

Table S1 Literature search strategy

1. PubMed

Search number	Query	Results
#1	"Nasopharyngeal Carcinoma"[Mesh]	5,718
#2	((((((((((((((((((Nasopharyngeal Carcinoma[Title/Abstract]) OR (Nasopharyngeal Carcinomas[Title/Abstract])) OR (nasopharynx tumor[Title/Abstract])) OR (epipharynx tumor[Title/Abstract])) OR (epipharynx tumour[Title/Abstract])) OR (nasopharyngeal neoplasms[Title/Abstract])) OR (nasopharyngeal tumor[Title/Abstract])) OR (nasopharyngeal tumour[Title/Abstract])) OR (nasopharynx tumour[Title/Abstract])) OR (rhinopharyngeal tumor[Title/Abstract])) OR (rhinopharynx tumor[Title/Abstract])) OR (rhinopharynx tumour[Title/Abstract])) OR (nasopharynx cancer[Title/Abstract])) OR (epipharynx cancer[Title/Abstract])) OR (nasopharyngeal cancer[Title/Abstract])) OR (rhinopharyngioma[Title/Abstract])) OR (rhinopharynx cancer[Title/Abstract])) OR (epipharyngeal carcinoma[Title/Abstract])) OR (epipharynx carcinoma[Title/Abstract])) OR (naso-pharyngeal carcinoma[Title/Abstract])) OR (nasopharyngeal carcinoma[Title/Abstract])) OR (postnasal space carcinoma[Title/Abstract])) OR (rhino-pharyngeal carcinoma[Title/Abstract])) OR (rhinopharyngeal carcinoma[Title/Abstract])) OR (rhinopharynx carcinoma[Title/Abstract]))	20,075
#3	((((((((((((((((((Nasopharyngeal Carcinoma[Title/Abstract]) OR (Nasopharyngeal Carcinomas[Title/Abstract])) OR (nasopharynx tumor[Title/Abstract])) OR (epipharynx tumor[Title/Abstract])) OR (epipharynx tumour[Title/Abstract])) OR (nasopharyngeal neoplasms[Title/Abstract])) OR (nasopharyngeal tumor[Title/Abstract])) OR (nasopharyngeal tumour[Title/Abstract])) OR (nasopharynx tumour[Title/Abstract])) OR (rhinopharyngeal tumor[Title/Abstract])) OR (rhinopharynx tumor[Title/Abstract])) OR (rhinopharynx tumour[Title/Abstract])) OR (nasopharynx cancer[Title/Abstract])) OR (epipharynx cancer[Title/Abstract])) OR (nasopharyngeal cancer[Title/Abstract])) OR (rhinopharyngioma[Title/Abstract])) OR (rhinopharynx cancer[Title/Abstract])) OR (epipharyngeal carcinoma[Title/Abstract])) OR (epipharynx carcinoma[Title/Abstract])) OR (naso-pharyngeal carcinoma[Title/Abstract])) OR (nasopharyngeal carcinoma[Title/Abstract])) OR (postnasal space carcinoma[Title/Abstract])) OR (rhino-pharyngeal carcinoma[Title/Abstract])) OR (rhinopharyngeal carcinoma[Title/Abstract])) OR (rhinopharynx carcinoma[Title/Abstract])) OR ("Nasopharyngeal Carcinoma"[Mesh])	20,192
#4	"Machine Learning"[Mesh]	51,433
#5	((((((((((((((((((machine learning[Title/Abstract]) OR (Transfer Learning[Title/Abstract])) OR (Deep learning[Title/Abstract])) OR (Hierarchical Learning[Title/Abstract])) OR (Ensemble Learning[Title/Abstract])) OR (artificial intelligence[Title/Abstract])) OR (Prediction model[Title/Abstract])) OR (random forest[Title/Abstract])) OR (neural network[Title/Abstract])) OR (ANN[Title/Abstract])) OR (Support vector machine[Title/Abstract])) OR (SVM[Title/Abstract])) OR (Gradient Boosting Machine[Title/Abstract])) OR (GBM[Title/Abstract])) OR (Nomogram[Title/Abstract])) OR (XGboost[Title/Abstract])) OR (Adaboost[Title/Abstract])) OR (Decision tree[Title/Abstract])) OR (External validation[Title/Abstract])) OR (Risk Prediction[Title/Abstract])) OR (Risk-Prediction[Title/Abstract])) OR (Radiomics[Title/Abstract])) OR (Radiomic[Title/Abstract])) OR (statistical learning[Title/Abstract])) OR (predictive analytics[Title/Abstract]))	265,748
#6	((((((((((((((((((machine learning[Title/Abstract]) OR (Transfer Learning[Title/Abstract])) OR (Deep learning[Title/Abstract])) OR (Hierarchical Learning[Title/Abstract])) OR (Ensemble Learning[Title/Abstract])) OR (artificial intelligence[Title/Abstract])) OR (Prediction model[Title/Abstract])) OR (random forest[Title/Abstract])) OR (neural network[Title/Abstract])) OR (ANN[Title/Abstract])) OR (Support vector machine[Title/Abstract])) OR (SVM[Title/Abstract])) OR (Gradient Boosting Machine[Title/Abstract])) OR (GBM[Title/Abstract])) OR (Nomogram[Title/Abstract])) OR (XGboost[Title/Abstract])) OR (Adaboost[Title/Abstract])) OR (Decision tree[Title/Abstract])) OR (External validation[Title/Abstract])) OR (Risk Prediction[Title/Abstract])) OR (Risk-Prediction[Title/Abstract])) OR (Radiomics[Title/Abstract])) OR (Radiomic[Title/Abstract])) OR (statistical learning[Title/Abstract])) OR (predictive analytics[Title/Abstract])) OR ("Machine Learning"[Mesh])	271,051
#7	"Radiotherapy"[Mesh]	204,166
#8	((((((((((((((((((Radiotherapies[Title/Abstract]) OR (Radiotherapy[Title/Abstract])) OR (Radiation Therapy[Title/Abstract])) OR (Radiation Therapies[Title/Abstract])) OR (Radiation Treatment[Title/Abstract])) OR (Radiation Treatments[Title/Abstract])) OR (Targeted Radiotherapies[Title/Abstract])) OR (Targeted Radiotherapy[Title/Abstract])) OR (Targeted Radiation Therapy[Title/Abstract])) OR (Targeted Radiation Therapies[Title/Abstract])) OR (bioradiant therapy[Title/Abstract])) OR (x ray therapy[Title/Abstract])) OR (x ray treatment[Title/Abstract])) OR (x-ray therapy[Title/Abstract]))	282,256
#9	((((((((((((((((((Radiotherapies[Title/Abstract]) OR (Radiotherapy[Title/Abstract])) OR (Radiation Therapy[Title/Abstract])) OR (Radiation Therapies[Title/Abstract])) OR (Radiation Treatment[Title/Abstract])) OR (Radiation Treatments[Title/Abstract])) OR (Targeted Radiotherapies[Title/Abstract])) OR (Targeted Radiotherapy[Title/Abstract])) OR (Targeted Radiation Therapy[Title/Abstract])) OR (Targeted Radiation Therapies[Title/Abstract])) OR (bioradiant therapy[Title/Abstract])) OR (x ray therapy[Title/Abstract])) OR (x ray treatment[Title/Abstract])) OR (x-ray therapy[Title/Abstract])) OR ("Radiotherapy"[Mesh])	376,249
#10	((((((((((((((((((Radiotherapies[Title/Abstract]) OR (Radiotherapy[Title/Abstract])) OR (Radiation Therapy[Title/Abstract])) OR (Radiation Therapies[Title/Abstract])) OR (Radiation Treatment[Title/Abstract])) OR (Radiation Treatments[Title/Abstract])) OR (Targeted Radiotherapies[Title/Abstract])) OR (Targeted Radiotherapy[Title/Abstract])) OR (Targeted Radiation Therapy[Title/Abstract])) OR (Targeted Radiation Therapies[Title/Abstract])) OR (bioradiant therapy[Title/Abstract])) OR (x ray therapy[Title/Abstract])) OR (x ray treatment[Title/Abstract])) OR (x-ray therapy[Title/Abstract])) OR ("Radiotherapy"[Mesh]) AND (((((((((((((((((((machine learning[Title/Abstract]) OR (Transfer Learning[Title/Abstract])) OR (Deep learning[Title/Abstract])) OR (Hierarchical Learning[Title/Abstract])) OR (Ensemble Learning[Title/Abstract])) OR (artificial intelligence[Title/Abstract])) OR (Prediction model[Title/Abstract])) OR (random forest[Title/Abstract])) OR (neural network[Title/Abstract])) OR (ANN[Title/Abstract])) OR (Support vector machine[Title/Abstract])) OR (SVM[Title/Abstract])) OR (Gradient Boosting Machine[Title/Abstract])) OR (GBM[Title/Abstract])) OR (Nomogram[Title/Abstract])) OR (XGboost[Title/Abstract])) OR (Adaboost[Title/Abstract])) OR (Decision tree[Title/Abstract])) OR (External validation[Title/Abstract])) OR (Risk Prediction[Title/Abstract])) OR (Risk-Prediction[Title/Abstract])) OR (Radiomics[Title/Abstract])) OR (Radiomic[Title/Abstract])) OR (statistical learning[Title/Abstract])) OR (predictive analytics[Title/Abstract])) OR ("Machine Learning"[Mesh])) AND (((((((((((((((((((Nasopharyngeal Carcinoma[Title/Abstract]) OR (Nasopharyngeal Carcinomas[Title/Abstract])) OR (nasopharynx tumor[Title/Abstract])) OR (epipharynx tumor[Title/Abstract])) OR (epipharynx tumour[Title/Abstract])) OR (nasopharyngeal neoplasms[Title/Abstract])) OR (nasopharyngeal tumor[Title/Abstract])) OR (nasopharyngeal tumour[Title/Abstract])) OR (rhinopharyngeal tumor[Title/Abstract])) OR (rhinopharynx tumor[Title/Abstract])) OR (rhinopharynx tumour[Title/Abstract])) OR (nasopharynx cancer[Title/Abstract])) OR (epipharynx cancer[Title/Abstract])) OR (nasopharyngeal cancer[Title/Abstract])) OR (rhinopharyngioma[Title/Abstract])) OR (rhinopharynx cancer[Title/Abstract])) OR (epipharyngeal carcinoma[Title/Abstract])) OR (epipharynx carcinoma[Title/Abstract])) OR (naso-pharyngeal carcinoma[Title/Abstract])) OR (nasopharyngeal carcinoma[Title/Abstract])) OR (postnasal space carcinoma[Title/Abstract])) OR (rhino-pharyngeal carcinoma[Title/Abstract])) OR (rhinopharyngeal carcinoma[Title/Abstract])) OR (rhinopharynx carcinoma[Title/Abstract])) OR ("Nasopharyngeal Carcinoma"[Mesh]))	217

2. Cochrane

Search number	Query	Results
#1	MeSH descriptor: [Nasopharyngeal Carcinoma] explode all trees	256
#2	(Nasopharyngeal Carcinoma):ti,ab,kw OR (Nasopharyngeal Carcinomas):ti,ab,kw OR (nasopharynx tumor):ti,ab,kw OR (epipharynx tumor):ti,ab,kw OR (epipharynx tumour):ti,ab,kw (Word variations have been searched)	1767
#3	(nasopharyngeal neoplasms):ti,ab,kw OR (nasopharyngeal tumor):ti,ab,kw OR (nasopharyngeal tumour):ti,ab,kw OR (nasopharynx tumour):ti,ab,kw OR (rhinopharyngeal tumor):ti,ab,kw (Word variations have been searched)	1308
#4	(rhinopharynx tumor):ti,ab,kw OR (rhinopharynx tumour):ti,ab,kw OR (nasopharynx cancer):ti,ab,kw OR (epipharynx cancer):ti,ab,kw OR (nasopharyngeal cancer):ti,ab,kw (Word variations have been searched)	1144
#5	(rhinopharyngioma):ti,ab,kw OR (rhinopharynx cancer):ti,ab,kw OR (epipharyngeal carcinoma):ti,ab,kw OR (epipharynx carcinoma):ti,ab,kw OR (naso-pharyngeal carcinoma):ti,ab,kw (Word variations have been searched)	6
#6	(nasopharyngeal carcinoma):ti,ab,kw OR (postnasal space carcinoma):ti,ab,kw OR (rhino-pharyngeal carcinoma):ti,ab,kw OR (rhinopharyngeal carcinoma):ti,ab,kw OR (rhinopharynx carcinoma):ti,ab,kw (Word variations have been searched)	1749
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	2608
#8	MeSH descriptor: [Machine Learning] explode all trees	274
#9	(machine learning):ti,ab,kw OR (Transfer Learning):ti,ab,kw OR (Deep learning):ti,ab,kw OR (Hierarchical Learning):ti,ab,kw OR (Ensemble Learning):ti,ab,kw (Word variations have been searched)	5292
#10	(artificial intelligence):ti,ab,kw OR (Prediction model):ti,ab,kw OR (random forest):ti,ab,kw OR (neural network):ti,ab,kw OR (ANN):ti,ab,kw (Word variations have been searched)	30863
#11	(Support vector machine):ti,ab,kw OR (SVM):ti,ab,kw OR (Gradient Boosting Machine):ti,ab,kw OR (GBM):ti,ab,kw OR (Nomogram):ti,ab,kw (Word variations have been searched)	2866
#12	(XGboost):ti,ab,kw OR (Adaboost):ti,ab,kw OR (Decision tree):ti,ab,kw OR (External validation):ti,ab,kw OR (Risk Prediction):ti,ab,kw (Word variations have been searched)	29984
#13	(Risk-Prediction):ti,ab,kw OR (Radiomics):ti,ab,kw OR (Radiomic):ti,ab,kw OR (statistical learning):ti,ab,kw OR (predictive analytics):ti,ab,kw (Word variations have been searched)	8734
#14	#8 OR #9 OR #10 OR #11 OR #12 OR #13	60698
#15	MeSH descriptor: [Radiotherapy] explode all trees	6696
#16	(Radiotherapy):ti,ab,kw OR (Radiotherapies):ti,ab,kw OR (Radiation Therapy):ti,ab,kw OR (Radiation Therapies):ti,ab,kw OR (Radiation Treatment):ti,ab,kw (Word variations have been searched)	48473
#17	(Radiation Treatments):ti,ab,kw OR (Targeted Radiotherapies):ti,ab,kw OR (Targeted Radiotherapy):ti,ab,kw OR (Targeted Radiation Therapy):ti,ab,kw OR (Targeted Radiation Therapies):ti,ab,kw (Word variations have been searched)	22991
#18	(bioradiant therapy):ti,ab,kw OR (x ray therapy):ti,ab,kw OR (x ray treatment):ti,ab,kw OR (x-ray therapy):ti,ab,kw (Word variations have been searched)	14410
#19	#15 OR #16 OR #17 OR #18	61883
#20	#7 AND #14 AND #19	72

3. Embase

Search number	Query	Results
#1	'nasopharynx tumor'/exp	32970
#2	'nasopharyngeal carcinomas':ab,ti OR 'nasopharynx tumor':ab,ti OR 'epipharynx tumor':ab,ti OR 'epipharynx tumour':ab,ti OR 'nasopharyngeal neoplasms':ab,ti OR 'nasopharyngeal tumor':ab,ti OR 'nasopharyngeal tumour':ab,ti OR 'nasopharynx tumour':ab,ti OR 'rhinopharyngeal tumor':ab,ti OR 'rhinopharynx tumor':ab,ti OR 'rhinopharynx tumour':ab,ti OR 'nasopharynx cancer':ab,ti OR 'epipharynx cancer':ab,ti OR 'nasopharyngeal cancer':ab,ti OR 'rhinopharyngioma':ab,ti OR 'rhinopharynx cancer':ab,ti OR 'epipharyngeal carcinoma':ab,ti OR 'epipharynx carcinoma':ab,ti OR 'naso-pharyngeal carcinoma':ab,ti OR 'nasopharyngeal carcinoma':ab,ti OR 'postnasal space carcinoma':ab,ti OR 'rhino-pharyngeal carcinoma':ab,ti OR 'rhinopharyngeal carcinoma':ab,ti OR 'rhinopharynx carcinoma':ab,ti	21961
#3	#1 OR #2	34881
#4	'machine learning'/exp	348615
#5	'machine learning':ab,ti OR 'transfer learning':ab,ti OR 'deep learning':ab,ti OR 'hierarchical learning':ab,ti OR 'ensemble learning':ab,ti OR 'artificial intelligence':ab,ti OR 'prediction model':ab,ti OR 'random forest':ab,ti OR 'neural network':ab,ti OR 'ann':ab,ti OR 'support vector machine':ab,ti OR 'svm':ab,ti OR 'gradient boosting machine':ab,ti OR 'gbm':ab,ti OR 'nomogram':ab,ti OR 'xgboost':ab,ti OR 'adaboost':ab,ti OR 'decision tree':ab,ti OR 'external validation':ab,ti OR 'risk prediction':ab,ti OR 'radiomics':ab,ti OR 'radiomic':ab,ti OR 'statistical learning':ab,ti OR 'predictive analytics':ab,ti	374079
#6	#4 OR #5	568645
#7	'radiotherapy'/exp	661590
#8	radiotherapy:ab,ti OR radiotherapies:ab,ti OR 'radiation therapy':ab,ti OR 'radiation therapies':ab,ti OR 'radiation treatment':ab,ti OR 'radiation treatments':ab,ti OR 'targeted radiotherapies':ab,ti OR 'targeted radiotherapy':ab,ti OR 'targeted radiation therapy':ab,ti OR 'targeted radiation therapies':ab,ti OR 'bioradiant therapy':ab,ti OR 'x ray therapy':ab,ti OR 'x ray treatment':ab,ti OR 'x-ray therapy':ab,ti	419142
#9	#8 OR #9	768587
#10	#3 AND #6 AND #9	456

4. Web of Science

Search number	Query	Results
#1	"Nasopharyngeal Carcinoma (Topic) OR Nasopharyngeal Carcinomas (Topic) OR nasopharynx tumor (Topic) OR epipharynx tumor (Topic) OR epipharynx tumour (Topic) OR nasopharyngeal neoplasms (Topic) OR nasopharyngeal tumor (Topic) OR nasopharyngeal tumour (Topic) OR nasopharynx tumour (Topic) OR rhinopharyngeal tumor (Topic) OR rhinopharynx tumor (Topic) OR rhinopharynx tumour (Topic) OR nasopharynx cancer (Topic) OR epipharynx cancer (Topic) OR nasopharyngeal cancer (Topic) OR rhinopharyngioma (Topic) OR epipharyngeal carcinoma (Topic) OR rhinopharynx cancer (Topic) OR epipharynx carcinoma (Topic) OR naso-pharyngeal carcinoma (Topic) OR nasopharyngeal carcinoma (Topic) OR postnasal space carcinoma (Topic) OR rhino-pharyngeal carcinoma (Topic) OR rhinopharyngeal carcinoma (Topic) OR rhinopharynx carcinoma (Topic)"	25554
#2	"machine learning (Topic) OR Transfer Learning (Topic) OR Deep learning (Topic) OR Hierarchical Learning (Topic) OR Ensemble Learning (Topic) OR artificial intelligence (Topic) OR Prediction model (Topic) OR random forest (Topic) OR neural network (Topic) OR ANN (Topic) OR Support vector machine (Topic) OR SVM (Topic) OR Gradient Boosting Machine (Topic) OR GBM (Topic) OR Nomogram (Topic) OR XGboost (Topic) OR Adaboost (Topic) OR Decision tree (Topic) OR External validation (Topic) OR Risk Prediction (Topic) OR Risk-Prediction (Topic) OR Radiomics (Topic) OR Radiomic (Topic) OR statistical learning (Topic) OR predictive analytics (Topic)"	2088885
#3	"Radiotherapy (Topic) OR Radiotherapies (Topic) OR Radiation Therapy (Topic) OR Radiation Therapies (Topic) OR Radiation Treatment (Topic) OR Radiation Treatments (Topic) OR Targeted Radiotherapies (Topic) OR Targeted Radiotherapy (Topic) OR Targeted Radiation Therapy (Topic) OR Targeted Radiation Therapies (Topic) OR bioradiant therapy (Topic) OR x ray therapy (Topic) OR x ray treatment (Topic) OR x-ray therapy (Topic)"	565709
#4	"(#3) AND #2) AND #1"	463

Table S2 List of excluded studies

DOI	Title
10.1016/j.ijrobp.2022.01.047	NTCP Modeling for High-Grade Temporal Radionecroses in a Large Cohort of Patients Receiving Pencil Beam Scanning Proton Therapy for Skull Base and Head and Neck Tumors
10.1016/j.radonc.2022.06.008	Longitudinal study of irradiation-induced brain functional network alterations in patients with nasopharyngeal carcinoma
10.1186/s40644-019-0203-y	Application of a machine learning method to whole brain white matter injury after radiotherapy for nasopharyngeal carcinoma
10.1002/hbm.23852	Radiation-induced brain structural and functional abnormalities in presymptomatic phase and outcome prediction
10.5599/admet.5.4.484	Identify the radiotherapy-induced abnormal changes in the patients with nasopharyngeal carcinoma
10.1016/j.ijrobp.2016.06.2111	Multimodal testing of DNA damage response markers for prediction of normal tissue toxicities following head and neck intensity modulated radiation therapy
10.1200/JCO.2022.40.16_suppl.e18063	Voxel-based radiomics outlines spatial heterogeneity of cerebral radiation necrosis (RN) associated with bevacizumab (Bev) response in head and neck radiotherapy (RT) patients
10.1016/j.ijrobp.2022.03.027	Efficacy and Safety of Apatinib for Radiation- induced Brain Injury Among Patients With Head and Neck Cancer: An Open-Label, Single-Arm, Phase 2 Study
10.3389/fonc.2021.720417	Blood-Brain Barrier Repair of Bevacizumab and Corticosteroid as Prediction of Clinical Improvement and Relapse Risk in Radiation-Induced Brain Necrosis: A Retrospective Observational Study
10.1158/1078-0432.CCR-20-1264	A radiomics model for predicting the response to bevacizumab in brain necrosis after radiotherapy

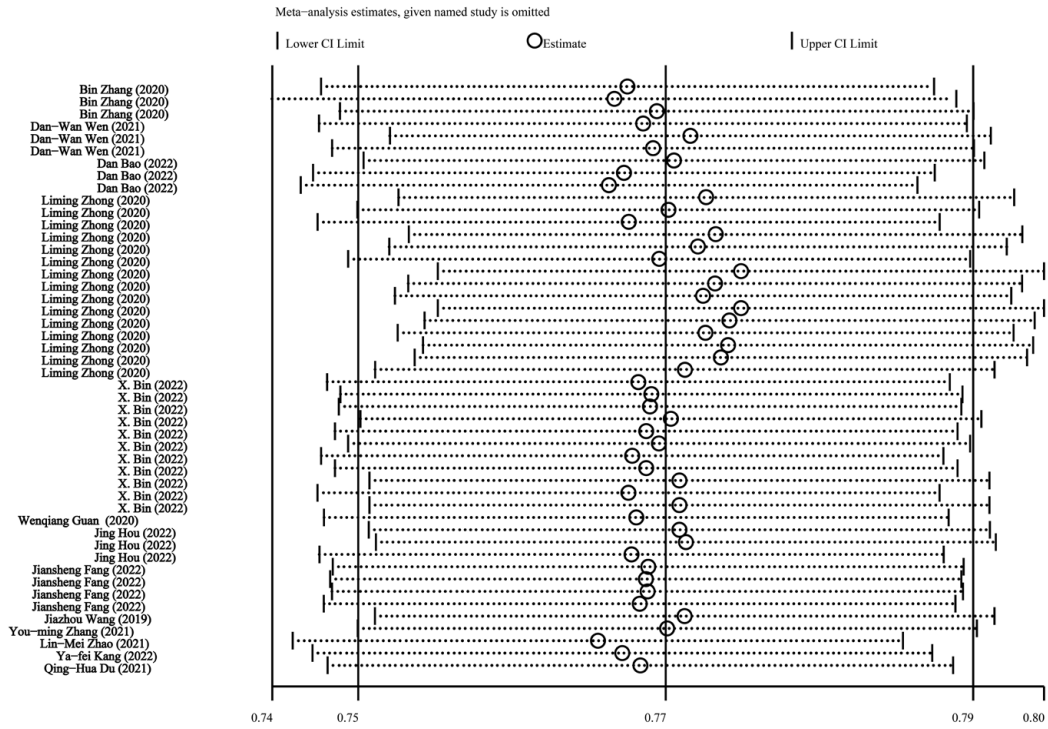
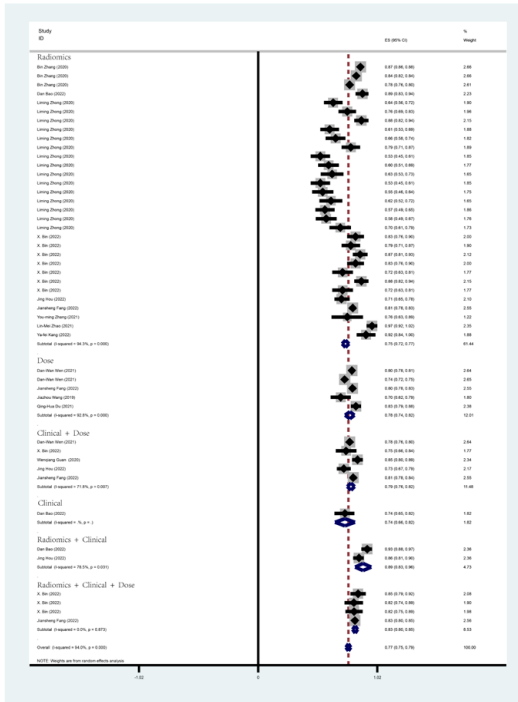
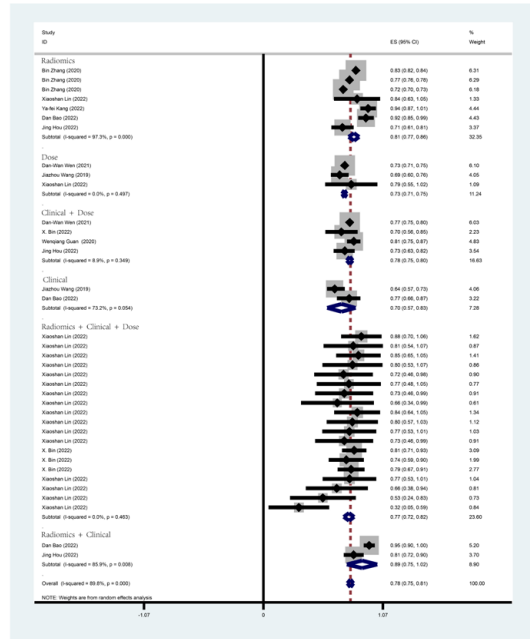


Figure S1 Sensitivity analyses of included models about C-index.

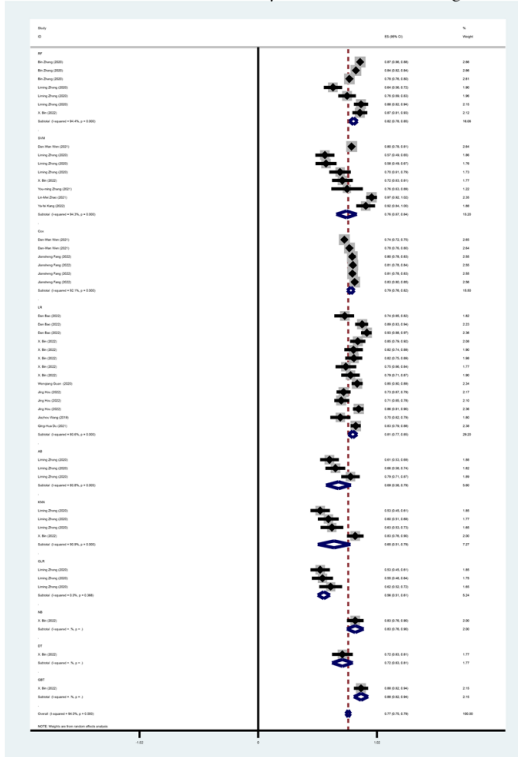
(a) Performance sorted by variable(training set)



(b) Performance sorted by variable(validation set)



(c) Performance sorted by ML method(training set)



(d) Performance sorted by ML method(validation set)

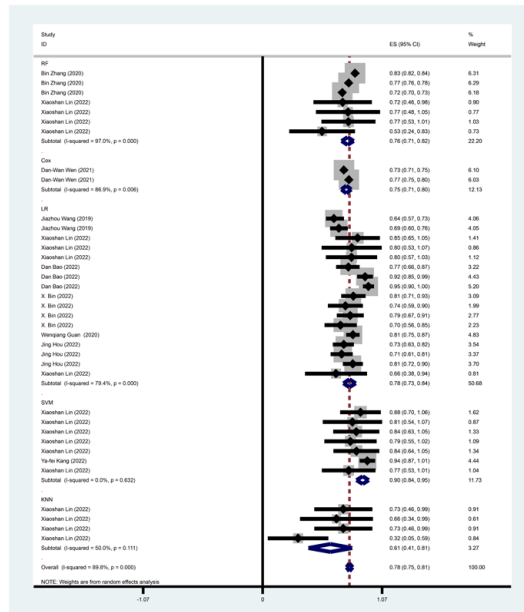


Figure S2 Forest plots of meta-analysis. (A) Performance sorted by variable (training set). (B) Performance sorted by variable (validation set). (C) Performance sorted by ML method (training set). (D) Performance sorted by ML method (validation set). ES, effect size; ML, machine learning; RF, random forest; KNN, k-nearest neighbors; AB, AdaBoost; GLR, generalized linear regression; SVM, support vector machines; LR, logistic regression; NB, Naive Bayes; DT, Decision Tree; GBM, Gradient Boosting Trees; Cox, cox proportional hazards.

Appendix 1

AMSTAR 2			
1. Did the research questions and inclusion criteria for the review include the components of PICO?			
For Yes:	Optional (recommended)		
√ Population	Timeframe for follow-up	√	Yes
√ Intervention			No
√ Comparator group			
√ Outcome			
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?			
For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following:	For Yes: As for partial yes, plus the protocol should be registered and should also have specified:		
√ review question(s)	√ a meta-analysis/synthesis plan, if appropriate, <i>and</i>	√	Yes
√ a search strategy	√ a plan for investigating causes of heterogeneity		Partial Yes
√ inclusion/exclusion criteria	√ justification for any deviations from the protocol		No
√ a risk of bias assessment			
3. Did the review authors explain their selection of the study designs for inclusion in the review?			
For Yes, the review should satisfy ONE of the following:			
√ <i>Explanation for</i> including only RCTs		√	Yes
√ OR <i>Explanation for</i> including only NRSI			No
OR <i>Explanation for</i> including both RCTs and NRSI			
4. Did the review authors use a comprehensive literature search strategy?			
For Partial Yes (all the following):	For Yes, should also have (all the following):		
√ searched at least 2 databases (relevant to research question)	√ searched the reference lists/bibliographies of included studies	√	Yes
√ provided key word and/or search strategy	√ searched trial/study registries		Partial Yes
√ justified publication restrictions (eg, language)	√ included/consulted content experts in the field where relevant, searched for grey literature		No
	√ conducted search within 24 months of completion of the review		
5. Did the review authors perform study selection in duplicate?			
For Yes, either ONE of the following:			
√ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include		√	Yes
OR two reviewers selected a sample of eligible studies <u>and</u> achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer			No
6. Did the review authors perform data extraction in duplicate?			
For Yes, either ONE of the following:			
√ at least two reviewers achieved consensus on which data to extract		√	Yes

from included studies OR two reviewers extracted data from a sample of eligible studies <u>and</u> achieved good agreement (at least 80 per cent), with the remainder extracted by one reviewer	No
7. Did the review authors provide a list of excluded studies and justify the exclusions?	
For Partial Yes: √ provided a list of all potentially relevant studies that were read in full text form but excluded from the review	For Yes, must also have: √ Justified the exclusion from the review of each potentially relevant study
	√ Yes Partial Yes No
8. Did the review authors describe the included studies in adequate detail?	
For Partial Yes (ALL the following): √ described populations √ described interventions √ described comparators √ described outcomes √ described research designs	For Yes, should also have ALL the following: √ described population in detail √ described intervention and comparator in detail (including doses where relevant) √ described study's setting √ timeframe for follow-up
	√ Yes Partial Yes No
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	
RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome
	Yes Partial Yes No Includes only NRSI
NRSI For Partial Yes, must have assessed RoB: √ from confounding, <i>and</i> √ from selection bias	For Yes, must also have assessed RoB: √ methods used to ascertain exposures and outcomes, <i>and</i> √ selection of the reported result from among multiple measurements or analyses of a specified outcome
	√ Yes Partial Yes No Includes only RCTs
10. Did the review authors report on the sources of funding for the studies included in the review?	
For Yes √ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	√ Yes No
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	
RCTs For Yes: The authors justified combining the data in a meta-analysis AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present	Yes No No meta-analysis

AND investigated the causes of any heterogeneity	conducted
For NRSI	
For Yes:	
√ The authors justified combining the data in a meta-analysis	√ Yes
√ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present	No
√ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available	No meta-analysis conducted
AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review	Not Applicable
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	
For Yes:	
included only low risk of bias RCTs	√ Yes
√ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect	No No meta-analysis conducted
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	
For Yes:	
included only low risk of bias RCTs	√ Yes
√ OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results	No
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	
For Yes:	
There was no significant heterogeneity in the results	
√ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	√ Yes No
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	
For Yes:	
√ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	√ Yes No No meta-analysis conducted
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	
For Yes:	
√ The authors reported no competing interests OR The authors described their funding sources and how they managed potential conflicts of interest	√ Yes No