

Table S1. Research strategy in MEDLINE and Chocrane
MEDLINE

| | Search formula |
|-----|--|
| L1 | S RESPIRATORY INSUFFICIENCY+NT/CT OR LUNG DISEASES, INTERSTITIAL+NT/CT OR PULMONARY DISEASE, CHRONIC OBSTRUCTIVE+NT/CT OR BRONCHIECTASIS+NT/CT |
| L2 | S RESPIRATORY(3A)(INSUFFICIEN? OR FAILUR?) OR INTERSTIT?(3A)(LUNG OR PULMONARY OR PNEUMON?) OR CHRONIC?(3A)OBSTRUCT?(3A)(LUNG OR PULMONARY OR AIRWAY OR AIRFLOW?) |
| L3 | S BRONCHIECTAS? OR FIBROS?(3A)(PULMONARY OR ALVEOLI?) OR EMPHYSEM?(3A)(PULMONARY OR FOCAL OR PANACINAR? OR PANLOBUL? OR CENTRIACINAR?) OR CHRONIC?(3A)BRONCHIT? OR ((CYSTIC FIBROSIS+NT/CT OR CYSTIC?(3A)FIBROS?) AND (LUNG OR PULMONARY)) |
| L4 | S (REFRACTORY? OR INTRACTABL?)(3A)(DYSPNE? OR DYSPNOE? OR BREATHLESS? OR BREATH(3A)SHORT?) OR *DYSPNEA+NT/CT OR (DYSPNE? OR DYSPNOE? OR BREATHLESS? OR BREATH?(3A)SHORT?)/TI |
| L5 | S ANALGESICS, OPIOID+NT/CT OR MORPHINE DERIVATIVES+NT/CT OR FENTANYL+NT/CT OR METHADONE+NT/CT OR TRAMADOL+NT/CT OR BUPRENORPHINE+NT/CT |
| L6 | S OPIOID? OR MORPHIN? OR OXYCODON? OR ?FENTANYL? OR METHADON? OR TRAMADOL? OR BUPRENORPHIN? OR ?CODEIN? OR HYDROMORPHON? |
| L7 | S (L1-L4) AND (L5 OR L6) |
| L8 | S END(2W)LIFE OR PALLIATIVE CARE+NT/CT OR TERMINAL CARE+NT/CT OR TERMINAL? OR PALLIAT? OR SEVERE? OR ADVANCED? |
| L9 | S NONCANCER? OR (NON OR WITHOUT)(W)CANCER? |
| L10 | S L8 AND L9 |
| L11 | S L8 NOT (NEOPLASMS+NT/CT OR (CANCER? OR CARCINOM? OR TUMOR? OR TUMOUR? OR NEOPLAS? OR MALIGNAN? OR ONCOLOG?)) |
| L12 | S L7 AND (L10 OR L11) |
| L13 | S L7 AND L6/TI AND (DYSPNE? OR DYSPNOE? OR BREATHLESSNES? OR BREATH?(3A)SHORT? OR BRONCHI? OR FIBROS? OR EMPHYSEM? OR RESPIRATORY(3A)(FAILUR? OR INSUFFICIEN?) OR INTERSTIT? OR OBSTRUCT? OR COPD OR COAD OR IP OR ILD)/TI |
| L14 | S L13 AND L9 |
| L15 | S L13 NOT (NEOPLASMS+NT/CT OR (CANCER? OR CARCINOM? OR TUMOR? OR TUMOUR? OR NEOPLAS? OR MALIGNAN? OR ONCOLOG?)) |
| L16 | S L14 OR L15 |
| L17 | S L12 OR L16 |
| L18 | S L17 AND (1980-2020)/PY AND (19800101-20201031)/UP AND (ENGLISH OR JAPANESE)/LA NOT EPUB?/FS |

Chochrane

| | Search formula |
|-----|---|
| #1 | [mh "RESPIRATORY INSUFFICIENCY"] OR [mh "LUNG DISEASES, INTERSTITIAL"] OR [mh "PULMONARY DISEASE, CHRONIC OBSTRUCTIVE"] OR [mh BRONCHIECTASIS] |
| #2 | (RESPIRATORY near/2 (INSUFFICIENC* OR FAILURE*) OR INTERSTITIAL near/3 (LUNG OR PULMONARY OR PNEUMONI*) OR CHRONIC near/3 OBSTRUCT* near/3 (LUNG OR PULMONARY OR AIRWAY OR AIRFLOW*)):ti,kw,ab |
| #3 | (BRONCHIECTAS* OR FIBROSIS near/3 (PULMONARY OR ALVEOLIT*) OR EMPHYSEMA near/3 (PULMONARY OR FOCAL OR PANACINAR OR PANLOBUAR OR CENTRIACINAR) OR CHRONIC near/3 BRONCHIT*):ti,kw,ab |
| #4 | ([mh "CYSTIC FIBROSIS"] OR CYSTIC near/3 FIBROSIS:ti,kw,ab) AND (LUNG OR PULMONARY):ti,kw,ab |
| #5 | ((REFRACTORY OR INTRACTABLE) near/3 (DYSPNE* OR DYSPNOE* OR BREATHLESS* OR BREATH near/3 SHORT*)):ti,kw,ab OR [mh DYPNEA[mj]] OR (DYSPNE* OR DYSPNOE* OR BREATHLESS* OR BREATH near/3 SHORT*):ti |
| #6 | #1 or #2 or #3 or #4 or #5 |
| #7 | [mh "ANALGESICS, OPIOID"] OR [mh "MORPHINE DERIVATIVES"] OR [mh FENTANYL] OR [mh METHADONE] OR [mh TRAMADOL] OR [mh BUPRENORPHINE] |
| #8 | (OPIOID* OR MORPHIN* OR OXYCODON* OR *FENTANYL* OR METHADON* OR TRAMADOL* OR BUPRENORPHIN* OR *CODEIN* OR HYDROMORPHON*):ti,kw,ab |
| #9 | #6 and (#7 or #8) |
| #10 | ([mh "PALLIATIVE CARE"] OR [mh "TERMINAL CARE"] OR (END near/2 LIFE OR TERMINAL* OR PALLIAT* OR SEVERE* OR ADVANCED*)):ti,kw,ab) |
| #11 | NONCANCER* OR (NON OR WITHOUT) next CANCER*:ti,kw,ab |
| #12 | #10 and #11 |
| #13 | #10 NOT ([mh NEOPLASMS] OR (CANCER* OR CARCINOM* OR TUMOR* OR TUMOUR* OR NEOPLAS* OR MALIGNAN* OR ONCOLOG*)):ti,kw,ab) |
| #14 | #9 and (#12 or #13) |
| #15 | #9 and (DYSPNE* OR DYSPNOE* OR BREATHLESS* OR BRONCHI* OR FIBROS* OR EMPHYSEM* OR FAILUR* OR INSUFFICIEN* OR INTERSTIT* OR OBSTRUCT* OR COPD OR COAD OR IP OR ILD):ti and (OPIOID* OR MORPHIN* OR OXYCODON* OR *FENTANYL* OR METHADON* OR TRAMADOL* OR BUPRENORPHIN* OR *CODEIN* OR HYDROMORPHON*):ti |
| #16 | #15 and #11 |
| #17 | #15 NOT ([mh NEOPLASMS] OR (CANCER* OR CARCINOM* OR TUMOR* OR TUMOUR* OR NEOPLAS* OR MALIGNAN* OR ONCOLOG*)):ti,kw,ab) |
| #18 | #14 or #16 or #17 |
| #19 | #18 with Cochrane Library publication date Between Jan 1980 and Oct 2020, in Cochrane Reviews, Cochrane Protocols, Clinical Answers, Editorials, Special Collections |
| #20 | #18 with Publication Year from 1980 to 2020, in Trials |
| #21 | #19 or #20 |

Table S2. Bias risk of the randomized controlled studies.

| Study | Random sequence generation (Selection bias) | Allocation concealment (Selection bias) | Blinding of participants and personnel (performance bias) | Binding of outcomes assessmnet (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|--|--|--|--|--|---|---|------------|
| Verberkt CA, (2020) ¹¹ | Low risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Currow D, (2020) ¹² | Low risk | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Kronborg-White S, (2020) ²⁹ | Low risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Ferreira DH, (2019) ²¹ | Low risk | Low risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Abdallah SJ, (2017) ³⁰ | Unclear risk | Unclear risk | Low risk | Unclear risk | High risk | Low risk | Low risk |
| Abernethy AP, (2003) ²⁵ | Low risk | Low risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk |
| Poole PJ, (1998) ³¹ | Low risk | Unclear risk | Unclear risk | Unclear risk | High risk | Low risk | Low risk |
| Light RW, (1996) ¹⁹ | Unclear risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Eiser N, (1991) ^{32 1} | Unclear risk | Unclear risk | Unclear risk | Unclear risk | High risk | Low risk | Low risk |
| Eiser N, (1991) ^{32 2} | Unclear risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Munck LK, (1990) ³³ | Unclear risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk |
| Light RW, (1989) ³⁴ | Unclear risk | Unclear risk | High risk | Unclear risk | Low risk | Low risk | Low risk |
| Rice KL, (1987) ³⁵ | Unclear risk | Unclear risk | Low risk | Unclear risk | High risk | Low risk | Low risk |

| | | | | | | | |
|---|-----------------|-----------------|--------------|-----------------|-----------|----------|-------------|
| Johnson MA, (1983) ³⁶ | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk |
| Woodcock AA, (1982) ¹⁸ | Unclear risk | Unclear risk | Unclear risk | Unclear risk | High risk | Low risk | Low risk |
| Woodcock AA, (1981) ³⁷ | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Low risk | Low risk | Low risk |

Table S3. Bias risk of non-randomized studies, observational studies, five retrospective studies.

| Study | Selection of participants (Selection bias) | Confounding variables (Selection bias) | Measurement of exposure (Performance bias) | Blinding of outcome assessments | Incomplete outcome data | Selective outcome reporting |
|-----------------------------------|--|--|--|---------------------------------|-------------------------|-----------------------------|
| Rocker GM, (2013) ³⁸ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Currow DC, (2011) ²⁶ | Low risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Allcroft P, (2013) ³⁹ | High risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk |
| Allen S, (2005) ⁴⁰ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Smallwood N, (2018) ⁴¹ | Low risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Vicent L, (2017) ⁴² | Low risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Takeyasu M, (2016) ⁴³ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Matsuda Y, (2017) ⁴⁴ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Bajwah S, (2012) ⁵ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Tsukuura H, (2013) ⁴⁵ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |
| Colman R, (2015) ⁴⁶ | High risk | Low risk | Low risk | Unclear risk | Low risk | Low risk |