Online Appendix D1 BTS Guideline for Pleural Disease

Section D Pleural malignancy

Question D1 Evidence Review and Protocol

D1 What is the diagnostic accuracy of radiology in adults with suspected pleural malignancy?

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Question Evidence Review

D1 What is the diagnostic accuracy of radiology in adults with suspected pleural malignancy?

Background

Detailed radiological evaluation is commonly performed as part of the assessment for patients with clinical or x-ray findings raising the possibility of pleural malignancy. A range of imaging tools are available including thoracic ultrasound (TUS), computed tomography (CT), positron emission tomography-computed tomography (PET-CT) and magnetic resonance imaging (MRI). Histological confirmation is the gold standard for diagnosis of pleural malignancy, but where tissue sampling is not possible a clinical diagnosis may be made on the basis of disease behaviour over time. This review evaluates the diagnostic accuracy of radiological tests to distinguish malignant from benign pleural pathology. The data presented should be supplemented by reference to Section 5 of the BTS Guideline for the investigation and management of pleural mesothelioma.[1]

Outcome

Diagnostic accuracy of radiological tests

Evidence Review

The initial literature search identified 47 papers. Fourteen studies were deemed suitable (Table D1a), but it should be noted that the high prevalence of malignancy in all groups is likely to be a source of bias.

Table D1a: Summary of included study details

Study	Design	No. patients	Malignant / benign	Modality
Bugalho 2014[2]	PCDS	133	66/67	US
Coolen 2015[3]	PCDS	100	67/33	MRI (DWI) and CT (limited signs)
Hallifax 2015[4]	RCS	370	202/168	CT
Luo 2001[5]	RCCS	64	40/24	MRI and CT
Leung 1990[6]	RCCS	74	39/35	CT
Qureshi 2009[7]	PCC	52	33/19	TUS and CT
Metintas 2002[8]	RCCS	215	138/77	CT
Porcel 2015a[9]	SR	639	407/232	PET/CT
Porcel 2015b[10]	PCS-VC	343 (derivation dataset)	115/228 (derivation dataset)	CT (derivation dataset)
Sun 2016[11]	RCCS	176	108/68	PET/CT
Tsim 2017[12]	PCS	315	195/120	CT
Tsim 2018[13]	PCCS	58	36/58	MRI and CT
Yang 2019[14]	PCS-VC	199 (derivation dataset)	84/199 (derivation dataset)	PET/CT (derivation dataset)
Yilmaz 2005[15]	RCCS	146	36/110	CT

CT – computed tomography; DWI – diffusion-weighted imaging; MRI – magnetic resonance imaging; PCC – prospective comparative cohort; PCS – prospective cohort study; PCS-VC – prospective cohort study/validation cohort; PCCS – prospective comparative cohort study; PDCS – prospective diagnostic cohort study; PET – positron-emission tomography; RCS – retrospective cohort study; RCCS – retrospective case-control series; SR – systematic review; US – ultrasound

Thoracic Ultrasound (TUS)

Ultrasound (US) is a valuable clinical tool for radiologists and physicians. It provides a real time assessment of the thorax, does not expose patients to ionising radiation and its principal role is in the evaluation of patients with pleural effusion at presentation. Two studies evaluated the *diagnostic* role of ultrasound in the diagnosis of malignant pleural effusion. The radiological signs of malignancy on TUS are similar to CT. TUS provides greater ability to assess the diaphragm but is unable to assess the mediastinum. The pooled estimates showed a sensitivity and specificity of 0.80 [0.71 to 0.87] and 0.90 [0.81 to 0.94] respectively [95% confidence intervals] (Figure D1a). Both studies also reported the sensitivity and specificity for individual US features to diagnose malignancy (Table D1b).[2,7]

Table D1b: Sensitivity and specificity values for individual US features of malignancy

Bugalho 2014[2]	**Sensitivity**	**Specificity**	**Qureshi 2009**[7]	**Sensitivity**	**Specificity**
Heterogeneous echogenic pattern present	0.80	0.57	Parietal pleural thickening >1cm	0.42	0.95
Septated pattern absent	0.92	0.25	Nodular pleural thickening	0.42	1.00
Swirling sign present	0.58	0.85	Visceral pleural thickening	0.15	1.00
Pleural/diaphragmatic thickness >10 mm	0.74	0.87	Diaphragmatic thickening >7mm	0.42	0.95
Pleural/diaphragmatic nodularity	0.79	0.91	Diaphragmatic layers resolved	0.30	0.95
Lung air bronchogram sign absent	0.92	0.31	Diaphragmatic nodules	0.30	1.00
Presence of chest wall invasion	0.03	1.00			
Peripheral lung lesion present	0.13	1.00			
Hepatic metastasis present	0.06	1.00			

Computed Tomography (CT)

Six studies provided an assessment of the overall accuracy of CT for the differentiation of malignant and benign pleural disease, but were heterogeneous in design, with variable CT scan technique, contrast timing and reporting strategies. The pooled estimates showed a sensitivity and specificity of 0.80 [0.62 to 0.90] and 0.81 [0.72 to 0.88] respectively [95% confidence intervals] (Figure D1b).[4,5,7,10,12,13]

Technical factors such as available scanner technology, slice thickness and use of intravenous contrast agent alter the diagnostic accuracy of the test and make comparisons between groups problematic. Tsim et al looked at the effect of timing of contrast agent and showed that sensitivity dropped from 0.61 to 0.27 and specificity from 0.82 to 0.69 with a delayed-phase scan and computed tomography pulmonary angiogram (CTPA) respectively for detection of malignancy (data acquisition should be obtained between 60-90 seconds following injection of intravenous contrast to optimise enhancement of the pleura). The same study revealed variability in accuracy between specialist thoracic and non-specialist radiologists with significantly higher sensitivity for specialists.[12]

Three studies have evaluated the CT features of pleural malignancy.[6,8,15] The principal radiological signs for detection of pleural malignancy on CT include pleural thickening that:

i) Is greater than 1 cm in depth
ii) Is circumferential
iii) Involves the mediastinal surface; and
iv) Has nodularity.

Limiting factors were the use of relatively old CT imaging technology and a slice thickness of 10 mm, which is likely to reduce sensitivity for detection of early signs of malignancy. A summary of the pooled analyses of the individual CT features is shown in Table D1c.

Table D1c: Pooled sensitivities and specificities for CT features associated with pleural malignancy

CT feature	No. studies	Sensitivity % [95% CI]	Specificity % [95% CI]
Circumferential pleural thickening	3	0.39 [0.24, 0.56]	0.97 [0.93, 0.98]
Nodular pleural thickening	3	0.40 [0.34, 0.46]	0.96 [0.92, 0.98]
Parietal pleural thickening >1 cm	3	0.40 [0.31, 0.49]	0.90 [0.67, 0.98]
Mediastinal pleural thickening	2	0.66 [0.55, 0.76]	0.85 [0.76, 0.91]

These features may be supplemented by a variety of other markers including nodularity of the fissures, demonstration of a lung lesion or liver metastasis and chest wall or diaphragmatic invasion. The presence of a pericardial effusion; cardiac dilatation; bilateral pleural effusions or loculation make a benign aetiology more likely.[6,10]

Positron Emission Tomography-Computed Tomography (PET-CT)

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography with fused CT images is becoming increasingly available across the UK. FDG uptake is not limited to malignant tissue and may be found in regions of inflammation or infection. Integration of morphological data and PET based on fused PET-CT is thought to increase the sensitivity and specificity of the test, and scoring systems that integrate pulmonary and extra-thoracic findings may be of value in increasing diagnostic accuracy of PET-CT. The PET-CT study pooled estimates for sensitivity and specificity were 0.89 [0.80 to 0.95] and 0.92 [0.88 to 0.95] respectively [95% confidence intervals] (Figure D1g).[11,14]

Porcel et al undertook a systematic review of the PET literature including 14 non-high risk of bias studies comprising 639 patients.[9] Only seven studies evaluated hybrid PET-CT, with the remainder assessing PET only imaging. Measures of diagnostic accuracy for integrated PET-CT data using qualitative and semi-quantitative reading (i.e. standardised uptake values [SUV]) are shown in Table D1d.

Table D1d: Diagnostic accuracy of integrated PET-CT comparing qualitative and semi-quantitative data

	No. studies	Sensitivity [95% CI]	Specificity [95% CI]	LR+ [95% CI]	LR- [95% CI]
Qualitative readings	5	0.85 [0.81, 0.94]	0.61 [0.44, 0.75]	2.32 [1.61, 3.45]	0.19 [0.11, 031]
Semi-quantitative readings	6	0.81 [0.66, 0.91]	0.74 [0.58, 0.85]	3.22 [2.00, 5.00]	0.26 [0.14, 0.43]

LR – likelihood ratio

Magnetic Resonance Imaging (MRI)

MRI in the evaluation of the pleura is relatively uncommon. Limitations to more widespread use include the length of time required for scanning, expertise in reporting and image acquisition and the relative lack of high-quality evidence for its use. Three papers, each assessing different techniques, met the criteria for inclusion. Luo et al assessed morphological assessment of the pleura, using Leung's criteria[6] with MRI, and found it comparable to CT assessment (sensitivity 0.98, specificity 0.92).[5] However, MRI was better able to detect subtle chest wall and/or diaphragmatic infiltration than CT. In addition, malignant pleural disease tended to be hyperintense on T_2-weighted images and gadolinium enhanced T_1-weighted images, unlike benign disease. Coolen et al identified the presence of multiple hyperintense foci on the pleura on high b-value diffusion-weighted images ("pointillism") as a marker of marker of malignancy (sensitivity 0.93, specificity 0.79).[3] Finally, Tsim et al. describe a novel marker of pleural malignancy defined by early contrast enhancement on dynamic contrast-enhanced images which, when combined with recognised morphological features, resulted in sensitivity and specificity of 0.92 and 0.78. However, comparison with CT evaluation in the same cohort (sensitivity 0.56, specificity 0.77) did not show a statistically significant difference.[13]

Imaging Techniques Summary

A summary of each imaging modality meta-analysis is shown in Table D1e and a summary of the MRI results is shown in Table D1f.

Table D1e: Summary of the diagnostic accuracy of thoracic ultrasound (TUS), CT and PET-CT

	Diagnostic accuracy		
Modality	**Pooled Sensitivity [95% CI]**	**Pooled Specificity [95% CI]**	**No. studies**
TUS*	0.80 [0.70, 0.87]	0.90 [0.81, 0.94]	2
CT	0.80 [0.62, 0.90]	0.81 [0.72, 0.88]	6
PET-CT	0.89 [0.80, 0.95]	0.92 [0.88, 0.95]	2

* Studies performed in patients with pleural effusion suspected of pleural malignancy

Table D1f: Summary of the diagnostic accuracy of MRI

	Diagnostic accuracy		
Modality	**Sensitivity**	**Specificity**	**No. studies**
MRI (morphological assessment of pleura)* [5]	0.98	0.92	1
MRI (high b-value diffusion-weighted images) [3]	0.93	0.79	1
MRI (dynamic contrast-enhanced images) [13]	0.92	0.78	1

* Assessment of T_1-weighted, T_2-weighted and contrast-enhanced T_1-weighted images

Evidence statements

TUS allows detailed evaluation of the peripheral pleura in the presence of a pleural effusion and has a moderate sensitivity and high specificity for diagnosing pleural malignancy (**Moderate**)

CT has a moderate sensitivity and specificity for the diagnosis of pleural malignancy (**Low**)

PET-CT has a high sensitivity and specificity for the diagnosis of pleural malignancy (**Low**)

Based on very limited evidence using different techniques, MRI may have a high sensitivity and specificity for diagnosing pleural malignancy (**Ungraded**)

Recommendations

- Ultrasound may be a useful tool at presentation to support a diagnosis of pleural malignancy, particularly in the context of a pleural effusion, where appropriate sonographic skills are present (**Conditional**)
- CT allows assessment of the entire thorax, and positive findings may support a clinical diagnosis of pleural malignancy when biopsy is not an option (**Conditional**), however a negative CT does not exclude malignancy (**Strong** – by consensus)
- PET/CT can be considered to support a diagnosis of pleural malignancy in adults when there are suspicious CT or clinical features and negative histological results, or when invasive sampling is not an option (**Conditional**)

Good Practice Points

- ✓ Imaging can play an important role in the assessment of pleural malignancy, but results should be interpreted in the context of clinical, histological and biochemical markers
- ✓ Features of malignancy may not be present on imaging at presentation. Unless a clear diagnosis is reached by other means (e.g. biopsy), monitoring with follow-up imaging of patients presenting with pleural thickening and unexplained unilateral pleural effusion should be considered to exclude occult malignancy
- ✓ MRI has potential as a diagnostic tool in pleural malignancy. Its clinical value has yet to be determined and its use should be limited to highly selected cases and research studies at the present time

Research Recommendations

- Further research is needed into the relative roles of thoracic ultrasound, CT, MRI and PET-CT for diagnosing malignant pleural disease in adults
- Further research is required to accurately assess the diagnostic accuracy of specific MRI techniques for the diagnosis of malignant pleural disease in adults

Meta-analyses

Diagnostic accuracy table contents and summary receiver operating characteristic (SROC) curve legend

Table contents

Pooled sensitivity [95% confidence intervals]

Pooled specificity [95% confidence intervals]

Likelihood ratio of a positive test result (LR+) [95% confidence intervals]

Likelihood ratio of a negative test result (LR-) [95% confidence intervals]

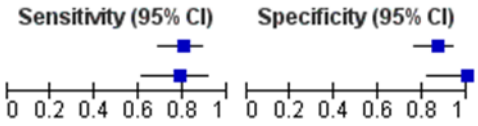
Diagnostic odds ratio (DOR, an indicator of the likelihood of a positive test result) [95% confidence intervals]

Summary receiver operating characteristic (SROC) curve legend

——	SROC
○	Study estimate
●	Summary point
·····	95% confidence region
- - -	95% prediction region

Figure D1a Thoracic ultrasound

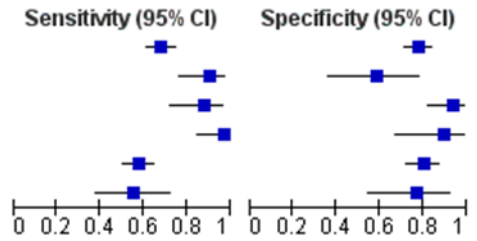
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bugalho 2014	53	9	13	58	0.80 [0.69, 0.89]	0.87 [0.76, 0.94]
Qureshi 2009	26	0	7	19	0.79 [0.61, 0.91]	1.00 [0.82, 1.00]

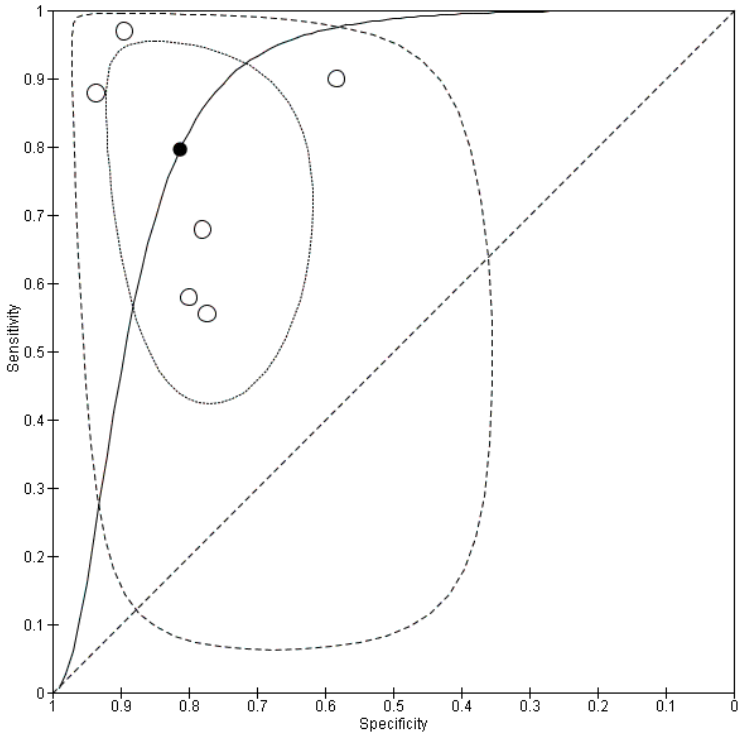


Pooled Sensitivity	0.798	[0.707, 0.866]
Pooled Specificity	0.895	[0.811, 0.945]
LR+	7.625	[2.851, 12.399]
LR-	0.226	[0.136, 0.315]
DOR	33.794	[5.170, 62.418]

Figure D1b Computed tomography

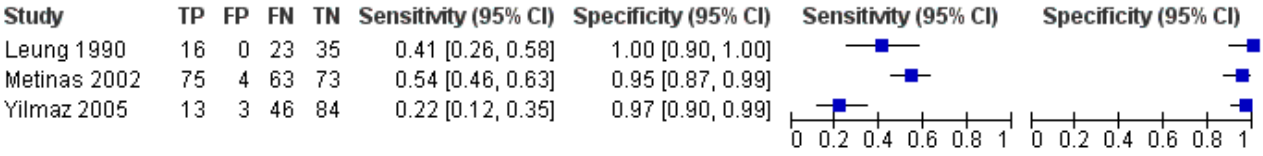
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hallifax 2015	137	37	65	131	0.68 [0.61, 0.74]	0.78 [0.71, 0.84]
Luo 2001	36	10	4	14	0.90 [0.76, 0.97]	0.58 [0.37, 0.78]
Porcel 2015	29	3	4	44	0.88 [0.72, 0.97]	0.94 [0.82, 0.99]
Qureshi 2009	32	2	1	17	0.97 [0.84, 1.00]	0.89 [0.67, 0.99]
Tsim 2017	113	24	82	96	0.58 [0.51, 0.65]	0.80 [0.72, 0.87]
Tsim 2018	20	5	16	17	0.56 [0.38, 0.72]	0.77 [0.55, 0.92]





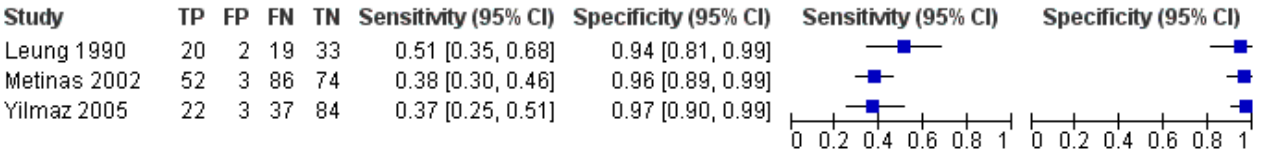
Pooled Sensitivity	0.796	[0.618, 0.904]
Pooled Specificity	0.813	[0.720, 0.880]
LR+	4.253	[2.114, 6.392]
LR-	0.251	[0.067, 0.435]
DOR	16.952	[-2.313, 36.217]

Figure D1c Circumferential pleural thickening



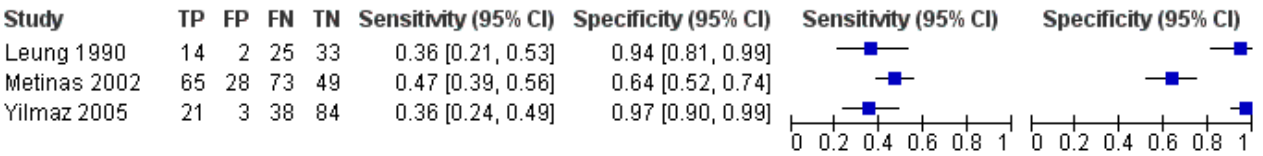
Pooled Sensitivity	0.388	[0.241, 0.558]
Pooled Specificity	0.965	[0.926, 0.984]
LR+	11.068	[2.641, 19.675]
LR-	0.635	[0.468, 0.801]
DOR	17.440	[1.443, 33.438]

Figure D1d Nodular pleural thickening



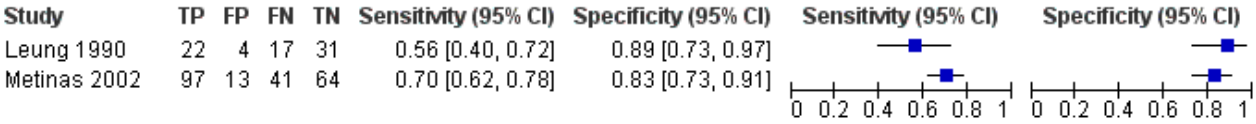
Pooled Sensitivity	0.398	[0.338, 0.462]
Pooled Specificity	0.960	[0.922, 0.980]
LR+	9.908	[3.005, 16.811]
LR-	0.627	[0.559, 0.694]
DOR	15.805	[3.891, 27.718]

Figure D1e Parietal pleural thickening >1 cm



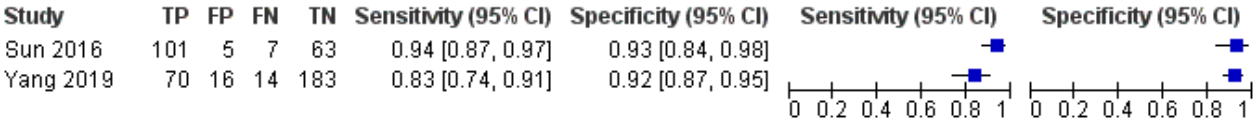
Pooled Sensitivity	0.398	[0.311, 0.492]
Pooled Specificity	0.902	[0.669, 0.976]
LR+	4.405	[-0.969, 9.059]
LR-	0.668	[0.578, 0.758]
DOR	6.057	[-1.941, 14.056]

Figure D1f Mediastinal pleural thickening



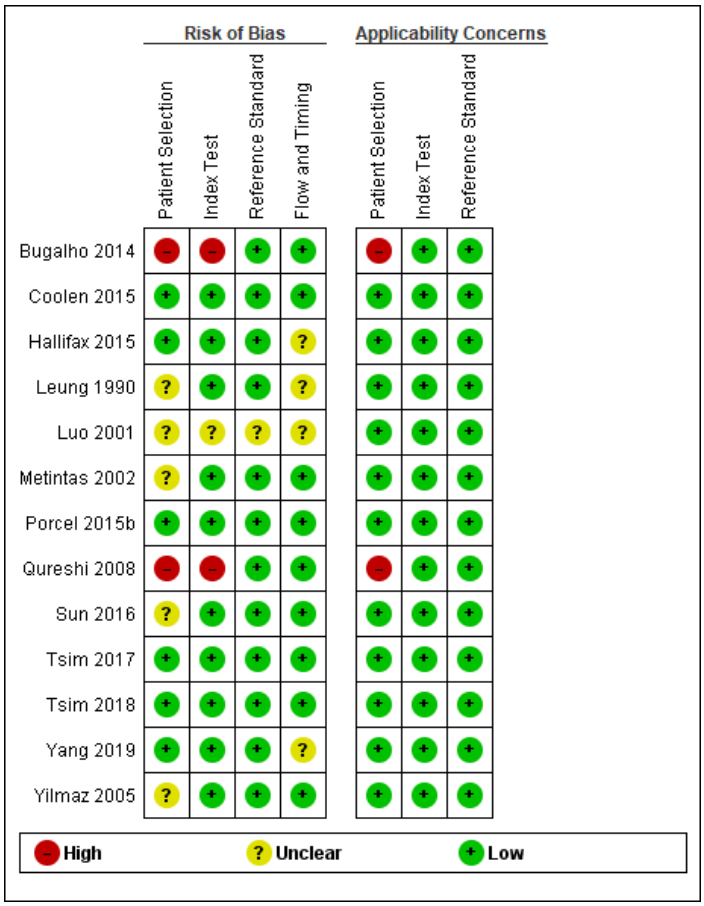
Pooled Sensitivity	0.663	[0.553, 0.758]
Pooled Specificity	0.852	[0.762, 0.912]
LR+	4.471	[2.329, 6.614]
LR-	0.395	[0.278, 0.512]
DOR	11.308	[4.082, 18.534]

Figure D1g PET-CT



Pooled Sensitivity	0.893	[0.800, 0.946]
Pooled Specificity	0.922	[0.879, 0.951]
LR+	11.494	[6.151, 16.836]
LR-	0.116	[0.039, 0.193]
DOR	99.082	[8.590, 189.574]

Risk of bias summary



GRADE analyses

Thoracic Ultrasound (TUS)

What is the diagnostic accuracy of thoracic ultrasound for diagnosing pleural malignancy in adults?
Patient or population: Adults aged 18+ with pleural effusion and suspected pleural malignancy
New test: Thoracic ultrasound
Pooled sensitivity: 0.80 (95% CI: 0.71 to 0.87) | **Pooled specificity**: 0.90 (95% CI: 0.81 to 0.94)

Test result	Number of results per 1,000 patients tested (95% CI)	Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence 20% Typically seen in		
True positives	**160** (141 to 173)	99 (2)	⨁⨁⨁◯ **MODERATE** [a]
False negatives	**40** (27 to 59)		
True negatives	**716** (649 to 756)	86 (2)	⨁⨁⨁◯ **MODERATE** [a]
False positives	**84** (44 to 151)		
	Prevalence 70% Typically seen in		
True positives	**559** (495 to 606)	99 (2)	⨁⨁⨁◯ **MODERATE** [a]
False negatives	**141** (94 to 205)		
True negatives	**269** (243 to 284)	86 (2)	⨁⨁⨁◯ **MODERATE** [a]
False positives	**31** (16 to 57)		

CI: Confidence interval

Explanations

a. No risk of bias, indirectness, inconsistency, imprecision or publication bias, but data downgraded as based on two studies

Computed Tomography (CT)

What is the diagnostic accuracy of CT for diagnosing pleural malignancy in adults?
Patient or population: Adults aged 18+ with suspected pleural malignancy
New test: CT
Pooled sensitivity: 0.80 (95% CI: 0.62 to 0.90) | **Pooled specificity**: 0.81 (95% CI: 0.72 to 0.88)

Test result	Number of results per 1,000 patients tested (95% CI)	Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence 20% Typically seen in		
True positives	**159** (124 to 181)	539 (6)	⨁⨁◯◯ **LOW** [a,b]
False negatives	**41** (19 to 76)		
True negatives	**650** (576 to 704)	400 (6)	⨁⨁◯◯ **LOW** [a,b]
False positives	**150** (96 to 224)		
	Prevalence 70% Typically seen in		
True positives	**557** (433 to 633)	539 (6)	⨁⨁◯◯ **LOW** [a,b]
False negatives	**143** (67 to 267)		
True negatives	**244** (216 to 264)	400 (6)	⨁⨁◯◯ **LOW** [a,b]
False positives	**56** (36 to 84)		

CI: Confidence interval

Explanations

a. Serious risk of bias as all patient in one study have significant pleural effusion therefore not applicable to patients with pleural malignancy and no effusion; unclear information provided in a second study

b. Some inconsistency - some spread in the data and 3/6 datasets lie out with the 95% confidence region

Positron Emission Tomography – Computed Tomography (PET-CT)

What is the diagnostic accuracy of PET-CT for diagnosing pleural malignancy in adults?

Patient or population: Adults aged 18+ with suspected pleural malignancy

New test: PET-CT

Pooled sensitivity: 0.89 (95% CI: 0.80 to 0.95) | **Pooled specificity**: 0.92 (95% CI: 0.88 to 0.95)

Test result	Number of results per 1,000 patients tested (95% CI)	Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence 20% Typically seen in		
True positives	**179** (160 to 189)	192 (2)	⨁⨁◯◯ **LOW** [a]
False negatives	**21** (11 to 40)		
True negatives	**738** (703 to 761)	267 (2)	⨁⨁◯◯ **LOW** [a]
False positives	**62** (39 to 97)		
	Prevalence 70% Typically seen in		
True positives	**625** (560 to 662)	192 (2)	⨁⨁◯◯ **LOW** [a]
False negatives	**75** (38 to 140)		
True negatives	**277** (264 to 285)	267 (2)	⨁⨁◯◯ **LOW** [a]
False positives	**23** (15 to 36)		

CI: Confidence interval

Explanations

a. Some risk of bias as unclear information provided in both studies

Recommendation Tables

Question Details

POPULATION:	Adults (18+) with suspected pleural malignancy
INDEX TESTS:	Thoracic ultrasound (TUS); computed tomography (CT); Positron Emission Tomography – Computed Tomography (PET-CT)
GOLD STANDARD:	Histology
OUTCOME:	Diagnostic accuracy of radiological tests for diagnosing pleural malignancy

Thoracic ultrasound (TUS)

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
☐	☐	☐	☒	☐

CONCLUSIONS

Recommendation

Thoracic ultrasound (TUS) may be a useful tool at presentation to support a diagnosis of pleural malignancy, particularly in the context of a pleural effusion, where appropriate sonographic skills are present

Justification

TUS allows detailed evaluation of the peripheral pleura in the presence of a pleural effusion and has a moderate sensitivity and high specificity for diagnosing pleural malignancy (**Moderate**)

Subgroup considerations

There were not enough data for subgroup consideration (mesothelioma)

Research priorities

Further research is needed into the role of TUS for diagnosing malignant pleural disease in adults

Computed tomography (CT)

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
☐	☐	☐	☒	☐

CONCLUSIONS

Recommendation

CT allows assessment of the entire thorax, and positive findings may support a clinical diagnosis of pleural malignancy when biopsy is not an option, however a negative CT does not exclude malignancy

Justification

CT has a moderate sensitivity and specificity for the diagnosis of pleural malignancy (**Low**)

Subgroup considerations

There were not enough data for subgroup consideration (mesothelioma)

Research priorities

Further research is needed into the role of CT for diagnosing malignant pleural disease in adults

Positron Emission Tomography – Computed Tomography (PET-CT)

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
TEST ACCURACY	Very inaccurate	Inaccurate	**Accurate**	Very accurate		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
☐	☐	☐	☒	☐

CONCLUSIONS

Recommendation
PET/CT can be considered to support a diagnosis of pleural malignancy in adults when there are suspicious CT or clinical features and negative histological results, or when invasive sampling is not an option
Justification
PET-CT has a high sensitivity and specificity for the diagnosis of pleural malignancy (**Low**)
Subgroup considerations
There were not enough data for subgroup consideration (mesothelioma)
Research priorities
Further research is needed into the role of PET-CT for diagnosing malignant pleural disease in adults

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Question Protocol

Field	Content
Review Question	What is the diagnostic accuracy of radiology in adults with suspected pleural malignancy?
Type of review question	Diagnostic accuracy
Objective of the review	When diagnosing pleural malignancy, is one imaging modality (CT, ultrasound, PET and MRI) superior than the others at providing a correct diagnosis?
Eligibility criteria – population / disease / condition / issue / domain	Adults (18+) with suspected pleural malignancy
Eligibility criteria – index test(s)	CT US PET MRI
Eligibility criteria – gold standard	Clinico-pathology
Outcomes and prioritisation	Diagnostic accuracy
Eligibility criteria – study design	RCTs Prospective comparative studies Case series of >100 patients
Other inclusion /exclusion criteria	Non-English language excluded unless full English translation Conference abstracts, Cochrane reviews, systematic reviews, reviews Cochrane reviews and systematic reviews can be referenced in the text, but **DO NOT** use in a meta-analysis

Proposed sensitivity / subgroup analysis, or meta-regression	Mesothelioma
Selection process – duplicate screening / selection / analysis	Agreement should be reached between Guideline members who are working on the question. If no agreement can be reached, a decision should be made by the Guideline co-chairs. If there is still no decision, the matter should be brought to the Guideline group and a decision will be made by consensus
Data management (software)	RevMan5 Meta-analysis data input. Evidence review/considered judgement. Storing Guideline text, tables, figures, etc. MetaDTA Data meta-analyses Gradepro Quality of evidence assessment / Recommendations
Information sources – databases and dates	MEDLINE, Embase, PubMED, Central Register of Controlled Trials and Cochrane Database of Systematic Reviews 1966 - present
Methods for assessing bias at outcome / study level	RevMan5 diagnostic accuracy full review template (based on QUADAS2) (follow instructions in '*BTS Guideline Process Handbook - Diagnostic Accuracy*')
Methods for quantitative analysis – combining studies and exploring (in)consistency	If 3 or more relevant studies: RevMan5 for forest plots, summary ROC plot MetaDTA to combine studies (pooled specificity, sensitivity, likelihood ratios, diagnostic odds ratio and confidence intervals) and calculate RevMan parameters for summary ROC plot (follow instructions in '*BTS Guideline Process Handbook - Diagnostic Accuracy*')
Meta-bias assessment – publication bias, selective reporting bias	GRADEpro Diagnostic accuracy quality of evidence assessment for each index test (follow instructions in '*BTS Guideline Process Handbook - Diagnostic Accuracy*')
Rationale / context – what is known	These tests are all used in the investigation of malignancy. Are there any data that demonstrate the utility of each modality?