR 'CNN':ti,ab,kw)
#3 ('x-ray computed tomography'/exp OR 'computed tomography scanner'/exp OR 'computed tomography':ti,ab,kw OR 'computer assisted tomography':ti,ab,kw OR 'ct':ti,ab,kw)
#4 ('invasiveness analysis':ti,ab,kw OR 'Invasive':ti,ab,kw OR 'invasiveness':ti,ab,kw OR 'risk':ti,ab,kw OR 'Risk Stratification':ti,ab,kw OR 'Risk assessment':ti,ab,kw OR 'risk management':ti,ab,kw OR 'subtype classification':ti,ab,kw OR 'histological assessment':ti,ab,kw)
#5 #1AND#2AND#3AND#4

3. Strategy for Cochrane Library (n=76):
#1 MeSH descriptor: [Lung Neoplasms] explode all trees
#2 MeSH descriptor: [Adenocarcinoma of Lung] explode all trees
#3 MeSH descriptor: [Solitary Pulmonary Nodule] explode all trees
#4 MeSH descriptor: [Adenocarcinoma, Bronchiolo-Alveolar] explode all trees
#5 MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees
#6 MeSH descriptor: [Carcinoma, Bronchogenic] explode all trees
#7 MeSH descriptor: [Bronchial Neoplasms] explode all trees
#8 MeSH descriptor: [Multiple Pulmonary Nodules] explode all trees
#9 (Bronchiolo-Alveolar Carcinomas):ti,ab,kw OR (Adenocarcinomas, Lung):ti,ab,kw OR (Carcinoma, Alveolar):ti,ab,kw OR (Bronchiolo-Alveolar Carcinoma):ti,ab,kw OR (Carcinomas, Bronchial):ti,ab,kw OR (Carcinomas, Alveolar):ti,ab,kw OR (Pulmonary Nodules, Multiple):ti,ab,kw OR (Non-Small-Cell Lung Carcinoma):ti,ab,kw OR (Cancer, Pulmonary):ti,ab,kw OR (Bronchiolar Carcinomas):ti,ab,kw OR (Carcinomas, Bronchiolar):ti,ab,kw OR (Lung Carcinomas, Non-Small-Cell):ti,ab,kw OR (Nonsmall Cell Lung Cancer):ti,ab,kw OR (Alveolar Carcinomas):ti,ab,kw OR (Neoplasm, Bronchial):ti,ab,kw OR (Adenocarcinomas, Alveolar):ti,ab,kw OR (Carcinoma, Bronchiolo-Alveolar):ti,ab,kw OR

(Carcinoma, Bronchiolar):ti,ab,kw OR (Lung Cancers):ti,ab,kw OR (Alveolar Adenocarcinomas):ti,ab,kw OR (Alveolar Cell Carcinoma):ti,ab,kw OR (Bronchiolo-Alveolar Adenocarcinoma):ti,ab,kw OR (Cancer, Lung):ti,ab,kw OR (Carcinomas, Bronchogenic):ti,ab,kw OR (Bronchiolar Carcinoma):ti,ab,kw OR (Neoplasms, Pulmonary):ti,ab,kw OR (Non-Small Cell Lung Cancer):ti,ab,kw OR (Carcinoma, Bronchioloalveolar):ti,ab,kw OR (Carcinoma, Non-Small Cell Lung):ti,ab,kw OR (Alveolar Adenocarcinoma):ti,ab,kw OR (Adenocarcinoma, Alveolar):ti,ab,kw OR (Bronchial Carcinoma):ti,ab,kw OR (Pulmonary Nodule, Multiple):ti,ab,kw OR (Carcinoma, Bronchial):ti,ab,kw OR (Carcinomas, Non-Small-Cell Lung):ti,ab,kw OR (Carcinomas, Bronchiolo-Alveolar):ti,ab,kw OR (Neoplasm, Pulmonary):ti,ab,kw OR (Non-Small-Cell Lung Carcinomas):ti,ab,kw OR (Neoplasms, Bronchial):ti,ab,kw OR (Bronchioloalveolar Carcinoma):ti,ab,kw OR (Bronchogenic Carcinomas):ti,ab,kw OR (Carcinoma, Non Small Cell Lung):ti,ab,kw OR (Alveolar Cell Carcinomas):ti,ab,kw OR (Lung Neoplasm):ti,ab,kw OR (Cancers, Pulmonary):ti,ab,kw OR (Bronchogenic Carcinoma):ti,ab,kw OR (Pulmonary Cancers):ti,ab,kw OR (Adenocarcinoma, Bronchiolo Alveolar):ti,ab,kw OR (Lung Adenocarcinoma):ti,ab,kw OR (Non Small Cell Lung Carcinoma):ti,ab,kw OR (Multiple Pulmonary Nodule):ti,ab,kw OR (Lung Cancer):ti,ab,kw OR (Cancer of Lung):ti,ab,kw OR (Lung Adenocarcinomas):ti,ab,kw OR (Neoplasm, Lung):ti,ab,kw OR (Adenocarcinomas, Bronchiolo-Alveolar):ti,ab,kw OR (Bronchial Neoplasm):ti,ab,kw OR (Adenocarcinoma, Lung):ti,ab,kw OR (Pulmonary Neoplasms):ti,ab,kw OR (Carcinomas, Bronchioloalveolar):ti,ab,kw OR (Bronchiolo-Alveolar Adenocarcinomas):ti,ab,kw OR (Lung Carcinoma, Non-Small-Cell):ti,ab,kw OR (Carcinoma, Bronchiolo Alveolar):ti,ab,kw OR (Cancer of the Lung):ti,ab,kw OR (Pulmonary Cancer):ti,ab,kw OR (Neoplasms, Lung):ti,ab,kw OR (Pulmonary Neoplasm):ti,ab,kw OR (Alveolar Carcinoma):ti,ab,kw OR (Carcinomas, Alveolar Cell):ti,ab,kw OR (Cancers, Lung):ti,ab,kw OR (Bronchial Carcinomas):ti,ab,kw OR (Bronchioloalveolar Carcinomas):ti,ab,kw OR (Carcinoma, Alveolar Cell):ti,ab,kw OR (pulmonary nodule):ti,ab,kw OR (lung nodule):ti,ab,kw OR (ground-glass nodule):ti,ab,kw OR (solid nodule):ti,ab,kw OR (subsolid nodule):ti,ab,kw OR (GGO):ti,ab,kw OR (pGGN):ti,ab,kw OR (PSN):ti,ab,kw OR (GGN):ti,ab,kw OR (mGGN):ti,ab,kw OR (SSN):ti,ab,kw OR (SPN):ti,ab,kw OR (NSN):ti,ab,kw OR (LUAD):ti,ab,kw
#10 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 MeSH descriptor: [Artificial Intelligence] explode all trees
#12 MeSH descriptor: [Neural Networks, Computer] explode all trees
#13 MeSH descriptor: [Knowledge Bases] explode all trees
#14 MeSH descriptor: [Biological Ontologies] explode all trees
#15 MeSH descriptor: [Robotics] explode all trees
#16 MeSH descriptor: [Unsupervised Machine Learning] explode all trees
#17 MeSH descriptor: [Fuzzy Logic] explode all trees
#18 MeSH descriptor: [Natural Language Processing] explode all trees
#19 MeSH descriptor: [Machine Learning] explode all trees
#20 MeSH descriptor: [Deep Learning] explode all trees
#21 MeSH descriptor: [Expert Systems] explode all trees
#22 MeSH descriptor: [Supervised Machine Learning] explode all trees
#23 MeSH descriptor: [Computer Heuristics] explode all trees
#24 (Vision System, Computer):ti,ab,kw OR (Machine Learning, Unsupervised):ti,ab,kw OR (Semi supervised Learning):ti,ab,kw OR (Computer Vision Systems):ti,ab,kw OR (Knowledge Representations):ti,ab,kw OR (Machine Learning, Supervised):ti,ab,kw OR (Remote Operation):ti,ab,kw OR (Systems, Computer Vision):ti,ab,kw OR (Network Models, Neural):ti,ab,kw OR (Intelligence, Artificial):ti,ab,kw OR (Computational Neural Network):ti,ab,kw OR (Network, Computer Neural):ti,ab,kw OR (Networks, Computational Neural):ti,ab,kw OR (Soft Robotics):ti,ab,kw OR (Neural Network Models):ti,ab,kw OR (Computer Vision System):ti,ab,kw OR (Perceptrons):ti,ab,kw OR (Soft Robotic):ti,ab,kw OR (System, Computer Vision):ti,ab,kw OR (Models, Neural Network):ti,ab,kw OR (Neural Network Model):ti,ab,kw OR (Networks, Computer Neural):ti,ab,kw OR (Learning, Unsupervised Machine):ti,ab,kw OR (Connectionist Model):ti,ab,kw OR (Intelligence, Computational):ti,ab,kw OR (Expert System):ti,ab,kw OR (Intelligence, Machine):ti,ab,kw OR (Learning, Hierarchical):ti,ab,kw OR (Neural Networks, Computational):ti,ab,kw OR (Operation, Remote):ti,ab,kw OR (Learning, Transfer):ti,ab,kw OR (Robotic, Soft):ti,ab,kw OR (Transfer Learning):ti,ab,kw OR (Learning, Active Machine):ti,ab,kw OR (Telerobotics):ti,ab,kw OR (Network, Neural):ti,ab,kw OR (Systems, Expert):ti,ab,kw OR (Model,

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Neural Network):ti,ab,kw OR (Models, Connectionist):ti,ab,kw OR (Perceptron):ti,ab,kw OR (Knowledge Bases):ti,ab,kw OR (Computational Intelligence):ti,ab,kw OR (Network, Computational Neural):ti,ab,kw OR (Learning from Labeled Data):ti,ab,kw OR (Reasoning, Computer):ti,ab,kw OR (Knowledge Representation):ti,ab,kw OR (Logic, Fuzzy):ti,ab,kw OR (Heuristics, Computer):ti,ab,kw OR (Neural Network, Computer):ti,ab,kw OR (Neural Network):ti,ab,kw OR (Bases, Knowledge):ti,ab,kw OR (Learning, Inductive Machine):ti,ab,kw OR (Operations, Remote):ti,ab,kw OR (Learning, Deep):ti,ab,kw OR (Learning, Supervised Machine):ti,ab,kw OR (Machine Learning, Inductive):ti,ab,kw OR (Model, Connectionist):ti,ab,kw OR (Hierarchical Learning):ti,ab,kw OR (Learning, Machine):ti,ab,kw OR (Networks, Neural):ti,ab,kw OR (Connectionist Models):ti,ab,kw OR (Semi-supervised Learning):ti,ab,kw OR (System, Expert):ti,ab,kw OR (Natural Language Processings):ti,ab,kw OR (Computer Reasoning):ti,ab,kw OR (Computer Neural Network):ti,ab,kw OR (Neural Network, Computational):ti,ab,kw OR (Heuristic, Computer):ti,ab,kw OR (Machine Learning with a Teacher):ti,ab,kw OR (Knowledgebase):ti,ab,kw OR (Language Processing, Natural):ti,ab,kw OR (Knowledge Base):ti,ab,kw OR (Knowledge Acquisition):ti,ab,kw OR (Base, Knowledge):ti,ab,kw OR (Computational Neural Networks):ti,ab,kw OR (Representation, Knowledge):ti,ab,kw OR (Vision Systems, Computer):ti,ab,kw OR (Learning, Semi-supervised):ti,ab,kw OR (Processings, Natural Language):ti,ab,kw OR (Acquisition, Knowledge):ti,ab,kw OR (Neural Networks):ti,ab,kw OR (Machine Intelligence):ti,ab,kw OR (Machine Learning, Active):ti,ab,kw OR (Active Machine Learning):ti,ab,kw OR (Knowledgebases):ti,ab,kw OR (Robotics, Soft):ti,ab,kw OR (Network Model, Neural):ti,ab,kw OR (Inductive Machine Learning):ti,ab,kw OR (Computer Heuristic):ti,ab,kw OR (Remote Operations):ti,ab,kw OR (Computer Neural Networks):ti,ab,kw OR (Language Processings, Natural):ti,ab,kw OR (Processing, Natural Language):ti,ab,kw OR (AI):ti,ab,kw OR (CNN):ti,ab,kw

#25 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24

#26 MeSH descriptor: [Tomography, X-Ray Computed] explode all trees

#27 (tomography scanners, x-ray computed):ti,ab,kw OR (computed tomography):ti,ab,kw OR (computer assisted tomography):ti,ab,kw OR (CT):ti,ab,kw OR (CAT):ti,ab,kw

#28 #26 OR #27

#29 (“invasiveness analysis”):ti,ab,kw OR (“Invasive”):ti,ab,kw OR (“invasiveness”):ti,ab,kw OR (“risk”):ti,ab,kw OR (“Risk Stratification”):ti,ab,kw OR (“Risk assessment”):ti,ab,kw OR (“risk management”):ti,ab,kw OR (“subtype classification”):ti,ab,kw OR (“histological assessment”):ti,ab,kw

#30 #10 AND #25 #28 AND #29

4. Strategy for Web of Science (n=1,066):

#1 TS=(“lung neoplasm*”) OR TS=(“pulmonary neoplasm*”) OR TS=(“lung cancer*”) OR TS=(“lung tumo*”) OR TS=(“lung carcinoma*”) OR TS=(“pulmonary cancer*”) OR TS=(“pulmonary tumo*”) OR TS=(“pulmonary carcinoma*”) OR TS=(“non-small-cell lung cancer*”) OR TS=(“lung adenocarcinoma*”) OR TS=(“pulmonary nodule*”) OR TS=(“lung nodule*”) OR TS=(“ground-glass nodule*”) OR TS=(“solid nodule*”) OR TS=(“subsolid nodule*”) OR TS=(“part-solid nodule*”) OR TS=(“non-solid nodule*”) OR TS=(“GGO”) OR TS=(“pGGN”) OR TS=(“PSN”) OR TS=(“NSN”) OR TS=(“GGN”) OR TS=(“mGGN”) OR TS=(“SPN”) OR TS=(“SSN”) OR TS=(“LUAD”)

#2 TS= (“machine learning”) OR TS=(“Artificial Intelligence”) OR TS=(“Machine Intelligence”) OR TS=(“Computational Intelligence”) OR TS=(“computer-aided”) OR TS= (“deep learning”) OR TS= (“Computer Reasoning”) OR TS= (“Computer Vision System*”) OR TS= (“Knowledge Representation”) OR TS= (“Knowledge Acquisition”) OR TS= (“Expert System*”) OR TS= (“Computer Heuristic*”) OR TS= (“Neural Network*”) OR TS=(“AI”) OR TS=(“CNN”)

#3 TS= (“Tomography, X-Ray Computed”) OR TS= (“computed tomography”) OR TS=(“computer assisted tomography”) OR TS=(“CT”) OR TS=(“CAT”)

#4 TS=(“invasiveness analysis”) OR TS=(“Invasive”) OR TS= (“invasiveness”) OR TS=(“Risk Stratification”) OR TS=(“Risk assessment”) OR TS=(“risk management”) OR TS=(“risk”) OR TS=(“subtype classification”) OR TS= (“histological assessment”)

#5 #1 AND #2 AND #3 AND #4

Appendix 2

Risk of Bias Assessment:
The detailed evaluation criteria:
DOMAIN 1: PATIENT SELECTION
A. Risk of Bias
Were the data sources clear?
Was a consecutive or random sample of patients enrolled?
Were the inclusion/exclusion criteria specified?
Did the study avoid inappropriate exclusions?
B. Applicability
Are there concerns that the included patients and setting do not match the review question?

DOMAIN 2: INDEX TEST(S)
A. Risk of Bias
Were the imaging acquisition protocol and the segmentation annotation method detailed?
Were the datasets composed of several types of scanners?
Was there an independent set of external validations?
B. Applicability
Are there concerns that the index test, its conduct, or interpretation differ from the review question?

DOMAIN 3: REFERENCE STANDARD
A. Risk of Bias
Was the reference standard adequate?
Is the reference standard likely to correctly classify the target condition?
B. Applicability
Are there concerns that the target condition as defined by the reference standard does not match the question?

DOMAIN 4: FLOW AND TIMING
A. Risk of Bias
Was the database clear partition into training, and validation sets?
Was there an appropriate interval between index tests and reference standard?

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Appendix 3

Studies that seemed promising for inclusion during the screening phase but were later excluded.

No.	Study	Reason for exclusion
1.	Chen X, Feng B, Chen Y, *et al.* A CT-based deep learning model for subsolid pulmonary nodules to distinguish minimally invasive adenocarcinoma and invasive adenocarcinoma. Eur J Radiol. 2021;145:110041.doi:10.1016/j.ejrad.2021.110041	No precise nodule segmentation
2.	Chen L, Qi H, Lu D, *et al.* A deep learning based CT image analytics protocol to identify lung adenocarcinoma category and high-risk tumor area. STAR Protoc. 2022;3(3):101485. doi:10.1016/j.xpro.2022.101485	No precise nodule segmentation
3.	K Gao R, Gao Y, Zhang J, Zhu C, Zhang Y, Yan C. A nomogram for predicting invasiveness of lung adenocarcinoma manifesting as pure ground-glass nodules: incorporating subjective CT signs and histogram parameters based on artificial intelligence. J Cancer Res Clin Oncol. 2023;149(17):15323-15333. doi:10.1007/s00432-023-05262-4	No precise nodule segmentation
4.	Le, V., Yang, D., Zhu, Y., Zheng, B., Bai, C., Nguyen, Q., & Shi, H. (2017). Automated Classification of Pulmonary Nodules for Lung Adenocarcinomas Risk Evaluation: An Effective CT Analysis by Clustering Density Distribution Algorithm. Journal of Medical Imaging and Health Informatics, 7, 1753-1758. for	No deep learning-based classification
5.	Gao C, Xiang P, Ye J, Pang P, Wang S, Xu M. Can texture features improve the differentiation of infiltrative lung adenocarcinoma appearing as ground glass nodules in contrast-enhanced CT?. Eur J Radiol. 2019;117:126-131. doi:10.1016/j.ejrad.2019.06.010e Medicine, 199(9). https://doi.org/10.1164/ajrccm-conference.2019.199.1_meetingabstracts.a2605	No deep learning-based classification
6.	Vaidya P, Bera K, Linden PA, *et al.* Combined Radiomic and Visual Assessment for Improved Detection of Lung Adenocarcinoma Invasiveness on Computed Tomography Scans: A Multi-Institutional Study. Front Oncol. 2022;12:902056.doi:10.3389/fonc.2022.902056, Lo, S.-C. B	No deep learning-based classification
7.	Zhang H, Wang S, Deng Z, Li Y, Yang Y, Huang H. Computed tomography-based radiomics machine learning models for prediction of histological invasiveness with sub-centimeter subsolid pulmonary nodules: a retrospective study. PeerJ. 2023;11:e14559. doi:10.7717/peerj.14559	No deep learning-based classification
8.	Chae HD, Park CM, Park SJ, Lee SM, Kim KG, Goo JM. Cd-glass nodules: differentiation of preinvasive lesions from invasive pulmonary adenocarcinomas. Radiology. 2014;273(1):285-293. doi:10.1148/radiol.14132187	No deep learning-based classification
9.	Sun J, Liu K, Tong H, *et al.* CT Texture Analysis for Differentiating Bronchiolar Adenoma, Adenocarcinoma In Situ, and Minimally Invasive Adenocarcinoma of the Lung. Front Oncol. 2021;11:634564. Published 2021 Apr 26. doi:10.3389/fonc.2021.634564 etection. Journal of Global Oncology, 5, 27–27. https://doi.org/10.1200/jgo.2019.5.suppl.27	No deep learning-based classification
10.	Sun J, Zhang L, Hu B, *et al.* Deep learning-based solid component measuring enabled interpretable prediction of tumor invasiveness for lung adenocarcinoma. Lung Cancer. 2023;186:107392. doi:10.1016/j.lungcan.2023.107392 18.08.020	No precise nodule segmentation
11.	Gong J, Liu J, Li H, *et al.* Deep Learning-Based Stage-Wise Risk Stratification for Early Lung Adenocarcinoma in CT Images: A Multi-Center Study. Cancers (Basel). 2021;13(13):3300. Published 2021 Jun 30. doi:10.3390/cancers13133300	No precise nodule segmentation
12.	Pei G, Wang D, Sun K, *et al.* Deep learning-enhanced radiomics for histologic classification and grade stratification of stage IA lung adenocarcinoma: a multicenter study. Front Oncol. 2023;13:1224455. doi:10.3389/fonc.2023.1224455	No precise nodule segmentation
13.	Li Q, Gu YF, Fan L, Li QC, Xiao Y, Liu SY. Effect of CT window settings on size measurements of the solid component in subsolid nodules: evaluation of prediction efficacy of the degree of pathological malignancy in lung adenocarcinoma. Br J Radiol. 2018;91(1088):20180251. doi:10.1259/bjr.20180251	No deep learning-based classification
14.	Lee J, Bartholmai B, Peikert T, *et al.* Evaluation of Computer-Aided Nodule Assessment and Risk Yield (CANARY) in Korean patients for prediction of invasiveness of ground-glass opacity nodule. PLoS One. 2021;16(6):e0253204.doi:10.1371/journal.pone.0253204	No deep learning-based classification

15.	Jiang B, Zhang Y, Zhang L, H de Bock G, Vliegenthart R, Xie X. Human-recognizable CT image features of subsolid lung nodules associated with diagnosis and classification by convolutional neural networks. Eur Radiol. 2021;31(10):7303-7315. doi:10.1007/s00330-021-07901-1	No precise nodule segmentation
16.	Deng J, Zhao M, Li Q, *et al.* Implementation of artificial intelligence in the histological assessment of pulmonary subsolid nodules. Transl Lung Cancer Res. 2021;10(12):4574-4586. doi:10.21037/tlcr-21-971	No precise nodule segmentation
17.	Garzelli L, Goo JM, Ahn SY, *et al.* Improving the prediction of lung adenocarcinoma invasive component on CT: Value of a vessel removal algorithm during software segmentation of subsolid nodules. Eur J Radiol. 2018;100:58-65. doi:10.1016/j.ejrad.2018.01.016	No deep learning-based classification
18.	Xiong Z, Zhao W, Tian D, *et al.* Invasiveness identification in pure ground-glass nodules: exploring the generalizability of radiomics based on external validation and stress testing. J Cancer Res Clin Oncol. 2023;149(14):12723-12735. doi:10.1007/s00432-023-05105-2	No deep learning-based classification
19.	Ren H, Liu F, Xu L, *et al.* Predicting the histological invasiveness of pulmonary adenocarcinoma manifesting as persistent pure ground-glass nodules by ultra-high-resolution CT target scanning in the lateral or oblique body position. Quant Imaging Med Surg. 2021;11(9):4042-4055. doi:10.21037/qims-20-1378	No deep learning-based classification
20.	Zhang R, Hong M, Cai H, *et al.* Predicting the pathological invasiveness in patients with a solitary pulmonary nodule via Shapley additive explanations interpretation of a tree-based machine learning radiomics model: a multicenter study. Quant Imaging Med Surg. 2023;13(12):7828-7841. doi:10.21037/qims-23-615	No deep learning-based classification
21.	Kim H, Lee D, Cho WS, *et al.* CT-based deep learning model to differentiate invasive pulmonary adenocarcinomas appearing as subsolid nodules among surgical candidates: comparison of the diagnostic performance with a size-based logistic model and radiologists. Eur Radiol. 2020;30(6):3295-3305. doi:10.1007/s00330-019-06628-4	No precise nodule segmentation
22.	Ye J, Ling J, Lv Y, Chen J, Cai J, Chen M. Pulmonary adenocarcinoma appearing as ground-glass opacity nodules identified using non-enhanced and contrast-enhanced CT texture analysis: A retrospective analysis. Exp Ther Med. 2020;19(4):2483-2490. doi:10.3892/etm.2020.8511	No deep learning-based classification
23.	Le V, Yang D, Zhu Y, *et al.* Quantitative CT analysis of pulmonary nodules for lung adenocarcinoma risk classification based on an exponential weighted grey scale angular density distribution feature. Comput Methods Programs Biomed. 2018;160:141-151. doi:10.1016/j.cmpb.2018.04.001	No deep learning-based classification
24.	Li S, Yu J, Meng X, *et al.* The feasibility of non-contrast enhanced plus contrast-enhanced computed tomography in discriminating invasive pure ground-glass opacity from pre-invasive pure ground-glass opacity. J Cardiothorac Surg. 2020;15(1):162. doi:10.1186/s13019-020-01159-2	No deep learning-based classification
25.	Liu RS, Ye J, Yu Y, *et al.* The predictive accuracy of CT radiomics combined with machine learning in predicting the invasiveness of small nodular lung adenocarcinoma. Transl Lung Cancer Res. 2023;12(3):530-546. doi:10.21037/tlcr-23-82	No deep learning-based classification
26.	Chen L, Zhang Z. The self-distillation trained multitask dense-attention network for diagnosing lung cancers based on CT scans. Med Phys. 2024;51(3):1738-1753. doi:10.1002/mp.16736	No invasiveness assessment
27.	Lin CY, Guo SM, Lien JJ, *et al.* Combined model integrating deep learning, radiomics, and clinical data to classify lung nodules at chest CT. Radiol Med. 2024;129(1):56-69. doi:10.1007/s11547-023-01730-6	No precise nodule segmentation
28.	Wang S, Wang R, Zhang S, *et al.* 3D convolutional neural network for differentiating pre-invasive lesions from invasive adenocarcinomas appearing as ground-glass nodules with diameters ≤3 cm using HRCT. Quant Imaging Med Surg. 2018;8(5):491-499. doi:10.21037/qims.2018.06.03	No precise nodule segmentation
29.	Wang D, Zhang T, Li M, Bueno R, Jayender J. 3D deep learning based classification of pulmonary ground glass opacity nodules with automatic segmentation. Comput Med Imaging Graph. 2021;88:101814. doi:10.1016/j.compmedimag.2020.101814	Lack of 2×2 data
30.	Zhao W, Yang J, Sun Y, *et al.* 3D Deep Learning from CT Scans Predicts Tumor Invasiveness of Subcentimeter Pulmonary Adenocarcinomas. Cancer Res. 2018;78(24):6881-6889. doi:10.1158/0008-5472.CAN-18-0696	Lack of 2×2 data

 https://dx.doi.org/10.21037/qims-24-1839

31.	Lv Y, Wei Y, Xu K, *et al.* 3D deep learning versus the current methods for predicting tumor invasiveness of lung adenocarcinoma based on high-resolution computed tomography images. Front Oncol. 2022;12:995870. Published 2022 Oct 21. doi:10.3389/fonc.2022.995870	No precise nodule segmentation
32.	Chen X, Feng B, Chen Y, *et al.* A CT-based deep learning model for subsolid pulmonary nodules to distinguish minimally invasive adenocarcinoma and invasive adenocarcinoma. Eur J Radiol. 2021;145:110041. doi:10.1016/j.ejrad.2021.110041	No precise nodule segmentation
33.	Gong J, Liu J, Hao W, *et al.* A deep residual learning network for predicting lung adenocarcinoma manifesting as ground-glass nodule on CT images. Eur Radiol. 2020;30(4):1847-1855. doi:10.1007/s00330-019-06533-w	No precise nodule segmentation
34.	Zhou J, Hu B, Feng W, *et al.* An ensemble deep learning model for risk stratification of invasive lung adenocarcinoma using thin-slice CT. NPJ Digit Med. 2023;6(1):119. Published 2023 Jul 5. doi:10.1038/s41746-023-00866-z	No precise nodule segmentation
35.	Yanagawa M, Niioka H, Hata A, *et al.* Application of deep learning (3-dimensional convolutional neural network) for the prediction of pathological invasiveness in lung adenocarcinoma: A preliminary study. Medicine (Baltimore). 2019;98(25):e16119. doi:10.1097/MD.0000000000016119	No precise nodule segmentation
36.	Zhang H, Wang D, Li W, *et al.* Artificial intelligence system-based histogram analysis of computed tomography features to predict tumor invasiveness of ground-glass nodules. Quant Imaging Med Surg. 2023;13(9):5783-5795. doi:10.21037/qims-23-31	No precise nodule segmentation
37.	Gao J, Qi Q, Li H, *et al.* Artificial-intelligence-based computed tomography histogram analysis predicting tumor invasiveness of lung adenocarcinomas manifesting as radiological part-solid nodules. Front Oncol. 2023;13:1096453. Published 2023 Feb 23. doi:10.3389/fonc.2023.1096453	No precise nodule segmentation
38.	Wang Y, Zhou L, Wang M, *et al.* Combination of generative adversarial network and convolutional neural network for automatic subcentimeter pulmonary adenocarcinoma classification. Quant Imaging Med Surg. 2020;10(6):1249-1264. doi:10.21037/qims-19-982	No precise nodule segmentation
39.	Ding H, Xia W, Zhang L, *et al.* CT-Based Deep Learning Model for Invasiveness Classification and Micropapillary Pattern Prediction Within Lung Adenocarcinoma. Front Oncol. 2020;10:1186. Published 2020 Jul 22. doi:10.3389/fonc.2020.01186	No precise nodule segmentation
40.	Kim H, Lee D, Cho WS, *et al.* CT-based deep learning model to differentiate invasive pulmonary adenocarcinomas appearing as subsolid nodules among surgical candidates: comparison of the diagnostic performance with a size-based logistic model and radiologists. Eur Radiol. 2020;30(6):3295-3305. doi:10.1007/s00330-019-06628-4	No precise nodule segmentation
41.	Kim H, Lee D, Cho WS, *et al.* CT-based deep learning model to differentiate invasive pulmonary adenocarcinomas appearing as subsolid nodules among surgical candidates: comparison of the diagnostic performance with a size-based logistic model and radiologists. Eur Radiol. 2020;30(6):3295-3305. doi:10.1007/s00330-019-06628-4	No precise nodule segmentation
42.	Yu Y, Wang N, Huang N, *et al.* Determining the invasiveness of ground-glass nodules using a 3D multi-task network. Eur Radiol. 2021;31(9):7162-7171. doi:10.1007/s00330-021-07794-0	No precise nodule segmentation
43.	Zuo Z, Zeng W, Peng K, *et al.* Development of a novel combined nomogram integrating deep-learning-assisted CT texture and clinical-radiological features to predict the invasiveness of clinical stage IA part-solid lung adenocarcinoma: a multicentre study. Clin Radiol. 2023;78(10):e698-e706. doi:10.1016/j.crad.2023.07.002	No precise nodule segmentation
44.	Yanagawa M, Niioka H, Kusumoto M, *et al.* Diagnostic performance for pulmonary adenocarcinoma on CT: comparison of radiologists with and without three-dimensional convolutional neural network. Eur Radiol. 2021;31(4):1978-1986. doi:10.1007/s00330-020-07339-x	No precise nodule segmentation
45.	Wang J, Chen X, Lu H, *et al.* Feature-shared adaptive-boost deep learning for invasiveness classification of pulmonary subsolid nodules in CT images. Med Phys. 2020;47(4):1738-1749. doi:10.1002/mp.14068	No precise nodule segmentation

46.	Huang H, Zheng D, Chen H, *et al.* Fusion of CT images and clinical variables based on deep learning for predicting invasiveness risk of stage I lung adenocarcinoma. Med Phys. 2022;49(10):6384-6394. doi:10.1002/mp.15903	No precise nodule segmentation
47.	Zhang T, Wang Y, Sun Y, *et al.* High-resolution CT image analysis based on 3D convolutional neural network can enhance the classification performance of radiologists in classifying pulmonary non-solid nodules. Eur J Radiol. 2021;141:109810. doi:10.1016/j.ejrad.2021.109810	No precise nodule segmentation
48.	Fang W, Zhang G, Yu Y, Chen H, Liu H. Identification of pathological subtypes of early lung adenocarcinoma based on artificial intelligence parameters and CT signs. Biosci Rep. 2022;42(1):BSR20212416. doi:10.1042/BSR20212416	No precise nodule segmentation
49.	Zhao ZR, Yu YH, Lin ZC, *et al.* Invasiveness assessment by artificial intelligence against intraoperative frozen section for pulmonary nodules≤3 cm. J Cancer Res Clin Oncol. 2023;149(10):7759-7765. doi:10.1007/s00432-023-04713-2	No precise nodule segmentation
50.	Marappan S, Mujib MD, Siddiqui AA, Aziz A, Khan S, Singh M. Lightweight Deep Learning Classification Model for Identifying Low-Resolution CT Images of Lung Cancer. Comput Intell Neurosci. 2022;2022:3836539. Published 2022 Aug 30. doi:10.1155/2022/3836539	No precise nodule segmentation
51.	Tao G, Shi D, Yu L, *et al.* Longitudinal prediction of lung nodule invasiveness by sequential modelling with common clinical computed tomography (CT) measurements: a prediction accuracy study. Transl Lung Cancer Res. 2022;11(5):845-857. doi:10.21037/tlcr-22-319	No precise nodule segmentation
52.	Chen L, Qi H, Lu D, *et al.* Machine vision-assisted identification of the lung adenocarcinoma category and high-risk tumor area based on CT images. Patterns (N Y). 2022;3(4):100464. Published 2022 Mar 3. doi:10.1016/j.patter.2022.100464	No deep learning-based classification
53.	Zuo Z, Wang P, Zeng W, Qi W, Zhang W. Measuring pure ground-glass nodules on computed tomography: assessing agreement between a commercially available deep learning algorithm and radiologists' readings. Acta Radiol. 2023;64(4):1422-1430. doi:10.1177/02841851221135406	No invasiveness assessment
54.	Ma C, Yue S. Minimum Sample Size Estimate for Classifying Invasive Lung Adenocarcinoma. Applied Sciences. 2022; 12(17):8469. https://doi.org/10.3390/app12178469	No deep learning-based classification
55.	Zhang Y, Qu H, Tian Y, *et al.* PB-LNet: a model for predicting pathological subtypes of pulmonary nodules on CT images. BMC Cancer. 2023;23(1):936. Published 2023 Oct 3. doi:10.1186/s12885-023-11364-6	No precise nodule segmentation
56.	Ashraf SF, Yin K, Meng CX, *et al.* Predicting benign, preinvasive, and invasive lung nodules on computed tomography scans using machine learning. J Thorac Cardiovasc Surg. 2022;163(4):1496-1505.e10. doi:10.1016/j.jtcvs.2021.02.010	No precise nodule segmentation
57.	Wang X, Li Q, Cai J, *et al.* Predicting the invasiveness of lung adenocarcinomas appearing as ground-glass nodule on CT scan using multi-task learning and deep radiomics. Transl Lung Cancer Res. 2020;9(4):1397-1406. doi:10.21037/tlcr-20-370	Lack of 2×2 data
58.	Zheng, J., Yang, D., Zhu, Y., Gu, W.H., Zheng, B., Bai, C., Zhao, L., Shi, H., Hu, J., Lu, S., Shi, W., & Wang, N. (2020). Pulmonary nodule risk classification in adenocarcinoma from CT images using deep CNN with scale transfer module. IET Image Process., 14, 1481-1489.	Lack of 2×2 data
59.	Ni Y, Yang Y, Zheng D, Xie Z, Huang H, Wang W. The Invasiveness Classification of Ground-Glass Nodules Using 3D Attention Network and HRCT. J Digit Imaging. 2020;33(5):1144-1154. doi:10.1007/s10278-020-00355-9	No precise nodule segmentation
60.	Zhao W, Sun Y, Kuang K, *et al.* ViSTA: A Novel Network Improving Lung Adenocarcinoma Invasiveness Prediction from Follow-Up CT Series. Cancers (Basel). 2022;14(15):3675. Published 2022 Jul 28. doi:10.3390/cancers14153675	No precise nodule segmentation
61.	K. Beck, S. Park, J.H. Hong, S.J. Na, Y.H. Ko.P2.16-02 Predicting Pathological Noninvasiveness in T1 Non-Small Cell Lung Cancer on Chest CT Scan Using Deep Learning Algorithm,Journal of Thoracic Oncology,Volume 13, Issue 10, Supplement,2018,Page S831, ISSN 1556-0864,https://doi.org/10.1016/j.jtho.2018.08.1477.	Conference abstract

62.	Y. She, J. Deng, D. Xie, C. Chen,MA03.07 Development and Validation of Deep Learning Model for Recognition of Histologic Subtype of Lung Adenocarcinoma from CT Images,Journal of Thoracic Oncology,Volume 13, Issue 10, Supplement,2018,Page S364, ISSN 1556-0864,https://doi.org/10.1016/j.jtho.2018.08.336.	Conference abstract
63.	Y. Saeki, S. Kitazawa, N. Kobayashi, S. Kikuchi, Y. Goto, Y. Sato,463P - Prediction of invasiveness in lung adenocarcinoma using machine learning algorithm based on 3D-CT imaging,Annals of Oncology,Volume 30, Supplement 9,2019,Page ix152,ISSN 0923-7534, https://doi.org/10.1093/annonc/mdz435.005.	Conference abstract
64.	Jiajun, D., She, Y., Wang, J., Wang, T., Zhao, M., Yang, W., Wen, Y., Sun, X., Xie, D., & Chen, C. (2020). Invasiveness assessment of deep leaning method for pulmonary subsolid nodules. European Respiratory Journal, 56. Doi:10.1183/13993003.congress-2020.4167	Conference abstract
65.	Zhang B, Yu F, Peng M (2020) Artificial intelligence-assisted CT characterizations and quantitative analysis for differentiating pre-invasive lesions from invasive adenocarcinomas in pulmonary subsolid nodules ≤ 2cm. Journal of Clinical Oncology 38	Conference abstract
66.	Lee J, Park SY, Kim JS (2021) Development of Machine Learning Based Algorithm for Prediction of Invasiveness of Early-Lung Adenocarcinoma by Using Chest Computed Tomography. Medical Physics 48	Conference abstract
67.	Paez R, Kammer MN, Balar A, *et al.* (2022) Risk Stratification of Pulmonary Nodules Using Longitudinal Risk Scores from the Lung Cancer Prediction Convolutional Neural Network (LCP CNN). American Journal of Respiratory and Critical Care Medicine 205. Doi:10.1164/ajrccm-conference.2022.205.1	Conference abstract
68.	Qi LL, Wu BT, Tang W, *et al.* (2020) Long-term follow-up of persistent pulmonary pure ground-glass nodules with deep learning–assisted nodule segmentation. European Radiology 30, 744-755	No invasiveness assessment
69.	Ahn Y, Lee SM, Noh HN, *et al.* (2021) Use of a Commercially Available Deep Learning Algorithm to Measure the Solid Portions of Lung Cancer Manifesting as Subsolid Lesions at CT: Comparisons with Radiologists and Invasive Component Size at Pathologic Examination. Radiology 299, 202-210.Doi: 10.1148/radiol.2021202803	No invasiveness assessment
70.	Cho H-h, Lee HY, Kim E, *et al.* (2021) Radiomics-guided deep neural networks stratify lung adenocarcinoma prognosis from CT scans. Communications Biology 4. Doi:10.1038/s42003-021-02814-7	No invasiveness assessment
71.	Qi LL, Wang JW, Yang L, *et al.* (2021) Natural history of pathologically confirmed pulmonary subsolid nodules with deep learning–assisted nodule segmentation. European Radiology 31, 3884-3897. Doi:10.1007/s00330-020-07450-z	No invasiveness assessment
72.	Gao R, Li T, Tang Y, *et al.* (2022) Reducing uncertainty in cancer risk estimation for patients with indeterminate pulmonary nodules using an integrated deep learning model. Computers in Biology and Medicine 150. Doi: 10.1016/j.compbiomed.2022.106113	No invasiveness assessment
73.	Zhang R, Wei Y, Wang D, *et al.* (2023) Deep learning for malignancy risk estimation of incidental sub-centimeter pulmonary nodules on CT images. European Radiology. Doi: 10.1007/s00330-023-10518-1	No invasiveness assessment
74.	Zhao B, Wang X, Sun K, *et al.* (2023) Correlation Between Intranodular Vessels and Tumor Invasiveness of Lung Adenocarcinoma Presenting as Ground-glass Nodules A Deep Learning 3-Dimensional Reconstruction Algorithm-based Quantitative Analysis on Noncontrast Computed Tomography Images. Journal of Thoracic Imaging 38, 297-303.Doi: 10.1097/rti.0000000000000731	No invasiveness assessment
75.	Maldonado F, Boland JM, Raghunath S, *et al.* (2013) Noninvasive Characterization of the Histopathologic Features of Pulmonary Nodules of the Lung Adenocarcinoma Spectrum using Computer-Aided Nodule Assessment and Risk Yield (CANARY)-A Pilot Study. Journal of Thoracic Oncology 8, 452-460.Doi: 10.1097/JTO.0b013e3182843721	No deep learning-based classification
76.	Raghunath S, Maldonado F, Rajagopalan S, *et al.* (2014) Noninvasive Risk Stratification of Lung Adenocarcinoma using Quantitative Computed Tomography. Journal of Thoracic Oncology 9, 1698-1703.Doi: 10.1097/jto.0000000000000319	No deep learning-based classification

77.	Maldonado F, Duan F, Raghunath SM, *et al.* (2015) Noninvasive Computed Tomography-based Risk Stratification of Lung Adenocarcinomas in the National Lung Screening Trial. American Journal of Respiratory and Critical Care Medicine 192, 737-744.Doi: 10.1164/rccm.201503-0443OC	No deep learning-based classification
78.	Liu J, Yang X, Li Y, *et al.* (2022) Development and validation of qualitative and quantitative models to predict invasiveness of lung adenocarcinomas manifesting as pure ground-glass nodules based on low-dose computed tomography during lung cancer screening. Quantitative Imaging in Medicine and Surgery 12, 2917-2931.Doi: 10.21037/qims-21-912	No deep learning-based classification
79.	Xia X, Gong J, Hao W, *et al.* Comparison and Fusion of Deep Learning and Radiomics Features of Ground-Glass Nodules to Predict the Invasiveness Risk of Stage-I Lung Adenocarcinomas in CT Scan. Front Oncol. 2020;10:418. Published 2020 Mar 31. doi:10.3389/fonc.2020.00418	Lack of 2×2 data

Table S1 Clinical characteristics of the selected studies

Author (year)	Nodule type	No. of Patient	No. of nodules	Diameter (mm)[a]	Pathological pattern				Tumor Location					Patient Characteristics	
					AAH	AIS	MIA	IAC	LUL	LLL	RUL	RML	RLL	Age (years)[a]	Gender (M:F)
Chunlong Fu 2023 (37)	GGN	911	999	NR	0	0	529	470	263	124	36	98	152	58.1±18.4	304:695
Jun Wang 2021 (36)	GGN	1626	1640	NR	125[b]	397[b]	309[b]	609b			NR			56±10.8[c]	400:1026[c]
Kang Qi 2024 (35)	pGGN	402	448	12.0±5.01	29	83	235	101	101	65	168	35	79	53.2±11.4	119:283
Sohee Park 2021 (32)	GGN	423	501	Three[d]	8	26	131	336	115[e]	68[e]	154[e]	38[e]	122[e]	Three[f]	181:242
Tianle Shen 2021 (34)	GGN	368	368	1.0 (0.2-4.5)	AAH+AIS (298)		618	875	670	328	949	198	469	57 (15-84)	924:1690
Xiang Wang 2021 (40)	GGN	622	687	Four[g]	113	148	115	311			NR			57 (27–87)	205:417
Yanqiu Wang 2021 (33)	GGN	156	470	NR	benign (143)	AIS+MIA (87)		240			NR			NR	NR
Yao Xu 2021 (38)	GGN	168	168	Two[h]	13	35	107	13	48	22	43	19	36	Two[i]	53:115

[a], denotes as years mean ± standard deviation or mean (range); [b], results of 1440 nodules in the internal set (external dataset: AAH+AIS+MIA =100, IACs =100); [c], 1426 patients in the internal set; [d], total: 13.6±5.9; development set: 13.9±6.2; validation set: 12.1±4.3; [e], four other nodules at the junction of the two lobes: RUL/RLL (n=2); RUL/RML (n=1); LUL/LLL (n=1); [f], total: 59.5±10.1; development set: 59.9±10.1; validation set: 58.0±10.0; [g], AAH: 11 (9–13); AIS: 11 (10–13); MIA:13 (11–16); IAC:18 (15–22); [h], noninvasive: 7.6±2.3; invasive: 9.1±3.9; [i], noninvasive: 46.8±10.4; invasive:49.8±13.0. NR, not reported; GGN, ground-glass nodule; pGGN, pure GGN; AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma; IAC, invasive adenocarcinoma; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; M:F, male: female.

Table S2 Characteristics of image scans

Author (year)	Imaging modality	Scanners	kVp	Reconstruction slice thickness (mm)	Reconstruction modality
Chunlong Fu 2023 (37)	CT	5	120	0.67, 1.0	NR
Jun Wang 2021 (36)	CT	2	120	1.0, 0.75	Sharp kernel (B46/C Filter)
Kang Qi 2024 (35)	CT	8	100 to 120	0.625 to 1.25	NR
Sohee Park 2021 (32)	CT	8	120	1, 1.25, 1.5	B50f kernel
Tianle Shen 2021 (34)	CT	1	NR	1, 5	NR
Xiang Wang 2021 (40)	CT	5	120	0.625, 1.0	STR
Yanqiu Wang 2021 (33)	CT	NR	NR	NR	NR
Yao Xu 2021 (38)	CT	2	120	0.625	NR

NR, not reported; CT, computed tomography; STR, standard algorithm reconstruction.

Table S3 Segmentation results

Author (year)	Manual or automatic	Segmentation method	Compared with the unsegmented model	Segmentation Performance (Dice)
Chunlong Fu 2023 (37)	Manual	ITK-SNAP	No	-
Jun Wang 2021 (36)	Automatic	IMAL-Net	Yes	81.9±1.0
Kang Qi 2024 (35)	Automatic	R3D-18 model for feature extraction; 3D-optimized modified version of the 2D U-Net	No	IAC:0.860 (0.814–0.887); other lesions: 0.838 (0.825–0.876)*
Sohee Park 2021 (32)	Automatic	built-in segmentation engine	No	training set: 0.754; tuning set: 0.742
Tianle Shen 2021 (34)	Manual	MIM software	Yes	-
Xiang Wang 2021 (40)	Manual	MITK	No	-
Yanqiu Wang 2021 (33)	Automatic	region adaptive MRF segmentation model	Yes	0.9144#
Yao Xu 2021 (38)	Manual	ITK-SNAP	Yes	-

*, results of the hold-out test set; #, denotes as overlapping area ratio. NR, not reported; RRCNN, recurrent residual convolutional neural network; MRF, Markov random field; IAC, invasive adenocarcinoma; MITK, Medical Imaging Interaction Toolkit.

Table S4 Summary of bias risks and applicability concerns across included studies using the QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Chunlong Fu 2023 (37)	☺	☺	☺	☺	?	?	☺
Jun Wang 2021 (36)	☹	☹	?	?	☺	☺	☺
Kang Qi 2024 (35)	☺	☺	☺	☺	☹	☺	☺
Sohee Park 2021 (32)	☺	☺	☺	☺	☺	☺	☺
Tianle Shen 2021 (34)	☺	☹	☺	?	☺	☺	☺
Xiang Wang 2021 (40)	☹	☹	?	☺	☺	☺	☺
Yanqiu Wang 2021 (33)	☺	☹	☺	?	☺	☺	☺
Yao Xu 2021 (38)	☺	☹	☺	?	☹	☺	☺

☺, low risk; ☹, High risk; ?, unclear risk.

Table S5 Comparison of classification performance between the human observers and the deep-learning models

Author (year)	Method	AUC	ACC	Sensitivity (%)	Specificity (%)	F1 (%)
Kang Qi 2024 (35)	AI model	0.911 (0.776–0.978)	76.9 (30/39)	50.0 (7/14)	92.0 (23/25)	60.9 (7/11.5)
	reader 1	NR	51.3 (20/39)	64.3 (9/14)	44.0 (11/25)	51.3 (20/39)
	reader 2	NR	79.5 (31/39)	85.7 (12/14)	76.0 (19/25)	75.0 (12/16.0)
	reader 3	NR	66.7 (26/39)	100.0 (14/14)	48.0 (12/25)	68.3 (14/20.5)
	reader 4	NR	71.8 (28/39)	28.6 (4/14)	96.0 (24/25)	42.1 (4/9.5)
Sohee Park 2021 (32)	AI model	0.956	NR	68.0 (56–79)	90.0 (79–96)	NR
	7-mm threshold*	0.835 (0.766–0.904)	76.5 (68.5–82.9)	62.2 (50.1–73.0)	90.7 (82.6–95.3)	NR
	5-mm threshold*	0.835 (0.766–0.904)	75.9 (69.2–81.6)	75.2 (65.2–83.1)	75.2 (65.2–83.1)	NR

*, average performance of six observers to evaluate the predictive value of measurements of the solid portion size. NR, not reported.

Table S6 GRADE summary of evidence

Test result	Study design	Factors that may decrease quality of evidence					Test property (95% CI)	Test result	Certainty of evidence
		Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias			
Sensitivity (TP + FN)	8 Cross-sectional study	Serious[1]	Seriou[s]2	Serious[3]	Not serious	Undetected	0.81 (0.73, 0.87)	TPs FNs	⊕◯◯◯ Very low
Specificity (FP + TN)	8 Cross-sectional study	Serious[1]	Serious[2]	Serious[3]	Not serious	Undetected	0.86 (0.80, 0.90)	FPs TNs	⊕◯◯◯ Very low

[1], several studies with high risk of bias in the QUADAS-2 domains: patient selection and index test. [2], two study with high concerns for applicability in the QUADAS-2 domains: patient selection. [3], large differences in sensitivity and specificity. CI, confidence interval.

