# Online Appendix D10 BTS Guideline for Pleural Disease

## Section D Pleural malignancy

## Question D10 Evidence Review and Protocol

**D10 For adults with malignant pleural effusion treated with indwelling pleural catheters, do intrapleural agents (talc or other pleurodesis agents) improve clinical outcomes?**

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## Question Evidence Review

### D10 For adults with malignant pleural effusion treated with indwelling pleural catheters, do intrapleural agents (talc or other pleurodesis agents) improve clinical outcomes?

#### Background

With the increasing use of indwelling pleural catheters (IPCs) to control breathlessness in patients with malignant pleural effusion (MPE), there has been interest in “combination” procedures, where a pleurodesis agent is inserted via a functioning IPC after a period of drainage. This review assesses the evidence for the clinical benefits of using this strategy.

#### Outcomes

Quality of life, length of hospital stay, need for re-intervention, symptoms (breathlessness, chest pain), complications and pleurodesis rates

#### Evidence Review

The initial literature search identified 10 papers, of which one was deemed relevant. The relevant study was a randomised controlled trial which compared pleurodesis patients with an indwelling pleural catheter (IPC) and expandable lung (defined as non-expandable lung less than 25%) who had talc or placebo (0.9% sodium chloride) instilled after 10 days of drainage.[1]

*Quality of Life*

Quality of life was measured using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) score and EuroQoL-5 dimensions-5 levels (EQ-5D-5L) score, with significantly greater improvements reported in differences in means across the study (70 days) for the talc slurry group ($p$ = 0.02, QLQ-C30 and $p$ = 0.04, EQ-5D-5L). Data are summarised in Table D10a.

*Length of Stay*

Length of hospital stay was not reported as these were day case procedures, but the number of days spent in hospital during the 70 days of the study was 4.1 ± 7.9 days in the talc group and 3.0 ± 5.2 days in the placebo group (mean ± SD), with no significance between the groups ($p$ = 0.74).[1]

*Re-intervention*

5/71 (7%) of patients in the talc group and 2/73 (3%) of patients in the placebo group underwent an additional therapeutic procedure for fluid management during the trial ($p$ = 0.25).[1]

*Symptoms (breathlessness, chest pain)*

Chest pain and breathlessness were reported as improved in both groups throughout the trial. Chest pain was significantly lower in the talc group at assessment points day 14, day 28 and across the duration of the study (70 days or until patient death) ($p$ = 0.04, 0.02 and 0.007 respectively) when compared to the placebo group, whereas breathlessness was only reported as significantly lower in the talc group at day 56 ($p$ = 0.04).[1]

*Complications*

Complications included underlying disease progression, distant fluid accumulation, IPC blockage and infection, but no significant differences were reported between the groups (talc slurry and placebo).[1]

*Pleurodesis rates*

43% of participants in the talc slurry group (30/69) and 23% (16/70) in the placebo group achieved successful pleurodesis by day 35 ($p$ = 0.008). Pleurodesis at day 70 was achieved by 51% of participants in the talc group, compared with 27% in the placebo group ($p$ = 0.003).[1]

Table D10a: Summary of quality of life, chest pain and breathlessness difference scores between administration of talc slurry or placebo via an indwelling pleural catheter

| **Outcome** | **Difference Talc slurry versus Sodium Chloride** [95% CI] | ***p*** |
|---|---|---|
| *Quality of life** | | |
| QLQ-C30 (mean score day 28) | 9.2 [1.1,17.4] | 0.01 |
| QLQ-C30 (mean score day 42) | 14.7 [5.9,23.5] | 0.001 |
| QLQ-C30 (‡ mean score across study) | 6.9 [1.2,12.6] | 0.02 |
| EQ-5D-5L (mean score day 28) | Data not reported | NS |
| EQ-5D-5L (mean score day 42) | 0.12 [0.01,0.22] | 0.03 |
| EQ-5D-5L (‡ mean score across study) | 0.07 [0.00,0.14] | 0.04 |
| *Symptoms† (breathlessness)* | | |
| VAS (mean score day 56) | -7.9 [-15.5,-0.3] | 0.04 |
| VAS (‡ mean score across study) | -3.6 [-8.5,1.3] | 0.15 |
| *Symptoms† (chest pain)* | | |
| VAS (mean score day 14) | -5.4 [-10.7,-0.1] | 0.04 |
| VAS (mean score day 28) | -6.8 [-12.6,-0.9] | 0.02 |
| VAS (‡ mean score across study) | -5.7 [-9.8,-1.6] | 0.007 |

* Positive difference score implies greater quality of life improvement in the talc slurry group; † Negative difference score implies greater symptoms in the sodium chloride (placebo) group; ‡ 70 days or until patient death

EQ-5D-5L – EuroQoL-5 dimensions-5 levels; QLQ-C30 – European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30; VAS – Visual analogue scale

**Evidence Statements**

Pleurodesis rates and quality of life may be improved in malignant pleural effusion patients with expandable lung (defined as >75% of hemithorax) who have talc instilled via an indwelling pleural catheter (**Ungraded**)

Chest pain and breathlessness may be reduced in malignant pleural effusion patients with expandable lung (defined as >75% of hemithorax) who have talc instilled via an indwelling pleural catheter (**Ungraded**)

Complication rates do not appear to differ between malignant pleural effusion patients treated with an indwelling pleural catheter and talc or placebo (**Ungraded**)

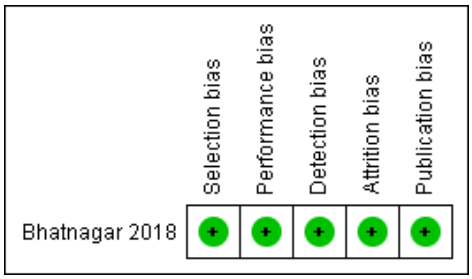
**Recommendation**

- 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)

**Research Recommendation**

- Research is needed to directly compare long term pleurodesis outcomes and quality of life comparing outpatient talc administered via IPC and in patient talc pleurodesis

## Risk of bias summary




## Reference

1. Bhatnagar R, Keenan EK, Morley AJ, et al. Outpatient talc administration by indwelling pleural catheter for malignant effusion. *New England Journal of Medicine.* 2018;378(14):1313-1322.

## Question Protocol

| Field | Content |
|---|---|
| Review Question | For adults with malignant pleural effusion treated with indwelling pleural catheters, do intrapleural agents (talc or pleurodesis agents) improve clinical outcomes? |
| Type of review question | Intervention review |
| Objective of the review | For patients with an MPE and an IPC in-situ, does the instillation of a pleurodesis agent, e.g. talc, lead to patients benefits, e.g. earlier pleurodesis. Are there any significant side effects? |
| Eligibility criteria – population / disease / condition / issue / domain | Adults (18+) with malignant pleural effusion treated with indwelling pleural catheters |
| Eligibility criteria – intervention(s) | Intrapleural agents (talc or pleurodesis agents) |
| Eligibility criteria – comparators(s) | No agent |
| Outcomes and prioritisation | Quality of life<br>Length of hospital stay<br>Need for re-intervention<br>Symptoms (breathlessness, chest pain)<br>Complications<br>Pleurodesis rates |
| 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 | Talc<br>Pleurodesis agent |
| 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 | We know that ward-based talc pleurodesis is effective in managing patients with MPE and that patients can also be treated as an out-patient with an IPC insertion and community drainage. Can these two techniques be safely combined and delivered in the out-patient setting? |