

Appendix A - The methodology checklist for the Taskforce statement

| | Yes | No |
|---|-----|----|
| Panel assembly | | |
| Experts from chest medicine and thoracic surgery | x | |
| Experts vetted for conflict of interest | x | |
| Patient representative | | x |
| Expert methodologist | x | |
| Literature review | | |
| Performed in collaboration with librarian | x | |
| Searched in multiple electronic databases (Medline/PUBMED, EMBASE, Cochrane Library) | x | |
| Reviewed reference list of retrieved articles | x | |
| Evidence synthesis | | |
| Pre-specified inclusion and exclusion criteria | x | |
| Evaluation of included studies for source of bias | x | |
| Explicitly summarised benefits and harms | x | |
| Grading system used | | x |
| Included studies evaluated | | |
| Recommendations for clinical practice | | x |
| Summary/opinions | x | |

Appendix B – PICO criteria for each question

1. What is the best definitive treatment for patients with symptomatic malignant pleural effusion (MPE)?

- P* Patients with symptomatic malignant pleural effusion
- I* Video-assisted Thoracoscopic Surgery (VATS), Local anaesthetic thoracoscopy (LAT), pleuroscopy, pleural endoscopy
- C* Indwelling pleural catheter (IPC), pleurodesis (talc slurry, intra-pleural bleomycin, intra-pleural tetracycline)
- O* Symptoms (breathlessness & CP), length of hospital stay

2. What is the optimal management for malignant pleural effusion with trapped lung?

- P* Patients with symptomatic malignant pleural effusion and trapped lung
- I* Indwelling pleural catheter, IPC
- C* Surgical decortication, Video-assisted thoracic surgical partial pleurectomy, VATS PP, pleurectomy decortication, P/D, Extended pleurectomy decortication, EPD
- O* Symptoms (breathlessness & CP), length of hospital stay, mortality

3. How should loculated malignant pleural effusion be managed?

- P* Patients with loculated malignant pleural effusion
- I* Video-assisted Thoracoscopic Surgery (VATS), Local anaesthetic thoracoscopy (LAT), pleuroscopy, pleural endoscopy
- C* Fibrinolytics (alteplase, Tissue plasminogen activator, TPA, streptokinase, dornase alpha, DNase), Indwelling pleural catheter, IPC
- O* Symptoms, length of stay, resolution of effusion

4. What factors predict prognosis in malignant pleural effusion?

Narrative synthesis to include literature review of prognostic scoring systems and prognostic factors.

5. Should patients with MPE and cancer that is sensitive to oncological treatment (e.g. chemotherapy, immunotherapy, targeted therapy) receive treatment prior to definitive management of their MPE? If so which cancers?

- P* Patients with malignant pleural effusion due to treatment-sensitive cancers (lymphoma, small cell lung cancer, breast cancer, ovarian cancer, germ cell tumour)
- I* Oncological treatment (chemotherapy, radiotherapy, immunotherapy, hormone therapy, targeted therapy) prior to malignant pleural effusion management
- C* Definitive pleural intervention (pleurodesis, indwelling pleural catheter) prior to oncological treatment
- O* Control of pleural effusion, symptoms, complications

6. In order to determine treatment in malignant pleural effusion, is a histological diagnosis always required or is cytology sufficient?

- P* Patients with a cytological diagnosis of malignant pleural effusion without histological confirmation or molecular staging
- I* Biopsy for histology
- C* Cytological diagnosis (including liquid biopsy)
- O* Number of procedures, time to diagnosis, personalised treatment plan

Appendix C – Search strategies for each PICO question

1. What is the best definitive treatment for patients with symptomatic malignant pleural effusion?

Summary – the following databases were searched:

MEDLINE 172 records identified

Embase 341 records identified

Cochrane Library 27 records

Cochrane Database of Systematic Reviews (CDSR) 0 records

Database of Abstracts of reviews of effectiveness (DARE) 1 record

Cochrane Central Register of Controlled Trials (CENTRAL) 23 records

Health Technology Assessment Database 1 record

NHS Economic Evaluation Database 2 records

MEDLINE via OVID 4th January 2017

Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

- 1 Pleural Effusion, Malignant/ (3488)
- 2 malignant pleura\$ effusion\$.mp. (2458)
- 3 1 or 2 (4641)
- 4 exp Thoracoscopy/ (12483)
- 5 Thoracic Surgery, Video-Assisted/ (5714)
- 6 VATS.mp. (3786)
- 7 video assisted thoracic surgery.mp. (2104)
- 8 video-assisted thoracic surgery.mp. (2104)
- 9 video assisted thoracoscopic surgery.mp. (2596)
- 10 video-assisted thoracoscopic surgery.mp. (2596)
- 11 local anaesthetic thoroscop\$.mp. (13)
- 12 local anesthetic thoroscop\$.mp. (4)
- 13 LAT.mp. (4972)
- 14 pleuroscopy.mp. (204)
- 15 pleural endoscopy.mp. (3)
- 16 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (19814)
- 17 indwelling pleural catheter\$.mp. (145)
- 18 in-dwelling pleural catheter\$.mp. (1)
- 19 IPC.mp. (3509)
- 20 Catheters, Indwelling/ (18293)
- 21 pleurodesis/ (1319)
- 22 pleurodesis.mp. (2597)
- 23 talc slurry.mp. (117)
- 24 intra-pleural bleomycin.mp. (0)
- 25 intra pleural bleomycin.mp. (0)
- 26 intrapleural bleomycin.mp. (12)
- 27 intra-pleural tetracycline.mp. (0)
- 28 intra pleural tetracycline.mp. (0)
- 29 intrapleural tetracycline.mp. (38)
- 30 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (24298)
- 31 3 and 16 and 30 (224)
- 32 limit 31 to english language (172)

Embase via OVID 4th January

Database: Embase <1974 to 2017 January 03>

- 1 Malignant Pleura Effusion/ (1488)
- 2 malignant pleura\$ effusion\$.mp. (3889)
- 3 1 or 2 (3889)
- 4 Thoracoscopy/ (12862)
- 5 Video Assisted Thoracoscopic Surgery/ (7661)
- 6 VATS.mp. (5935)
- 7 video assisted thoracic surgery.mp. (2736)
- 8 video-assisted thoracic surgery.mp. (2736)
- 9 video assisted thoracoscopic surgery.mp. (8854)
- 10 video-assisted thoracoscopic surgery.mp. (8854)
- 11 local anaesthetic thoracoscop\$.mp. (28)
- 12 local anesthetic thoracoscop\$.mp. (10)
- 13 LAT.mp. (5461)
- 14 pleuroscopy.mp. (316)
- 15 pleural endoscopy.mp. (6)
- 16 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (27253)
- 17 indwelling pleural catheter\$.mp. (285)
- 18 in-dwelling pleural catheter\$.mp. (7)
- 19 IPC.mp. (4283)
- 20 Indwelling Catheter/ (10226)
- 21 pleurodesis/ (4218)
- 22 pleurodesis.mp. (4694)
- 23 talc slurry.mp. (168)
- 24 intra-pleural bleomycin.mp. (1)
- 25 intra pleural bleomycin.mp. (1)
- 26 intrapleural bleomycin.mp. (13)
- 27 intra-pleural tetracycline.mp. (0)
- 28 intra pleural tetracycline.mp. (0)
- 29 intrapleural tetracycline.mp. (40)
- 30 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (19049)
- 31 3 and 16 and 30 (400)
- 32 limit 31 to english language (341)

The Cochrane Library 4th January 2017

- #1 MeSH descriptor: [Pleural Effusion, Malignant] explode all trees
- #2 malignant pleura* effusion*:ti,ab,kw (Word variations have been searched)
- #3 #1 or #2
- #4 MeSH descriptor: [Thoracoscopy] explode all trees
- #5 MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees
- #6 VATS:ti,ab,kw (Word variations have been searched)
- #7 video assisted thoracic surgery:ti,ab,kw (Word variations have been searched)
- #8 video-assisted thoracic surgery:ti,ab,kw (Word variations have been searched)
- #9 video assisted thoracoscopic surgery:ti,ab,kw (Word variations have been searched)
- #10 video-assisted thoracoscopic surgery:ti,ab,kw (Word variations have been searched)
- #11 local anaesthetic thoracoscop*:ti,ab,kw (Word variations have been searched)
- #12 local anesthetic thoracoscop*:ti,ab,kw (Word variations have been searched)
- #13 LAT:ti,ab,kw (Word variations have been searched)
- #14 pleuroscopy:ti,ab,kw (Word variations have been searched)
- #15 pleural endoscopy:ti,ab,kw (Word variations have been searched)
- #16 #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15

- #17 indwelling pleural catheter*:ti,ab,kw (Word variations have been searched)
- #18 in-dwelling pleural catheter*:ti,ab,kw (Word variations have been searched)
- #19 IPC:ti,ab,kw (Word variations have been searched)
- #20 MeSH descriptor: [Catheters, Indwelling] explode all trees
- #21 MeSH descriptor: [Pleurodesis] explode all trees
- #22 pleurodesis:ti,ab,kw (Word variations have been searched)
- #23 talc slurry:ti,ab,kw (Word variations have been searched)
- #24 intra-pleural bleomycin:ti,ab,kw (Word variations have been searched)
- #25 intra pleural bleomycin:ti,ab,kw (Word variations have been searched)
- #26 intrapleural bleomycin:ti,ab,kw (Word variations have been searched)
- #27 intra-pleural tetracycline:ti,ab,kw (Word variations have been searched)
- #28 intra pleural tetracycline:ti,ab,kw (Word variations have been searched)
- #29 intrapleural tetracycline:ti,ab,kw (Word variations have been searched)
- #30 #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29
- #31 #3 and #16 and #30

2. What is the optimal management for malignant pleural effusion with trapped lung?

Summary – the following databases were searched:

MEDLINE 27 records identified

Embase 53 records identified

Cochrane Library 8 records

Cochrane Database of Systematic Reviews (CDSR) 0 records

Database of Abstracts of reviews of effectiveness (DARE) 1 record

Cochrane Central Register of Controlled Trials (CENTRAL) 7 records

Health Technology Assessment Database 0 records

NHS Economic Evaluation Database 0 records

MEDLINE

Via Ovid 6th January 2017

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

- 1 Pleural Effusion, Malignant/ (3489)
- 2 malignant pleur\$ effusion\$.mp. (2466)
- 3 1 or 2 (4648)
- 4 trapped lung\$.mp. (149)
- 5 (lung adj (trap\$ or entrap\$)).mp. (41)
- 6 4 or 5 (185)
- 7 3 and 6 (61)
- 8 Catheters, Indwelling/ (18298)
- 9 IPC.mp. (3513)
- 10 indwelling pleural catheter\$.mp. (145)
- 11 in-dwelling pleural catheter\$.mp. (1)
- 12 8 or 9 or 10 or 11 (21809)
- 13 7 and 12 (19)
- 14 Pleural Effusion, Malignant/ (3489)
- 15 malignant pleur\$ effusion\$.mp. (2466)
- 16 14 or 15 (4648)
- 17 trapped lung\$.mp. (149)

- 18 (lung adj (trap\$ or entrap\$)).mp. (41)
- 19 17 or 18 (185)
- 20 16 and 19 (61)
- 21 Thoracic Surgery, Video-Assisted/ (5718)
- 22 VATS.mp. (3789)
- 23 video assisted thoracic surgery.mp. (2104)
- 24 video-assisted thoracic surgery.mp. (2104)
- 25 video assisted thoracoscopic surgery.mp. (2597)
- 26 video-assisted thoracoscopic surgery.mp. (2597)
- 27 (VATS adj PP).mp. (0)
- 28 partial pleurectomy.mp. (43)
- 29 (video\$ adj4 partial pleurectomy).ti,ab. (4)
- 30 pleurectomy decortication.mp. (161)
- 31 EPD.mp. (901)
- 32 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (9606)
- 33 20 and 32 (13)
- 34 13 or 33 (27)
- 35 from 34 keep 1-27 (27)

Embase

Via Ovid 6th January 2017

Database: Embase <1974 to 2017 January 05>

- 1 Malignant Pleura Effusion/ (1492)
- 2 malignant pleur\$ effusion\$.mp. (3899)
- 3 1 or 2 (3899)
- 4 trapped lung\$.mp. (278)
- 5 (lung adj (trap\$ or entrap\$)).mp. (88)
- 6 4 or 5 (347)
- 7 3 and 6 (116)
- 8 Indwelling Catheter/ (10233)
- 9 IPC.mp. (4285)
- 10 indwelling pleural catheter\$.mp. (285)
- 11 in-dwelling pleural catheter\$.mp. (7)
- 12 8 or 9 or 10 or 11 (14583)
- 13 7 and 12 (44)
- 14 Malignant Pleura Effusion/ (1492)
- 15 malignant pleur\$ effusion\$.mp. (3899)
- 16 14 or 15 (3899)
- 17 trapped lung\$.mp. (278)
- 18 (lung adj (trap\$ or entrap\$)).mp. (88)
- 19 17 or 18 (347)
- 20 16 and 19 (116)
- 21 Video Assisted Thoracoscopic Surgery/ (7669)
- 22 VATS.mp. (5940)
- 23 video assisted thoracic surgery.mp. (2741)
- 24 video-assisted thoracic surgery.mp. (2741)
- 25 video assisted thoracoscopic surgery.mp. (8862)
- 26 video-assisted thoracoscopic surgery.mp. (8862)
- 27 (VATS adj PP).mp. (0)
- 28 partial pleurectomy.mp. (66)

- 29 (video\$ adj4 partial pleurectomy).ti,ab. (7)
- 30 pleurectomy decortication.mp. (280)
- 31 EPD.mp. (1154)
- 32 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (12636)
- 33 20 and 32 (18)
- 34 13 or 33 (53)

Cochrane Library 6th January 2017

- #1 MeSH descriptor: [Pleural Effusion, Malignant] explode all trees
- #2 malignant pleur* effusion*:ti,ab,kw (Word variations have been searched)
- #3 #1 or #2
- #4 trapped lung*:ti,ab,kw (Word variations have been searched)
- #5 (lung near (trap* or entrap*)):ti,ab,kw (Word variations have been searched)
- #6 #4 or #5
- #7 #3 and #6
- #8 MeSH descriptor: [Catheters, Indwelling] explode all trees
- #9 IPC:ti,ab,kw or indwelling pleural catheter*:ti,ab,kw or in-dwelling pleural catheter*:ti,ab,kw (Word variations have been searched)
- #10 #8 or #9
- #11 #7 and #10
- #12 MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees
- #13 VATS:ti,ab,kw or "video assisted thoracic surgery":ti,ab,kw or "video-assisted thoracic surgery":ti,ab,kw or "video assisted thoracoscopic surgery":ti,ab,kw or " video-assisted thoracoscopic surgery":ti,ab,kw (Word variations have been searched)
- #14 VATS near/1 PP:ti,ab,kw or partial pleurectomy:ti,ab,kw or video* near/4 partial pleurectomy:ti,ab,kw or pleurectomy decortication:ti,ab,kw or EPD:ti,ab,kw (Word variations have been searched)
- #15 #12 or #13 or #14
- #16 #7 and #15
- #17 #11 or #16

3. How should septated & loculated malignant pleural effusion be managed?

Summary – the following databases were searched:

MEDLINE 103 records identified

Embase 52 records identified

Cochrane Library 2 records

Cochrane Database of Systematic Reviews (CDSR) 0 records

Database of Abstracts of reviews of effectiveness (DARE) 0 records

Cochrane Central Register of Controlled Trials (CENTRAL) 2 records

Health Technology Assessment Database 0 records

NHS Economic Evaluation Database 0 records

MEDLINE

Via Ovid 9th January 2017

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

- 1 pleural effusion, malignant/ (3489)
- 2 (loculat\$ or complex or septat\$).ti,ab. (1144868)

- 3 1 and 2 (111)
- 4 (malignant pleural effusion adj5 (loculat\$ or complex or septat\$)).ti,ab. (4)
- 5 3 or 4 (113)
- 6 limit 5 to english language (103)

Embase

Via Ovid 9th January 2017

Database: Embase <1974 to 2017 January 05>

- 1 Malignant pleura effusion/ (1486)
- 2 (loculat\$ or complex or septat\$).ti,ab. (1141646)
- 3 1 and 2 (49)
- 4 (malignant pleural effusion adj5 (loculat\$ or complex or septat\$)).ti,ab. (9)
- 5 3 or 4 (56)
- 6 limit 5 to english language (52)

Cochrane Library 9th January 2017

- #1 MeSH descriptor: [Pleural Effusion, Malignant] explode all trees
- #2 (loculat* or complex or septat*):ti,ab,kw (Word variations have been searched)
- #3 #1 and #2
- #4 (malignant pleural effusion) near/5 (loculat* or complex or septat*):ti,ab,kw (Word variations have been searched)
- #5 #3 or #4

4. What factors predict prognosis in malignant pleural effusion?

Summary – the following databases were searched:

MEDLINE 676 records identified

Embase 1045 records identified

Cochrane Library 141 records

Cochrane Database of Systematic Reviews (CDSR) 3 records

Database of Abstracts of reviews of effectiveness (DARE) 0 records

Cochrane Central Register of Controlled Trials (CENTRAL) 1382 records

Health Technology Assessment Database 0 records

NHS Economic Evaluation Database 0 records

MEDLINE

Via Ovid 11th January 2017

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

- 1 ((prognosis or prognostic or survival or outcome\$) adj3 (score\$ or scoring or predict\$)).ti,ab. (142406)
- 2 Pleural Effusion, Malignant/ (3491)
- 3 malignant pleura\$ effusion.mp. (1652)
- 4 malignant pleural mesothelioma.mp. (3238)
- 5 (EORTC or LENT or CALGB).mp. (9757)
- 6 2 or 3 or 4 or 5 (17048)
- 7 1 and 6 (690)
- 8 limit 7 to english language (676)

Embase

Via Ovid 11th January 2017

Database: Embase <1974 to 2017 January 10>

- 1 ((prognosis or prognostic or survival or outcome\$) adj3 (score\$ or scoring or predict\$)).ti,ab.
(188427)
- 2 Malignant Pleura Effusion/ (1488)
- 3 malignant pleura\$ effusion.mp. (3113)
- 4 malignant pleural mesothelioma.mp. (4433)
- 5 (EORTC or LENT or CALGB).mp. (15323)
- 6 2 or 3 or 4 or 5 (22660)
- 7 1 and 6 (1070)
- 8 limit 7 to english language (1045)

Cochrane Library 9th January 2017

- #1 MeSH descriptor: [Pleural Effusion, Malignant] explode all trees
- #2 malignant pleura* effusion:ti,ab,kw (Word variations have been searched)
- #3 malignant pleural mesothelioma:ti,ab,kw (Word variations have been searched)
- #4 (EORTC or LENT or CALGB):ti,ab,kw (Word variations have been searched)
- #5 #1 or #2 or #3 or #4
- #6 (prognosis or prognostic or survival or outcome*) near/3 (score* or scoring or predict*):ti,ab,kw
(Word variations have been searched)
- #7 #5 and #6

5. Should patients with malignant pleural effusion and cancer that is sensitive to oncological treatment (e.g. chemotherapy, immunotherapy, targeted therapy) receive treatment prior to definitive management of their MPE? If so which cancers?

Summary – the following databases were searched:

MEDLINE 257 records identified

Embase 286 records identified

Cochrane Library 44 records

Cochrane Database of Systematic Reviews (CDSR) 0 records

Database of Abstracts of reviews of effectiveness (DARE) 0 records

Cochrane Central Register of Controlled Trials (CENTRAL) 44 records

Health Technology Assessment Database 0 records

NHS Economic Evaluation Database 0 records

MEDLINE

Via Ovid 13th January 2017

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

- 1 Pleural Effusion, Malignant/ (3491)
- 2 Malignant pleura\$ effusion.mp. (1652)
- 3 1 or 2 (4275)
- 4 Lymphoma/ (54779)
- 5 Small Cell Lung Carcinoma/ (3085)
- 6 Breast Neoplasms/ (283396)
- 7 Ovarian Neoplasms/ (79995)
- 8 "Neoplasms, Germ Cell and Embryonal"/ (8957)

- 9 Germinoma/ (3121)
- 10 4 or 5 or 6 or 7 or 8 or 9 (421445)
- 11 lymphoma.ti,ab. (151057)
- 12 (small cell lung adj (cancer\$ or neoplasm\$)).ti,ab. (56193)
- 13 (breast adj (cancer\$ or neoplasm\$)).ti,ab. (256513)
- 14 (ovarian adj (cancer\$ or neoplasm\$)).ti,ab. (52724)
- 15 (germ cell tumour\$ or germ cell tumor\$).ti,ab. (11064)
- 16 11 or 12 or 13 or 14 or 15 (513676)
- 17 10 or 16 (673735)
- 18 3 and 17 (1114)
- 19 Drug Therapy/ (31435)
- 20 drug therapy/ or chemoradiotherapy/ or chemotherapy, adjuvant/ (76526)
- 21 exp Radiotherapy/ (174182)
- 22 exp Immunotherapy/ (270920)
- 23 Hormone Replacement Therapy/ (9807)
- 24 Molecular Targeted Therapy/ (22333)
- 25 19 or 20 or 21 or 22 or 23 or 24 (526207)
- 26 (chemotherap\$ or radiotherap\$ or immunotherap\$ or hormone replacement therap\$ or targeted therap\$).ti,ab. (577344)
- 27 25 or 26 (964203)
- 28 18 and 27 (305)
- 29 limit 28 to english language (257)

Embase

Via Ovid 13th January 2017

Database: Embase <1974 to 2017 January 10>

- 1 Malignant Pleura Effusion/ (1488)
- 2 Malignant pleura\$ effusion.mp. (3113)
- 3 1 or 2 (3113)
- 4 Lymphoma/ (110307)
- 5 Small Cell Lung Carcinoma/ (212)
- 6 Small Cell Lung Cancer/ (4086)
- 7 Lung Small Cell Cancer/ (19297)
- 8 Breast Cancer/ (320895)
- 9 Ovary Tumor/ (30520)
- 10 Germ cell tumor/ (15504)
- 11 4 or 5 or 6 or 7 or 8 or 9 or 10 (488491)
- 12 lymphoma.ti,ab. (182097)
- 13 (small cell lung adj (cancer\$ or neoplasm\$)).ti,ab. (72722)
- 14 (breast adj (cancer\$ or neoplasm\$)).ti,ab. (306059)
- 15 (ovarian adj (cancer\$ or neoplasm\$)).ti,ab. (62684)
- 16 (germ cell tumour\$ or germ cell tumor\$).ti,ab. (13336)
- 17 12 or 13 or 14 or 15 or 16 (618693)
- 18 11 or 17 (767259)
- 19 3 and 18 (889)
- 20 Chemotherapy/ (234955)
- 21 chemoradiotherapy/ or chemotherapy, adjuvant/ (70602)
- 22 exp Radiotherapy/ (449000)
- 23 exp Immunotherapy/ (172040)
- 24 Hormone Substitution/ (35337)
- 25 Molecularly Targeted Therapy/ (19537)
- 26 20 or 21 or 22 or 23 or 24 or 25 (846757)

- 27 (chemotherap\$ or radiotherap\$ or immunotherap\$ or hormone replacement therap\$ or targeted therap\$).ti,ab. (744222)
- 28 26 or 27 (1130917)
- 29 19 and 28 (320)
- 30 limit 29 to english language (286)

Cochrane Library 13th January 2017

- #1 MeSH descriptor: [Pleural Effusion, Malignant] explode all trees
- #2 Malignant pleura* effusion:ti,ab,kw (Word variations have been searched)
- #3 #1 or #2
- #4 MeSH descriptor: [Lymphoma] explode all trees
- #5 MeSH descriptor: [Small Cell Lung Carcinoma] explode all trees
- #6 MeSH descriptor: [Breast Neoplasms] explode all trees
- #7 MeSH descriptor: [Ovarian Neoplasms] explode all trees
- #8 MeSH descriptor: [Neoplasms, Germ Cell and Embryonal] explode all trees
- #9 MeSH descriptor: [Germinoma] explode all trees
- #10 #4 or #5 or #6 or #7 or #8 or #9
- #11 lymphoma:ti,ab,kw (Word variations have been searched)
- #12 small cell lung near/1 (cancer* or neoplasm*):ti,ab,kw (Word variations have been searched)
- #13 breast near/1 (cancer* or neoplasm*):ti,ab,kw (Word variations have been searched)
- #14 ovarian near/1 (cancer* or neoplasm*):ti,ab,kw (Word variations have been searched)
- #15 (germ cell tumour*) or (germ cell tumor*):ti,ab,kw (Word variations have been searched)
- #16 #11 or #12 or #13 or #14 or #15
- #17 #3 and (#10 or #16)
- #18 MeSH descriptor: [Drug Therapy] explode all trees
- #19 MeSH descriptor: [Chemoradiotherapy] explode all trees
- #20 MeSH descriptor: [Chemotherapy, Adjuvant] explode all trees
- #21 MeSH descriptor: [Radiotherapy] explode all trees
- #22 MeSH descriptor: [Immunotherapy] explode all trees
- #23 MeSH descriptor: [Hormone Replacement Therapy] explode all trees
- #24 MeSH descriptor: [Molecular Targeted Therapy] explode all trees
- #25 #18 or #19 or #20 or #21 or #22
- #26 (chemotherap* or radiotherap* or immunotherap* or hormone replacement therap* or targeted therap*):ti,ab,kw (Word variations have been searched)
- #27 #25 or #26
- #28 #17 and #27

6. Question 6 - In order to determine treatment in malignant pleural effusion, is a histological diagnosis always required or is cytology sufficient?

Summary – the following databases were searched:

- MEDLINE 987 records identified
- Embase 650 records identified

*Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Via Ovid 14th February 2017*

- 1 Pleural Effusion, Malignant/ (3262)
- 2 Malignant pleura\$ effusion.ti,ab. (1525)

- 3 1 or 2 (3977)
- 4 exp Biopsy/ (251622)
- 5 biops\$.ti,ab. (339380)
- 6 exp histological techniques/ (706358)
- 7 exp histochemistry/ (449080)
- 8 exp fluorescent antibody technique/ (116898)
- 9 exp histocytological preparation techniques/ (236867)
- 10 exp microdissection/ (3079)
- 11 exp microtomy/ (8911)
- 12 exp replica techniques/ (8586)
- 13 exp "staining and labeling"/ (169591)
- 14 exp tissue embedding/ (7844)
- 15 exp tissue preservation/ (66122)
- 16 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (1147659)
- 17 3 and 16 (811)
- 18 exp cytological techniques/ (1366851)
- 19 cell count/ (60797)
- 20 cell culture techniques/ (40931)
- 21 cell migration assays/ (401)
- 22 cell separation/ (38995)
- 23 cell tracking/ (1494)
- 24 cytodiagnosis/ (15162)
- 25 karyometry/ (1516)
- 26 cytogenetic analysis/ (5423)
- 27 cytophotometry/ (1045)
- 28 enzyme-linked immunospot assay/ (905)
- 29 histochemistry/ (72568)
- 30 histocytological preparation techniques/ (1436)
- 31 Biomarkers, Tumor/an [Analysis] (35316)
- 32 Neoplastic Cells, Circulating/ (8364)
- 33 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 (1390594)
- 34 3 and 33 (929)
- 35 17 or 34 (1147)
- 36 limit 35 to english language (987)

Embase

Via Ovid 14th February 2017

Database: Embase <1974 to 2017 Week 06>

- 1 Pleural Effusion, Malignant/ (197)
- 2 Malignant pleura\$ effusion.ti,ab. (2335)
- 3 1 or 2 (2401)
- 4 exp Biopsy/ (618468)
- 5 biops\$.ti,ab. (492133)
- 6 exp histology/ (1168556)
- 7 exp histochemistry/ (116963)
- 8 exp fluorescent antibody technique/ (30029)
- 9 exp microdissection/ (10231)
- 10 exp microtomy/ (2492)
- 11 exp staining/ (248558)
- 12 exp tissue embedding/ (1168556)
- 13 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 (2035078)
- 14 3 and 13 (548)

- 15 exp cytology/ (755612)
- 16 exp cell count/ (348483)
- 17 cell culture technique/ (640)
- 18 cell migration assay/ (1800)
- 19 cell separation/ (13927)
- 20 cell tracking/ (2752)
- 21 exp cytodagnosis/ (62461)
- 22 karyometry/ (1198)
- 23 cytophotometry/ (1370)
- 24 enzyme linked immunospot assay/ (9229)
- 25 Tumor Marker/an (7049)
- 26 Circulating Tumor Cell/ (6831)
- 27 15 or 6 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 (1835767)
- 28 3 and 27 (550)
- 29 14 or 28 (756)
- 30 limit 29 to english language (650)

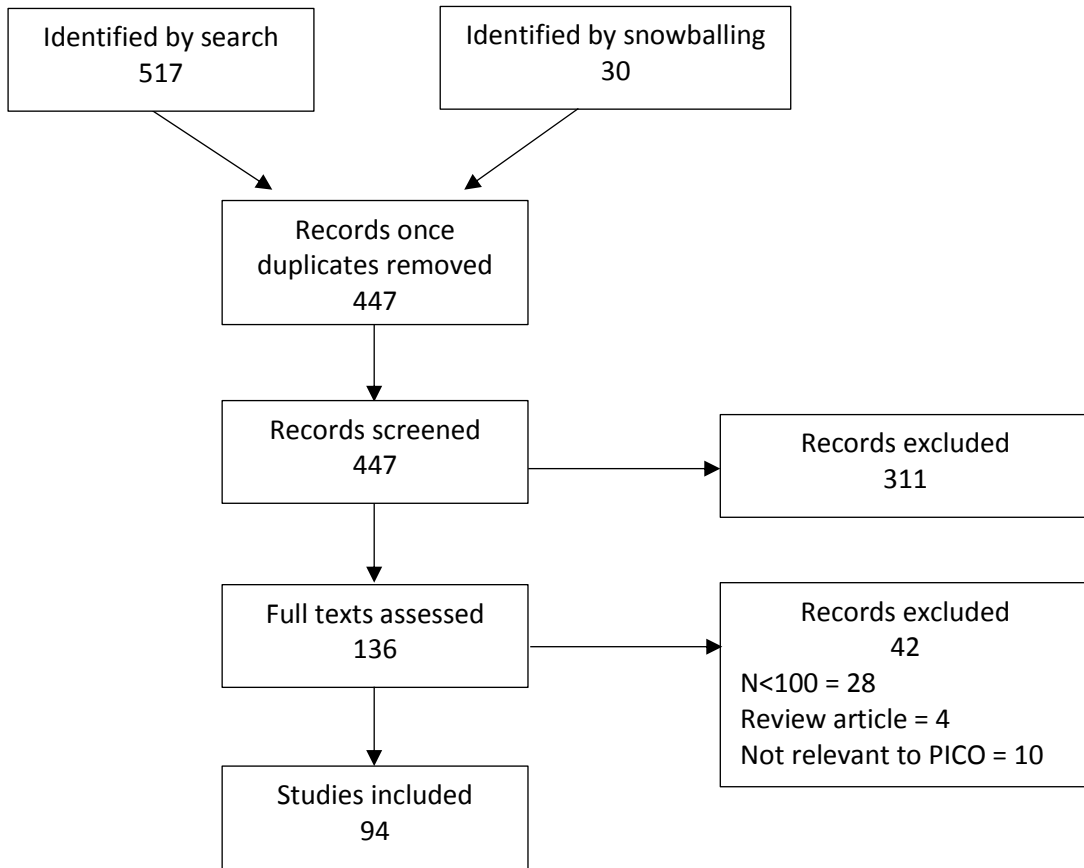
Appendix D – Eligibility criteria for each PICO question

| PICO | Inclusion criteria | Exclusion criteria |
|----------|---|---|
| 1 | <p>Systematic reviews Meta-analyses Randomised controlled trials Large observational studies (n>100) Smaller observational studies (n<100) if novel data, or if only report of a certain intervention</p> | <p>Opinion pieces & editorials Letters Non-formal review articles Case reports Conference abstracts Laboratory studies Animal studies Trials comparing pleurodesis agents Papers relating to trapped lung or loculated effusion (PICO 2 & 3)</p> |
| 2 | <p>Systematic reviews Meta-analyses Randomised controlled trials, Observational studies where n>1</p> | <p>Opinion pieces & editorials Letters Non-formal review articles Case studies Conference abstracts Laboratory studies Animal studies Pleurodesis papers Papers reporting trapped lung incidence or trapped lung as an outcome</p> |
| 3 | <p>Systematic reviews Meta-analyses Randomised controlled trials, Observational studies Non-formal review articles Case reports</p> | <p>Opinion pieces & editorials Letters Conference abstracts Laboratory studies Animal studies Papers reporting incidence of loculated effusions or loculations as an outcome</p> |
| 4 | <p>Systematic reviews Meta-analyses Randomised controlled trials, Observational studies n>100 Prognostic biomarkers or biomarkers that affect clinical decision making</p> | <p>Opinion pieces & editorials Letters Non-formal review articles Case reports Conference abstracts Laboratory studies Animal studies Papers describing prognostic factors for a specific tumour type that may include malignant pleural effusions, but do not relate specifically to people with effusions Predictors of pleurodesis success Diagnostic & disease specific biomarkers Molecular markers and histochemistry</p> |
| 5 | <p>Systematic reviews Meta-analyses Randomised controlled trials, Observational studies Case reports</p> | <p>Opinion pieces & editorials Letters Non-formal review articles Conference abstracts Laboratory studies Animal studies</p> |

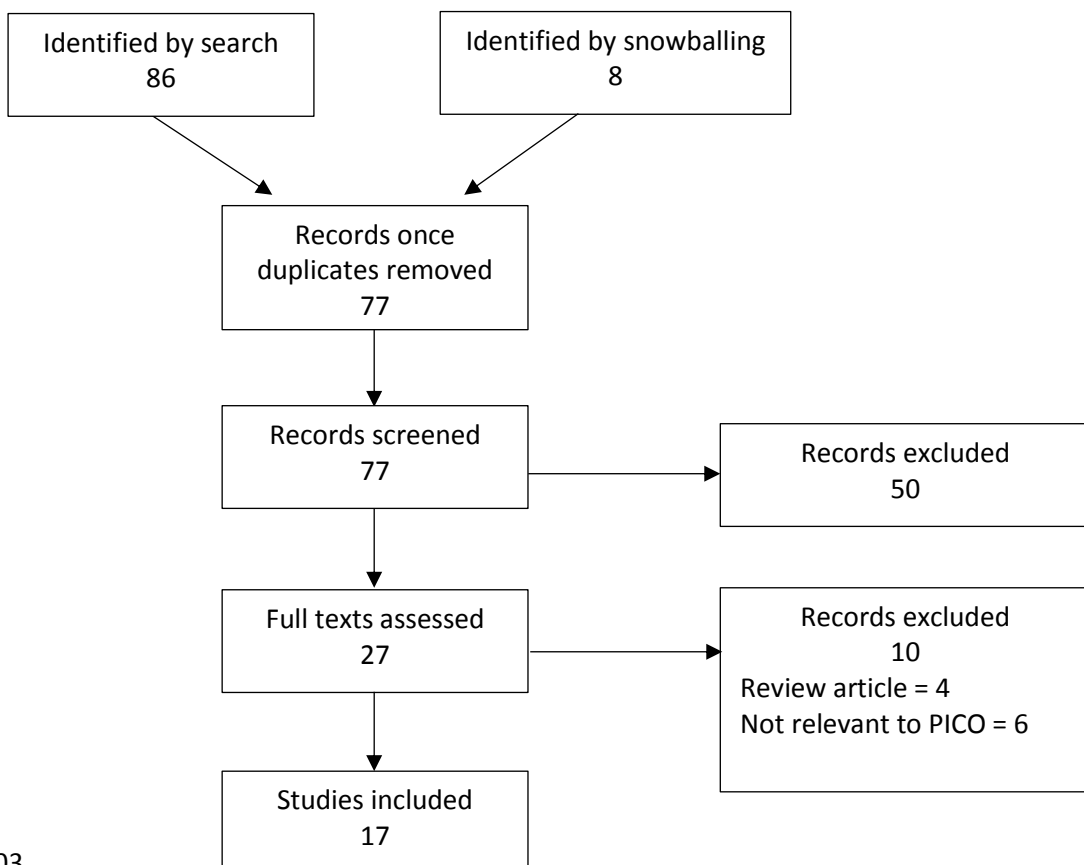
| | | |
|-----------------|---|--|
| <p>6</p> | <p>Systematic reviews Meta-analyses Randomised controlled trials, Observational studies Blood biomarkers Circulating tumour cells Liquid biopsy</p> | <p>Opinion pieces & editorials Letters Non-formal review articles Case reports Conference abstracts Laboratory studies Animal studies Papers comparing cytokines/cell populations in benign vs malignant effusions Papers comparing specific biopsy techniques Paediatric tumours Papers describing molecular pathways/mechanistic processes Papers focussing on specific cell receptors or markers</p> |
|-----------------|---|--|

Appendix E – PRISMA diagram for each PICO question

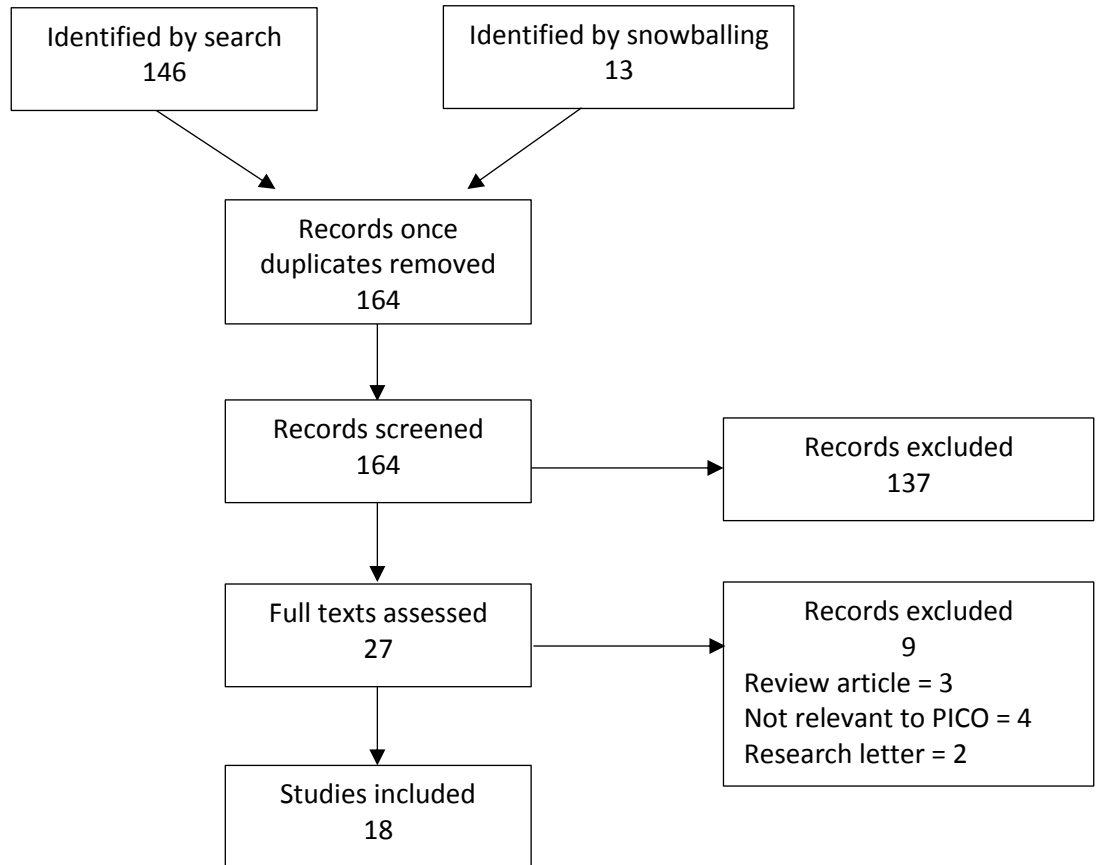
PRISMA diagram for PICO question 1



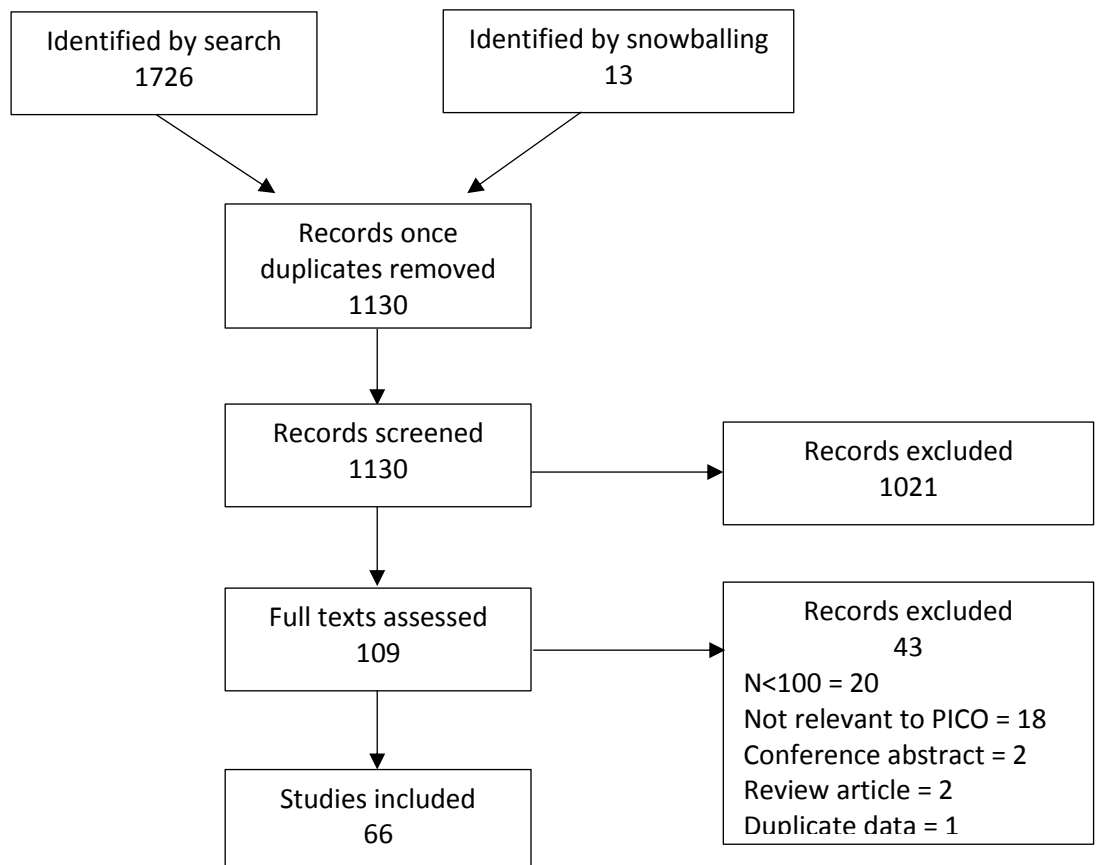
PRISMA diagram for PICO question 2



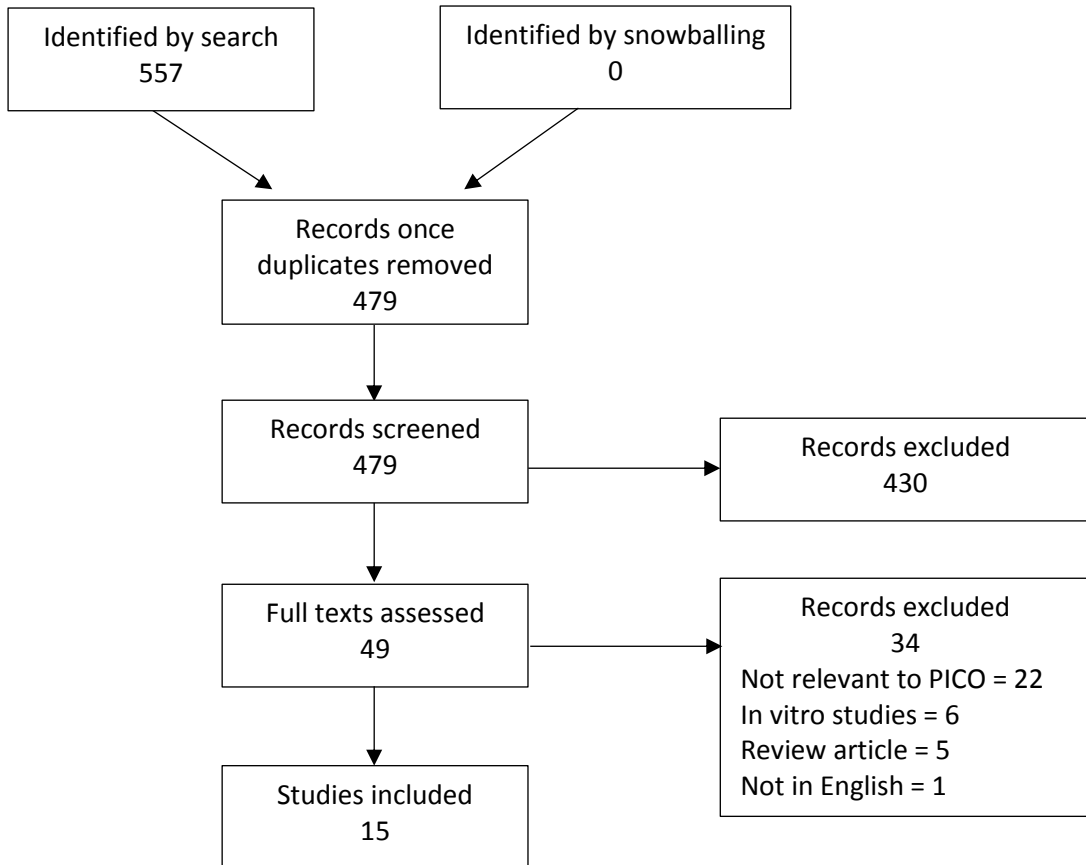
PRISMA diagram for PICO question 3



PRISMA diagram for PICO question 4



PRISMA diagram for PICO question 5



PRISMA diagram for PICO question 6

