

**Management of Malignant Pleural Effusions: An Official American Thoracic Society /
Society of Thoracic Surgeons / Society of Thoracic Radiology Clinical Practice Guideline
*Online Supplement***

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1. Committee composition

The guidelines panel included specialists from multiple disciplines with expertise in the management of MPE and experts in guideline development methodology. Two patients with MPE and their primary caregivers provided insight about important, patient-centered outcomes and reviewed the manuscript.

2. Conflict of Interest management and sponsorship

Committee members disclosed all potential conflicts of interest. Individuals with manageable conflicts took part in discussions of the evidence but did not participate in formulating or grading recommendations.

ATS staff provided logistical support and funding. However, the topics discussed and the final recommendations were not influenced by the views and interests of ATS, other participating societies, or Doctor Evidence.

3. Formulating clinical questions

The committee used expert opinion to identify seven specific questions of importance to patients with known or suspected MPE, their caregivers, and clinicians who treat patients with MPE. Suspected MPE was defined as a pleural effusion in a patient with known malignancy, where other causes (i.e. infection or congestive heart failure) have been excluded. A list of outcomes of interest for each of the clinical questions was created. Outcomes were then rated as “critical”, “important”, or “less important.” As suggested by the GRADE method, only outcomes that were considered ‘critical’ or ‘important’ were considered. Questions were formulated using the Patient/Intervention/Comparator/Outcome (PICO) format.

4. Literature search

Literature searches were conducted using the standard methodology provided by the Cochrane Handbook for Systematic Reviews and recommended by the ATS. We searched for studies published from January 1, 1974 through December 31, 2017 within Medline, EMBASE, and the Cochrane Database of Systematic Reviews using the search strategies described in this supplement (Tables E1-E7). For each PICO question, two panel members (PICO leads) conducted a title and abstract review. Full texts of potentially relevant studies were reviewed by PICO leads to determine eligibility. Using a standardized data collection instrument, we abstracted relevant data on study characteristics, types of participants, interventions and outcomes of interest. Literature search and data abstraction for PICO4 was performed by evidence-based medicine experts at Doctor Evidence (Santa Monica, California, USA), a vendor that specializes in evidence based medicine analytics, employing the same methodology and framework as used for the other PICO questions. Full details of their methodology can be found in the accompanying meta-analysis for PICO4.

5. Evidence review and development of clinical recommendations

We used GRADEpro Guideline Development Tool online software (McMaster University, Hamilton, ON, Canada) to develop evidence profiles for each PICO question (7, 9, 10). The evidence profiles summarized the quality of evidence and results for each outcome of importance, with the exception of select binary outcomes (mortality, need for further pleural interventions, cellulitis, empyema) from PICO 4. To summarize these select results from multiple studies, we reported a risk-of-bias assessment and performed meta-analysis using random effects models within Review Manager software (RevMan), version 5.3 (Copenhagen:

The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We pooled results for RCTs and observational studies separately and favored evidence from RCTs when making recommendations. We applied evidence from observational studies only when data from RCTs were not available or inconclusive. More detailed methods for the meta-analysis for PICO4 have been provided elsewhere (Iyer et al, Submitted to *Annals ATS*, 2018).

The overall quality of evidence for each outcome was defined as the degree of confidence that an estimate of the effect is correct. The evidence quality therefore depends on overall risk of bias, precision, consistency, directness of the evidence, risk of publication bias, presence of dose-effect, magnitude of effect and the effect of plausible residual confounding. The quality of evidence was categorized as high, moderate, low or very low (table E1).

Recommendations were described as ‘strong’ or ‘conditional’ (also referred to as ‘weak’) and the categorization was based on the evidence to decision framework, which includes the following items: priority of the clinical problem, magnitude of the desirable effects, magnitude of the undesirable effects, overall certainty of the evidence (quality of evidence), variability in patient values, the balance of desirable and undesirable effects of the intervention, acceptability of the intervention and feasibility of implementing the recommendation (11). Recommendations were decided by consensus and none of the PICO questions required voting. The implication of the strength of recommendations for different stakeholders is provided in table E2.

6. Quality of Evidence

Table 1. Quality of Evidence (Confidence in estimates) Grades (8)

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

7. Implication of Recommendations

Table 2. Implication of the strength of recommendation for different users of the guideline

	Strong recommendation	Weak or Conditional recommendation
Patients	Most patients in this situation would want the recommended intervention.	The majority of individuals in this situation would want the suggested intervention, but many would not.
Clinicians	Most patients should receive the recommended course of action.	Different choices will be appropriate for different patients, and that the clinician must help each patient arrive at a management decision consistent with her or his values and preferences.
Policy makers	The recommendation can be adapted as policy in most situations including for the use as performance indicators.	Policies are also more likely to vary between regions/health systems. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

Adapted from the GRADE Handbook (8)

8. Search Strategy Tables

Table E3a: Pre-specified search strategy and study selection criteria for (PICO 1) the use of ultrasound to guide pleural interventions for the management of malignant pleural effusions.

Medline (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Malignant Pleural Effusions	("Pleural Effusion, Malignant"[Mesh] OR "Chylothorax"[Mesh] OR "Chylothorax" OR ("Neoplasms"[Mesh] OR "neoplasm" OR "neoplasms" OR "cancer" OR "cancers" OR "tumor" OR "tumors" OR "tumour" OR "tumours" OR "Malignant" OR "Malignancy" OR "Malignancies") AND ("pleural effusion" OR "pleura effusion" OR "pleura effusions" OR "pleural effusions"))	16,264
2	Pleural Intervention	(Thoracostomy[Mesh] OR Thoracoscopy[Mesh] OR Thoracentesis[Mesh] OR "thoracostomy" OR "thoracostomies" OR "thoracoscopy" OR "thoracoscopies" OR "pleural endoscopy" OR "pleural endoscopies" OR "pleuroscopy" OR "pleuroscopies" OR "thoroscopic surgery" OR "video assisted thoracic surgery" OR "VATS" OR "thoracentesis" OR "thoracenteses" OR "thoracocentesis" OR "thoracocenteses" OR "pleural aspiration" OR "pleural aspirations" OR "pleurocentesis" OR "pleurocenteses" OR "chest aspiration" OR "chest aspirations" OR "intercostal drain" OR "Chest drainage" OR "chest drain")	37,866
3	Ultrasound	("Ultrasonography"[Mesh] OR "ultrasonograph" OR "ultrasonographs" OR "ultrasonography" OR "ultrasonographies" OR "ultrasound" OR "ultrasounds" OR "Echotomography" OR "ultrasonic imaging")	1,338,193
4		#1 AND #2 AND #3	720

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion, (b) compared patients who underwent ultrasound examination before pleural intervention to those who did not, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the

systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3b: Pre-specified search strategy and study selection criteria for (PICO 2) the decision to drain a malignant pleural effusion in an asymptomatic patient.

Medine (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Malignant Pleural Effusions	("Pleural Effusion, Malignant"[Mesh] OR "Chylothorax"[Mesh] OR "Chylothorax" OR ("Neoplasms"[Mesh] OR "neoplasm" OR "neoplasms" OR "cancer" OR "cancers" OR "tumor" OR "tumors" OR "tumour" OR "tumours" OR "Malignant" OR "Malignancy" OR "Malignancies") AND ("pleural effusion" OR "pleura effusion" OR "pleura effusions" OR "pleural effusions"))	16,264
2	Pleural Intervention	(Thoracostomy[Mesh] OR Thoracoscopy[Mesh] OR Thoracentesis[Mesh] OR "thoracostomy" OR "thoracostomies" OR "thoracoscopy" OR "thoracoscopies" OR "pleural endoscopy" OR "pleural endoscopies" OR "pleuroscopy" OR "pleuroscopies" OR "thorascopic surgery" OR "video assisted thoracic surgery" OR "VATS" OR "thoracentesis" OR "thoracenteses" OR "thoracocentesis" OR "thoracocenteses" OR "pleural aspiration" OR "pleural aspirations" OR "pleurocentesis" OR "pleurocenteses" OR "chest aspiration" OR "chest aspirations" OR "intercostal drain" OR "Chest drainage" OR "chest drain")	37,866
3	Asymptomatic	("Asymptomatic Diseases"[Mesh] OR "Asymptomatic" OR "presymptomatic" OR "pre-symptomatic" OR "symptomless")	139,991
4		#1 AND #2 AND #3	79

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled asymptomatic patients with known or suspected malignant pleural effusion, (b) compared patients who underwent therapeutic drainage to those who did not, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3c: Pre-specified search strategy and study selection criteria for (PICO 3) the use of pleural manometry and large-volume thoracentesis in the management of malignant pleural effusions.

Medline (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Malignant Pleural Effusions	("Pleural Effusion, Malignant"[Mesh] OR "Chylothorax"[Mesh] OR "Chylothorax" OR ("Neoplasms"[Mesh] OR "neoplasm" OR "neoplasms" OR "cancer" OR "cancers" OR "tumor" OR "tumors" OR "tumour" OR "tumours" OR "Malignant" OR "Malignancy" OR "Malignancies") AND ("pleural effusion" OR "pleura effusion" OR "pleura effusions" OR "pleural effusions"))	16,264
2	Manometry	(Manometry[Mesh] OR "Manometry" OR "Manometries" OR "Tonometry" OR "tonometries" OR "manometer" OR "manometers")	35,430
3	large volume thoracentesis	((("high volume") OR "large volume")) AND ("Paracentesis"[Mesh] OR Thoracostomy[Mesh] OR Thoracoscopy[Mesh] OR Thoracentesis[Mesh] OR Chest Tubes[Mesh] OR Catheterization, Peripheral[Mesh] OR Drainage[Mesh] OR Talc[Mesh] OR "thoracostomy" OR "thoracostomies" OR "thoracoscopy" OR "thoracoscopies" OR "pleural endoscopy" OR "pleural endoscopies" OR "pleuroscopy" OR "pleuroscopies" OR "thoroscopic surgery" OR "video assisted thoracic surgery" OR "VATS" OR "thoracentesis" OR "thoracenteses" OR "thoracocentesis" OR "thoracocenteses" OR "pleural aspiration" OR "pleural aspirations" OR "pleurocentesis" OR "pleurocenteses" OR "chest aspiration" OR "chest aspirations" OR "pleurx" OR "chest tube" OR "chest tubes" OR "drainage" OR "talc" OR "talcum" OR "poudrage" OR "slurry" OR "paracentesis" OR "paracenteses" OR ("catheterization" OR "catheters" OR "catheter" OR Catheterization[Mesh] OR Catheters, Indwelling[Mesh]) AND ("pigtail" OR "pleura" OR "pleural") OR "Pleurodesis"[Mesh] OR "pleurodesis"))	851
4		#1 OR (#2 AND #3)	41

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion, (b) compared patients who underwent ultrasound examination before pleural intervention to those who did not, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3d: Pre-specified search strategy and study selection criteria for (PICO 4) the use of indwelling pleural catheter versus chemical pleurodesis for the first-line management of malignant pleural effusions.

Medine (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Malignant Pleural Effusions	"Pleural Effusion, Malignant/therapy"[Mesh]	1,230
2	Pleural catheter	(pleural catheter [tiab] OR pleural catheter [ot] OR pleural catheters [tiab] OR pleural catheters [ot])	293
3	Pleural drain	Pleurx [tiab] OR pleurx [ot] OR "Pleural port" [tiab] OR "pleural ports" [tiab] OR "pleural port" [ot] OR "pleural ports" [ot] OR "indwelling tunneled catheter" [tiab] OR "indwelling tunneled catheters" [tiab] OR "indwelling tunneled catheter" [ot] OR "indwelling tunneled catheters" [ot] OR Pleural drain [tiab] OR pleural drains [tiab] OR Pleural drain [ot] OR pleural drains [ot]	155
4	Pigtail catheter	((pigtail catheter [tiab] OR pigtail catheters [tiab] OR pig-tail catheter [tiab] OR pig-tail catheters [tiab] OR pigtail catheter [ot] OR pigtail catheters [ot] OR pig-tail catheter [ot] OR pig-tail catheters [ot]) AND (pleura [tiab] OR pleural [tiab] OR pleura [ot] OR pleural [ot] OR effusion [tiab] OR effusions [tiab] OR effusion [ot] OR effusions [ot] OR chylothorax [tiab] OR chylothorax [ot]))	97
5	Indwelling Pleural catheter	("Catheters, Indwelling"[Mesh] AND (pleura [tiab] OR pleural [tiab] OR pleura [ot] OR pleural [ot] OR effusion [tiab] OR effusions [tiab] OR effusion [ot] OR effusions [ot] OR chylothorax [tiab] OR chylothorax [ot]))	333
6	Malignant Pleural Effusion Catheter	(Catheters, Indwelling [Mesh]) AND (Pleural Effusion, Malignant [Mesh])	130
7	Pleural drainage	("Drainage/instrumentation"[Mesh] AND (pleura [tiab] OR pleural [tiab] OR pleura [ot] OR pleural [ot] OR effusion [tiab] OR effusions [tiab] OR effusion [ot] OR effusions [ot] OR chylothorax [tiab] OR chylothorax [ot]))	470
8	Small bore catheter	(small-bore catheter* [tiab] AND (pleura [tiab] OR pleural [tiab] OR pleura [ot] OR pleural [ot] OR effusion [tiab] OR effusions [tiab] OR effusion [ot] OR effusions [ot] OR chylothorax [tiab] OR chylothorax [ot]))	40
9		#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	2008

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion without non-expandable lung or prior intervention, (b) compared patients

who underwent indwelling pleural catheter placement versus chemical pleurodesis, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3e: Pre-specified search strategy and study selection criteria for (PICO 5) the use of talc slurry versus talc poudrage for the management of malignant pleural effusions.

Medine (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Malignant Pleural Effusions	("Pleural Effusion, Malignant"[Mesh] OR "Chylothorax"[Mesh] OR "Chylothorax" OR (("Neoplasms"[Mesh] OR "neoplasm" OR "neoplasms" OR "cancer" OR "cancers" OR "tumor" OR "tumors" OR "tumour" OR "tumours" OR "Malignant" OR "Malignancy" OR "Malignancies") AND ("pleural effusion" OR "pleura effusion" OR "pleura effusions" OR "pleural effusions"))	16,264
2	Talc	"Talc"[Mesh] OR "talc" OR "talcum" OR "talcum powder"	2,641
3	Slurry or poudrage	"Talc pleurodesis" OR "pleurodesis" OR "poudrage" OR "slurry"	8,497
4		#1 AND #2 AND #3	496

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion without non-expandable lung or prior intervention, (b) compared patients who underwent talc pleurodesis via slurry versus poudrage, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3f: Pre-specified search strategy and study selection criteria for (PICO 6) the use of indwelling pleural catheter versus chemical pleurodesis for the management of malignant pleural effusions in patients with non-expandable lung, loculated effusion, or prior failed pleurodesis.

Medline (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Pleurodesis	"Pleurodesis"[Mesh] OR pleurodesis	2,528
2	Failure or recurrent pleural effusion	(Treatment Failure[Mesh] OR "failure" OR "failed" OR "fail") OR (("Recurrence"[Mesh] OR "relapse" OR "relapses" OR "relapsed" OR "recurrent" OR "recurrence") AND ("Pleural Effusion"[Mesh] OR "Chylothorax"[Mesh] OR "pleural effusion" OR "pleural effusions" OR "pleura effusion" OR "pleura effusions" OR "chylothorax" OR "trapped lung" OR "lung entrapment"))	1,052,537
3	Pleural catheter	(Thoracostomy[Mesh] OR Thoracoscopy[Mesh] OR Thoracentesis[Mesh] OR Chest Tubes[Mesh] OR Catheterization, Peripheral[Mesh] OR Drainage[Mesh] OR Talc[Mesh] OR "thoracostomy" OR "thoracostomies" OR "thoracoscopy" OR "thoracoscopies" OR "pleural endoscopy" OR "pleural endoscopies" OR "pleuroscopy" OR "pleuroscopies" OR "thoroscopic surgery" OR "video assisted thoracic surgery" OR "VATS" OR "thoracentesis" OR "thoracenteses" OR "thoracocenteses" OR "pleural aspiration" OR "pleural aspirations" OR "pleurocentesis" OR "pleurocenteses" OR "chest aspiration" OR "chest aspirations" OR "pleurx" OR "chest tube" OR "chest tubes" OR "drainage" OR "talc" OR "talcum" OR "poudrage" OR "slurry") OR (("pleural" OR "pleura" OR "pigtail") AND (Catheterization[Mesh] OR Catheters, Indwelling[Mesh] OR "catheter" OR "catheters" OR "catheterization"))	155,737
4		#1 AND #2 AND #3	632

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion with non-expandable lung, loculations, or prior failed intervention, (b) compared patients who underwent indwelling pleural catheter placement versus chemical pleurodesis, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published

after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

Table E3g: Pre-specified search strategy and study selection criteria for (PICO 7) the use of medical therapy alone versus medical therapy plus discontinuation of catheter in the management of indwelling pleural catheter infections in patients with malignant pleural effusions.

Medine (PubMed) search strategy to identify evidence:

Step	Concept	Search Term	Result
1	Indwelling Pleural Catheter	pleural catheter [tiab] OR pleural catheter [ot] OR pleural catheters [tiab] OR pleural catheters [ot] OR Pleurx [tiab] OR pleurx [ot] OR "Pleural port" [tiab] OR "pleural ports" [tiab] OR "pleural port" [ot] OR "pleural ports" [ot] OR "indwelling tunneled catheter" [tiab] OR "indwelling tunneled catheters" [tiab] OR "indwelling tunneled catheter" [ot] OR "indwelling tunneled catheters" [ot] OR Pleural drain [tiab] OR pleural drains [tiab] OR Pleural drain [ot] OR pleural drains [ot] OR ("Catheters, Indwelling"[Mesh] AND (pleura [tiab] OR pleural [tiab] OR pleura [ot] OR pleural [ot] OR effusion [tiab] OR effusions [tiab] OR effusion [ot] OR effusions [ot] OR chylothorax [tiab] OR chylothorax [ot]))	630
2	Infection	"Infection"[Mesh] OR "Empyema"[Mesh] OR "pleuritis" OR "empyema" OR "infection" OR "infected"	1,666,510
3		#1 AND #2	144

*The same search terms were adapted to strategies to search EMBASE, the Cochrane Central Register of Controlled Clinical Trials, and the Cochrane Database of Systematic Reviews.

Study selection criteria Studies were selected if they (a) enrolled patients with known or suspected malignant pleural effusion with indwelling pleural catheter and associated infection, (b) compared patients who underwent discontinuation versus maintenance of the catheter, and (c) measured patient-important outcomes. We initially sought published systematic reviews that included trials that met these selection criteria, with the plan to search step-wise for randomized trials and then observational studies if no suitable systematic reviews were identified. If such systematic reviews were identified, we planned to combine the systematic review with relevant studies published after the systematic review. Studies identified in this fashion were to be supplemented with unsystematic observations from the committee members.

9. Flow Chart of Search Results (PRISMA) Diagrams

Figure E1: Flow of information through a systematic review examining (PICO #1) the use of ultrasound to guide pleural interventions for the management of malignant pleural effusions

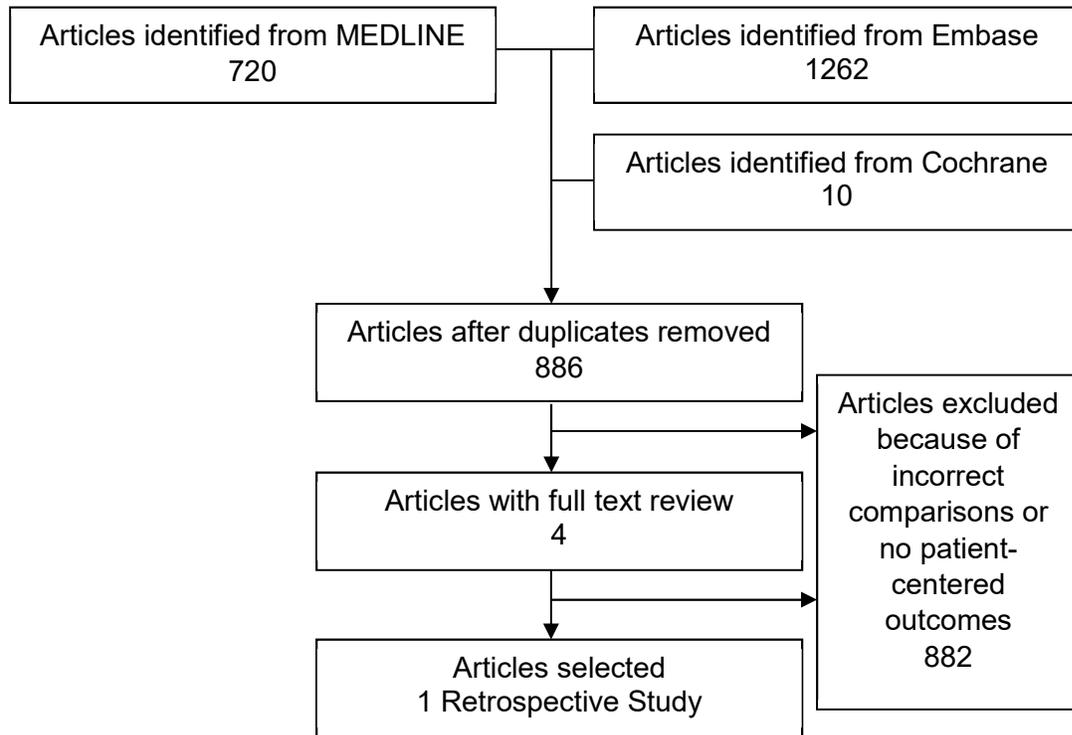


Figure E2: Flow of information through a systematic review examining (PICO #2) the decision to drain a malignant pleural effusion in an asymptomatic patient.

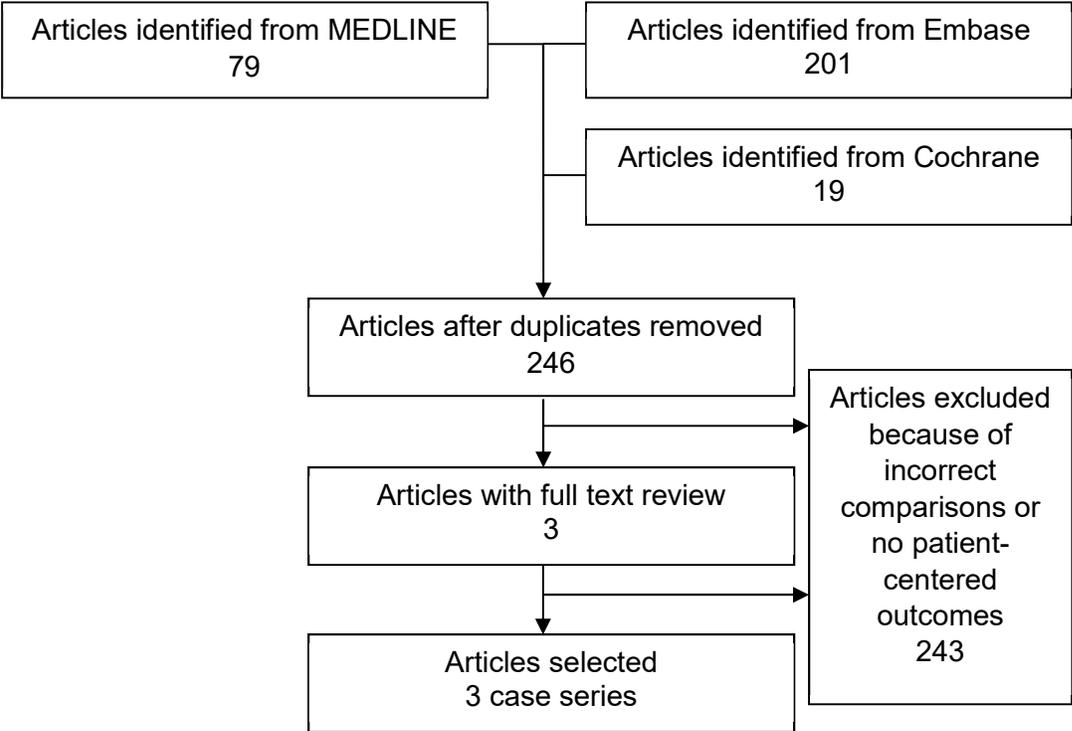


Figure E3: Flow of information through a systematic review examining (PICO #3) the use of pleural manometry and large-volume thoracentesis in the management of malignant pleural effusions.

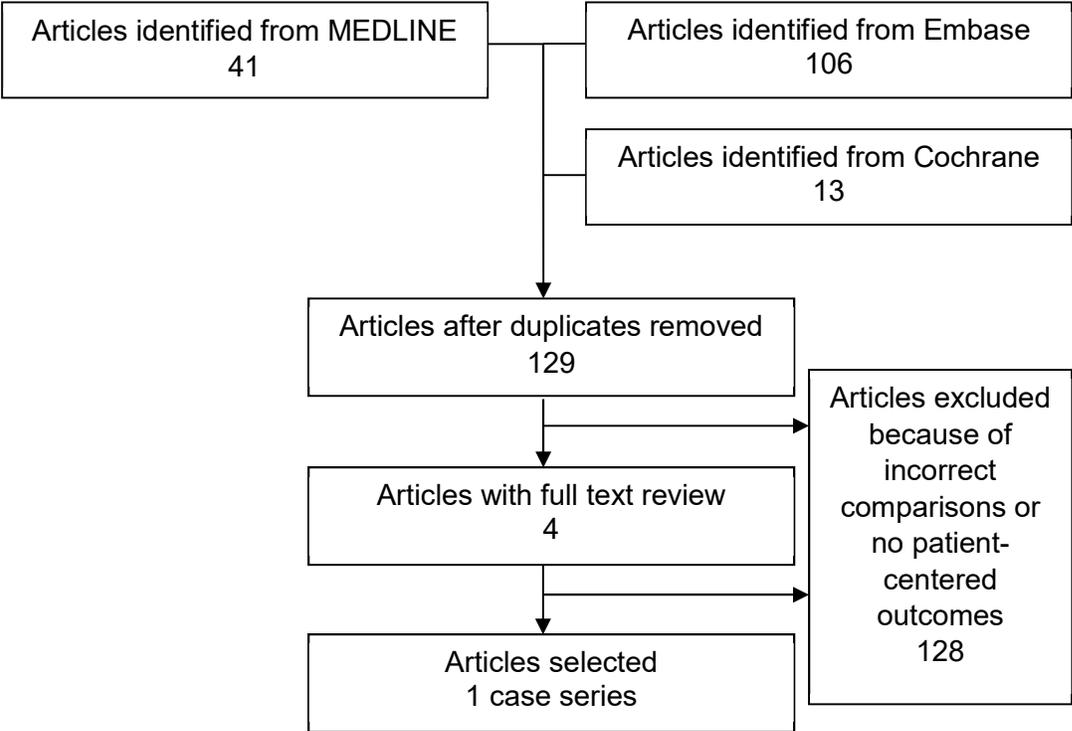


Figure E4: Flow of information through a systematic review examining (PICO #4) the use of indwelling pleural catheter versus chemical pleurodesis for the first-line management of malignant pleural effusions.

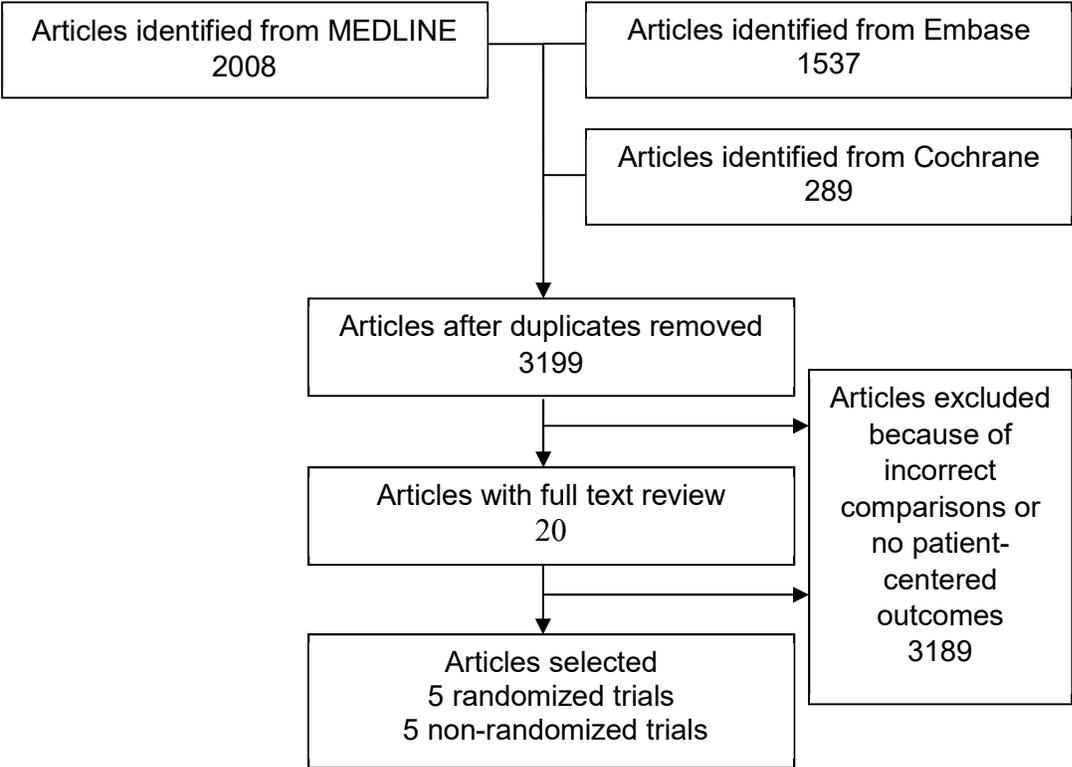


Figure E5: Flow of information through a systematic review examining (PICO #5) the use of talc slurry versus talc poudrage for the management of malignant pleural effusions.

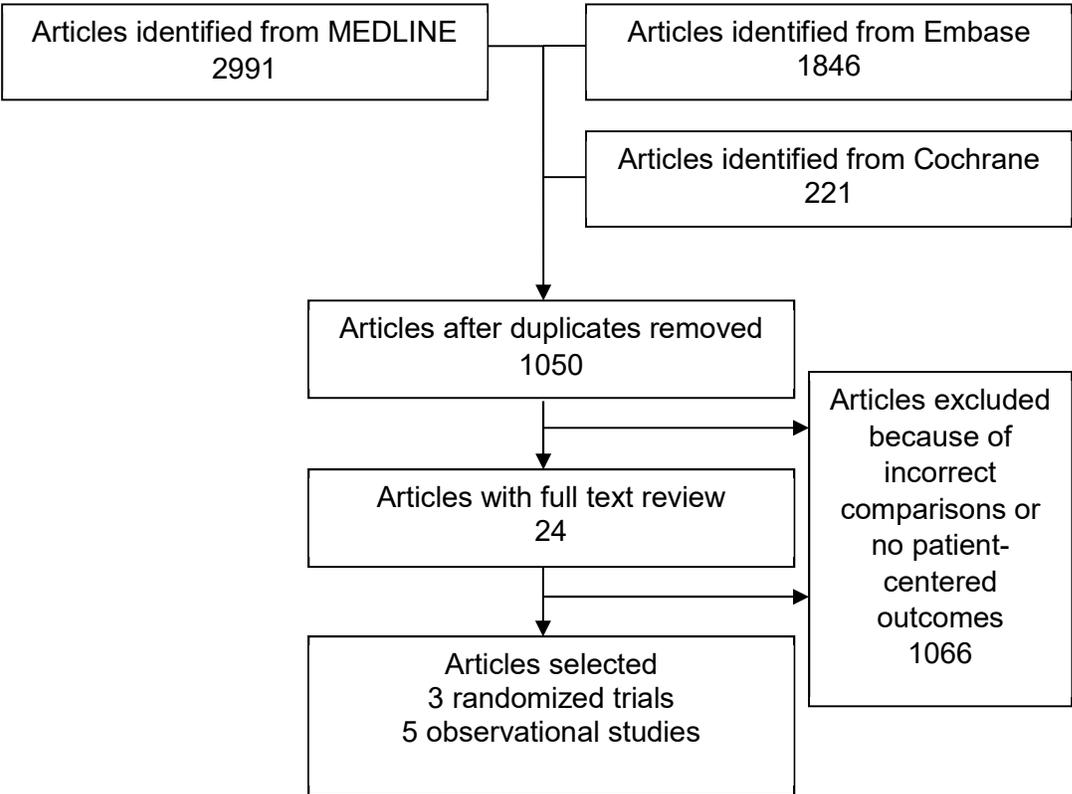


Figure E6: Flow of information through a systematic review examining (PICO #6) the use of indwelling pleural catheter versus chemical pleurodesis for the management of malignant pleural effusions in patients with non-expandable lung, loculated effusion, or prior failed pleurodesis..

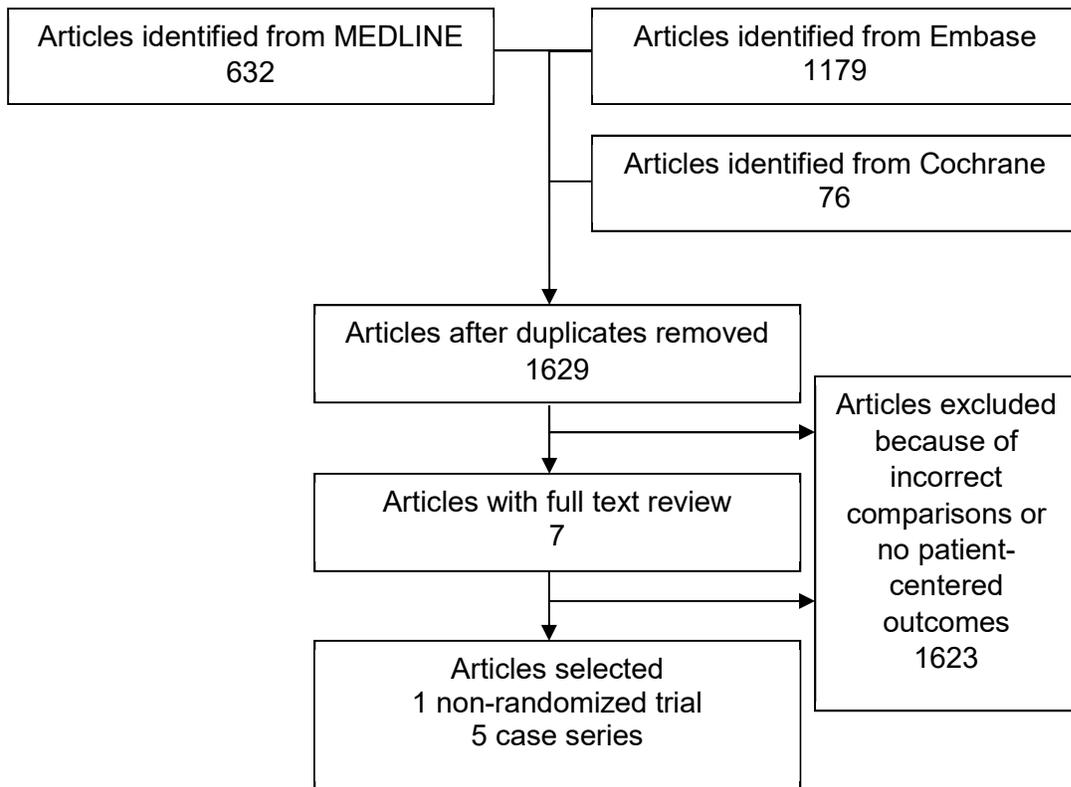
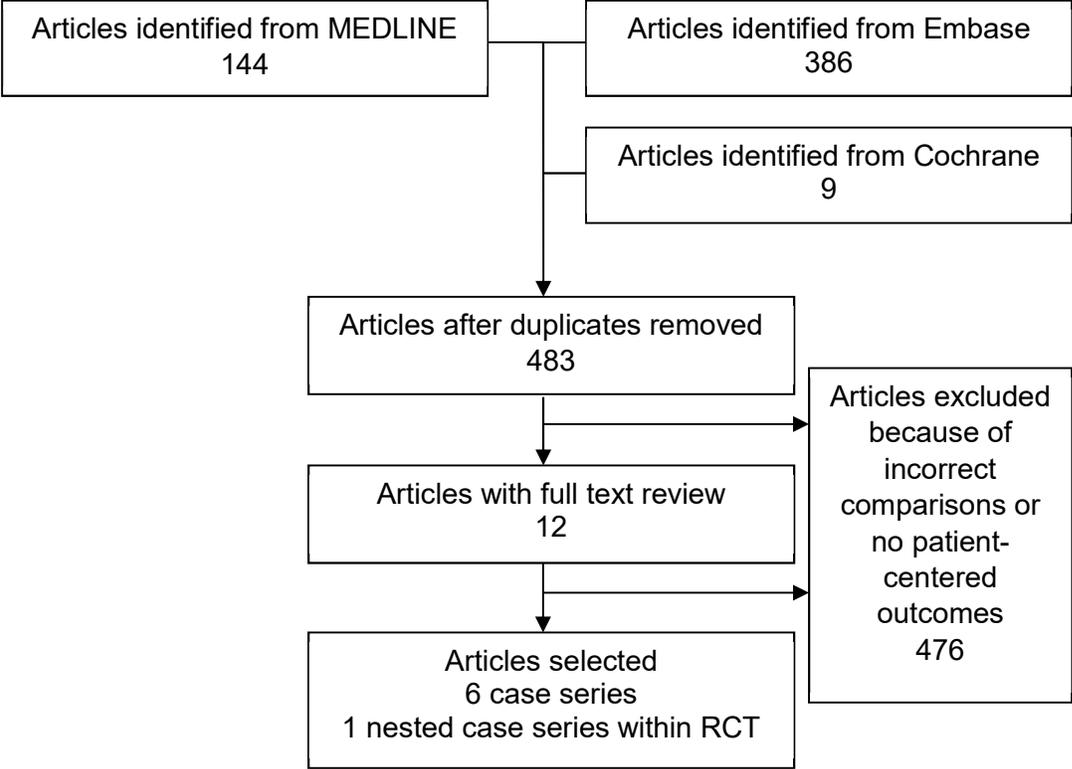


Figure E7: Flow of information through a systematic review examining (PICO #7) the use of medical therapy alone versus medical therapy plus discontinuation of catheter in the management of indwelling pleural catheter infections in patients with malignant pleural effusions.



10. Evidence Profiles

Table E4a: Evidence Profile for PICO 1

Author(s):

Date:

Question: In patients with symptomatic MPE, should thoracic ultrasound be used to guide pleural interventions?

Setting:

Bibliography:

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	thoracic ultrasound	no image guidance	Relative (95% CI)	Absolute (95% CI)		
Pneumothorax rate requiring chest tube after thoracentesis for malignant pleural effusion												
1 ¹	observational studies	serious ^a	not serious	not serious	not serious	none	0/310 (0.0%)	3/135 (2.2%)	not estimable		⊕○○○ VERY LOW	CRITICAL
Pneumothorax rate related to thoracentesis for malignant pleural effusion (assessed with: Retrospective review)												
1 ¹	observational studies	serious ^a	not serious	not serious	not serious	none	3/310 (1.0%)	12/135 (8.9%)	RR 0.10 (0.03 to 0.37)	8 fewer per 100 (from 6 fewer to 9 fewer)	⊕○○○ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Unclear whether post-procedure xray showed procedure-related pneumothorax or pneumothorax ex vacuo.

References

1. Cavanna, . . 2014.

Table E4b: Evidence Profile for PICO 2

Question: In patients with MPE who are asymptomatic, should pleural drainage be performed?

*Because there were no studies directly comparing interventions, results from non-comparative studies are provided in the text.

Table E4c: Evidence Profile for PICO 3

Question: Should the management of patients with MPE be guided by large-volume thoracentesis and pleural manometry?

*Because there were no studies directly comparing interventions, results from non-comparative studies are provided in the text.

Table E4d: Evidence Profile for PICO 4 (with risk of bias assessment)

Author(s):

Date:

Question: In patients with symptomatic MPE with known or suspected expandable lung, should IPCs or chemical pleurodesis be used as first-line definitive pleural intervention?

Setting:

Bibliography:

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Indwelling pleural catheter	pleurodesis	Relative (95% CI)	Absolute (95% CI)		
Dyspnea at 30 days (assessed with: Visual Analog Scale in mm)												
1 ¹	randomised trials	serious ^a	not serious	not serious	not serious	none	73	71	-	mean 2.58 mm higher (5.91 lower to 11.08 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Improvement in dyspnea at 30 days (assessed with: Change in Borg score at rest)												
1 ²	randomised trials	serious ^a	not serious	not serious	very serious ^b	none	62	28	-	MD 0.4 points higher (0 to 0)	⊕○○○ VERY LOW	
Improvement in Baseline Dyspnea at 6 weeks (assessed with: Decrease in Visual Analog Scale by 10mm)												
1 ³	randomised trials	serious	not serious	not serious	very serious	none	42/49 (85.7%)	35/47 (74.5%)	RR 0.70 (0.29 to 1.64)	22 fewer per 100 (from 48 more to 53 fewer)	⊕○○○ VERY LOW	CRITICAL
Improvement in Dyspnea at 6 weeks (assessed with: change in modified Borg score at rest)												
1 ⁴	randomised trials	serious ^a	not serious	not serious	serious ^c	none	18	18	-	MD 0.6 points higher (0 to 0)	⊕⊕○○ LOW	
Hospital length of stay												
1 ¹	randomised trials	serious ^a	not serious	not serious	not serious ^d	none	73	71	-	median 2 days fewer (0 to 0)	⊕⊕⊕○ MODERATE	CRITICAL
Hospital length of stay												
1 ³	randomised trials	serious ^a	not serious	not serious	not serious ^d	none	51	52	-	median 4 days fewer (0 to 0)	⊕⊕⊕○ MODERATE	CRITICAL
Hospital length of stay												
1 ⁴	randomised trials	serious ^a	not serious	not serious	not serious ^d	none	46	48	-	median 5 days fewer (0 to 0)	⊕⊕⊕○ MODERATE	

Bleeding requiring intervention												
2 ^{5,6}	observational studies	serious	not serious	not serious	serious	none	2/93 (2.2%)	3/81 (3.7%)	RR 0.58 (0.09 to 3.38)	2 fewer per 100 (from 3 fewer to 9 more)	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; MD: Mean difference; RR: Risk ratio

Explanations

- a. Investigators not blinded
- b. Mean (SD) listed for both groups, but mean difference calculated by methodologist. Range of mean difference not listed, and standard deviations were two-fold higher than reported means.
- c. Means for both groups listed in table; mean difference calculated by methodologists; unable to assess range of mean difference.
- d. Post-randomization length of stay reported; total hospital length of stay showed similar differences favoring IPC.

References

1. Thomas, . AMPLE. 2017.
2. Putnam, . . 1999.
3. Davies, . TIME2. JAMA; 2012.
4. Boshuizen, . NVALT-14. 2017.
5. Srour, . . Can Resp J; 2013.
6. Hunt, . . 2012.

	Thomas 2017	Putnam 1999	Dermmy 2012	Davies 2012	Boshuizen 2017	
	+	?	?	+	+	Random sequence generation (selection bias)
	+	?	?	?	?	Allocation concealment (selection bias)
	+	+	+	+	+	Blinding of participants and personnel (performance bias): Adverse outcomes, objective
	-	-	-	-	-	Blinding of participants and personnel (performance bias): Self-reported
	+	+	+	+	+	Blinding of outcome assessment (detection bias): Adverse outcome, objective
	-	-	-	-	-	Blinding of outcome assessment (detection bias): Self-reported
	+	-	+	+	-	Incomplete outcome data (attrition bias)
	+	+	+	+	+	Selective reporting (reporting bias)
	+	+	+	+	+	Other bias

Figure E8: Pooled relative risks (RR) for PICO4 using random effects model comparing indwelling pleural catheter (IPC) with chemical pleurodesis for (a) 3-month mortality, (b) repeat pleural procedures, (c) pleural infection, and (d) cellulitis.

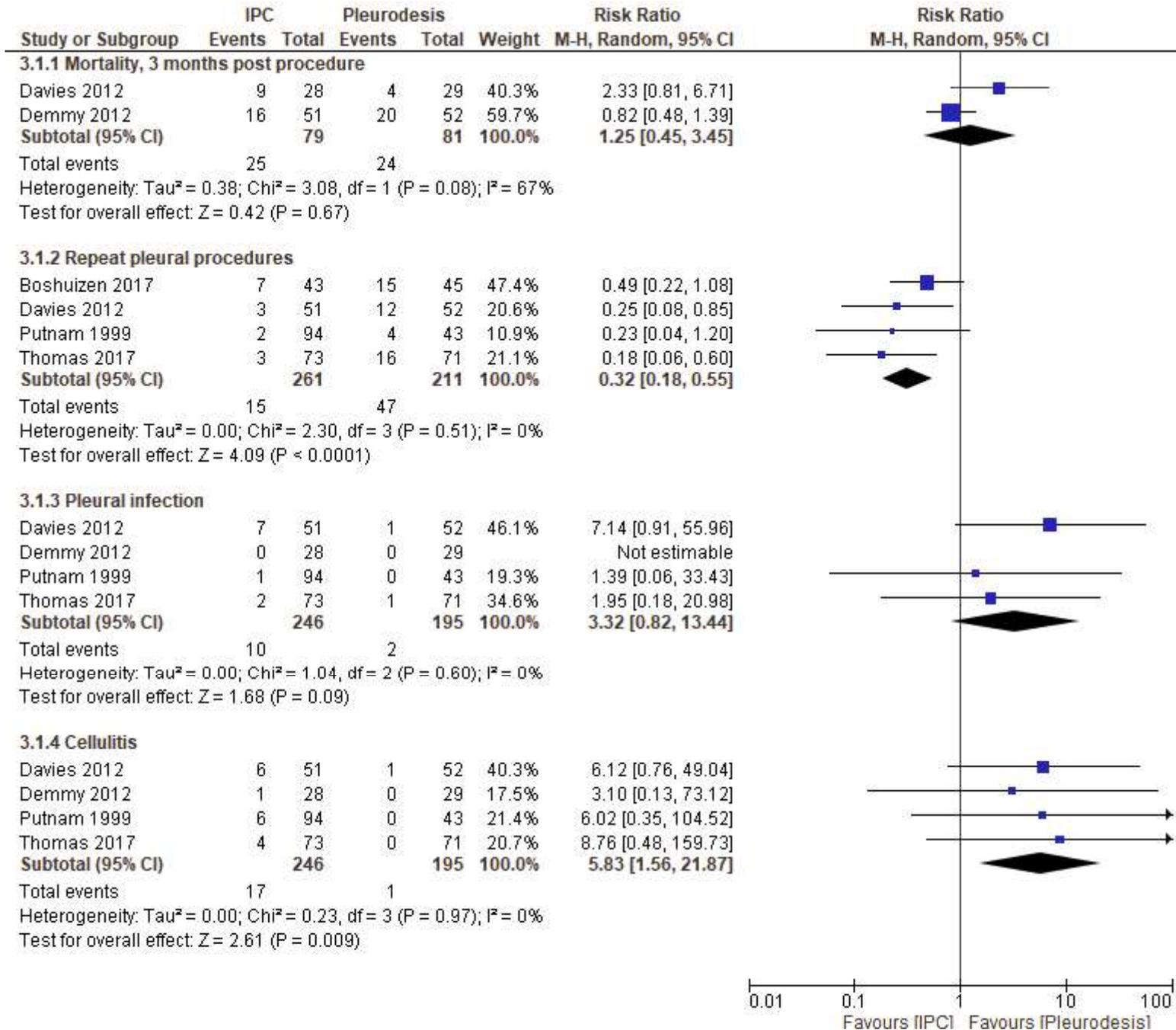


Table E4e: Evidence Profile for PICO 5

Author(s):
Date:
Question: Talc poudrage compared to talc slurry for pleurodesis in symptomatic malignant pleural effusions
Setting:
Bibliography:

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	talc poudrage	talc slurry	Relative (95% CI)	Absolute (95% CI)		
30-day mortality												
2 ^{1,2}	randomised trials	not serious	very serious ^a	not serious	serious ^b	none	25/207 (12.1%)	33/193 (17.1%)	RR 0.70 (0.43 to 1.12)	5 fewer per 100 (from 2 more to 10 fewer)	⊕○○○ VERY LOW	CRITICAL
30-day mortality												
2 ^{3,4}	observational studies	very serious ^c	serious ^d	not serious	not serious	none	3/154 (1.9%)	9/103 (8.7%)	RR 0.22 (0.06 to 0.80)	7 fewer per 100 (from 2 fewer to 8 fewer)	⊕○○○ VERY LOW	CRITICAL
Respiratory Failure requiring mechanical ventilation												
2 ^{5,6}	randomised trials	serious ^e	not serious	not serious	very serious	none	18/251 (7.2%)	9/225 (4.0%)	RR 1.74 (0.81 to 3.74)	3 more per 100 (from 1 fewer to 11 more)	⊕○○○ VERY LOW	CRITICAL
Treatment failure requiring more ipsilateral procedures (assessed with: need for more procedures)												
2 ^{6,7}	randomised trials	serious ^f	not serious	not serious	serious	none	5/58 (8.6%)	5/59 (8.5%)	RR 1.02 (0.31 to 3.30)	0 fewer per 100 (from 6 fewer to 19 more)	⊕⊕○○ LOW	CRITICAL
Treatment failure requiring more ipsilateral procedures (assessed with: need for more procedures)												
3 ^{3,8,9}	observational studies	very serious	serious	not serious	very serious	none	39/162 (24.1%)	46/142 (32.4%)	RR 0.74 (0.51 to 1.06)	8 fewer per 100 (from 2 more to 16 fewer)	⊕○○○ VERY LOW	CRITICAL
Repeat pleural procedures (assessed with: Subsequent Pleural Procedures Per Patient Day of Life)												
1 ¹⁰	observational studies	serious ⁹	not serious	not serious	not serious	none	673	1779	-	median 0.33 Talc Slurry higher (0 to 0)	⊕○○○ VERY LOW	CRITICAL
Inpatient stay days (assessed with: Inpatient days associated with pleural procedures per day of Life)												

1 ¹⁰	observational studies	serious ⁹	not serious	not serious	not serious	none	673	1779	-	median 0.012 Talc Slurry higher (0 to 0)	⊕○○○ VERY LOW	IMPORTANT
30 day- 6 month recurrence (radiologic) free survival (follow up: range 30 days to 6 months; assessed with: Chest x-ray and CT scan)												
2 ^{6,7}	randomised trials	serious ^h	not serious	not serious	not serious	none	142/207 (68.6%)	110/191 (57.6%)	RR 1.19 (1.02 to 1.39)	109 more per 1,000 (from 12 more to 225 more)	⊕⊕⊕○ MODERATE	IMPORTANT
Empyema												
2 ^{6,7}	randomised trials	serious	not serious	not serious ⁶	very serious	none	2/253 (0.8%)	3/226 (1.3%)	RR 0.89 (0.18 to 4.30)	0 fewer per 100 (from 1 fewer to 4 more)	⊕○○○ VERY LOW	IMPORTANT
Bleeding requiring transfusion												
1 ⁶	randomised trials	serious	not serious	not serious	very serious	none	10/223 (4.5%)	5/196 (2.6%)	RR 1.76 (0.61 to 5.05)	2 more per 100 (from 1 fewer to 10 more)	⊕○○○ VERY LOW	IMPORTANT
Pneumonia												
2 ^{6,7}	randomised trials	serious	not serious	not serious	serious	none	22/253 (8.7%)	9/226 (4.0%)	RR 2.18 (1.02 to 4.64)	5 more per 100 (from 0 fewer to 14 more)	⊕⊕○○ LOW	IMPORTANT
Cellulitis												
3 ^{5,6,7}	randomised trials	serious	not serious	not serious	very serious	none	2/281 (0.7%)	3/255 (1.2%)	RR 0.6 (0.1 to 3.6)	0 fewer per 100 (from 1 fewer to 3 more)	⊕○○○ VERY LOW	NOT IMPORTANT
Fever												
2 ^{6,7}	randomised trials	not serious	not serious	not serious	very serious	none	67/253 (26.5%)	71/226 (31.4%)	RR 0.84 (0.63 to 1.11)	5 fewer per 100 (from 3 more to 12 fewer)	⊕⊕○○ LOW	NOT IMPORTANT

CI: Confidence interval; RR: Risk ratio

Explanations

- a. Mortality noted in one study; zero mortality in second study.
- b. Confidence interval does not exclude an appreciable benefit or an appreciable harm.
- c. Data from one cohort and one retrospective study with limited data on patient selection.
- d. Very few events; majority (7/9) of deaths in Talc slurry group come from one study.
- e. No objective criteria provided and no blinding.
- f. Few events, variable follow up periods- not all patients followed up in one study.
- g. Database study with incomplete data entry, selection bias
- h. Variable follow up periods

References

1. Dresler, . . Chest; 2005.
2. Terra, . . Chest; 2009.
3. Stefani, . . European Journal of Cardio-thoracic Surgery; 2006.
4. Luh, . . Thorac Cardio Surg; 2006.
5. Yim, . . 1996.
6. Dresler, . . 2005.
7. Terra, . . 2009.
8. Fysh, . . Thorax; 2013.
9. Erickson, . . The American Surgeon; 2002.
10. Ost, . . Chest; 2017.

Table E4f: Evidence Profile for PICO 6

Author(s):

Date:
Question: In patients with symptomatic MPE with non-expandable lung, failed pleurodesis or loculated effusion, should an IPC or chemical pleurodesis be used?

Setting:

Bibliography:

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	indwelling pleural catheter	chemical pleurodesis	Relative (95% CI)	Absolute (95% CI)		
Mortality at 1 year												
1 ¹	observational studies	very serious	not serious	not serious	very serious	none	25/34 (73.5%)	3/7 (42.9%)	RR 1.72 (0.71 to 4.13)	309 more per 1,000 (from 124 fewer to 1,000 more)	⊕○○○ VERY LOW	CRITICAL
Length of stay 2 days or less												
1 ^{1,a}	observational studies	very serious	not serious	not serious	very serious	none	19/34 (55.9%)	0/7 (0.0%)	not estimable		⊕○○○ VERY LOW	CRITICAL
Length of stay 2 days or less												
1 ^{2,b}	observational studies	very serious	not serious	not serious	not serious	none	27/63 (42.9%)	-	-	-	⊕○○○ VERY LOW	CRITICAL
Empyema												
4 ^{1,2,3,4,b}	observational studies	very serious	not serious	not serious	very serious	none	7/290 (2.4%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT
Cellulitis												
4 ^{1,2,3,4,b}	observational studies	very serious	not serious	not serious	very serious	none	11/290 (3.8%)	-	-	-	⊕○○○ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single center, retrospective review. All patients with expandable lung underwent VATS pleurodesis; all complicated pleural spaces underwent IPC placement.
 b. Case series of IPC patients with no comparison arm.

References

1. Ohm, . . 2003.
2. Thornton, . . 2010.
3. Bazerbashi, . . 2009.
4. Qureshi, . . 2008.

Table E4g: Evidence Profile for PICO 7

Question: In patients with IPC-associated infection, should catheter removal be done in addition to medical therapy?

*Because there were no studies directly comparing interventions, pooled results from non-comparative studies are provided in the text.

11. Evidence to Decision Frameworks

Table E5a: Evidence to Decision Framework for PICO1

QUESTION

Should thoracic ultrasound vs. no image guidance be used for interventions of malignant pleural effusions?	
POPULATION:	interventions of malignant pleural effusions
INTERVENTION:	thoracic ultrasound
COMPARISON:	no image guidance
MAIN OUTCOMES:	Pneumothorax rate requiring chest tube after thoracentesis for malignant pleural effusion; Pneumothorax rate related to thoracentesis for malignant pleural effusion;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input checked="" type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know		

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input type="radio"/> Small <input checked="" type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know		

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input checked="" type="radio"/> No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input type="radio"/> Probably favors the intervention<input checked="" type="radio"/> Favors the intervention<input type="radio"/> Varies<input type="radio"/> Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input checked="" type="radio"/> Don't know		

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input checked="" type="radio"/> No included studies		

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Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input checked="" type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies		

Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies

EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input checked="" type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

In patients with malignant pleural effusion, we recommend that ultrasound imaging be used to guide pleural interventions.

Justification

This recommendation is based not only on the limited observational evidence for ultrasound guidance for management of malignant effusions, but also on the stronger evidence from larger studies in the management of pleural effusions of all types described above. The decision to use ultrasound guidance for pleural interventions in patients with malignant effusions will depend on local expertise, availability, and access to ultrasound machines.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

Research Priorities Future studies should further investigate the utility of using ultrasound to identify intercostal vessels, with the goal of decreasing the small, but real, risk of hemorrhagic complications associated with pleural procedures. Additionally, ultrasound can be used to evaluate for non-expandable lung prior to thoracentesis, however, these techniques need to be simplified, and potentially correlated with pleural manometry.

Table E5b: Evidence to Decision Framework for PICO2

QUESTION

Should pleural intervention vs. expectant management be used for asymptomatic malignant pleural effusions?	
POPULATION:	asymptomatic malignant pleural effusions
INTERVENTION:	pleural intervention
COMPARISON:	expectant management
MAIN OUTCOMES:	No studies directly addressing the question.;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know		

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input checked="" type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know		

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention<input type="radio"/> Varies<input checked="" type="radio"/> Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input checked="" type="radio"/> Don't know		

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input checked="" type="radio"/> No included studies		

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Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input checked="" type="radio"/> Don't know		

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies		

● Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies

EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input checked="" type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
---	--	---	--	---

CONCLUSIONS

Recommendation

In patients with asymptomatic malignant pleural effusions, we recommend against pleural interventions. (Grade 2C)

Justification

- **Patients should be queried more deeply on symptoms.
- **Effusions with 1/3 or greater should be considered for referral for intervention.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

Table E5c: Evidence to Decision Framework for PICO3

QUESTION

Should therapeutic thoracentesis with or without pleural manometry vs. no therapeutic thoracentesis be used for subsequent decision on IPC or chemical pleurodesis?	
POPULATION:	subsequent decision on IPC or chemical pleurodesis
INTERVENTION:	therapeutic thoracentesis with or without pleural manometry
COMPARISON:	no therapeutic thoracentesis
MAIN OUTCOMES:	No studies directly addressing the question.;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input checked="" type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies		

Don't know

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Large <input type="radio"/> Moderate <input type="radio"/> Small <input checked="" type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know</p>		

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies</p>		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<p><input type="radio"/> Important uncertainty or variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input checked="" type="radio"/> No important uncertainty or variability</p>		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input checked="" type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention<input type="radio"/> Varies<input type="radio"/> Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input checked="" type="radio"/> Don't know		

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input checked="" type="radio"/> No included studies		

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention <input type="radio"/> Varies<input checked="" type="radio"/> No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Reduced<input type="radio"/> Probably reduced<input type="radio"/> Probably no impact<input type="radio"/> Probably increased<input type="radio"/> Increased <input type="radio"/> Varies<input type="radio"/> Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> No<input type="radio"/> Probably no<input type="radio"/> Probably yes<input type="radio"/> Yes <input type="radio"/> Varies		

Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies

EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input checked="" type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

In patients with symptomatic malignant pleural effusion, we suggest therapeutic thoracentesis be performed prior to definitive pleural interventions (Grade 2C).

Justification

*With dissent

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

Table E5d: Evidence to Decision Framework for PICO4

QUESTION

Should Indwelling pleural catheter vs. pleurodesis be used for first-line therapy in malignant pleural effusions?	
POPULATION:	first-line therapy in malignant pleural effusions
INTERVENTION:	Indwelling pleural catheter
COMPARISON:	pleurodesis
MAIN OUTCOMES:	Dyspnea at 30 days; Improvement in dyspnea at 30 days; Improvement in Baseline Dyspnea at 6 weeks; Improvement in Dyspnea at 6 weeks; Hospital length of stay; Hospital length of stay; Hospital length of stay; Bleeding requiring intervention; Survival; 30-day mortality; 42-day mortality; Treatment failure (need for ipsilateral procedures); Treatment failure (need for ipsilateral procedures at 1 year); Cellulitis; Empyema; Empyema; Treatment failure (need for more ipsilateral procedures); Cellulitis; Dyspnea at 6 weeks;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Malignant Pleural Effusions affect a significant proportion of patients with cancer. Palliation of symptoms is the mainstay of therapy. Available modalities for palliation of symptoms associated with MPE include Indwelling Pleural Catheters and Pleurodesis. Both modalities have advantages and disadvantages and choosing the right option will impact the quality of life for patients with limited expected survival.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies		

Don't know

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input checked="" type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know		

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input checked="" type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or		

variability

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input checked="" type="radio"/> Does not favor either the intervention or the comparison<input type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention<input type="radio"/> Varies<input type="radio"/> Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input checked="" type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input type="radio"/> Don't know		

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input checked="" type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input type="radio"/> No included studies		

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Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input checked="" type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input checked="" type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies		

Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies

EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input checked="" type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

In patients with Malignant Pleural Effusions with known or suspected expandable lung and no prior definitive therapy, we recommend that either Indwelling Pleural Catheters or chemical pleurodesis be used for management of dyspnea.

Justification

Indwelling Pleural Catheters' advantages over Pleurodesis are a decrease in the need for additional interventions, better control of dyspnea and a decrease in length of hospitalization. However, the risk of infections is higher with Indwelling Pleural Catheters when compared to Pleurodesis. Based on a low quality of the evidence reviewed, the recommendation is for either the intervention or comparison.

Subgroup considerations

Not considered.

Implementation considerations

Not considered.

Monitoring and evaluation

Not considered.

Research priorities

Not considered.

Table E5e: Evidence to Decision Framework for PICO5

QUESTION

Should talc poudrage vs. talc slurry be used for pleurodesis in symptomatic malignant pleural effusions?	
POPULATION:	pleurodesis in symptomatic malignant pleural effusions
INTERVENTION:	talc poudrage
COMPARISON:	talc slurry
MAIN OUTCOMES:	30-day mortality; 30-day mortality; Respiratory Failure requiring mechanical ventilation; Treatment failure requiring more ipsilateral procedures; Treatment failure requiring more ipsilateral procedures; Repeat pleural procedures; Inpatient stay days; 30 day- 6 month recurrence (radiologic) free survival; Empyema; Bleeding requiring transfusion; Pneumonia; Cellulitis; Fever;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Malignant pleural effusion (MPE) is a common clinical problem which results in breathlessness and other symptoms, often presenting acutely. It is known that around 90% of MPE cases will re-accumulate after initial drainage, and therefore definitive pleural intervention (to prevent recurrent presentation with breathlessness and minimise symptoms) is a priority in care.</p> <p>Pleurodesis involves the administration of a drug or material in the pleural space to cause inflammation, and thereby create adhesions, obliterating the pleural space and preventing fluid re-accumulation. Talc pleurodesis is the most widely used pleurodesis agent, but there are two delivery methods - talc poudrage which is conducted at either surgical or medical thoracoscopy (when talc is blown in as a dry powder) or talc slurry, when talc is injected through a chest tube, mixed with sterile fluid and done at the bedside.</p>	<p>The high incidence, large amount of suffering and symptoms caused by MPE means that establishing the optimal treatment for recurrent MPE is a high priority for clinicians and patients.</p>
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

<input checked="" type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know		
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input checked="" type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input type="radio"/> Don't know		In favour of poudrage - lower 30 day mortality, and less requirement for pleural procedures. However, on less important outcomes to decision making (pneumonia, bleeding requiring transfusion), small evidence favouring slurry.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input checked="" type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	Small numbers of patients in direct comparative studies with high risk of bias. Wide confidence intervals reflecting significant uncertainty.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Important uncertainty or	The outcomes of requirement for further pleural procedures and adverse event outcomes are highly likely to be valued, as are the main side effect	

variability <input type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability	outcomes. However, the key outcome of either breathlessness or quality of life assessment has not been addressed in any of the appraised studies. This is important as treatment of symptoms is the treatment intent.	
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Balance of effects
 Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input checked="" type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	<p>There is no strong evidence to favour either talc poudrage or slurry as treatment. There is very weak evidence of increased efficacy (in need for further pleural interventions at 1 month) and of lower serious adverse events (mortality) in favour of poudrage. However, there is also very weak evidence against poudrage of increased minor complications (pneumonia) with poudrage.</p> <p>Overall, the evidence therefore does not favour either talc poudrage or talc slurry</p>	

Resources required
 How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	No specific health economic assesment has been attempted in the appraised studies.	

Certainty of evidence of required resources
 What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low	Not applicable.	

<input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies		
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Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input checked="" type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	There are large numbers of patients treated with VATS and medical thoracoscopy in previous case series and randomised trials, with good acceptance of the intervention.	
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Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Medical thoracoscopy and surgical VATS are widely available, but not available in every hospital.	

SUMMARY OF JUDGEMENTS

		JUDGEMENT					
PROBLEM	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED	Very low	Low	Moderate	High			No included studies

RESOURCES							
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input checked="" type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

In patients with symptomatic malignant pleural effusion with expandable lung who are fit to undergo thoracoscopy, we recommend the use of either talc poudrage or talc slurry for pleurodesis.

Justification

Overall justification

The recommendation for either talc poudrage or talc slurry pleurodesis is made on the basis of only very weak evidence of improved outcome (need for further pleural procedures at 1 month, i.e. pleurodesis success) and reduced mortality for poudrage, and very weak evidence of increased complications (pneumonia, bleeding) favouring talc slurry.

There is no direct evidence comparing quality of life, time in hospital or breathlessness comparing these two interventions.

Detailed justification

Desirable Effects

Very weak evidence of improved outcome (need for further pleural procedures at 1 month, i.e. pleurodesis success) and reduced mortality favoring talc poudrage.

Undesirable Effects

Very weak evidence of increased complications (pneumonia, bleeding) favouring talc slurry.

Subgroup considerations

The largest trial to date (Dresler et al) reported increased pleurodesis efficacy favouring poudrage compared with slurry in the subgroup of patients with expandable lung, and with MPE due to either lung cancer or breast cancer (82% versus 67% pleurodesis success at 1 month). The certainty of this estimate is poor due to post-hoc subgroup analysis.

Implementation considerations

Monitoring and evaluation

Complication rates of both slurry and poudrage pleurodesis should be monitored.

Research priorities

1. Patient reported outcome measures of breathlessness / QOL comparing the intervention with standard care
2. Prospective randomised study of patients with expandable lung comparing talc poudrage and slurry (underway - see Maskell et al, ISRCTN47845793).

Table E5f: Evidence to Decision Framework for PICO6

QUESTION

Should indwelling pleural catheter vs. chemical pleurodesis be used for malignant pleural effusions with loculations or prior failed pleurodesis?	
POPULATION:	malignant pleural effusions with loculations or prior failed pleurodesis
INTERVENTION:	indwelling pleural catheter
COMPARISON:	chemical pleurodesis
MAIN OUTCOMES:	Mortality at 1 year; Length of stay 2 days or less; Length of stay 2 days or less; Empyema; Cellulitis;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	The clinical problem of malignant pleural effusion (MPE) with loculation, failed talc pleurodesis or trapped lung (where pleurodesis will not be successful, and is usually not attempted) is significant with 15% of patients in randomised trials demonstrating trapped lung, and 30% failing talc pleurodesis. In patients with MPE with these conditions, the use of an indwelling pleural catheter (IPC) may offer long term drainage of fluid thereby relieving symptoms and preventing admission to hospital.	The frequency of loculation, trapped lung or failed pleurodesis in MPE are high, and the implications for this to patient symptoms and clinicians sufficient such that this should be seen as a priority.
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies	The evidence suggests IPCs are associated with shorter hospital stay in these conditions than pleurodesis. However, the number of patients assessed in these studies (in both IPC and pleurodesis groups) is very small.	

Don't know

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	The evidence suggests IPCs are associated with shorter hospital stay in these conditions than pleurodesis. However, the number of patients assessed in these studies (in both IPC and pleurodesis groups) is very small.	Although there appears to be an excess of 30 day mortality in the IPC patients, very few patients with pleurodesis for these conditions were reported. Empyema and cellulitis rates with IPC are 2.4% and 3.8% respectively, and these outcomes are not reported for pleurodesis in the assessed studies.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	Very few patients in small numbers of studies, providing wide confidence intervals.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability	The main outcomes here assessed include important safety outcomes (mortality, infection) and efficacy outcomes (time in hospital). The "missing" outcome is of an assessment of patient focussed or reported breathlessness, which is not reported in any of the assessed studies, and represents an evidence gap in answering this question.	

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input checked="" type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention<input type="radio"/> Varies<input type="radio"/> Don't know	Accepting overall large uncertainty of any effects observed, there is moderate evidence for beneficial outcomes (reduced hospital stay) favouring the intervention and weak evidence for side effects favouring the comparator (infection). Overall, the evidence therefore probably favours intervention (IPC) although the evidence is weak.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input checked="" type="radio"/> Don't know	There is no direct Health Economic (HE) comparison of IPC with talc pleurodesis for these conditions. The reduction in hospital stay is likely to result in cost benefits for initial treatment, but IPC may be more expensive longer term as it requires ongoing support and equipment.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input checked="" type="radio"/> No included studies	Not applicable	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Favors the comparison<input type="radio"/> Probably favors the comparison<input type="radio"/> Does not favor either the intervention or the comparison<input type="radio"/> Probably favors the intervention<input type="radio"/> Favors the intervention <input type="radio"/> Varies<input checked="" type="radio"/> No included studies	There is no data of the quality needed to assess cost-effectiveness.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Reduced<input checked="" type="radio"/> Probably reduced<input type="radio"/> Probably no impact<input type="radio"/> Probably increased<input type="radio"/> Increased <input type="radio"/> Varies<input type="radio"/> Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> No<input type="radio"/> Probably no<input type="radio"/> Probably yes<input checked="" type="radio"/> Yes <input type="radio"/> Varies		

Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	IPCs are already in widespread clinical use and therefore demonstrated to be implementable. Clinicians should be aware of the requirements for ongoing use for their patients, including sufficient support, advice and contact with the respiratory team as needed for issues with IPC use such as complications.	

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	No	Probably no	Probably yes	Yes		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
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies

EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input checked="" type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

In patients with symptomatic malignant pleural effusions with trapped lung, failed pleurodesis or loculated effusion, we suggest the use of indwelling pleural catheters over chemical pleurodesis.

Justification

Overall justification

Detailed justification

Desirable Effects

Moderate evidence of benefit (for time in hospital)

Undesirable Effects

Weak evidence of increased adverse events (skin and pleural infection).

Certainty of evidence

There is very poor certainty of evidence given the size and quality of assessed studies

Subgroup considerations

None

Implementation considerations

Ensure clinicians have sufficient resource to support the use of IPCs in the long term for their patients

Monitoring and evaluation

Patients with IPC should be closely monitored for possible infection.

Research priorities

There is a clear need for studies to directly address if IPC or pleurodesis are efficacious in treating the symptom of breathlessness in patients with trapped lung, loculated effusion and failed talc pleurodesis. This is an evidence gap and a research priority for this key question, as treatment of breathlessness is the treatment intent.

Table E5f: Evidence to Decision Framework for PICO7

QUESTION

Should All patients with infected IPC vs. be used for infected indwelling pleural catheters?	
POPULATION:	infected indwelling pleural catheters
INTERVENTION:	All patients with infected IPC
COMPARISON:	
MAIN OUTCOMES:	Death attributable to infection in all case series; Death attributable to infection in case series that commented on catheter removal;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTEREST:	

ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Though there are several trials that report the incidence of pleural infection in patients who have received IPCs, there are no prospective trials investigating outcomes between patients who were treated with antibiotics and catheter removal vs being treated with antibiotics and keeping the catheter in place.	
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	There is considerable practice pattern variation amongst centers throughout the world in the treatment of IPC related pleural infection.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large <input type="radio"/> Moderate <input type="radio"/> Small <input type="radio"/> Trivial <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	<p>There is considerable practice pattern variation amongst centers throughout the world in the treatment of IPC related pleural infection.</p>	<p>From the largest retrospective series, including more than 1,000 patients, the incidence of pleural infection in patients who have IPCs is 5%, with an overall mortality of 2.9%. That being said, amongst the patients who developed pleural infection, there was a 6% mortality. Factors associated with mortality are not known.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies		

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> Possibly important uncertainty or variability <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input checked="" type="radio"/> Varies <input type="radio"/> Don't know 	<p>As IPC related infections are managed in a variety of ways (oral vs. IV antibiotics, inpatient vs outpatient therapy, keeping vs removing the IPC) the associated costs can vary significantly. Further study is required.</p>	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies 		

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Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input checked="" type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies	As the large majority of patients who develop IPC related infection have good outcomes, current evidence suggests that patients can be treated in a variety of ways, and treatment decisions should be made on an individual basis.	

Don't know

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
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CONCLUSIONS

Recommendation

In patients with indwelling pleural catheter infections, we suggest treating through the infection without catheter removal. Clinicians should consider catheter removal when there is no clinical improvement or evidence of worsening infection.

Justification

There are a paucity of data suggesting catheter removal is superior to keeping the catheter in place. Likewise, data do not support IV over oral antibiotics.

As the large majority of patients who develop IPC related infection have good outcomes, current evidence suggests that patients can be treated in a variety of ways, and treatment decisions should be made on an individual basis.

Subgroup considerations

Considerations should be made based on the clinical status of the patient, including signs / symptoms of pleural sepsis / systemic inflammatory response, imaging studies.

Implementation considerations

Considerations as to resources available to provide home IV antibiotic therapy, the proximity of the patient to the care-team as well as the patient's local support network should be taken into account.

Monitoring and evaluation

Patients with IPC related pleural infection require close monitoring to assure clinical improvement with the implemented treatment plan. Should there be any worsening of the patients clinical status, it is imperative to escalate intervention appropriately (i.e. switch from oral to IV antibiotics, consider catheter removal, re-discuss the patient's course with a multi-disciplinary team).

Research priorities

Future studies should investigate the best treatment for IPC related pleural infection. Outcomes should include mortality, resource utilization and need for escalation of care.