

## Bijlage Zoekverantwoording

### 1.Evidence based

#### Key question 1

---

##### Key question

*Bij patiënten met dyspneu in de palliatieve fase bij COPD, hartfalen, of kanker: is er een effect van medicatie op dyspneu, inspanningstolerantie, fysiek functioneren of kwaliteit van leven t.o.v. placebo, geen behandeling of andere (medicamenteuze of non-medicamenteuze) behandeling)?*

P: Patiënten met dyspneu en kanker in de palliatieve fase, of vergevorderde stadia van COPD of hartfalen

I: Medicamenteuze behandeling

- a. opioïden (morphine, fentanyl, oxycodon, hydromorfine)
- b. corticosteroïden
- c. benzodiazepines

C: Andere (medicamenteuze of non-medicamenteuze) interventie

O: Dyspneu, inspanningstolerantie, fysiek functioneren, kwaliteit van leven

##### Search strategy

---

Search date: January 19, 2015

Databases: OVID Medline, Embase and the Cochrane Library (see appendix for search strings).

Search limits:

- Publication date: 2000-2014;
- English and Dutch only;
- Study design: meta-analyses, systematische reviews, randomised controlled trials (RCT), controlled clinical trials (CCT)

##### Search Results

---

**Table 1. Overall search results.**

Database	Number of hits
OVID Medline	428
OVID PreMedline	18
EMBASE.com	978
Cochrane Database of Systematic Reviews	27
DARE	3
HTA database	0
CENTRAL	271

<b>Total hits</b>	<b>1725</b>
N excluded (language, year, duplicates)	445
<b>Total unique eligible hits</b>	<b>1280</b>

## Excluded studies

---

1280 unique hits were screened on title and abstract (**Fout! Verwijzingsbron niet gevonden.**). Of these, 1415 were excluded. The most important reasons for exclusion were:

1. Other population: patients with other diseases and/or no dyspnea (in palliative or advanced stage)
2. Other intervention: interventions other than those specified
3. Wrong study design: narrative reviews, observational studies

Of the remaining 45 papers, the full-text was retrieved. Based on the full-text, an additional 31 studies were excluded. [Table 2](#) provides an overview of these excluded studies.

## Included studies

---

The following 9 systematic reviews were included:

- Bailey CD, Wagland R, Dabbour R, Caress A, Smith J, Molassiotis A. An integrative review of systematic reviews related to the management of breathlessness in respiratory illnesses. *BMC Pulmonary Medicine*. 2010;10(63)
- Ben-Aharon I, Gafter-Gvili A, Leibovici L, Stemmer SM. Interventions for alleviating cancer-related dyspnea: a systematic review and meta-analysis. *Acta Oncol*. 2012;51(8):996-1008
- DiSalvo WM, Joyce MM, Tyson LB, Culkin AE, Mackay K. Putting evidence into practice: evidence-based interventions for cancer-related dyspnea. *Clin J Oncol Nurs*. 2008;12(2):341-52
- Jennings AL, Davies AN, Higgins JP, Broadley K. Opioids for the palliation of breathlessness in terminal illness. *Cochrane Database of Systematic Reviews*. 2001;4(4):CD002066
- Lorenz KA, Lynn J, Dy SM, Shugarman LR, Wilkinson A, Mularski RA, et al. Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med*. 2008;148(2):147-59
- Marciniuk DD, Goodridge D, Hernandez P, Rucker G, Balter M, Bailey P, et al. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. *Can Respir J*. 2011;18(2):69-78
- Simon ST, Higginson IJ, Booth S, Harding R, Bausewein C. Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. *Cochrane Database of Systematic Reviews*. 2010;1(1):CD007354
- Simon ST, Koskeroglu P, Gaertner J, Voltz R. Fentanyl for the relief of refractory breathlessness: a systematic review. *J Pain Symptom Manage*. 2013;46(6):874-86
- Viola R, Kiteley C, Lloyd NS, Mackay JA, Wilson J, Wong RK, et al. The management of dyspnea in cancer patients: a systematic review. *Support Care Cancer*. 2008;16(4):329-37

The following 5 primary studies were included:

- Cuervo Pinna MA. A randomized crossover clinical trial to evaluate the efficacy of oral transmucosal fentanyl citrate in the treatment of dyspnea on exertion in patients with advanced cancer. *J Pain Symptom Manage*. 2014;47(6):e4-5
- Gamborg H, Riis J, Christrup L, Krantz T. Effect of intraoral and subcutaneous morphine on dyspnea at rest in terminal patients with primary lung cancer or lung metastases. *J Opioid Manag*. 2013;9(4):269-74
- Hui D, Xu A, Frisbee-Hume S, Chisholm G, Morgado M, Reddy S, et al. Effects of prophylactic subcutaneous fentanyl on exercise-induced breakthrough dyspnea in cancer patients: a preliminary double-blind, randomized, controlled trial. *J Pain Symptom Manage*. 2014;47(2):209-17
- Oxberry SG, Bland JM, Clark AL, Cleland JG, Johnson MJ. Repeat dose opioids may be effective for breathlessness in chronic heart failure if given for long enough. *J Palliat Med*. 2013;16(3):250-5

- Oxberry SG, Torgerson DJ, Bland JM, Clark AL, Cleland JG, Johnson MJ. Short-term opioids for breathlessness in stable chronic heart failure: a randomized controlled trial. *Eur J Heart Fail.* 2011;13(9):1006-12

**Table 2. Key question 1: overview of excluded studies based on full-text evaluation.**

Author	Reference	Title	Reason
Aaron SD	N Engl J Med 2003 348(26):2618-25	Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease	Geen vergevorderd stadium
Ben-Aharon I	J Clin Oncol 2008 26(14):2396-404	Interventions for alleviating cancer-related dyspnea: a systematic review	Updated by Ben-Aharon 2012
Booth S	European Journal of Cancer 2011 47(S77)	The efficacy of benzodiazepines for palliating dyspnoea: A systematic review	Abstract
Clemens K.E	J. Pain Symptom Manage. 2007 33(4):473-481	Symptomatic Therapy of Dyspnea with Strong Opioids and Its Effect on Ventilation in Palliative Care Patients	Geen vergelijkende studie
Clemens KE	Support Care Cancer 2009 17(4):367-77	Use of oxygen and opioids in the palliation of dyspnoea in hypoxic and non-hypoxic palliative care patients: a prospective study	Geen vergelijkende studie
Jennings AL	Thorax 2002 57(11):939-44	A systematic review of the use of opioids in the management of dyspnoea	Idem als Cochrane review
Kallet RH	Respir Care 2007 52(7):900-10	The role of inhaled opioids and furosemide for the treatment of dyspnea	Narratieve review gebaseerd op PubMed search; geen quality appraisal
Navigante AH	Medicina Paliativa 2003 10(1):14-9	Morphine plus midazolam versus oxygen therapy on severe dyspnea management in the last week of life in hipoxemic advanced cancer patients. Spanish	Spaans
Simon S	Cochrane Database Syst. Rev. 2008 4):	Benzodiazepines for the relief of breathlessness in malignant and advanced non-malignant diseases in adults	Updated by Simon 2010
Simon ST	J Pain Symptom Manage 2013 45(3):561-78	Episodic breathlessness in patients with advanced disease: a systematic review	Gaat niet over behandeling
Walters JAE	Cochrane Database of Systematic Reviews 2014 12):	Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease	Niet specifiek over vergevorderd stadium
Wiseman R	Aust Fam Physician 2013 42(3):137-40	Chronic refractory dyspnoea--evidence based management	Geen quality appraisal
Dy SM	Cancer J 2010; 16(5): 507-513	Evidence-based approaches to other symptoms in advanced cancer	Geen quality appraisal
Bausewein C	Dtsch. Arztebl. int 2013 110(33-34):563-71; quiz 572	Shortness of breath and cough in patients in palliative care	Geen quality appraisal
Beller EM	Cochrane Database of Systematic Reviews 2015 1):	Palliative pharmacological sedation for terminally ill adults	Geen vergelijkende studies gevonden
Booth S	Nat Clin Pract Oncol 2008 5(2):90-100	The etiology and management of intractable breathlessness in patients with advanced cancer: a systematic review of pharmacological therapy	Geen quality appraisal
Jantarakupt P	Oncol Nurs Forum 2005 32(4):785-97	Dyspnea management in lung cancer: applying the evidence from chronic obstructive pulmonary disease	Narrative review
Mercadante S	J Pain Symptom Manage 2011 41(4):754-60	Palliative sedation in patients with advanced cancer followed at home: a systematic review	Geen specifieke analyse voor dyspneu
Oxberry SG	Am Heart J 2012 164(2):229-35	Minimally clinically important difference in chronic breathlessness: every little helps	Geen interventie-studie
Shearer FA	Cochrane Database of Systematic Reviews 2014 2):	Opioids for treating dyspnoea in patients with chronic heart failure	Protocol

Author	Reference	Title	Reason
Walters JA	Cochrane Database Syst Rev 2009 1):CD001288	Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease	Foute context (acute exacerbaties)
Wilt TJ	Ann Intern Med 2007 147(9):639-53	Management of stable chronic obstructive pulmonary disease: a systematic review for a clinical practice guideline	Verkeerde interventies
Brown SJ	Ann Pharmacother 2005 39(6):1088-92	Nebulized morphine for relief of dyspnea due to chronic lung disease	Geen quality appraisal
Foral PA	Chest 2004 125(2):691-4	Nebulized opioids use in COPD	Narratieve review gebaseerd op PubMed search; geen quality appraisal
Liu C	J Cardiovasc Pharmacol 2014 63(4):333-8	Cardiac outcome prevention effectiveness of glucocorticoids in acute decompensated heart failure: COPE-ADHF study	Foute context (acute decompensatie)
Abernethy AP	BMJ 2003 327(7414):523-8	Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea	Geïnccludeerd in geïnccludeerde review
Bruera E	J Pain Symptom Manage 2005 29(6):613-8	Nebulized versus subcutaneous morphine for patients with cancer dyspnea: a preliminary study	Geïnccludeerd in geïnccludeerde review
Charles MA	J Pain Symptom Manage 2008 36(1):29-38	Relief of incident dyspnea in palliative cancer patients: a pilot, randomized, controlled trial comparing nebulized hydromorphone, systemic hydromorphone, and nebulized saline	Geïnccludeerd in geïnccludeerde review
Johnson MJ	Eur J Heart Fail 2002 4(6):753-6	Morphine for the relief of breathlessness in patients with chronic heart failure--a pilot study	Geïnccludeerd in geïnccludeerde review
Navigante AH	J Pain Symptom Manage 2006 31(1):38-47	Midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer	Geïnccludeerd in geïnccludeerde review
Navigante AH	J. Pain Symptom Manage 2010; 39: 820-830	Morphine versus midazolam as upfront therapy to control dyspnea perception in cancer patients while its underlying cause is sought or treated	Geïnccludeerd in geïnccludeerde review

## Key question 2

---

### Key question

*Bij patiënten met dyspneu en COPD, hartfalen of kanker in de palliatieve fase: is er een effect van niet-medicamenteuze therapie op dyspneu, inspanningstolerantie, fysiek functioneren en kwaliteit van leven t.o.v. geen behandeling of andere niet-medicamenteuze interventie?*

P: Patiënten met dyspneu en kanker in de palliatieve fase, of vergevorderde stadia van COPD of hartfalen

I: Niet-medicamenteuze behandeling:

- instructie en voorlichting
- ademhalingsoefeningen
- ontspanningsoefeningen
- psychologische ondersteuning
- acupunctuur/acupressuur
- hulpmiddelen bij het lopen
- vibratie thoraxwand
- neurostimulatie
- luchtbevochtiging
- ventilator
- zuurstof
- niet-invasieve beademing
- uitzuigen

C: Geen therapie of andere niet-medicamenteuze interventie

O: Dyspneu, inspanningstolerantie, fysiek functioneren, kwaliteit van leven

### Search strategy

---

Search date: February 20, 2015

Databases: OVID Medline, Embase and the Cochrane Library (see appendix for search strings).

Search limits:

- Publication date: 2000-2014;
- English and Dutch only;
- Study design: meta-analyses, systematische reviews, randomised controlled trials (RCT), controlled clinical trials (CCT)
- 

### Search Results

---

**Table 3. Overall search results.**

Database	Number of hits
OVID Medline	759

OID PreMedline	18
EMBASE.com	334
Cochrane Database of Systematic Reviews	166
DARE	9
HTA database	0
CENTRAL	466
<b>Total hits</b>	<b>1752</b>
N excluded (language, year, duplicates)	400
<b>Total unique eligible hits</b>	<b>1352</b>

## Excluded studies

---

1352 unique hits were screened on title and abstract (Table 3). Of these, 1283 were excluded. The most important reasons for exclusion were:

1. Other population: patients with other diseases and/or no dyspnea (in palliative or advanced stage)
2. Other intervention: interventions other than those specified
3. Wrong study design: narrative reviews, observational studies

Of the remaining 69 papers, the full-text was retrieved. Based on the full-text, an additional 44 studies were excluded. Table 4 provides an overview of these excluded studies.

## Included studies

---

The following 18 systematic reviews were included:

- Bailey CD, Wagland R, Dabbour R, Caress A, Smith J, Molassiotis A. An integrative review of systematic reviews related to the management of breathlessness in respiratory illnesses. *BMC pulmonary medicine*. 2010;10(63)
- Bausewein C, Booth S, Gysels M, Higginson I. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *Cochrane Database of Systematic Reviews*. 2008;2(2):CD005623
- Ben-Aharon I, Gafter-Gvili A, Leibovici L, Stemmer S.M. Interventions for alleviating cancer-related dyspnea: A systematic review and meta-analysis. *Acta Oncol*. 2012;51(8):996-1008
- Bradley JM, Lasserson T, Elborn S, Macmahon J, O'Neill B. A systematic review of randomized controlled trials examining the short-term benefit of ambulatory oxygen in COPD. *Chest*. 2007;131(1):278-85
- Chen H, Liang B-M, Xu Z-B, Tang Y-J, Wang K, Xiao J, et al. Long-term non-invasive positive pressure ventilation in severe stable chronic obstructive pulmonary disease: a meta-analysis. *Chin Med J*. 2011;124(23):4063-70
- Cranston JM, Crockett A, Currow D. Oxygen therapy for dyspnoea in adults. *Cochrane Database of Systematic Reviews*. 2008;3(3):CD004769
- DiSalvo WM, Joyce MM, Tyson LB, Culkin AE, Mackay K. Putting evidence into practice: evidence-based interventions for cancer-related dyspnea. *Clin J Oncol Nurs*. 2008;12(2):341-52
- Holland AE, Hill CJ, Jones AY, McDonald CF. Breathing exercises for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2012;10
- Kolodziej MA, Jensen L, Rowe B, Sin D. Systematic review of noninvasive positive pressure ventilation in severe stable COPD. *Eur Respir J*. 2007;30(2):293-306
- Lee EJ, Frazier SK. The efficacy of acupressure for symptom management: a systematic review. *J Pain Symptom Manage*. 2011;42(4):589-603
- Marciniuk DD, Goodridge D, Hernandez P, Rocker G, Balter M, Bailey P, et al. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: a Canadian Thoracic Society clinical practice guideline. *Can Respir J*. 2011;18(2):69-78
- Norweg A, Collins EG. Evidence for cognitive-behavioral strategies improving dyspnea and related distress in COPD. *International Journal of Copd*. 2013;8:439-51

- Osadnik CR, McDonald CF, Miller BR, Hill CJ, Tarrant B, Steward R, et al. The effect of positive expiratory pressure (PEP) therapy on symptoms, quality of life and incidence of re-exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease: a multicentre, randomised controlled trial. *Thorax*. 2014;69(2):137-43
- Pan L, Guo Y, Liu X, Yan J. Lack of efficacy of neuromuscular electrical stimulation of the lower limbs in chronic obstructive pulmonary disease patients: a meta-analysis. *Respirology*. 2014;19(1):22-9
- Struik FM, Lacasse Y, Goldstein R, Kerstjens HA, Wijkstra PJ. Nocturnal non-invasive positive pressure ventilation for stable chronic obstructive pulmonary disease. *Cochrane Database Syst Review* 2013; 6: CD002878
- Towler P, Molassiotis A, Brearley SG. What is the evidence for the use of acupuncture as an intervention for symptom management in cancer supportive and palliative care: an integrative overview of reviews. *Support Care Cancer*. 2013;21(10):2913-23
- Uronis HE, Currow DC, McCrory DC, Samsa GP, Abernethy AP. Oxygen for relief of dyspnoea in mildly- or non-hypoxaemic patients with cancer: a systematic review and meta-analysis. *Br J Cancer*. 2008;98(2):294-9
- Uronis H, McCrory DC, Samsa G, Currow D, Abernethy A. Symptomatic oxygen for non-hypoxaemic chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2011;6(6):CD006429

The review of Pan et al. was not identified by the search and was included by the working group.

The following 8 primary studies were included:

- Barton R, English A, Nabb S, Rigby AS, Johnson MJ. A randomised trial of high vs low intensity training in breathing techniques for breathless patients with malignant lung disease: a feasibility study. *Lung Cancer*. 2010;70(3):313-9
- Bausewein C, Booth S, Gysels M, Kuhnback R, Higginson IJ. Effectiveness of a hand-held fan for breathlessness: a randomised phase II trial. *BMC Palliative Care*. 2010;9:22
- Dreher M, Doncheva E, Schwoerer A, Waltersbacher S, Sonntag F, Kabitz HJ, et al. Preserving oxygenation during walking in severe chronic obstructive pulmonary disease: noninvasive ventilation versus oxygen therapy. *Respiration*. 2009;78(2):154-60
- Duiverman ML, Wempe JB, Bladder G, Vonk JM, Zijlstra JG, Kerstjens HAM, et al. Two-year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: a randomized controlled trial. *Respiratory research*. 2011;12(112)
- Hui D, Morgado M, Chisholm G, Withers L, Nguyen Q, Finch C, et al. High-flow oxygen and bilevel positive airway pressure for persistent dyspnea in patients with advanced cancer: a phase II randomized trial. *J Pain Symptom Manage*. 2013;46(4):463-73
- Moore RP, Berlowitz DJ, Denehy L, Pretto JJ, Brazzale DJ, Sharpe K, et al. A randomised trial of domiciliary, ambulatory oxygen in patients with COPD and dyspnoea but without resting hypoxaemia. *Thorax*. 2011;66(1):32-7
- Ozalevli S, Ozden A, Gocen Z, Cimrin AH. Comparison of six-minute walking tests conducted with and without supplemental oxygen in patients with chronic obstructive pulmonary disease and exercise-induced oxygen desaturation. *Ann Saudi Med*. 2007;27(2):94-100
- Suzuki M, Muro S, Ando Y, Omori T, Shiota T, Endo K, et al. A randomized, placebo-controlled trial of acupuncture in patients with chronic obstructive pulmonary disease (COPD): the COPD-acupuncture trial (CAT). *Arch Intern Med*. 2012;172(11):878-86



**Table 4. Key question 2: overview of excluded studies based on full-text evaluation.**

Reference	Reason
Abernethy AP, McDonald CF, Frith PA, Clark K, Herndon JE, 2nd, Marcello J, et al. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. <i>Lancet</i> . 2010;376(9743):784-93	Al geïnccludeerd in geïnccludeerde review
Bruera E, Sweeney C, Willey J, Palmer JL, Strasser F, Morice RC, et al. A randomized controlled trial of supplemental oxygen versus air in cancer patients with dyspnea. <i>Palliat Med</i> . 2003;17(8):659-63	Al geïnccludeerd in geïnccludeerde review
Clini E, Sturani C, Rossi A, Viaggi S, Corrado A, Donner CF, et al. The Italian multicentre study on noninvasive ventilation in chronic obstructive pulmonary disease patients.[Erratum appears in <i>Eur Respir J</i> . 2002 Dec;20(6):1617]. <i>Eur Respir J</i> . 2002;20(3):529-38	Al geïnccludeerd in geïnccludeerde review
Crisafulli E, Costi S, De Blasio F, Biscione G, Americi F, Penza S, et al. Effects of a walking aid in COPD patients receiving oxygen therapy. <i>Chest</i> . 2007;131(4):1068-74	Al geïnccludeerd in geïnccludeerde review
Donesky-Cuenca D, Nguyen HQ, Paul S, Carriero-Kohlman V. Yoga therapy decreases dyspnea-related distress and improves functional performance in people with chronic obstructive pulmonary disease: a pilot study. <i>J Altern Complement Med</i> . 2009;15(3):225-34	Foute interventie
Galbraith S, Fagan P, Perkins P, Lynch A, Booth S. Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial. <i>J Pain Symptom Manage</i> . 2010;39(5):831-8	Al geïnccludeerd in geïnccludeerde review
Jolliet P, Tassaux D, Roeseler J, Burdet L, Broccard A, D'Hoore W, et al. Helium-oxygen versus air-oxygen noninvasive pressure support in decompensated chronic obstructive disease: A prospective, multicenter study. <i>Crit Care Med</i> . 2003;31(3):878-84	Foute context (acuut)
Lewith GT, Prescott P, Davis CL. Can a standardized acupuncture technique palliate disabling breathlessness: a single-blind, placebo-controlled crossover study. <i>Chest</i> . 2004;125(5):1783-90	Al geïnccludeerd in geïnccludeerde review
Maggiore SM, Richard J-CM, Abroug F, Diehl JL, Antonelli M, Sauder P, et al. A multicenter, randomized trial of noninvasive ventilation with helium-oxygen mixture in exacerbations of chronic obstructive lung disease. <i>Crit Care Med</i> . 2010;38(1):145-51	Foute context (acuut)
Nava S, Ferrer M, Esquinas A, Scala R, Groff P, Cosentini R, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. <i>Lancet Oncol</i> . 2013;14(3):219-27	Foute context (acuut)
Philip J, Gold M, Milner A, Di Iulio J, Miller B, Spruyt O. A randomized, double-blind, crossover trial of the effect of oxygen on dyspnea in patients with advanced cancer. <i>J Pain Symptom Manage</i> . 2006;32(6):541-50	Al geïnccludeerd in geïnccludeerde review
Struik FM, Sprooten RTM, Kerstjens HAM, Bladder G, Zijnen M, Asin J, et al. Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. <i>Thorax</i> . 2014;69(9):826-34	Foute context (acuut)
Vickers AJ, Feinstein MB, Deng GE, Cassileth BR. Acupuncture for dyspnea in advanced cancer: a randomized, placebo-controlled pilot trial [ISRCTN89462491]. <i>BMC Palliative Care</i> . 2005;4(5):18	Al geïnccludeerd in geïnccludeerde review
Antonelli M, Conti G, Pelosi P, Gregoretti C, Pennisi MA, Costa R, et al. New treatment of acute hypoxemic respiratory failure: noninvasive pressure support ventilation delivered by helmet--a pilot controlled trial. <i>Crit Care Med</i> . 2002;30(3):602-8.	Foute populatie (acute respiratory failure), foute vergelijking
Bausewein C, Simon ST. Shortness of breath and cough in patients in palliative care. <i>Dtsch</i> . 2013;110(33-34):563-71; quiz 72.	Geen quality appraisal
Ben-Aharon I, Gafter-Gvili A, Paul M, Leibovici L, Stemmer SM. Interventions for alleviating cancer-related dyspnea: a systematic review. <i>J Clin Oncol</i> . 2008;26(14):2396-404.	Updated by Ben-Aharon 2012
Booth S, Wade R. Oxygen or air for palliation of breathlessness in advanced cancer. <i>J R Soc Med</i> . 2003;96(5):215-8.	Narrative review
Chan CWH, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy: results of a psychoeducational randomized controlled trial. <i>J Pain Symptom Manage</i> . 2011;41(2):347-57.	Niet alle patiënten hadden dyspneu
Connors et al. An evaluation of a a physiotherapy led non-pharmacological bresthlessness programme for patientws with intrathoracic malignancy. <i>Palliat med</i> 2007; 21: 285-287	Complexe interventie, individueel effect van interventies niet te achterhalen
Davis CL, Lewith GT, Broomfield J, Prescott P. A pilot project to assess the methodological issues involved in evaluating acupuncture as a treatment for disabling breathlessness. <i>J Altern Complement Med</i> . 2001;7(6):633-9.	Geen informatie over stadium

Reference	Reason
Deng et al. The effect of non-pharmacological staged interventions on fatigue and dyspnea in patients with chronic obstructive pulmonary disease: a randomized controlled trial. <i>Int J Nursing Pract</i> 2013; 19: 636-643	Complexe interventie, individueel effect van interventies niet te achterhalen
Fridlender ZG, Arish N, Laxer U, Berkman N, Leibovitz A, Fink G, et al. Randomized controlled crossover trial of a new oscillatory device as add-on therapy for COPD. <i>COPD</i> . 2012;9(6):603-10.	Vooral COPD st. II-III
Garcia-Talavera I, Figueira M, Aguirre-Jaime A. A randomised trial of domiciliary, ambulatory oxygen in patients with COPD and dyspnoea but without resting hypoxaemia. <i>Thorax</i> . 2011;66(7):631-2; author reply 2.	Letter
Goktalay T, Akdemir SE, Alpaydin AO, Coskun AS, Celik P, Yorgancioglu A. Does high-frequency chest wall oscillation therapy have any impact on the infective exacerbations of chronic obstructive pulmonary disease? A randomized controlled single-blind study. <i>Clin Rehabil</i> . 2013;27(8):710-8.	Foute context (infective exacerbations)
Higginson et al. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. <i>Lancet Respir Med</i> 2014; 2: 979-87	Complexe interventie, individueel effect van interventies niet te achterhalen
Hui D, Morgado M, Chisholm GB, Withers L, Nguyen Q, Finch C, et al. High-flow oxygen (HFO) and bilevel positive airway pressure (BiPAP) for refractory dyspnea in patients with advanced cancer: A randomized controlled trial. <i>J Clin Oncol</i> . 2013;31(15 SUPPL. 1).	Abstract
Jantarakupt P, Porock D. Dyspnea management in lung cancer: applying the evidence from chronic obstructive pulmonary disease. <i>Oncol Nurs Forum</i> . 2005;32(4):785-97.	Narrative review
Mahajan AK, Diette GB, Hatipoglu U, Bilderback A, Ridge A, Harris VW, et al. High frequency chest wall oscillation for asthma and chronic obstructive pulmonary disease exacerbations: a randomized sham-controlled clinical trial. <i>Respiratory research</i> . 2011;12(120).	Vooral astma, verkeerde context (acuut)
Mishra EK, Corcoran J, Hallifax R, Stradling J, Maskell N, Rahman N. Defining the minimal important difference for the visual analogue scale for dyspnoea in patients with malignant pleural effusions. <i>Thorax</i> . 2013;68:A171.	Abstract
Mularski RA, Munjas BA, Lorenz KA, Sun S, Robertson SJ, Schmelzer W, et al. Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. <i>J Altern Complement Med</i> . 2009;15(10):1083-90.	Ook COPD st. I-III
Nicolini A, Mollar E, Grecchi B, Landucci N. Comparison of intermittent positive pressure breathing and temporary positive expiratory pressure in patients with severe chronic obstructive pulmonary disease. <i>Arch Bronconeumol</i> . 2014;50(1):18-24.	Foute interventie (PEP)
Osadnik CR, McDonald CF, Miller BR, Hill CJ, Tarrant B, Steward R, et al. The effect of positive expiratory pressure (PEP) therapy on symptoms, quality of life and incidence of re-exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease: a multicentre, randomised controlled trial. <i>Thorax</i> . 2014;69(2):137-43.	Foute context (acuut), interventie niet in PICO
Principi T, Pantanetti S, Catani F, Elisei D, Gabbanelli V, Pelaia P, et al. Noninvasive continuous positive airway pressure delivered by helmet in hematological malignancy patients with hypoxemic acute respiratory failure. <i>Intensive Care Med</i> . 2004;30(1):147-50.	Foute vergelijking
Rueda J-R, Sola I, Pascual A, Subirana Casacuberta M. Non-invasive interventions for improving well-being and quality of life in patients with lung cancer. <i>Cochrane Database of Systematic Reviews</i> . 2011;9(9):CD004282.	Beantwoord PICO niet
Seamark DA, Seamark CJ, Halpin DMG. Palliative care in chronic obstructive pulmonary disease: a review for clinicians. <i>J R Soc Med</i> . 2007;100(5):225-33.	Narrative review
Smith TA, Davidson PM, Lam LT, Jenkins CR, Ingham JM. The use of non-invasive ventilation for the relief of dyspnoea in exacerbations of chronic obstructive pulmonary disease; a systematic review. <i>Respirology</i> . 2012;17(2):300-7.	Foute context (acuut)
Sola I, Thompson E, Subirana M, Lopez C, Pascual A. Non-invasive interventions for improving well-being and quality of life in patients with lung cancer. <i>Cochrane Database of Systematic Reviews</i> . 2004;4(4):CD004282.	Ge-updated
Storre JH, Huttmann SE, Ekkernkamp E, Walterspacher S, Schmoor C, Dreher M, et al. Oxygen supplementation in noninvasive home mechanical ventilation: the crucial roles of CO2 exhalation systems and leakages. <i>Respir Care</i> . 2014;59(1):113-20.	Foute vergelijking
Uronis HE, Ekström MP, Currow DC et al. Oxygen for relief of dyspnoea in people with chronic obstructive pulmonary disease who would not qualify for home oxygen: a systematic review and meta-analysis. <i>Thorax</i> . 2014 Dec 3. pii: thoraxjnl-2014-205720	Samenvatting van Cochrane review
Valenza MC, Valenza-Pena G, Torres-Sanchez I, Gonzalez-Jimenez E, Conde-Valero A, Valenza-Demet G. Effectiveness of controlled breathing techniques on anxiety and depression in hospitalized patients with COPD: a randomized clinical Trial. <i>Respir Care</i> . 2014;59(2):209-15.	Foute context: infectieuze exacerbatie; geen stadia gerapporteerd
Whale CA, MacLaran SJA, Whale CI, Barnett M. Pilot study to assess the credibility of acupuncture in acute exacerbations of chronic obstructive pulmonary disease. <i>Acupunct Med</i> . 2009;27(1):13-5.	Foute context: acute exacerbatie; geen stadia gerapporteerd

Reference	Reason
Wu H-S, Wu S-C, Lin J-G, Lin L-C. Effectiveness of acupressure in improving dyspnoea in chronic obstructive pulmonary disease. J Adv Nurs. 2004;45(3):252-9.	Ook COPD st. I-III
Yu DSF, Lee DTF, Woo J. Effects of relaxation therapy on psychologic distress and symptom status in older Chinese patients with heart failure. J Psychosom Res. 2007;62(4):427-37.	Meerderheid NYHA I-II
Zhao I, Yates P. Non-pharmacological interventions for breathlessness management in patients with lung cancer: a systematic review. Palliat Med. 2008;22(6):693-701.	Complexe interventie, individueel effect van interventies niet te achterhalen

## Search strings Question 1

- medline (ovid)

---

- 1 exp DYS/PNEA/ (15779)
- 2 (dyspnoe\$ or dyspne\$).mp. (37968)
- 3 dyspnoeic.mp. (161)
- 4 breathless\$.mp. (3192)
- 5 (breathing adj3 labored).mp. (171)
- 6 (breathing adj3 laboured).mp. (38)
- 7 (breathing adj3 difficult\$).mp. (1341)
- 8 or/1-7 (41332)
- 9 Lung Diseases, Obstructive/ (17896)
- 10 exp Pulmonary Disease, Chronic Obstructive/ (37064)
- 11 emphysema\$.mp. (28045)
- 12 (chronic\$ adj3 bronchiti\$).mp. (10077)
- 13 (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp. (80668)
- 14 COPD.mp. (24299)
- 15 COAD.mp. (186)
- 16 COBD.mp. (11)
- 17 AECB.mp. (205)
- 18 or/9-17 (111704)
- 19 exp Heart Failure/ (88210)
- 20 (heart adj2 failure\*).tw. (102700)
- 21 (cardiac adj2 failure\*).tw. (11714)
- 22 (myocardial adj2 failure\*).tw. (2330)
- 23 (heart adj2 decompensat\*).tw. (2155)
- 24 heart failure.tw. (102175)
- 25 cardiac failure.tw. (9677)
- 26 or/19-25 (140772)
- 27 exp Neoplasms/ (2621559)
- 28 Neoplasm Staging/ (125122)
- 29 cancer\$.ti,ab. (1035026)
- 30 tumor\$.ti,ab. (941350)
- 31 tumour\$.ti,ab. (198532)

- 32 carcinoma\$.ti,ab. (459327)
- 33 neoplasm\$.ti,ab. (95382)
- 34 lymphoma.ti,ab. (109223)
- 35 melanoma.ti,ab. (74309)
- 36 staging.ti,ab. (49428)
- 37 metastas\$.ti,ab. (216580)
- 38 metastatic.ti,ab. (138252)
- 39 exp Neoplasm Metastasis/ (158363)
- 40 exp neoplastic processes/ (339813)
- 41 neoplastic process\$.ti,ab. (2288)
- 42 non small cell.ti,ab. (30863)
- 43 adenocarcinoma\$.ti,ab. (93863)
- 44 squamous cell.ti,ab. (65141)
- 45 nsclc.ti,ab. (18092)
- 46 osteosarcoma\$.ti,ab. (14839)
- 47 phyllodes.ti,ab. (1277)
- 48 cystosarcoma\$.ti,ab. (551)
- 49 fibroadenoma\$.ti,ab. (2925)
- 50 (non adj small adj cell).ti,ab. (30863)
- 51 (non adj2 small adj2 cell).ti,ab. (31069)
- 52 (nonsmall adj2 cell).ti,ab. (1772)
- 53 plasmacytoma\$.ti,ab. (5203)
- 54 myeloma.ti,ab. (35791)
- 55 multiple myeloma.ti,ab. (23333)
- 56 lymphoblastoma\$.ti,ab. (277)
- 57 lymphocytoma\$.ti,ab. (288)
- 58 lymphosarcoma\$.ti,ab. (3839)
- 59 immunocytoma.ti,ab. (402)
- 60 sarcoma\$.ti,ab. (71340)
- 61 hodgkin\$.ti,ab. (51183)
- 62 (nonhodgkin\$ or non hodgkin\$.ti,ab. (29387)
- 63 or/27-62 (3020105)
- 64 18 or 26 or 63 (3248106)

- 65 Narcotics/ (14532)
- 66 \*"Analgesics, Opioid"/ (19666)
- 67 (opioïd\$ or morphine or morfine or hydromorphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone).mp. (138260)
- 68 exp Adrenal Cortex Hormones/ (337600)
- 69 (17-ketosteroid\$ or androstenedione or androsterone or "estrone sulfate" or etiocholanolone or prasterone or dehydroepiandrosterone or hydroxycorticosteroid\$ or "11 hydroxycorticosteroid\$" or 17-hydrocorticosteroid\$ or deoxycorticosterone or deoxycorticosterone or pregnenolone or corticosteroid\$ or hydrocortisone or budesonide or prednisolone or methylprednisolone or efcortisol or hydrocortone or "solu cortef" or budesonide or entocort\$ or budenofalk or equilein or 18-hydroxycorticosterone or aldosterone or corticosterone or hydrocortisone or hydrocortisone or tetrahydrocortisol or tetrahydrocortisol or cortison or cortodoxone).mp. (267557)
- 70 exp Benzodiazepines/ (58527)
- 71 benzodiazepine\$.mp. (36609)
- 72 (adinazolam or alprazolam or bentazepam or bromazepam or brotizolam or chlordiazepoxide or cinolazepam or clobazam or clonazepam or clorazepate or clotiazepam or cloxazolam or delorazepam or demoxepam or desmethyldiazepam or diazepam or estazolam or etizolam or etozolam or fludiazepam or flunitrazepam or flurazepam or flutoprazepam or halazepam or haloxazolam or ketazolam or loprazolam or lorazepam or lormetazepam or medazepam or metaclazepam or mexazolam or midazolam or nimetazepam or nitrazepam or nordazepam or oxazepam or oxazolam or pinazepam or prazepam or quazepam or temazepam or tetrazepam or tofisopam or triazolam).mp. (50494)
- 73 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 (605122)
- 74 randomized controlled trial.pt. (380681)
- 75 controlled clinical trial.pt. (88346)
- 76 randomized.ab. (279544)
- 77 placebo.ab. (147491)
- 78 clinical trials as topic.sh. (170246)
- 79 randomly.ab. (198505)
- 80 trial.ti. (120264)
- 81 74 or 75 or 76 or 77 or 78 or 79 or 80 (872399)
- 82 exp animals/ not humans.sh. (3969827)
- 83 81 not 82 (800180)
- 84 meta-analysis.mp.pt. or review.pt. or search:.tw. (2072081)
- 85 83 or 84 (2749075)
- 86 8 and 64 and 73 and 85 (590)
- 87 limit 86 to yr="2000 -Current" (428)

## PreMedline (OVID)

---

- 2 (dyspnoe\$ or dyspne\$).mp. (2808)
- 3 dyspnoeic.mp. (19)

- 4 breathless\$.mp. (340)
- 5 (breathing adj3 labored).mp. (9)
- 6 (breathing adj3 laboured).mp. (2)
- 7 (breathing adj3 difficult\$.mp. (162)
- 8 or/2-7 (3260)
- 11 emphysema\$.mp. (1141)
- 12 (chronic\$ adj3 bronchiti\$.mp. (267)
- 13 (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp. (4327)
- 14 COPD.mp. (2680)
- 15 COAD.mp. (17)
- 16 COBD.mp. (0)
- 17 AECB.mp. (15)
- 18 or/11-17 (6060)
- 20 (heart adj2 failure\*).tw. (7624)
- 21 (cardiac adj2 failure\*).tw. (605)
- 22 (myocardial adj2 failure\*).tw. (119)
- 23 (heart adj2 decompensat\*).tw. (242)
- 24 heart failure.tw. (7592)
- 25 cardiac failure.tw. (446)
- 26 or/20-25 (8053)
- 29 cancer\$.ti,ab. (91727)
- 30 tumor\$.ti,ab. (66356)
- 31 tumour\$.ti,ab. (12751)
- 32 carcinoma\$.ti,ab. (30052)
- 33 neoplasm\$.ti,ab. (6831)
- 34 lymphoma.ti,ab. (6672)
- 35 melanoma.ti,ab. (4606)
- 36 staging.ti,ab. (4002)
- 37 metastas\$.ti,ab. (18480)
- 38 metastatic.ti,ab. (12030)
- 41 neoplastic process\$.ti,ab. (138)
- 42 non small cell.ti,ab. (3718)
- 43 adenocarcinoma\$.ti,ab. (7028)

- 44 squamous cell.ti,ab. (5327)
- 45 nsclc.ti,ab. (2651)
- 46 osteosarcoma\$.ti,ab. (1109)
- 47 phyllodes.ti,ab. (114)
- 48 cystosarcoma\$.ti,ab. (16)
- 49 fibroadenoma\$.ti,ab. (195)
- 50 (non adj small adj cell).ti,ab. (3718)
- 51 (non adj2 small adj2 cell).ti,ab. (3728)
- 52 (nonsmall adj2 cell).ti,ab. (168)
- 53 plasmacytoma\$.ti,ab. (234)
- 54 myeloma.ti,ab. (2076)
- 55 multiple myeloma.ti,ab. (1699)
- 56 lymphoblastoma\$.ti,ab. (11)
- 57 lymphocytoma\$.ti,ab. (9)
- 58 lymphosarcoma\$.ti,ab. (91)
- 59 immunocytoma.ti,ab. (1)
- 60 sarcoma\$.ti,ab. (4742)
- 61 hodgkin\$.ti,ab. (2329)
- 62 (nonhodgkin\$ or non hodgkin\$).ti,ab. (1500)
- 63 or/29-62 (159745)
- 64 18 or 26 or 63 (172397)
- 67 (opioid\$ or morphine or morfine or hydromorphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone).mp. (7059)
- 69 (17-ketosteroid\$ or androstenedione or androsterone or "estrone sulfate" or etiocholanolone or prasterone or dehydroepiandrosterone or hydroxycorticosteroid\$ or "11 hydroxycorticosteroid\$" or 17-hydrocorticosteroid\$ or deoxycorticosterone or deoxycorticosterone or pregnenolone or corticosteroid\$ or hydrocortisone or budesonide or prednisolone or methylprednisolone or efcortisol or hydrocortone or "solu cortef" or budesonide or entocort\$ or budenofalk or equilein or 18-hydroxycorticosterone or aldosterone or corticosterone or hydrocortisone or hydrocortisone or tetrahydrocortisol or tetrahydrocortisol or cortison or cortodoxone).mp. (9289)
- 71 benzodiazepine\$.mp. (1390)
- 72 (adinazolam or alprazolam or bentazepam or bromazepam or brotizolam or chlordiazepoxide or cinolazepam or clobazam or clonazepam or clorazepate or clotiazepam or cloxazolam or delorazepam or demoxepam or desmethyldiazepam or diazepam or estazolam or etizolam or etozolam or fludiazepam or flunitrazepam or flurazepam or flutoprazepam or halazepam or haloxazolam or ketazolam or loprazolam or lorazepam or lormetazepam or medazepam or metaclazepam or mexazolam or midazolam or nimetazepam or nitrazepam or nordazepam or oxazepam or oxazolam or pinazepam or prazepam or quazepam or temazepam or tetrazepam or tofisopam or triazolam).mp. (1710)
- 73 67 or 69 or 71 or 72 (18467)



- 74 randomized controlled trial.pt. (764)
- 75 controlled clinical trial.pt. (84)
- 76 randomized.ab. (25645)
- 77 placebo.ab. (9273)
- 79 randomly.ab. (23043)
- 80 trial.ti. (10810)
- 81 74 or 75 or 76 or 77 or 79 or 80 (54433)
- 84 meta-analysis.mp.pt. or review.pt. or search:.tw. (52394)
- 85 81 or 84 (101887)
- 86 8 and 64 and 73 and 85 (18)
- 87 limit 86 to yr="2000 -Current" (18)

### EMBASE (via embase.com)

#1	'neoplasm'/exp	3477142
#2	cancer*:ab,ti OR tumor*:ab,ti OR tumour*:ab,ti OR carcinoma*:ab,ti OR neoplasm*:ab,ti OR lymphoma:ab,ti OR melanoma:ab,ti OR metastas*:ab,ti OR metastatic:ab,ti OR (non:ab,ti AND small:ab,ti AND cell:ab,ti) OR adenocarcinoma*:ab,ti OR (squamous:ab,ti AND cell:ab,ti) OR nscl:ab,ti OR osteosarcoma*:ab,ti OR phyllodes:ab,ti OR cystosarcoma*:ab,ti OR fibroadenoma*:ab,ti OR plasmacytoma*:ab,ti OR myeloma*:ab,ti OR lymphoblastoma*:ab,ti OR lymphocytoma*:ab,ti OR sarcoma*:ab,ti OR hodgkin*:ab,ti OR nonhodgkin*:ab,ti	2990009
#3	'chronic obstructive lung disease'/exp OR emphysema*:ab,ti OR (chronic* NEAR/3 bronchiti*):ab,ti OR (obstruct* NEAR/3 (pulmonary OR lung* OR airway* OR airflow* OR bronch* OR respirat*)):ab,ti OR copd:ab,ti OR coad:ab,ti OR cobd:ab,ti OR aecb:ab,ti	146325
#4	'heart failure'/exp OR (heart NEAR/2 failure*):ab,ti OR (myocardial NEAR/2 failure*):ab,ti OR (cardiac NEAR/2 failure*):ab,ti OR (heart NEAR/2 decompensat*):ab,ti	355413
#5	#1 OR #2 OR #3 OR #4	4425976
#6	'dyspnea'/de OR dyspnoe*:ab,ti OR dyspne*:ab,ti OR breathless*:ab,ti OR (breathing NEAR/3 labored):ab,ti OR (breathing NEAR/3 laboured):ab,ti OR (breathing NEAR/3 difficult*):ab,ti	111255
#7	'narcotic agent'/exp OR 'narcotic analgesic agent'/exp OR opioid*:ab,ti OR morphine:ab,ti OR morfine:ab,ti OR hydromorphone:ab,ti OR buprenorphine:ab,ti OR codeine:ab,ti OR dextromoramide:ab,ti OR diphenoxylate:ab,ti OR dipipanone:ab,ti OR dextropropoxyphene:ab,ti OR propoxyphene:ab,ti OR diamorphine:ab,ti OR dihydrocodeine:ab,ti OR alfentanil:ab,ti OR fentanyl:ab,ti OR remifentanil:ab,ti OR meptazinol:ab,ti OR methadone:ab,ti OR nalbuphine:ab,ti OR oxycodone:ab,ti OR papaveretum:ab,ti OR pentazocine:ab,ti OR meperidine:ab,ti OR pethidine:ab,ti OR phenazocine:ab,ti OR hydrocodone:ab,ti OR hydromorphone:ab,ti OR levorphanol:ab,ti OR oxymorphone:ab,ti OR butorphanol:ab,ti OR dezocine:ab,ti OR sufentanil:ab,ti OR ketobemidone:ab,ti OR 'corticosteroid'/exp OR '17 ketosteroid':ab,ti OR androstenedione:ab,ti OR androsterone:ab,ti OR 'estrone sulfate':ab,ti OR etiocholanolone:ab,ti OR prasterone:ab,ti OR dehydroepiandrosterone:ab,ti OR hydroxycorticosteroid*:ab,ti OR '11 hydroxycorticosteroid':ab,ti OR '17 hydrocorticosteroid':ab,ti OR deoxycorticosterone:ab,ti OR pregnenolone:ab,ti OR corticosteroid*:ab,ti OR prednisolone:ab,ti OR methylprednisolone:ab,ti OR efcortisol:ab,ti OR hydrocortone:ab,ti OR 'solu cortef':ab,ti OR budesonide:ab,ti OR entocort*:ab,ti OR budenofalk:ab,ti OR equilein:ab,ti OR '18 hydroxycorticosterone':ab,ti OR aldosterone:ab,ti OR corticosterone:ab,ti OR hydrocortisone:ab,ti OR tetrahydrocortisol:ab,ti OR cortison:ab,ti OR cortodoxone:ab,ti OR 'benzodiazepine derivative'/exp OR benzodiazepine*:ab,ti OR adinazolam:ab,ti OR alprazolam:ab,ti OR bentazepam:ab,ti OR bromazepam:ab,ti OR brotizolam:ab,ti OR chlordiazepoxide:ab,ti OR cinolazepam:ab,ti OR clobazam:ab,ti OR clonazepam:ab,ti OR clorazepate:ab,ti OR clotiazepam:ab,ti OR cloxazolam:ab,ti OR delorazepam:ab,ti OR demoxepam:ab,ti OR desmethyldiazepam:ab,ti OR diazepam:ab,ti OR estazolam:ab,ti OR etizolam:ab,ti OR etozolam:ab,ti OR fludiazepam:ab,ti OR flunitrazepam:ab,ti OR flurazepam:ab,ti OR flutoprazepam:ab,ti OR halazepam:ab,ti OR haloxazolam:ab,ti OR ketazolam:ab,ti OR loprazolam:ab,ti OR lorazepam:ab,ti OR lormetazepam:ab,ti OR medazepam:ab,ti OR metaciazepam:ab,ti OR mexazolam:ab,ti OR midazolam:ab,ti OR nimetazepam:ab,ti OR nitrazepam:ab,ti OR nordazepam:ab,ti OR oxazepam:ab,ti OR oxazolam:ab,ti OR pinazepam:ab,ti OR prazepam:ab,ti OR quazepam:ab,ti OR temazepam:ab,ti OR tetrazepam:ab,ti OR tofisopam:ab,ti OR triazolam:ab,ti	1204905
#8	#5 AND #6 AND #7	10682
#9	#8 AND ([cochrane review]/lim OR [systematic review]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND ([dutch]/lim OR [english]/lim) AND [2000-2015]/py	978

## cochrane library (via wiley)

---

- #1 MeSH descriptor: [Neoplasms] 1 tree(s) exploded
- #2 MeSH descriptor: [Neoplasm Staging] this term only
- #3 MeSH descriptor: [Neoplasm Metastasis] 1 tree(s) exploded
- #4 MeSH descriptor: [Neoplastic Processes] 1 tree(s) exploded
- #5 (cancer\* or tumor\* or tumour\* or carcinoma\* or neoplasm\* or lymphoma or melanoma or metastas\* or metastatic or (non and small and cell) or adenocarcinoma\* or (squamous and cell) or nslc or osteosarcoma\* or phyllodes or cystosarcoma\* or fibroadenoma\* or plasmacytoma\* or myeloma\* or lymphoblastoma\* or lymphocytoma\* or sarcoma\* or hodgkin\* or nonhodgkin\*):ti,ab
- #6 #1 or #2 or #3 or #4 or #5
- #7 MeSH descriptor: [Lung Diseases, Obstructive] 1 tree(s) exploded
- #8 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] 1 tree(s) exploded
- #9 emphysema\*:ti,ab
- #10 (chronic\* and bronchiti\*):ti,ab
- #11 (obstruct\* and (pulmonary or lung\* or airway\* or airflow\* or bronch\* or respirat\*)):ti,ab
- #12 (COPD or COAD or COBD or AECB):ti,ab
- #13 #7 or #8 or #9 or #10 or #11 or #12
- #14 MeSH descriptor: [Heart Failure] 1 tree(s) exploded
- #15 (heart and failure):ti,ab
- #16 (cardiac and failure):ti,ab
- #17 (myocardial and failure):ti,ab
- #18 (heart and decompensat\*):ti,ab
- #19 #14 or #15 or #16 or #17 or #18
- #20 #6 or #13 or #19
- #21 MeSH descriptor: [Dyspnea] 1 tree(s) exploded
- #22 (dyspnoe\* or dyspne\*):ti,ab
- #23 breathless\*:ti,ab
- #24 (breathing and (labored or laboured or difficult\*)):ti,ab
- #25 #21 or #22 or #23 or #24
- #26 #20 and #25
- #27 MeSH descriptor: [Analgesics, Opioid] 1 tree(s) exploded
- #28 (opiod\* or morphine or morfine or hydromorphine or buprenorphine or codeine or dextromoramide or diphenoxylate or dipipanone or dextropropoxyphene or propoxyphene or diamorphine or dihydrocodeine or alfentanil or fentanyl or remifentanil or meptazinol or methadone or nalbuphine or oxycodone or papaveretum or pentazocine or meperidine or pethidine or phenazocine or hydrocodone or hydromorphone or levorphanol or oxymorphone or butorphanol or dezocine or sufentanil or ketobemidone):ti,ab

#29 MeSH descriptor: [Adrenal Cortex Hormones] 1 tree(s) exploded

#30 (17-ketosteroid\* or androstenedione or androsterone or "estrone sulfate" or etiocholanolone or prasterone or dehydroepiandrosterone or hydroxycorticosteroid\* or "11 hydroxycorticosteroid\*" or 17-hydrocorticosteroid\* or deoxycorticosterone or deoxycorticosterone or pregnenolone or corticosteroid\* or hydrocortisone or budesonide or prednisolone or methylprednisolone or efcortisol or hydrocortone or "solu cortef" or budesonide or entocort\* or budenofalk or equilein or 18-hydroxycorticosterone or aldosterone or corticosterone or hydrocortisone or hydrocortisone or tetrahydrocortisol or tetrahydrocortisol or cortison or cortodoxone):ti,ab

#31 MeSH descriptor: [Benzodiazepines] 1 tree(s) exploded

#32 benzodiazepine\*:ti,ab

#33 (adinazolam or alprazolam or bentazepam or bromazepam or brotizolam or chlordiazepoxide or cinolazepam or clobazam or clonazepam or clorazepate or clotiazepam or cloxazolam or delorazepam or demoxepam or desmethyldiazepam or diazepam or estazolam or etizolam or etozolam or fludiazepam or flunitrazepam or flurazepam or flutoprazepam or halazepam or haloxazolam or ketazolam or loprazolam or lorazepam or lormetazepam or medazepam or metaclazepam or mexazolam or midazolam or nimetazepam or nitrazepam or nordazepam or oxazepam or oxazolam or pinazepam or prazepam or quazepam or temazepam or tetrazepam or tofisopam or triazolam):ti,ab

#34 #27 or #28 or #29 or #30 or #31 or #32 or #33

#35 #26 and #34

## Search strings Question 2

### 1.medline (ovid)

---

- 1 exp DYSPNEA/ (15903)
- 2 (dyspnoe\$ or dyspne\$).mp. (38234)
- 3 dyspnoeic.mp. (163)
- 4 breathless\$.mp. (3218)
- 5 (breathing adj3 labored).mp. (171)
- 6 (breathing adj3 laboured).mp. (38)
- 7 (breathing adj3 difficult\$).mp. (1356)
- 8 or/1-7 (41631)
- 9 Lung Diseases, Obstructive/ (17907)
- 10 exp Pulmonary Disease, Chronic Obstructive/ (37494)
- 11 emphysema\$.mp. (28155)
- 12 (chronic\$ adj3 bronchiti\$).mp. (10089)
- 13 (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp. (81301)
- 14 COPD.mp. (24637)
- 15 COAD.mp. (186)
- 16 COBD.mp. (11)
- 17 AECB.mp. (206)
- 18 refractory dyspnoe\$.mp. (17)
- 19 chronic dyspne\$.mp. (114)

- 20 or/9-19 (112509)
- 21 exp Heart Failure/ (88948)
- 22 (heart adj2 failure\*).tw. (103634)
- 23 (cardiac adj2 failure\*).tw. (11766)
- 24 (myocardial adj2 failure\*).tw. (2352)
- 25 (heart adj2 decompensat\*).tw. (2187)
- 26 heart failure.tw. (103104)
- 27 cardiac failure.tw. (9709)
- 28 or/21-27 (141913)
- 29 exp Neoplasms/ (2637332)
- 30 Neoplasm Staging/ (126191)
- 31 cancer\$.ti,ab. (1045723)
- 32 tumor\$.ti,ab. (948677)
- 33 tumour\$.ti,ab. (199584)
- 34 carcinoma\$.ti,ab. (461921)
- 35 neoplasm\$.ti,ab. (95796)
- 36 lymphoma.ti,ab. (109894)
- 37 melanoma.ti,ab. (74861)
- 38 staging.ti,ab. (49776)
- 39 metastas\$.ti,ab. (218423)
- 40 metastatic.ti,ab. (139422)
- 41 exp Neoplasm Metastasis/ (159331)
- 42 exp neoplastic processes/ (342311)
- 43 neoplastic process\$.ti,ab. (2299)
- 44 non small cell.ti,ab. (31255)
- 45 adenocarcinoma\$.ti,ab. (94567)
- 46 squamous cell.ti,ab. (65677)
- 47 nsclc.ti,ab. (18365)
- 48 osteosarcoma\$.ti,ab. (14968)
- 49 phyllodes.ti,ab. (1281)
- 50 cystosarcoma\$.ti,ab. (551)
- 51 fibroadenoma\$.ti,ab. (2931)
- 52 (non adj small adj cell).ti,ab. (31255)

- 53 (non adj2 small adj2 cell).ti,ab. (31461)
- 54 (nonsmall adj2 cell).ti,ab. (1781)
- 55 plasmacytoma\$.ti,ab. (5220)
- 56 myeloma.ti,ab. (35983)
- 57 multiple myeloma.ti,ab. (23499)
- 58 lymphoblastoma\$.ti,ab. (277)
- 59 lymphocytoma\$.ti,ab. (288)
- 60 lymphosarcoma\$.ti,ab. (3842)
- 61 immunocytoma.ti,ab. (402)
- 62 sarcoma\$.ti,ab. (71693)
- 63 hodgkin\$.ti,ab. (51389)
- 64 (nonhodgkin\$ or non hodgkin\$).ti,ab. (29520)
- 65 or/29-64 (3039510)
- 66 20 or 28 or 65 (3269245)
- 80 exp Respiratory Therapy/ (90183)
- 81 breathing technique\$.mp. (331)
- 82 breathing exercise\$.mp. (3048)
- 83 acupuncture.mp. (18409)
- 84 acupressure.mp. (690)
- 85 exp Relaxation Techniques/ (7271)
- 86 relaxation.mp. (83285)
- 87 exp counseling/ (33693)
- 88 exp psychotherapy/ (152282)
- 89 non-pharmacological.mp. (3660)
- 90 walking/ (20626)
- 91 Dependent Ambulation/ (113)
- 92 Physical Therapy Modalities/is [Instrumentation] (1398)
- 93 Exercise Therapy/is [Instrumentation] (862)
- 94 mobility limitation/ (2488)
- 95 Vibration/tu [Therapeutic Use] (798)
- 96 exp Electric Stimulation Therapy/ (59977)
- 97 moist\$.mp. (18517)
- 98 Ventilators, Mechanical/ (7880)

- 99 Noninvasive Ventilation/ (395)
- 100 suction/ (10472)
- 101 airway clearance.mp. (449)
- 102 aspiration.mp. (58742)
- 103 handheld fan.mp. (5)
- 104 exp OXYGEN/ (148769)
- 105 exp OXYGEN INHALATION THERAPY/ (21638)
- 106 (oxygen\$ and (therap\$ or treat\$)).mp. (138210)
- 107 (therap\$ or treat\$).mp. (4984942)
- 108 104 and 107 (29180)
- 109 105 or 106 or 108 (144800)
- 110 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 109 (647351)
- 112 randomized controlled trial.pt. (384167)
- 113 controlled clinical trial.pt. (88541)
- 114 randomized.ab. (282620)
- 115 placebo.ab. (148584)
- 116 clinical trials as topic.sh. (170815)
- 117 randomly.ab. (200449)
- 118 trial.ti. (121742)
- 119 112 or 113 or 114 or 115 or 116 or 117 or 118 (879535)
- 120 exp animals/ not humans.sh. (3986356)
- 121 119 not 120 (806716)
- 122 meta-analysis.mp,pt. or review.pt. or search:.tw. (2086988)
- 123 121 or 122 (2769349)
- 126 8 and 66 and 110 and 123 (1053)
- 127 limit 126 to yr="2000 - 2014" (759)

## **PreMedline (OVID)**

---

- 2 (dyspnoe\$ or dyspne\$).mp. (2862)
- 3 dyspnoeic.mp. (19)
- 4 breathless\$.mp. (346)
- 5 (breathing adj3 labored).mp. (10)
- 6 (breathing adj3 laboured).mp. (2)
- 7 (breathing adj3 difficult\$).mp. (164)

- 8 or/2-7 (3324)
- 11 emphysema\$.mp. (1207)
- 12 (chronic\$ adj3 bronchiti\$).mp. (286)
- 13 (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp. (4512)
- 14 COPD.mp. (2784)
- 15 COAD.mp. (18)
- 16 COBD.mp. (0)
- 17 AECB.mp. (15)
- 18 refractory dyspnoe\$.mp. (1)
- 19 chronic dyspne\$.mp. (10)
- 20 or/11-19 (6321)
- 22 (heart adj2 failure\*).tw. (7945)
- 23 (cardiac adj2 failure\*).tw. (629)
- 24 (myocardial adj2 failure\*).tw. (127)
- 25 (heart adj2 decompensat\*).tw. (255)
- 26 heart failure.tw. (7912)
- 27 cardiac failure.tw. (461)
- 28 or/22-27 (8387)
- 31 cancer\$.ti,ab. (95188)
- 32 tumor\$.ti,ab. (68672)
- 33 tumour\$.ti,ab. (13175)
- 34 carcinoma\$.ti,ab. (30952)
- 35 neoplasm\$.ti,ab. (7085)
- 36 lymphoma.ti,ab. (6994)
- 37 melanoma.ti,ab. (4844)
- 38 staging.ti,ab. (4204)
- 39 metastas\$.ti,ab. (19080)
- 40 metastatic.ti,ab. (12427)
- 43 neoplastic process\$.ti,ab. (138)
- 44 non small cell.ti,ab. (3863)
- 45 adenocarcinoma\$.ti,ab. (7249)
- 46 squamous cell.ti,ab. (5471)
- 47 nscl.ti,ab. (2769)

- 48 osteosarcoma\$.ti,ab. (1145)
- 49 phyllodes.ti,ab. (124)
- 50 cystosarcoma\$.ti,ab. (18)
- 51 fibroadenoma\$.ti,ab. (203)
- 52 (non adj small adj cell).ti,ab. (3863)
- 53 (non adj2 small adj2 cell).ti,ab. (3873)
- 54 (nonsmall adj2 cell).ti,ab. (180)
- 55 plasmacytoma\$.ti,ab. (235)
- 56 myeloma.ti,ab. (2179)
- 57 multiple myeloma.ti,ab. (1792)
- 58 lymphoblastoma\$.ti,ab. (11)
- 59 lymphocytoma\$.ti,ab. (9)
- 60 lymphosarcoma\$.ti,ab. (92)
- 61 immunocytoma.ti,ab. (1)
- 62 sarcoma\$.ti,ab. (4893)
- 63 hodgkin\$.ti,ab. (2443)
- 64 (nonhodgkin\$ or non hodgkin\$).ti,ab. (1581)
- 65 or/31-64 (165521)
- 66 20 or 28 or 65 (178693)
- 81 breathing technique\$.mp. (38)
- 82 breathing exercise\$.mp. (72)
- 83 acupuncture.mp. (1637)
- 84 acupressure.mp. (119)
- 86 relaxation.mp. (14480)
- 89 non-pharmacological.mp. (635)
- 97 moist\$.mp. (4127)
- 101 airway clearance.mp. (55)
- 102 aspiration.mp. (4626)
- 103 handheld fan.mp. (0)
- 106 (oxygen\$ and (therap\$ or treat\$)).mp. (9716)
- 110 or/81-110 (35130)
- 112 randomized controlled trial.pt. (620)
- 113 controlled clinical trial.pt. (77)



- 114 randomized.ab. (26770)
- 115 placebo.ab. (9567)
- 117 randomly.ab. (23685)
- 118 trial.ti. (11269)
- 119 112 or 113 or 114 or 115 or 117 or 118 (56283)
- 122 meta-analysis.mp,pt. or review.pt. or search:.tw. (54584)
- 123 119 or 122 (105685)
- 126 8 and 66 and 110 and 123 (18)
- 127 limit 126 to yr="2000 - 2014" (18)

### EMBASE (via embase.com)

#1	'neoplasm'/exp	3522387
#2	cancer*:ab,ti OR tumor*:ab,ti OR tumour*:ab,ti OR carcinoma*:ab,ti OR neoplasm*:ab,ti OR lymphoma:ab,ti OR melanoma:ab,ti OR metastas*:ab,ti OR metastatic:ab,ti OR (non:ab,ti AND small:ab,ti AND cell:ab,ti) OR adenocarcinoma*:ab,ti OR (squamous:ab,ti AND cell:ab,ti) OR nscl:ab,ti OR osteosarcoma*:ab,ti OR phyllodes:ab,ti OR cystosarcoma*:ab,ti OR fibroadenoma*:ab,ti OR plasmacytoma*:ab,ti OR myeloma*:ab,ti OR lymphoblastoma*:ab,ti OR lymphocytoma*:ab,ti OR sarcoma*:ab,ti OR hodgkin*:ab,ti OR nonhodgkin*:ab,ti	3032421
#3	'chronic obstructive lung disease'/exp OR emphysema*:ab,ti OR (chronic* NEAR/3 bronchiti*):ab,ti OR (obstruct* NEAR/3 (pulmonary OR lung* OR airway* OR airflow* OR bronch* OR respirat*)):ab,ti OR copd:ab,ti OR coad:ab,ti OR cobd:ab,ti OR aecb:ab,ti	147701
#4	'heart failure'/exp OR (heart NEAR/2 failure*):ab,ti OR (myocardial NEAR/2 failure*):ab,ti OR (cardiac NEAR/2 failure*):ab,ti OR (heart NEAR/2 decompensat*):ab,ti	359212
#5	#1 OR #2 OR #3 OR #4	4479802
#6	'dyspnea'/de OR dyspnoe*:ab,ti OR dyspne*:ab,ti OR breathless*:ab,ti OR (breathing NEAR/3 labored):ab,ti OR (breathing NEAR/3 laboured):ab,ti OR (breathing NEAR/3 difficult*):ab,ti	112881
#7	#5 AND #6	56271
#8	'education'/exp	1067531
#9	'counseling'/exp	113370
#10	'breathing exercise'/exp	4954
#11	'relaxation training'/exp	8585
#12	'psychotherapy'/exp	195037
#13	('non pharmacological' NEAR/1 intervention*):ab,ti	1253
#14	'acupuncture'/exp	33716
#15	'walking aid'/exp	4604
#16	'vibration'/exp	52459
#17	'electrostimulation therapy'/exp	183353
#18	moist:ab,ti	5629
#19	'ventilator'/exp	17822
#20	'noninvasive ventilation'/exp	2527
#21	'oxygen'/exp	151508
#22	'suction'/exp	7543
#23	'aspiration'/exp	21000
#24	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	1764747
#25	#7 AND #24 AND ([cochrane review]/lim OR [systematic review]/lim OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND ([dutch]/lim OR [english]/lim) AND [2000-2015]/py	334

### cochrane library (via wiley)

- #1 MeSH descriptor: [Neoplasms] 1 tree(s) exploded
- #2 MeSH descriptor: [Neoplasm Staging] this term only
- #3 MeSH descriptor: [Neoplasm Metastasis] 1 tree(s) exploded

- #4 MeSH descriptor: [Neoplastic Processes] 1 tree(s) exploded
- #5 (cancer\* or tumor\* or tumour\* or carcinoma\* or neoplasm\* or lymphoma or melanoma or metastas\* or metastatic or (non and small and cell) or adenocarcinoma\* or (squamous and cell) or nslc or osteosarcoma\* or phyllodes or cystosarcoma\* or fibroadenoma\* or plasmacytoma\* or myeloma\* or lymphoblastoma\* or lymphocytoma\* or sarcoma\* or hodgkin\* or nonhodgkin\*):ti,ab
- #6 #1 or #2 or #3 or #4 or #5
- #7 MeSH descriptor: [Lung Diseases, Obstructive] 1 tree(s) exploded
- #8 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] 1 tree(s) exploded
- #9 emphysema\*:ti,ab
- #10 (chronic\* and bronchiti\*):ti,ab
- #11 (obstruct\* and (pulmonary or lung\* or airway\* or airflow\* or bronch\* or respirat\*)):ti,ab
- #12 (COPD or COAD or COBD or AECB):ti,ab
- #13 #7 or #8 or #9 or #10 or #11 or #12
- #14 MeSH descriptor: [Heart Failure] 1 tree(s) exploded
- #15 (heart and failure):ti,ab
- #16 (cardiac and failure):ti,ab
- #17 (myocardial and failure):ti,ab
- #18 (heart and decompensat\*):ti,ab
- #19 #14 or #15 or #16 or #17 or #18
- #20 #6 or #13 or #19
- #21 MeSH descriptor: [Dyspnea] 1 tree(s) exploded
- #22 (dyspnoe\* or dyspne\*):ti,ab
- #23 breathless\*:ti,ab
- #24 (breathing and (labored or laboured or difficult\*)):ti,ab
- #25 #21 or #22 or #23 or #24
- #26 #20 and #25
- #27 MeSH descriptor: [Respiratory Therapy] 1 tree(s) exploded
- #28 (breathing and (technique\* or exercise\*)):ti,ab
- #29 (acupuncture or acupressure):ti,ab
- #30 MeSH descriptor: [Relaxation Therapy] 1 tree(s) exploded
- #31 relaxation:ti,ab
- #32 MeSH descriptor: [Counseling] 1 tree(s) exploded
- #33 MeSH descriptor: [Psychotherapy] 1 tree(s) exploded
- #34 non-pharmacological:ti,ab
- #35 MeSH descriptor: [Walking] 1 tree(s) exploded

- #36 MeSH descriptor: [Dependent Ambulation] explode all trees
- #37 MeSH descriptor: [Physical Therapy Modalities] 1 tree(s) exploded and with qualifier(s): [Instrumentation - IS]
- #38 MeSH descriptor: [Exercise Therapy] 1 tree(s) exploded and with qualifier(s): [Instrumentation - IS]
- #39 MeSH descriptor: [Mobility Limitation] 1 tree(s) exploded
- #40 MeSH descriptor: [Vibration] 1 tree(s) exploded and with qualifier(s): [Therapeutic use - TU]
- #41 MeSH descriptor: [Electric Stimulation Therapy] 1 tree(s) exploded
- #42 moist\*:ti,ab
- #43 MeSH descriptor: [Ventilators, Mechanical] explode all trees
- #44 MeSH descriptor: [Noninvasive Ventilation] 1 tree(s) exploded
- #45 MeSH descriptor: [Suction] explode all trees
- #46 (airway and clearance):ti,ab
- #47 aspiration:ti,ab
- #48 (handheld and fan):ti,ab
- #49 MeSH descriptor: [Oxygen] 1 tree(s) exploded
- #50 MeSH descriptor: [Oxygen Inhalation Therapy] explode all trees
- #51 #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50
- #52 #26 and #51
- #53 #20 and #51

## *2.Consensus based*

Consensus based teksten zijn gebaseerd op evidence. Deze evidence is door de werkgroepleden zelf verzameld en verwerkt. Voor consensus based richtlijnteksten is er geen systematisch literatuuronderzoek uitgevoerd en worden de artikelen niet methodologisch beoordeeld. Er wordt geen level of evidence toegekend aan de studies en er wordt geen niveau van bewijs toegekend aan de conclusies. In de formulering van de conclusies wordt wel rekening gehouden met de onderliggende evidence.