# Online Appendix A5 BTS Guideline for Pleural Disease

## Section A Spontaneous pneumothorax

## Question A5 Evidence Review and Protocol

**A5 In adults with spontaneous pneumothorax what is the optimal operation for improving clinical outcomes?**

### Contents

## Question Evidence Review

### A5 In adults with spontaneous pneumothorax what is the optimal operation for improving clinical outcomes?

#### Background

Thoracic surgery for pneumothorax can be broadly divided into two different types, i) resection of lung parenchyma (often visible sub-pleural blebs or bullae) to remove the suspected source of the current air leak and prevent future potential sources of air leaks; and ii) surgical pleurodesis to obliterate the pleural space via an inflammatory symphysis of the visceral and parietal pleura to prevent the accumulation of air within that space and prevent any future episodes of pneumothorax. The former requires a 'bullectomy' a form of wedge resection using stapler equipment and can also include the use of a 'sealant' (such as glue and a mesh) to further fortify the site of lung resection. The latter can be achieved through a number of different methods intra-operatively including pleural abrasion, partial pleurectomy and talc poudrage. The aim of this review was to compare these two main types of pneumothorax surgery for the treatment of spontaneous pneumothorax in adults.

#### Outcomes

Pneumothorax recurrence, length of hospital stay, further treatment (surgery, chest drain, conservative management), pain and breathlessness, duration of air leak, complications, quality of life and mortality

#### Evidence review

The literature search identified 133 abstracts for review, of which 10 studies were relevant to the review. Two studies were randomised controlled trials[1,2] and the remainder retrospective cohort studies[3-10]. One study specifically investigated secondary pneumothorax in patients with emphysema.[2] All studies reported data outcomes for patients undergoing bullectomy alone (+/- sealant) and those underdoing surgical pleurodesis.

It should be noted that there were differences within the data that should be taken into consideration:

i) The commonest form of surgical pleurodesis within the studies was pleural abrasion, with talc pleurodesis and pleurectomy being under-represented within these studies. It has previously been published that pleural abrasion may represent a weaker form of pleurodesis in comparison to the other two methods.[11]

ii) There is variability within the two surgical groups in a number of studies e.g. whether a sealant was used during a bullectomy, the type of sealant used in a bullectomy and the type of surgical pleurodesis.

*Pneumothorax recurrence*

All studies reported on pneumothorax recurrence, but meta-analysis (Figure A5a) showed no difference in the rate of pneumothorax recurrence between bullectomy (93 per 1000 patients (75 to 114)) and surgical pleurodesis (93 per 1000) for the treatment of spontaneous pneumothorax in adults.

*Length of hospital stay*

Length of hospital stay was reported in four studies.[1-3,5] Meta-analysis showed no difference in the length of hospital stay between pneumothorax treatment with bullectomy or surgical pleurodesis, but there was significant inconsistency between the studies (Figure A5b).

*Further treatment (surgery, chest drain, conservative management)*

Three studies reported the need for further treatment[1,3,5], but meta-analyses showed no difference in the need for further treatment, the need for surgery, the need for chest drain or the need for conservative management following bullectomy or surgical pleurodesis (Figure A5c and Table A5a).

Table A5a: Comparison of the risk of need for further treatment following bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax in adults

| Further treatment | No. datasets | **Risk of need for further treatment** (per 1000 patients) Bullectomy | Surgical pleurodesis |
|---|---|---|---|
| Combined* | 8 | 42 (32 to 54) | 42 |
| Further surgery | 3 | 50 (34 to 76) | 49 |
| Chest drain | 2 | 28 (17 to 47) | 44 |
| Conservative management | 3 | 45 (28 to 73) | 45 |

* Combined – combined subgroup data (further surgery, chest drain and conservative management)

*Pain and breathlessness*

Pain was reported in two studies[1,5], but was reported in different formats, A summary of the results is shown in Table A5b.

Table A5b: Comparison of post-operative chest pain following surgical pleurodesis or bullectomy alone for the treatment of pneumothorax

| Study | Pain type | Bullectomy | Surgical pleurodesis | *p* |
|---|---|---|---|---|
| | | VAS (mean ± SD score) (mm) | | |
| Horio 2002[5] | Post-operative chest pain | 11.8 ± 0.9 | 11.0 ± 8.5 | NS |
| | | % patients (no. patients) | | |
| Lee 2014[1] | Residual pain | 38.6% (292/757) | 51.3% (337/657) | <0.001 |
| | Occasional pain* | 34.3% (260/757) | 42.9% (282/657) | NS |
| | Intermittent pain† | 3.8% (29/757) | 5.2% (34/657) | NS |
| | Daily pain‡ | 0.4% (3/757) | 3.2% (21/657) | NS |

* Not requiring analgesia

† Requiring intermittent analgesia

‡ Requiring daily analgesia

NS – not significant; VAS – visual analogue scale

Breathlessness was not reported in any study.

*Duration of air leak*

Seven studies reported on duration of air leak, with six reporting actual duration[1-3,5,8,10] and six reporting duration greater than 5 days[1,3-5,8,10], but meta-analysis showed no difference in the duration of air leak (Figure A5d), or the duration of air leak greater than five days (Figure A5e) between bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax.

*Complications*

Seven studies reported on complications[1-5,8,10], but three reported no complications in both experiment arms (bullectomy and surgical pleurodesis), so could not be included in the meta-analysis[4,5,8]. Meta-analysis of the remaining studies[1-3,10] showed no difference in the risk of complications between bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax (62 per 1000 patients (44 to 88) compared with 81 per 1000 respectively) (Figure A5f).

*Quality of life*

No studies reported on quality of life.

*Mortality*

Seven studies reported mortality rate at day 30 following bullectomy alone or surgical pleurodesis for the treatment of pneumothorax.[2,3,5-9] Six of these studies reported no deaths in either experimental arm (bullectomy or surgical pleurodesis)[2,3,5,7-9], with the final study reporting two deaths following surgical pleurodesis (2/235 subjects), but both subjects underwent thoracotomy prior to adoption of VATS[6].

**Evidence statements**

There appears to be no difference in pneumothorax recurrence (**Very low**), length of hospital stay (**Very low**), the need for further treatment (surgery, chest drain or conservative management) (**Very low**), duration of air leak (**Very low**), complications (**Very low**) or mortality (**Ungraded**) following bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax in adults

There was insufficient evidence to comment on pain and breathlessness and quality of life following bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax in adults

**Recommendation**

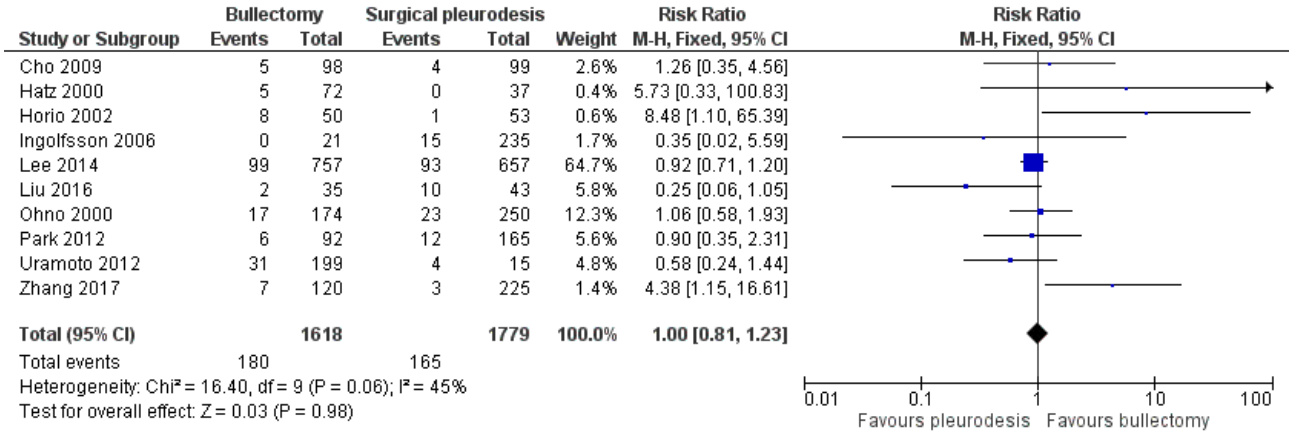
- Surgical pleurodesis and/or bullectomy can be considered for the treatment of spontaneous pneumothorax in adults (**Conditional**)

**Research Recommendation**

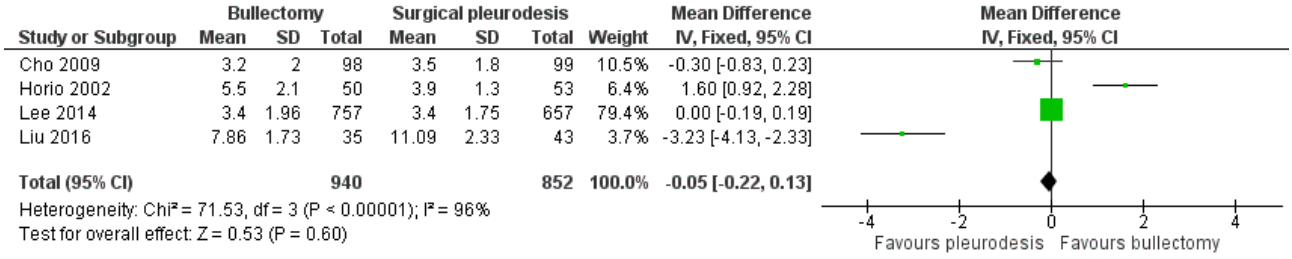
- Further research is needed to determine optimal type of surgical pleurodesis (e.g. pleurectomy, abrasion, talc) and adjunct (e.g. bullectomy) for the treatment of spontaneous pneumothorax in adults

## Meta-analyses

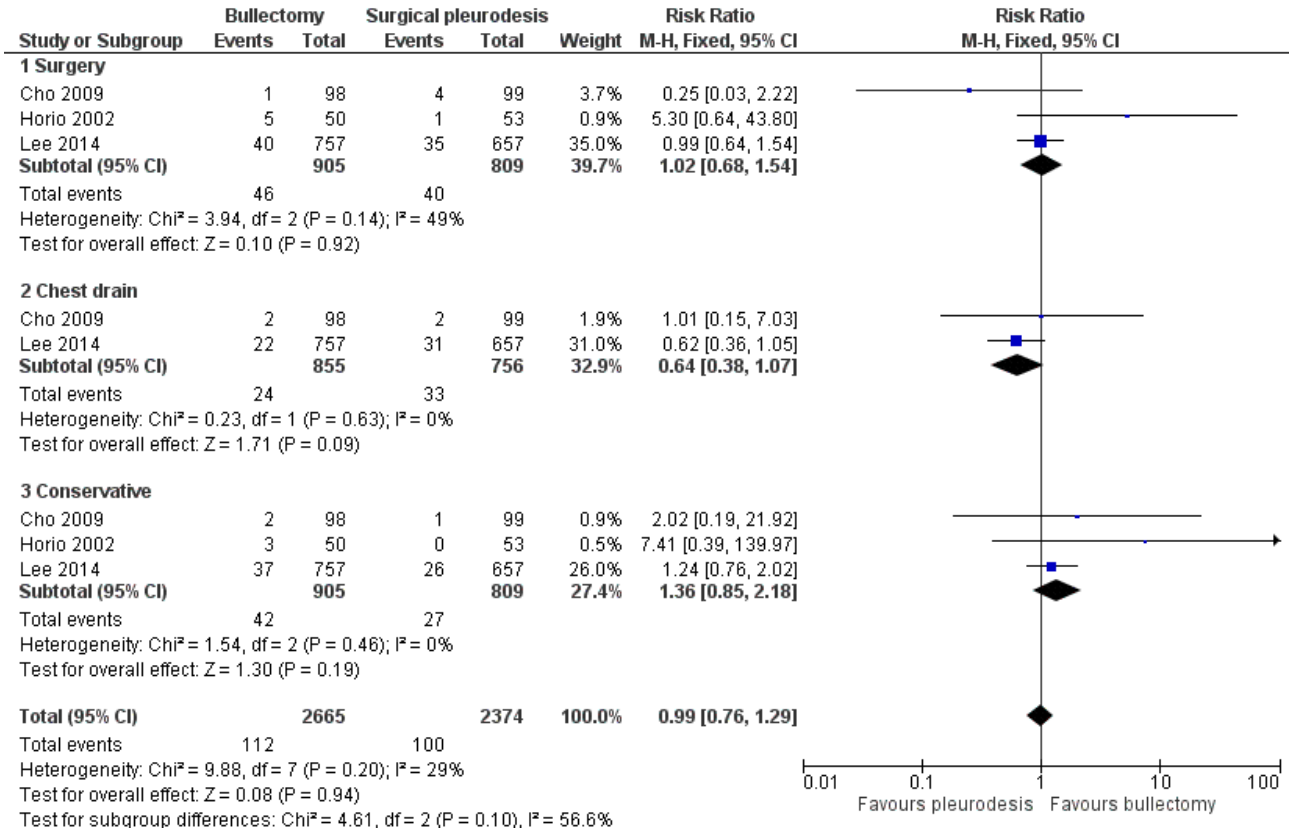
### *Figure A5a Pneumothorax recurrence*



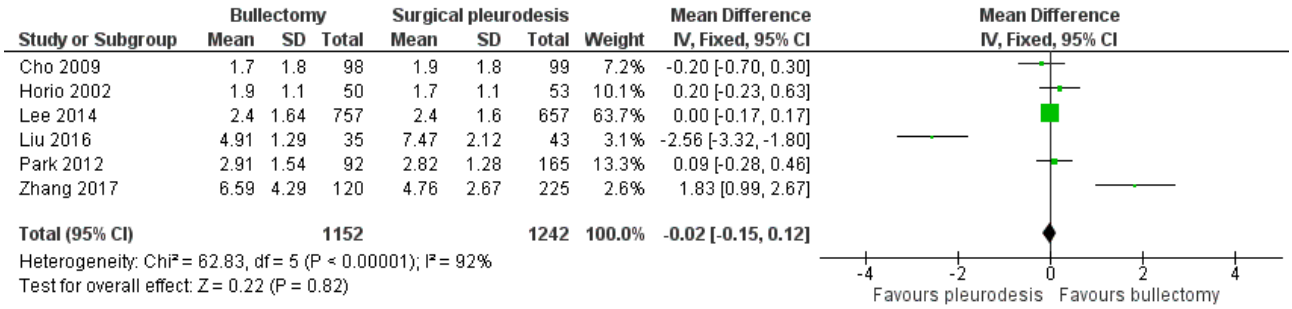

### *Figure A5b Length of hospital stay*



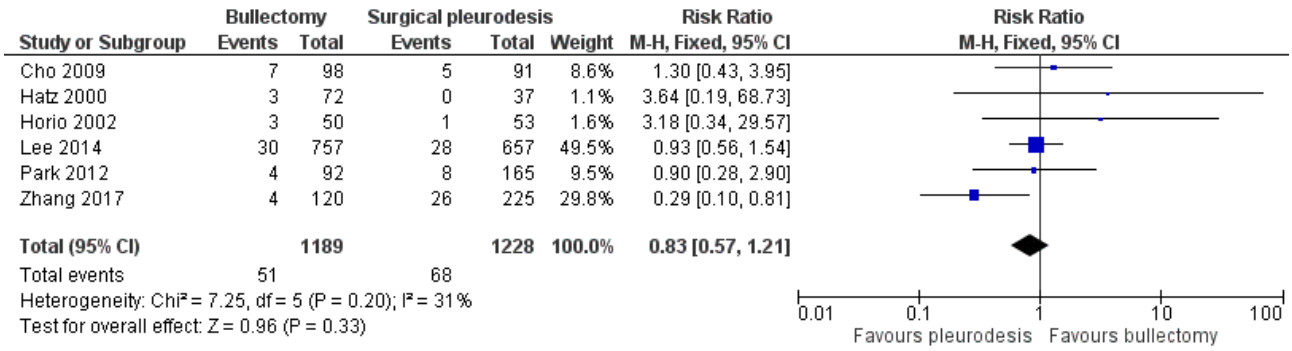

### *Figure A5c Further treatment (surgery, chest drain, conservative management)*



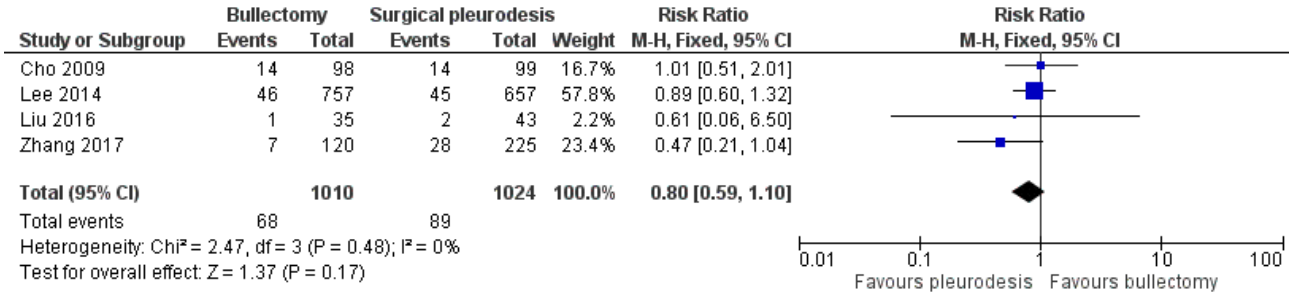
### *Figure A5d Duration of air leak – chest drain in situ*



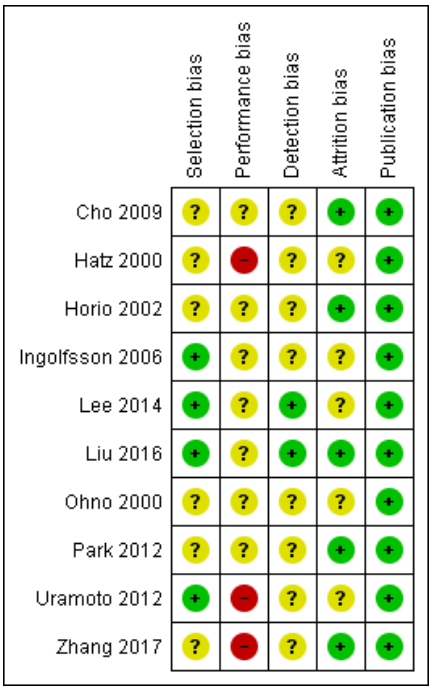

### *Figure A5e Duration of air leak – prolonged air leak*




### *Figure A5f Complications*



## Risk of bias summary




## GRADE analyses

**In adults with spontaneous pneumothorax what is the optimal operation for improving clinical outcomes?**

**Population**: Adults (18+) with spontaneous pneumothorax undergoing surgery

**Intervention**: Bullectomy alone

**Comparator**: Surgical pleurodesis (talc, abrasion, other technique)

| Outcome | Number of participants (studies) | Estimate of effect | Quality of the Evidence (GRADE) |
|---|---|---|---|
| **Length of hospital stay** | 1792 (4 studies) | 0.05 days lower (0.22 lower to 0.13 higher) in the intervention group | ⨁◯◯◯ **VERY LOW** [a,b] |
| **Duration of air leak (chest drain in situ)** | 2394 (6 studies) | 0.02 days lower (0.15 lower to 0.12 higher) in the intervention group | ⨁◯◯◯ **VERY LOW** [a,b] |

**Explanations**

a. High risk of bias across the studies

b. Serious inconsistency across the studies

**In adults with spontaneous pneumothorax what is the optimal operation for improving clinical outcomes?**

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**Comparator**: Surgical pleurodesis (talc, abrasion, other technique)

| Outcome | Number of participants (studies) | Relative effect (95% CI) | Anticipated absolute effects | | Quality of the Evidence (GRADE) |
|---|---|---|---|---|---|
| | | | Pleurodesis | Bullectomy | |
| **Recurrence** | 3397 (10 studies) | RR 1.00 (0.81 to 1.23) | **93 per 1000** | **93 per 1000** (75 to 114) | ⨁◯◯◯ **VERY LOW** [a,b] |
| **Further treatment** | 5039 (3 studies) | RR 0.99 (0.76 to 1.29) | **42 per 1000** | **42 per 1000** (32 to 54) | ⨁◯◯◯ **VERY LOW** [a,b,c] |
| **Further treatment – surgery** | 1714 (3 studies) | RR 1.02 (0.68 to 1.54) | **49 per 1000** | **50 per 1000** (34 to 76) | ⨁◯◯◯ **VERY LOW** [a,b,c] |
| **Further treatment – chest drain** | 1611 (2 studies) | RR 0.64 (0.85 to 2.18) | **44 per 1000** | **28 per 1000** (17 to 47) | ⨁◯◯◯ **VERY LOW** [a,d,e] |
| **Further treatment – conservative** | 1714 (3 studies) | RR 1.36 (0.85 to 2.18) | **33 per 1000** | **45 per 1000** (28 to 73) | ⨁◯◯◯ **VERY LOW** [a,d,e] |
| **Duration of air leak – prolonged air leak** | 2417 (6 studies) | RR 0.83 (0.59 to 1.1) | **87 per 1000** | **70 per 1000** (51 to 96) | ⨁◯◯◯ **VERY LOW** [a,d,e] |
| **Complications** | 2034 (4 studies) | RR 0.8 (0.54 to 1.08) | **81 per 1000** | **62 per 1000** (44 to 88) | ⨁◯◯◯ **VERY LOW** [a,e] |

**CI:** Confidence interval

**Explanations**

a. High risk of bias across the studies
b. Serious inconsistency across the studies
c. Serious imprecision, CIs cross both MIDs
d. Some inconsistency across the studies
e. Some imprecision, CIs cross one MID

## Recommendation Table

### Question Details

| | |
|---|---|
| **POPULATION:** | Adults (18+) with spontaneous pneumothorax undergoing surgery |
| **INTERVENTION:** | Bullectomy alone |
| **COMPARISON:** | Surgical pleurodesis (talc, abrasion, other technique) |
| **OUTCOMES:** | Pneumothorax recurrence; length of hospital stay; further treatment (surgery, chest drain, conservative management); pain and breathlessness; duration of air leak; complications; quality of life; mortality |

### 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 |
| **BALANCE OF EFFECTS** | Favours the comparison | Probably favours the comparison | **Does not favour the intervention or the comparison** | Probably favours the intervention | Favours the intervention | Varies | Don't know |

### TYPE OF RECOMMENDATION

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

## CONCLUSIONS

### Recommendation

Surgical pleurodesis and/or bullectomy can be considered for the treatment of spontaneous pneumothorax in adults

### Justification

There appears to be no difference in pneumothorax recurrence (**Very low**), length of hospital stay (**Very low**), the need for further treatment (surgery, chest drain or conservative management) (**Very low**), duration of air leak (**Very low**), complications (**Very low**) or mortality (**Ungraded**) following bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax in adults

There was insufficient evidence to comment on pain and breathlessness and quality of life following bullectomy or surgical pleurodesis for the treatment of spontaneous pneumothorax in adults

### Subgroup considerations

There were no subgroups to consider

### Research priorities

Further research is needed to determine optimal type of surgical pleurodesis (e.g. pleurectomy, abrasion, talc) and adjunct (e.g. bullectomy) for the treatment of spontaneous pneumothorax in adults

## References


1. Lee S, Kim HR, Cho S, et al. Staple line coverage after bullectomy for primary spontaneous pneumothorax: a randomized trial. *Annals of Thoracic Surgery.* 2014;98(6):2005-2011.
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## Question Protocol

| Field | Content |
|---|---|
| Review Question | In adults with spontaneous pneumothorax undergoing surgery, what is the optimal operation for improving clinical outcomes? |
| Type of review question | Intervention review |
| Objective of the review | A question comparing surgical techniques in patients with spontaneous pneumothorax undergoing surgery (Bullectomy alone versus talc poudrage, pleurectomy or abrasion). Which is the best surgical approach? |
| Eligibility criteria – population / disease / condition / issue / domain | Adults (18+) with spontaneous pneumothorax undergoing surgery |
| Eligibility criteria – intervention(s) | Bullectomy alone |
| Eligibility criteria – comparators(s) | Surgical pleurodesis (talc, abrasion, other technique) |
| Outcomes and prioritisation | Recurrence<br>Length of hospital stay<br>Further treatment (pleural and surgical procedures)<br>Pain / breathlessness<br>Duration of air leak<br>Complications<br>Quality of life<br>Mortality |
| Eligibility criteria – study design | RCTs<br>Prospective comparative studies<br>Case series of >100 patients |
| Other inclusion /exclusion criteria | Non-English language excluded unless full English translation<br>Conference abstracts, Cochrane reviews, systematic reviews, reviews<br>Cochrane reviews and systematic reviews can be referenced in the text, but **DO NOT** use in a meta-analysis |
| Proposed sensitivity / subgroup analysis, or meta-regression | None |

| | |
|---|---|
| Selection process – duplicate screening / selection / analysis | Agreement should be reached between Guideline members who are working on the question. If no agreement can be reached, a decision should be made by the Guideline co-chairs. If there is still no decision, the matter should be brought to the Guideline group and a decision will be made by consensus |
| Data management (software) | RevMan5 — Pairwise meta-analyses<br>Evidence review/considered judgement.<br>Storing Guideline text, tables, figures, etc.<br>Gradeprofiler — Quality of evidence assessment<br>Gradepro — Recommendations |
| Information sources – databases and dates | MEDLINE, Embase, PubMED, Central Register of Controlled Trials and Cochrane Database of Systematic Reviews<br>1966 - present |
| Methods for assessing bias at outcome / study level | RevMan5 intervention review template and NICE risk of bias checklist<br>(follow instructions in '*BTS Guideline Process Handbook – Intervention Review'*) |
| Methods for quantitative analysis – combining studies and exploring (in)consistency | If 3 or more relevant studies:<br>RevMan5 for meta-analysis, heterogeneity testing and forest plots<br>(follow instructions in '*BTS Guideline Process Handbook – Intervention Review'*) |
| Meta-bias assessment – publication bias, selective reporting bias | GRADEprofiler — Intervention review quality of evidence assessment for each outcome<br>(follow instructions in '*BTS Guideline Process Handbook – Intervention Review'*) |
| Rationale / context – what is known | In patients undergoing surgical treatment for their spontaneous pneumothorax a number of different surgical techniques are employed. We need to review the current literature to answer the question; What is the best technique in terms of patient satisfaction and low recurrence rates? |