

# British Thoracic Society Guideline for pleural disease

Mark E Roberts,<sup>1</sup> Najib M Rahman ,<sup>2,3,4</sup> Nick A Maskell,<sup>5</sup> Anna C Bibby,<sup>5</sup> Kevin G Blyth ,<sup>6,7</sup> John P Corcoran ,<sup>8</sup> Anthony Edey,<sup>9</sup> Matthew Evison ,<sup>10</sup> Duneesha de Fonseka ,<sup>11</sup> Rob Hallifax,<sup>12</sup> Susan Harden,<sup>13</sup> Iain Lawrie,<sup>14</sup> Eric Lim,<sup>15</sup> David McCracken,<sup>16</sup> Rachel Mercer,<sup>17</sup> Eleanor K Mishra ,<sup>18</sup> Andrew G Nicholson,<sup>19</sup> Farinaz Noorzad,<sup>20</sup> Kirstie S Opstad,<sup>21</sup> Maria Parsonage,<sup>22</sup> Andrew E Stanton ,<sup>23</sup> Steven Walker<sup>5</sup>

For numbered affiliations see end of article.

## Correspondence to

Dr Mark E Roberts, Department of Respiratory Medicine, King's Mill Hospital, Sutton-in-Ashfield, UK; mark.roberts@nhs.net

Published Online First  
8 August 2023

## INTRODUCTION

The following is a summary of the British Thoracic Society (BTS) Guideline for pleural disease and includes a summary of the guideline recommendations and good practice points (GPPs). The full guideline is published as a separate Thorax Supplement<sup>1</sup> and is available from the BTS website.<sup>2</sup> Please refer to the full guideline for full information about each section.<sup>1</sup> All online supplemental appendices are also available via the BTS website.<sup>2</sup>

## BACKGROUND

The aim of the guideline was to provide evidence-based guidance on the investigation and management of pleural disease. Pleural disease is common and represents a major and rapidly developing subspecialty that presents to many different hospital services. Since the last BTS Guideline for pleural disease published in 2010,<sup>3–9</sup> many high quality and practice changing studies, using patient centred outcomes, have been published. The paradigms for the investigation and management of pleural disease have therefore shifted, so this guideline aimed to capture this evidence and use it to answer the most important questions relevant to today's practice.

## Target audience for the guideline

The guideline will be of interest to UK based clinicians caring for adults with pleural disease, including chest physicians, respiratory trainees, specialist respiratory nurses, specialist lung cancer nurses, specialist pleural disease nurses, pathologists, thoracic surgeons, thoracic surgeon trainees, acute physicians, oncologists, emergency physicians, hospital practitioners, intensive care physicians, palliative care physicians, radiologists, other allied health professional and patients and carers.

## Areas covered by the guideline

The guideline focuses on the investigation and management of pleural disease in adults and covers four broad areas of pleural disease:

- Spontaneous pneumothorax
- Undiagnosed unilateral pleural effusion
- Pleural infection
- Pleural malignancy

Adult patients in both inpatient and ambulatory settings are considered.

The guideline does not cover mesothelioma (as alternative guidance is available<sup>10</sup>), benign (non-infectious, non-pneumothorax) pleural disease or rare pleural diseases. Guidance on pleural interventions is also covered in the BTS Clinical Statement on Pleural Procedures.<sup>11</sup>

## Methodology

BTS guidelines use the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology for guideline development.<sup>12</sup> GRADE is a systematic and transparent process for assessing the quality of the evidence and the full GRADE process involves:

- Systematic review,
- Critical appraisal; and
- GRADE analysis.

Full details of the BTS process are available in the BTS Guideline production manual (<https://www.brit-thoracic.org.uk/quality-improvement/guidelines/>).

## Clinical questions, patient-centred outcomes and literature search

Clinical questions were defined from the scope of the guideline formulated into PICO (population, intervention, comparator, and outcome) style framework diagnostic accuracy, intervention or prognostic review formats. Patient-centred outcomes were agreed by the group for each question.

The PICO framework formed the basis of the literature search. The initial searches were completed by the University of York, and the latter stages by BTS Head Office. Systematic electronic database searches were conducted to identify all papers that may be relevant to the guideline. For each question, the following databases were searched: Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. The search strategy is available for review in Online Appendix 1 (accessible via the full guideline).

## Critical appraisal and GRADE analysis of the evidence

After an initial screening to determine relevance to the clinical questions, each paper was assessed to determine if it addressed:



► <http://dx.doi.org/10.1136/thorax-2022-219630>



© Author(s) (or their employer(s)) 2023. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Roberts ME, Rahman NM, Maskell NA, et al. *Thorax* 2023;78:1143–1156.

**Table 1** GRADE score definitions

Grade	Definition
High	⊕⊕⊕⊕ High confidence that the true effect is close to the estimated effect
Moderate	⊕⊕⊕○ Moderate confidence that the true effect is close to the estimated effect
Low	⊕⊕○○ Low confidence that the true effect is close to the estimated effect
Very Low	⊕○○○ Very low confidence that the true effect is close to the estimated effect
Ungraded	GRADE analysis not possible, but evidence deemed important

- The clinical question population.
- The index test and reference standard (for diagnostic accuracy questions), the intervention and comparator (for intervention questions), or the exposure and referent (for prognostic questions).
- The study type(s) defined in the clinical question protocol; and
- The clinical question outcome(s).

Each full paper fulfilling the above criteria was ‘accepted’ for inclusion. In circumstances where there was little, or no supporting evidence that fulfilled the above criteria, the full paper inclusion strategy was widened to include evidence that partially addressed the clinical question.

Following data extraction from the ‘accepted’ papers, evidence profiles were generated for each of the clinical questions and the quality of the evidence was assessed using the GRADE principles.<sup>12</sup> Where GRADE analysis was not possible, but the evidence was deemed important enough to be included in the guideline, the evidence has been listed as (Ungraded), denoting that inclusion was reached by consensus of the guideline development group. A definition of the GRADE scores is shown in **table 1**.

The direction and strength of the recommendations are then based on the quality of the evidence, the balance of desirable and undesirable outcomes and the values and preferences of patients/ carers. GRADE specifies two categories of strength for a recommendation as shown in **table 2**.

From the outset, it was acknowledged that there would be little high-quality evidence for some of the clinical questions identified. In this instance, low grade evidence was considered, along with the expert opinion of the GDG via consensus at the meetings.

Good practice points (GPPs) were also developed by informal consensus in areas where there was no quality evidence, but the GDG felt that some guidance, based on the clinical experience of the GDG, might be helpful to the reader. These are indicated as shown below:

- ✓ Advised best practice based on the clinical experience of the GDG.

In some instances where evidence was limited, but GDG members felt that it was important to include a recommendation rather than a GPP, recommendations were agreed by informal consensus and categorised as (Conditional – by consensus), based on the same criteria detailed in **table 1**.

## Stakeholders

Stakeholders were identified at the start of the process. All stakeholder organisations were notified when the guideline was available for public consultation and a list of all stakeholders is listed in Appendix 4 to the full guideline.

## SUMMARY OF RECOMMENDATIONS AND GOOD PRACTICE POINTS

### Spontaneous pneumothorax

Acute management for spontaneous pneumothorax

#### Recommendations

- ▶ Conservative management can be considered for the treatment of minimally symptomatic (ie, no significant pain or breathlessness and no physiological compromise) or asymptomatic primary spontaneous pneumothorax in adults regardless of size. (Conditional – by consensus)
- ▶ Ambulatory management should be considered for the initial treatment of primary spontaneous pneumothorax in adults with good support and in centres with available expertise and follow-up facilities. (Conditional)
- ▶ In patients not deemed suitable for conservative or ambulatory management, needle aspiration or tube drainage should be considered for the initial treatment of primary spontaneous pneumothorax in adults. (Conditional)
- ▶ Chemical pleurodesis can be considered for the prevention of recurrence of secondary spontaneous pneumothorax in adults (eg, patients with severe COPD who significantly decompensated in the presence of a pneumothorax, even during / after the first episode). (Conditional)
- ▶ Thoracic surgery can be considered for the treatment of pneumothorax in adults at initial presentation if recurrence prevention is deemed important (eg, patients presenting with tension pneumothorax, or those in high risk occupations). (Conditional)

#### Good practice points

- ✓ When establishing local ambulatory treatment pathways, planning and coordination between with the emergency department, general medicine and respiratory medicine is vital.
- ✓ When performing chemical pleurodesis for the treatment of pneumothorax in adults, adequate analgesia should be provided before and after treatment.
- ✓ All treatment options should be discussed with the patient to determine their main priority, with consideration for the least invasive option.

**Table 2** Explanation of the terminology used in BTS recommendations

Strength	Benefits and risks	Implications
Strong Recommended, so “offer”	Benefits appear to outweigh the risks (or vice versa) for the majority of the target group	Most service users would want to, or should receive this intervention
Conditional Suggested, so “consider”	Risks and benefits are more closely balanced, or there is more uncertainty in likely service users’ values and preferences	Service users should be supported to arrive at a decision based on their values and preferences

Optimal management after the resolution of a first episode of pneumothorax

#### *Good practice points*

- ✓ Elective surgery may be considered for patients in whom recurrence prevention is deemed important (eg, at risk professionals (divers, airline pilots, military personnel), or those who developed a tension pneumothorax at first episode).
- ✓ Elective surgery should be considered for patients with a second ipsilateral or first contralateral pneumothorax.
- ✓ Discharge and activity advice should be given to all patients post pneumothorax.

Optimal management for spontaneous pneumothorax and ongoing air leak

#### *Good practice point*

- ✓ If a patient is not considered fit for surgery, autologous blood pleurodesis or endobronchial therapies should be considered for the treatment of pneumothorax with persistent air leak in adults.

Optimal surgical approach and surgical operation for pneumothorax management

#### *Recommendations*

- Video-assisted thoracoscopy access can be considered for surgical pleurodesis in the general management of pneumothorax in adults. (Conditional)
- Thoracotomy access and surgical pleurodesis should be considered for the lowest level of recurrence risk required for specific (eg, high risk) occupations. (Conditional)
- Surgical pleurodesis and/or bullectomy should be considered for the treatment of spontaneous pneumothorax in adults. (Conditional)

### **Investigation of the undiagnosed unilateral pleural effusion**

Radiology for diagnosing unilateral pleural effusions of benign aetiology

#### *Good practice points*

- ✓ Imaging findings of a unilateral pleural effusion should be interpreted in the context of clinical history and knowledge of pleural fluid characteristics.
- ✓ CT follow-up should be considered for patients presenting with pleural infection to exclude occult malignancy if there are ongoing symptoms, or other clinically concerning features.
- ✓ PET-CT should not be used in the assessment of pleural infection.

Image guided versus non-image guided intervention for suspected unilateral pleural effusion

#### *Recommendation*

- Image-guided thoracentesis should always be used to reduce the risk of complications. (Strong – by consensus)

Optimal volume and container for pleural aspiration samples

#### *Recommendations*

- 25–50 mL of pleural fluid should be submitted for cytological analysis in patients with suspected malignant pleural effusion (MPE). (Strong – by consensus)
- Pleural fluid should be sent in both plain and blood culture bottle tubes in patients with suspected pleural infection. (Strong – by consensus)

#### *Good practice points*

- ✓ At least 25 mL, and where possible 50 mL, of pleural fluid should be sent for initial cytological examination.
- ✓ If volumes of  $\geq 25$  mL cannot be achieved, smaller volumes should also be sent, but clinicians should be aware of the reduced sensitivity.
- ✓ If small volume aspirate (<25 mL) has been non-diagnostic, a larger volume should be sent, if achievable, except when there is high suspicion of a tumour type associated with low pleural fluid cytology sensitivity (especially mesothelioma).
- ✓ Pleural fluid samples should be processed by direct smear and cell block preparation.
- ✓ In patients with an undiagnosed pleural effusion where pleural infection is possible and volume of fluid sample available allows, microbiological samples should be sent in both white top containers and volumes of 5–10 mL inoculated into (aerobic and anaerobic) blood culture bottles.
- ✓ In cases where volume available does not allow 5–10 mL inoculation, volumes of 2–5 mL should be prioritised to blood culture bottles rather than a plain, sterile container.

Pleural fluid tests (biomarkers) for diagnosing unilateral pleural effusion

#### *Recommendations*

- Pleural fluid cytology should be used as an initial diagnostic test in patients with suspected secondary pleural malignancy, accepting that a negative cytology should lead to consideration of further investigation. (Conditional)
- Pleural fluid biomarkers should not be used for diagnosing secondary pleural malignancy. (Conditional)
- In high prevalence populations, pleural fluid adenosine deaminase (ADA) and/or interferon gamma (IFN-gamma) test(s) can be considered for diagnosing tuberculous pleural effusion. (Conditional)
- In low prevalence populations, pleural fluid adenosine deaminase (ADA) can be considered as an exclusion test for tuberculous pleural effusion. (Conditional)
- Tissue sampling for culture and sensitivity should be the preferred option for all patients with suspected tuberculous pleural effusion. (Strong – by consensus)
- Pleural fluid antinuclear antibody (ANA) should be considered to support a diagnosis of lupus pleuritis. (Conditional)

#### *Good practice points*

- ✓ The clinical utility of pleural fluid cytology varies by tumour sub-type, including diagnostic sensitivity and predictive value for response to subsequent cancer therapies. This should be taken into consideration when planning the most suitable diagnostic strategy (for example, direct biopsies in those with a likely low cytological yield can be considered).
- ✓ Pleural fluid N-terminal pro brain natriuretic peptide (NT-proBNP) is useful when considering heart failure as a cause in unilateral pleural effusions but not superior to serum NT-proBNP and therefore should not be ordered routinely.

Serum biomarkers for diagnosing unilateral pleural effusion

#### *Recommendations*

- Serum NT-proBNP should be considered to support a diagnosis of heart failure in patients with unilateral pleural effusion suspected of having heart failure. (Conditional)

**Good practice points**

- ✓ Serum biomarkers should not currently be used to diagnose secondary pleural malignancy, pleural infection or autoimmune pleuritis.
- ✓ Serum biomarkers should not routinely be used to diagnosis tuberculous pleural effusion, but may be considered in high prevalence areas.
- ✓ Serum biomarkers, including NT-proBNP, should not be used in isolation for diagnosing unilateral pleural effusion, as multiple conditions may co-exist.

**Pleural biopsy for diagnosing unilateral pleural effusion****Recommendations**

- Thoracoscopic or image-guided pleural biopsy may be used depending on the clinical indication and local availability of techniques (including need for control of pleural fluid). (Strong)
- Blind (non-image guided) pleural biopsies should not be conducted. (Strong – by consensus)

**Pleural infection****Predicting clinical outcomes of pleural infection****Recommendation**

- RAPID (renal, age, purulence, infection source, dietary factors) scoring should be considered for risk stratifying adults with pleural infection and can be used to inform discussions with patients regarding potential outcome from infection. (Conditional)

**Pleural fluid, or radiology parameters for determining which patients can be treated with intercostal drainage****Recommendations**

- For patients with parapneumonic effusion (PPE) or suspected pleural infection, where diagnostic aspiration does not yield frank pus, immediate pH analysis should be performed. (Strong – by consensus)
- For patients with suspected complex parapneumonic effusion (CPPE):
  - If pleural fluid pH  $\leq 7.2$  this implies a high risk of CPPE or pleural infection and an intercostal drain (ICD) should be inserted if the volume of accessible pleural fluid on ultrasound makes it safe to do so. (Strong – by consensus)
  - If pleural fluid pH is  $>7.2$  and  $<7.4$  this implies an intermediate risk of CPPE or pleural infection. Pleural fluid lactate dehydrogenase (LDH) should be measured and if  $>900 \text{ IU/L}$  intercostal drainage should be considered, especially if other clinical parameters support CPPE (specifically ongoing temperature, high pleural fluid volume, low pleural fluid glucose ( $72 \text{ mg/dL} \leq 4.0 \text{ mmol/L}$ ), pleural contrast enhancement on CT or septation on ultrasound). (Strong – by consensus)
  - If pleural fluid pH  $\geq 7.4$  this implies a low risk of CPPE or pleural infection and there is no indication for immediate drain. (Strong – by consensus)
- In the absence of readily available immediate pleural fluid pH measurement, an initial pleural fluid glucose  $<3.3 \text{ mmol/L}$  may be used as an indicator of high probability of CPPE/pleural infection and can be used to inform decision to insert intercostal drain in the appropriate clinical context. (Strong – by consensus)

**Good practice points**

- ✓ Clinicians should be mindful of alternative diagnoses that can mimic parapneumonic effusion (PPE) with a low pH and potential for loculations (eg, rheumatoid effusion, effusions due to advanced malignancy/mesothelioma).
- ✓ Pleural fluid samples taken for pH measurement should not be contaminated with local anaesthetic or heparin (eg, by extruding all heparin from an arterial blood gas syringe) as this lowers pleural fluid pH. Delays in obtaining a pleural fluid pH will also increase pleural fluid pH.
- ✓ In patients where a clinical decision is made not to insert an ICD at initial diagnostic aspiration, regular clinical reviews should be performed and repeat thoracocentesis considered to ensure that CPPE is not missed.

**Optimal initial drainage strategy for established pleural infection****Recommendation**

- Initial drainage of pleural infection should be undertaken using a small bore chest tube (14F or smaller). (Conditional – by consensus)

**Good practice points**

- ✓ Due to the lack of supporting evidence, early surgical drainage under video-assisted thoracoscopy surgery (VATS) or thoracotomy should not be considered over chest tube ("medical") drainage for the initial treatment of pleural infection.
- ✓ Due to lack of supporting evidence, medical thoracoscopy should not be considered as initial treatment for pleural infection.

**Intrapleural therapy for managing pleural infection****Recommendations**

- Combination tissue plasminogen activator (TPA) and DNase should be considered for the treatment of pleural infection, where initial chest tube drainage has ceased and leaves a residual pleural collection. (Conditional – by consensus)
- Saline irrigation can be considered for the treatment of pleural infection when intrapleural TPA and DNase therapy or surgery is not suitable. (Conditional – by consensus)
- Single agent tissue plasminogen activator (TPA) or DNase should not be considered for treatment of pleural infection. (Conditional – by consensus)
- Streptokinase should not be considered for treatment of pleural infection. (Conditional)

**Good practice points**

- ✓ Patient consent should be taken when using TPA and DNase as there is a potential risk of bleeding.
- ✓ When administering TPA plus DNase the regime should be 10 mg TPA twice daily (10 mg two times per day)+5 mg DNase two times per day for 3 days, based on randomised controlled trial data. Based on retrospective case series data, lower dose 5 mg TPA two times per day+5 mg DNase two times per day for 3 days may be as effective, and can be used if considered necessary.
- ✓ Reduced doses of TPA may be considered in those with a potentially higher bleeding risk (eg, those on therapeutic anticoagulation which cannot be temporarily ceased).
- ✓ For details on administration of intrapleural treatments, please refer to the BTS Clinical Statement on Pleural Procedures.<sup>11</sup>

## Optimal surgical approach and surgical method for managing pleural infection

### *Recommendation*

- VATS access should be considered over thoracotomy for adults in the surgical management of pleural infection. (Conditional)

### *Good practice points*

- ✓ When selecting a surgical access for the treatment of pleural infection in adults, it is important to ensure the technique can facilitate optimal clearance of infected material and achieve lung re-expansion where appropriate.
- ✓ Extent of surgery should be tailored according to patient and empyema stage when the lung is not completely trapped (drainage vs debridement)
- ✓ Decortication should be a decision that is individualised to the patient with a trapped lung based on assessment of patient fitness and empyema stage.

## Pleural malignancy

### Optimal imaging modality for diagnosing pleural malignancy

### *Recommendations*

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

### *Good practice points*

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

## Systemic therapy for reducing the need for definitive pleural intervention for malignant pleural effusion

### *Recommendation*

- Definitive pleural intervention should not be deferred until after systemic anti-cancer therapy (SACT). (Conditional – by consensus)

## Managing malignant pleural effusion

### Pleural aspiration with no pleurodesis agent versus talc slurry pleurodesis

### *Recommendation*

- Management of malignant pleural effusion (MPE) using talc pleurodesis (or another method) is recommended in

preference to repeated aspiration especially in those with a better prognosis, but the relative risks and benefits should be discussed with the patient. (Conditional – by consensus)

### *Good practice points*

- ✓ Decisions on the best treatment modality should be based on patient choice.
- ✓ Informed decision making should include the role of inpatient vs ambulatory management and the potential risk of requiring further pleural interventions.

## Indwelling pleural catheter versus talc slurry pleurodesis

### *Recommendation*

- Patients without known non-expandable lung should be offered a choice of indwelling pleural catheter (IPC) or pleurodesis as first line intervention in the management of MPE. The relative risks and benefits should be discussed with patients to individualise treatment choice. (Conditional)

### *Good practice points*

- ✓ The psychological implications and potential altered body image aspects of having a semi-permanent tube drain in situ should not be underestimated and must be considered prior to insertion.
- ✓ All patients who have had an IPC inserted should be referred to the community nursing team on discharge for an early assessment of the wound site, symptom control, support with IPC drainage and removal of sutures.
- ✓ Patients and their relatives should be supported to perform community drainage and complete a drainage diary if they feel able to do so, to promote independence and self-management.
- ✓ Complications such as infection refractory to community management, suspected drain fracture, loculations or blockage with persistent breathlessness should be referred back to the primary pleural team for further assessment.

## Thoracoscopy and talc poudrage pleurodesis versus chest drain and talc slurry pleurodesis

### *Recommendation*

- Talc slurry or talc poudrage may be offered to patients with MPE to control fluid and reduce the need for repeated procedures. (Conditional)

### *Good practice point*

- ✓ Where a diagnostic procedure is being conducted at thoracoscopy (pleural biopsies), if talc pleurodesis is reasonable, this should be conducted during the same procedure via poudrage.

## Surgical pleurodesis, or surgical decortication versus talc slurry pleurodesis

### *Recommendation*

- In selected patients considered fit enough for surgery, either surgical talc pleurodesis or medical talc slurry can be considered for the management of patients with MPE. The relative risks, benefits and availability of both techniques should be discussed with patients to individualise treatment choice. (Conditional – by consensus)

**Good practice points**

- ✓ Informed decision-making should include the role of surgery versus ambulatory management with an IPC for the management of MPE in selected patients.
- ✓ Decortication surgery may improve pleurodesis success in malignant pleural effusion patients with non-expandable lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery).

**Managing malignant pleural effusion and non-expandable lung**

Pleural aspiration, talc slurry pleurodesis, talc poudrage pleurodesis, decortication surgery or indwelling pleural catheter (IPC)

**Good practice points**

- ✓ Decisions on treatment modality for malignant pleural effusion and non-expanded lung should be based on patient choice, with the relative risks and benefits of each modality discussed with the patient, but patients should be made aware of the limited evidence base regarding treatment options for non-expandable lung.
- ✓ IPCs are effective at controlling symptoms in non-expandable lung and should be considered, but it may be appropriate to undertake pleural aspiration first to assess symptomatic response.
- ✓ Pleural aspiration may result in a need for multiple procedures so alternatives should be discussed with the patient.
- ✓ In patients with radiologically significant (>25%) non-expandable lung requiring intervention for a symptomatic MPE, current evidence suggests the use of an indwelling pleural catheter rather than talc pleurodesis.
- ✓ In MPE patients with less than 25% non-expandable lung, talc slurry pleurodesis may improve quality of life, chest pain, breathlessness and pleurodesis rates.
- ✓ Decortication surgery may improve pleurodesis success in selected MPE patients with non-expanded lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery).

**Managing malignant pleural effusion and septated effusion (on radiology)**

Intrapleural enzymes versus surgery, or no treatment

**Good practice points**

- ✓ Intrapleural fibrinolytics can be considered in highly selected symptomatic patients with MPE to try to improve breathlessness.
- ✓ Intrapleural fibrinolytics may be used in patients with MPE and septated effusion and an indwelling pleural catheter (IPC) to improve drainage if flushing the IPC with normal saline or heparinised saline does not improve drainage.
- ✓ Surgery can be considered for palliation of symptoms in a minority of patients with significantly septated MPE and associated symptoms and otherwise good prognosis and performance status.

**Managing malignant pleural effusion treated with an indwelling pleural catheter (IPC)**

Symptom-based/conservative drainage versus daily drainage

**Recommendations**

- Where IPC removal is a priority, daily IPC drainages are recommended to offer increased rates of pleurodesis when

compared with less frequent drainages of symptom-guided or alternate drainage regimes. (Conditional)

- Patients should be advised that they do not require daily drainage to control symptoms of breathlessness and chest pain if they wish to opt for a less intensive regime. (Strong – by consensus)

**Good practice points**

- ✓ Decisions on the optimal drainage should be based on patient choice.
- ✓ Informed decision making should include the explanation of the effect of drainage regimes on the patient-centre outcomes such as breathlessness and the possibility of auto-pleurodesis during the disease course.
- ✓ Although daily drainage may result in earlier removal of IPC, there may be an associated cost associated with the increased number of drainage events (both to the healthcare system, and to the patient). This has been addressed in a modelling study<sup>13</sup> and should be considered.

**Intrapleural agents (talc or other pleurodesis agents)****Recommendation**

- Instillation of talc via an indwelling pleural catheter (IPC) should be offered to patients with expandable lung where the clinician or patient deems achieving pleurodesis and IPC removal to be important. (Conditional – by consensus)

**Intrapleural chemotherapy versus systemic treatment for treating pleural malignancy****Recommendation**

- Intrapleural chemotherapy should not be routinely used for the treatment of MPE. (Conditional – by consensus)

**Good practice point**

- ✓ All patients of good performance status with metastatic malignancy should be considered for systemic anti-cancer therapy (SACT) as standard of care as per national guidelines.

**Using prognostic or predictive scores to provide prognostic information for patients with malignant pleural effusion****Good practice points**

- ✓ Clinicians may consider using a validated risk score for malignant pleural effusion if the information is of use in planning treatments or in discussion with patients.
- ✓ Patients with pleural malignancy should be managed in a multi-disciplinary way, including referral to specialist palliative care services where appropriate.

Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply recommendations for the management of patients. The recommendations cited here are a guide and may not be appropriate for use in all situations. The guidance provided does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

**Author affiliations**

<sup>1</sup>Respiratory Medicine, Sherwood Forest Hospitals NHS Foundation Trust, Nottinghamshire, UK

<sup>2</sup>University of Oxford, Oxford Respiratory Trials Unit, Oxford, UK

<sup>3</sup>Oxford NIHR Biomedical Research Centre, Oxford, UK

<sup>4</sup>Oxford Pleural Unit, Churchill Hospital, Oxford, UK

<sup>5</sup>Academic Respiratory Unit, University of Bristol and North Bristol NHS Trust, UK

<sup>6</sup>Glasgow Pleural Disease Unit, Queen Elizabeth University Hospital, Glasgow, UK

- <sup>7</sup>School of Cancer Sciences, University of Glasgow/Cancer Research UK Beatson Institute, Glasgow, UK  
<sup>8</sup>Interventional Pulmonology Service, University Hospitals Plymouth NHS Trust, Plymouth, UK  
<sup>9</sup>North Bristol NHS Trust, Westbury on Trym, UK  
<sup>10</sup>North West Lung Centre, Manchester University NHS Foundation Trust, Manchester, UK  
<sup>11</sup>Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK  
<sup>12</sup>Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK  
<sup>13</sup>Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia  
<sup>14</sup>Manchester University NHS Foundation Trust, Manchester, UK  
<sup>15</sup>Academic Division of Thoracic Surgery, The Royal Brompton Hospital and Imperial College London, London, UK  
<sup>16</sup>Regional Respiratory Centre, Belfast Health and Social Care Trust, Belfast, UK  
<sup>17</sup>Portsmouth Hospitals University NHS Trust, Portsmouth, UK  
<sup>18</sup>Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK  
<sup>19</sup>Department of Histopathology, Royal Brompton and Harefield Hospitals, Guy's and St Thomas' NHS Foundation Trust and National Heart and Lung Institute, London, UK  
<sup>20</sup>St George's University Hospitals NHS Foundation Trust, London, UK  
<sup>21</sup>British Thoracic Society, London, UK  
<sup>22</sup>North Cumbria Integrated Care NHS Foundation Trust, Cumbria, UK  
<sup>23</sup>Freeman Hospital, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK

**Twitter** Nick A Maskell @BristolARU, Anna C Bibby @BristolARU, Kevin G Blyth @kevingblyth, Matthew Evison @matthewevison1, Duneesha de Fonseka @defonseka, Eleanor K Mishra @EleanorKMishra, Maria Parsonage @Parsonage and Andrew E Stanton @andrewestanton

**Contributors** MER, NMR and NAM were the lead authors responsible for the final document. All authors agreed the outline and content of the document and authored sections of the document and the clinical question reviews.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared. BTS Declarations of Interest forms have been completed by all members for each year they were part of the GDG. Details of these forms can be obtained from BTS Head Office. 'Declarations of Interests' was a standing item at each GDG meeting.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Commissioned; internally peer reviewed.

#### ORCID iDs

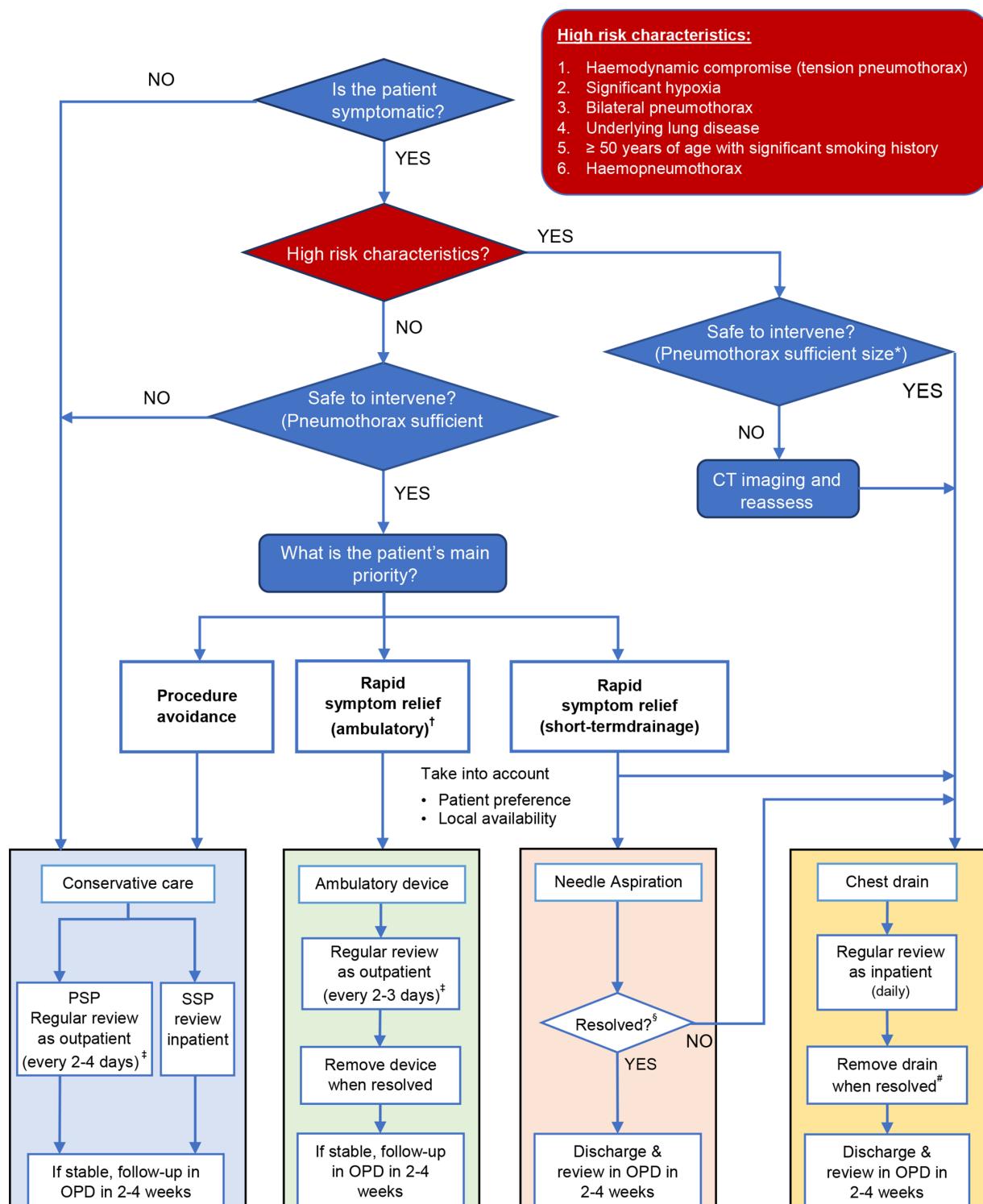
- Najib M Rahman <http://orcid.org/0000-0003-1195-1680>  
Kevin G Blyth <http://orcid.org/0000-0003-2972-6641>  
John P Corcoran <http://orcid.org/0000-0002-0480-7819>  
Matthew Evison <http://orcid.org/0000-0003-4066-5253>  
Duneesha de Fonseka <http://orcid.org/0000-0002-0060-9671>  
Eleanor K Mishra <http://orcid.org/0000-0002-5903-3005>  
Andrew E Stanton <http://orcid.org/0000-0001-6758-7051>

#### REFERENCES

- 1 British Thoracic Society. Pleural disease guideline. *Thorax*. Forthcoming; 2023.
- 2 British Thoracic Society (BTS). Quality improvement: pleural disease. Available: <https://www.brit-thoracic.org.uk/quality-improvement/guidelines/pleural-disease/> [Accessed 01 Mar 2023].
- 3 Du Rand I, Maskell N. Introduction and methods: British thoracic society pleural disease guideline 2010. *Thorax* 2010;65 Suppl 2:ii1–3.
- 4 Hooper C, Lee YCG, Maskell N, et al. Investigation of a unilateral pleural effusion in adults: British thoracic society pleural disease guideline. *Thorax* 2010;65 Suppl 2:ii4–17.
- 5 MacDuff A, Arnold A, Harvey J, et al. Management of spontaneous Pneumothorax: British thoracic society pleural disease guideline. *Thorax* 2010;65 Suppl 2:ii18–31.
- 6 Roberts ME, Neville E, Berrisford RG, et al. Management of a malignant pleural effusion: British thoracic society pleural disease guideline. *Thorax* 2010;65 Suppl 2:ii32–40.
- 7 Davies HE, Davies RJO, Davies CWH, et al. Management of pleural infection in adults: British thoracic society pleural disease guideline. *Thorax* 2010;65 Suppl 2:ii41–53.
- 8 Rahman NM, Ali NJ, Brown G, et al. Local anaesthetic thoracoscopy: British thoracic society pleural disease guideline. *Thorax* 2010;65 Suppl 2:ii54–60.
- 9 Havelock T, Teoh R, Laws D, et al. Pleural procedures and thoracic ultrasound: British thoracic society pleural disease guideline 2010. *Thorax* 2010;65 Suppl 2:ii61–76.
- 10 Woolhouse I, Bishop L, Darlison L, et al. British thoracic society guideline for the investigation and management of malignant pleural Mesothelioma. *Thorax* 2018;73:i1–30.
- 11 British Thoracic Society. Clinical statement on pleural procedures. *Thorax* 2023. Forthcoming; 2023.
- 12 BMJ Best Practice. What is GRADE? 2022. Available: <https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/> [Accessed 01 Mar 2023].
- 13 Shafiq M, Simkovich S, Hossen S, et al. Indwelling pleural catheter drainage strategy for malignant effusion: a cost-effectiveness analysis. *Ann Am Thorac Soc* 2020;17:746–53.

### APPENDIX 1 – CLINICAL PATHWAYS/DECISION TREES

#### Pneumothorax Pathway



\* Pneumothorax of sufficient size to intervene depends on clinical context but, in general, usually ≥ 2cm laterally or apically on CXR, or any size on CT scan which can be safely accessed with radiological support.

† If ambulatory pathway available locally.

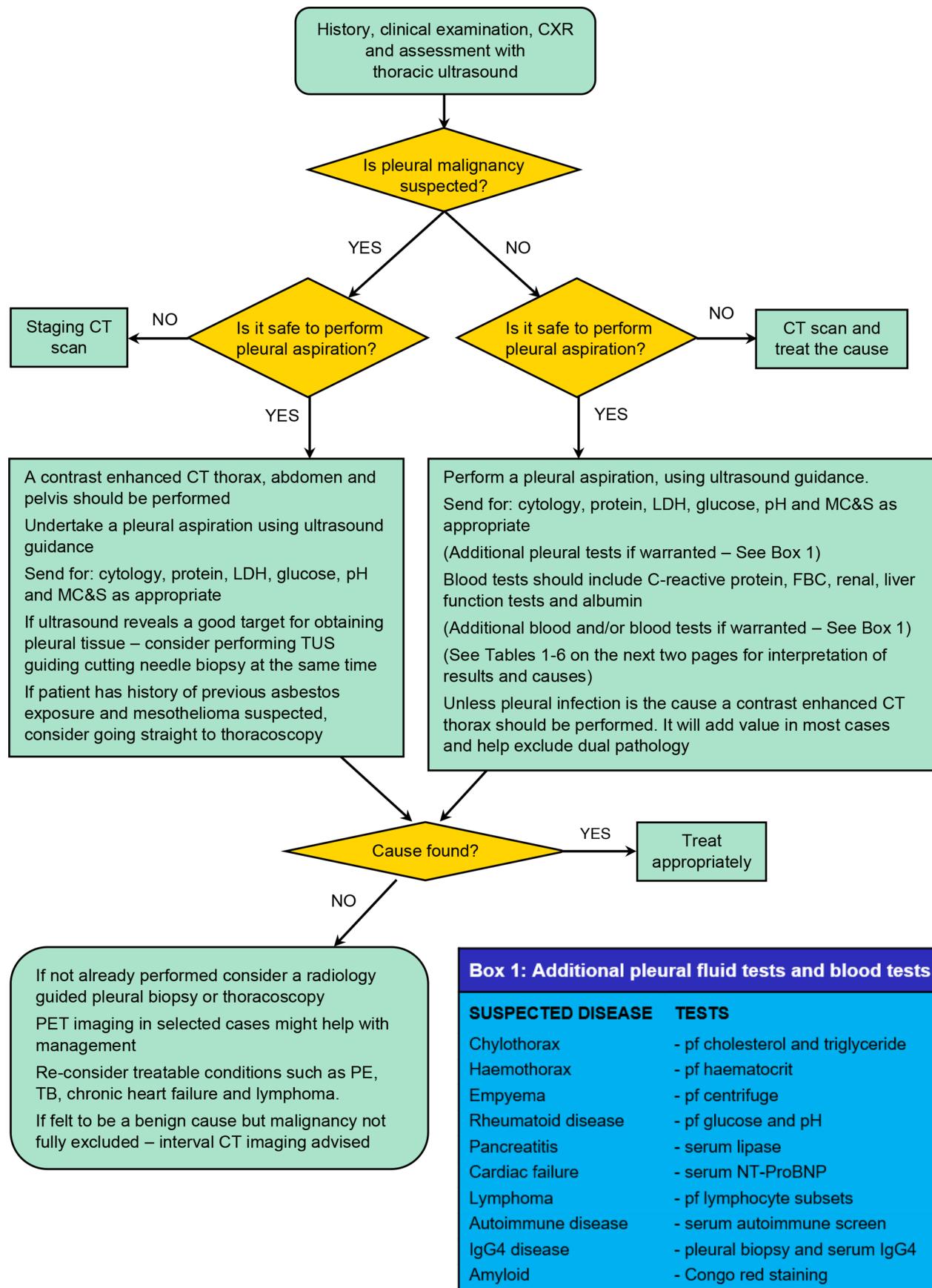
‡ At review, if enlarging pneumothorax or symptoms consider chest drain insertion and admission.

§ Success: improvement in symptoms and sustained improvement on CXR.

# Talc pleurodesis can be considered on the first episode of pneumothorax in high risk patients in whom repeat pneumothorax would be hazardous (eg, severe COPD).

CXR, chest X-ray; COPD, chronic obstructive pulmonary disease; OPD, outpatient department; PSP, primary spontaneous pneumothorax; SSP, secondary spontaneous pneumothorax.

## Unilateral pleural effusion diagnostic pathway



CXR, chest X-ray; FBC, full blood count; LDH, lactate dehydrogenase; NT-proBNP, N-terminal prohormone brain natriuretic peptide; PE, pulmonary embolism; TB, tuberculosis; TUS, thoracic ultrasound.

## Guideline summary

### Unilateral pleural effusion diagnostic pathway – Tables 1–6

Table 1

Light's criteria
Pleural fluid is an exudate if one or more of the following criteria are met:
<ul style="list-style-type: none"><li>• Pleural fluid protein divided by serum protein is &gt;0.5</li><li>• Pleural fluid lactate dehydrogenase (LDH) divided by serum LDH is &gt;0.6</li><li>• Pleural fluid LDH &gt;2/3 the upper limits of laboratory normal value for serum LDH</li></ul>

Table 2

Transudates	Exudates
<b>Common</b> <ul style="list-style-type: none"><li>• Congestive cardiac failure</li><li>• Liver cirrhosis</li><li>• Hypoalbuminaemia</li><li>• Nephrotic syndrome</li></ul>	<b>Common</b> <ul style="list-style-type: none"><li>• Malignancy</li><li>• Pleural infection</li><li>• Pulmonary embolism</li><li>• Autoimmune pleuritis</li></ul>
<b>Less common</b> <ul style="list-style-type: none"><li>• Nephrotic syndrome</li><li>• Mitral stenosis</li><li>• Peritoneal dialysis</li><li>• Chronic hypothyroidism</li><li>• Constrictive pericarditis</li></ul>	<b>Less common</b> <ul style="list-style-type: none"><li>• Drugs</li><li>• Lymphatic disorders</li><li>• Meigs syndrome</li><li>• Post-coronary artery bypass graft</li><li>• Benign asbestos related pleural effusion</li></ul>

Table 3

Causes of lymphocytic pleural effusion
Malignancy
Tuberculosis
Lymphoma
Congestive cardiac failure
Post-coronary bypass graft
Rheumatoid arthritis
Chylothorax
Yellow nail syndrome

Table 4

Causes of bilateral pleural effusions
Congestive cardiac failure
Hypoalbuminaemia
Renal failure
Liver failure
SLE and other autoimmune diseases
Widespread malignancy including abdominal/pelvic malignancy
Bilateral pulmonary embolus

Table 5

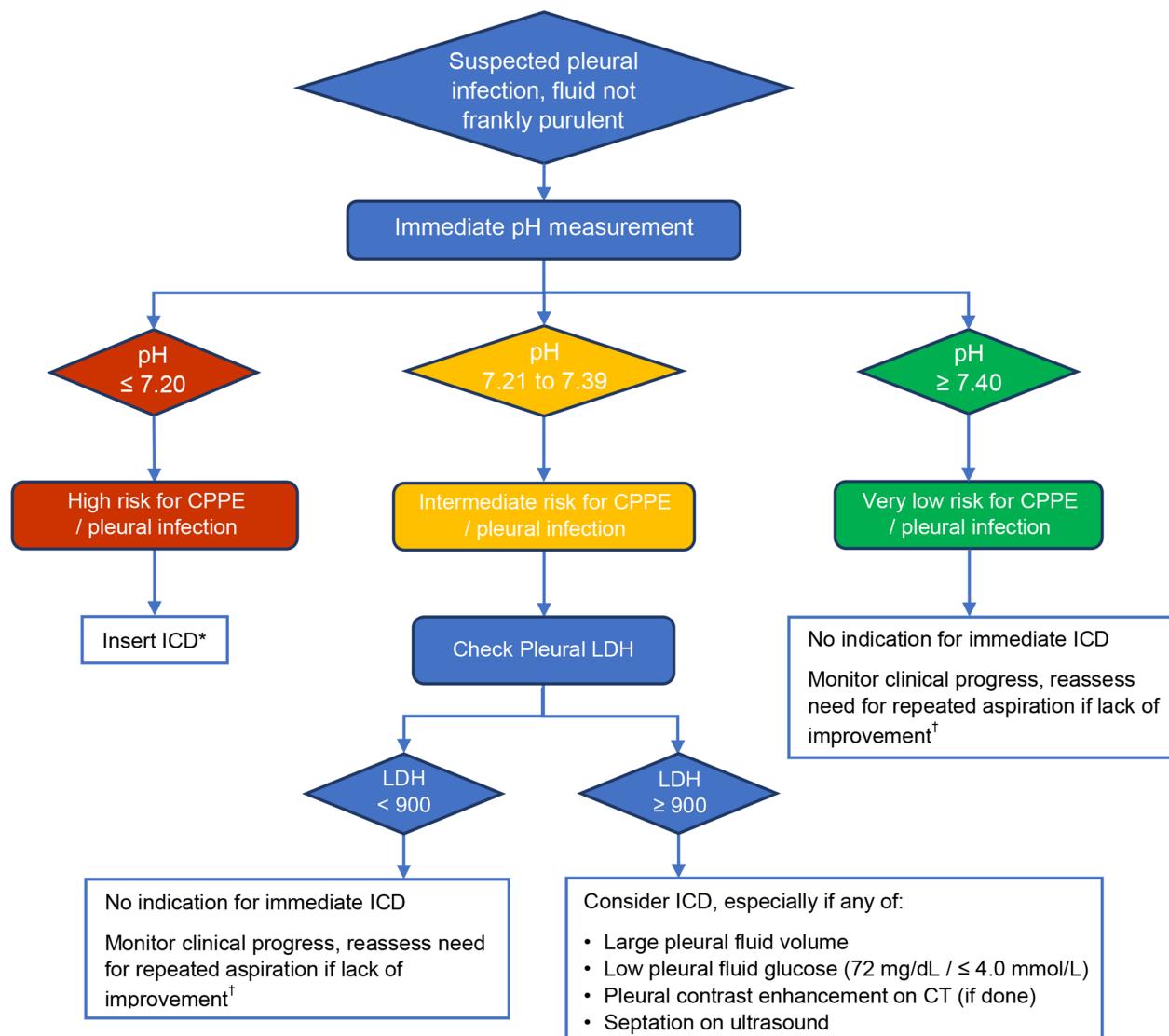
Pleural fluid lipid values in chylothorax and pseudochylothorax	
<b>Chylothorax:</b>	
• Triglycerides	– high >1.24 mmol/L (110 mg/dL)
• Cholesterol	– low
• Cholesterol crystals	– absent
• Chylomicrons	– usually present
<b>Pseudochylothorax:</b>	
• Triglycerides	– low
• Cholesterol	– high >5.18 mmol/L (200 mg/dL)
• Cholesterol crystals	– often present
• Chylomicrons	– absent

Table 6

Causes of chylothorax and pseudochylothorax	
<b>Chylothorax:</b>	
• Trauma:	thoracic surgery (especially if involving posterior mediastinum, for example, oesophagectomy), thoracic injuries
• Neoplasm:	lymphoma or metastatic carcinoma
• Miscellaneous:	disorders of lymphatics (including lymphangioliomyomatosis), tuberculosis, cirrhosis, obstruction of the central veins, chyloascites
• Idiopathic (about 10%)	
<b>Pseudochylothorax:</b>	
• Tuberculosis	
• Rheumatoid arthritis	

## Guideline summary

### Suspected pleural infection, non-purulent fluid – initial decision tree



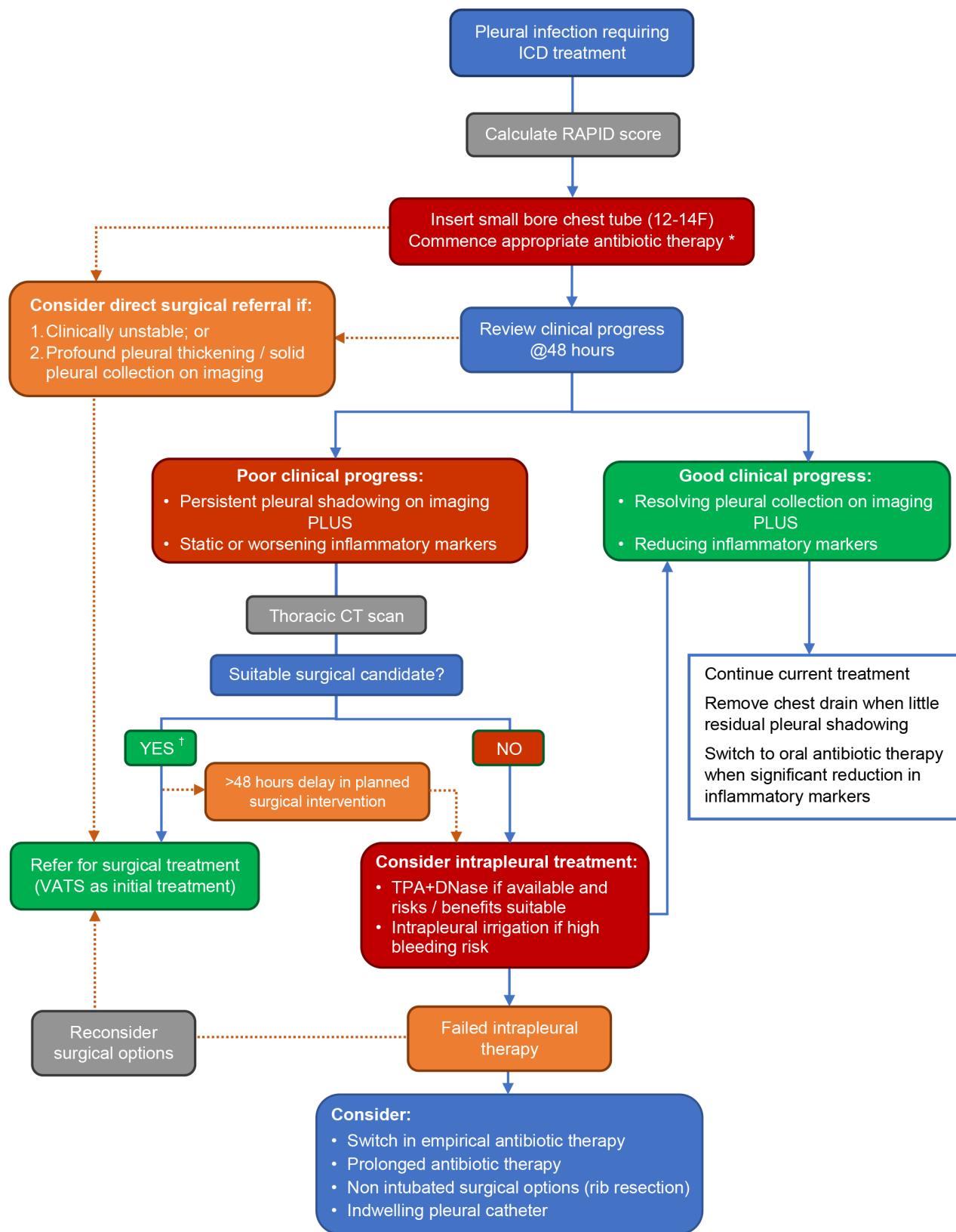
\* Assuming ultrasound demonstrates safe volume of accessible pleural fluid.

<sup>†</sup> As evidenced by ongoing temperature, persisting elevation of inflammatory markers. Those with septations and pleural pH >7.4 should also be considered for drainage.

Initial pH	Level of risk for CPPE / pleural infection	Initial action regarding drainage
≤ 7.2	High risk	Insert ICD, assuming ultrasound demonstrates safe volume of accessible pleural fluid
> 7.2 to < 7.4	Intermediate risk	Check LDH and review other parameters which may support CPPE / pleural infection. Consider ICD insertion if LDH > 900, especially if any of the following: <ul style="list-style-type: none"><li>• Large pleural fluid volume</li><li>• Low pleural fluid glucose (72 mg/dL / ≤ 4.0 mmol/L)</li><li>• Pleural contrast enhancement on CT</li><li>• Septation on ultrasound</li></ul>
≥ 7.4	Very low risk	No indication for immediate ICD

CPPE, complex parapneumonic effusion; LDH, lactate dehydrogenase; ICD, intercostal drain.

## Pleural infection treatment pathway

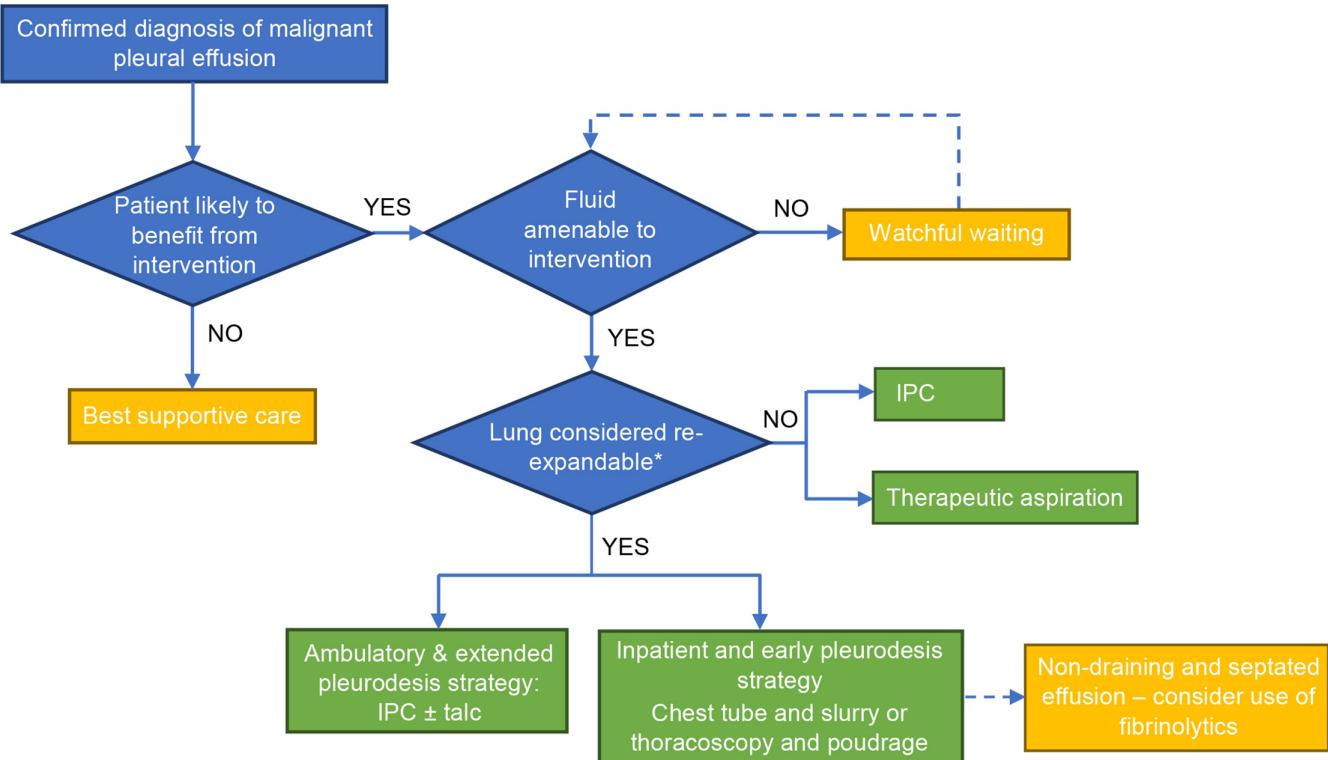


\* Antibiotic therapy should be based on likely organisms initially and adapted according to positive culture results, with consideration of anaerobic cover throughout.

† Intrapleural treatment may be considered prior to surgical treatment in liaison with surgical expertise.

ICD, intercostal drain; TPA, tissue plasminogen activator; VATS, video-assisted thoracoscopic surgery.

## Malignant pleural effusion pathway



IPC, indwelling pleural catheter.