

ADAPTED FOR FUROPEAN NURSES BY FONS

Dyspnea

Improving symptom management in cancer care through evidence based practice









Welcome to the Euro PEPs

The European Oncology Nursing Society is pleased to present its first set of "Putting Evidence into Practice" guidelines to improve the care of cancer patients in Europe.

Improvement in patient care is an ongoing process. There is a gap between the evidence that is available and what is actually implemented. This knowledge gap impacts on patient's in poor or inappropriate care that is detrimental to cancer patients. Results from research studies reveal that nurses insufficiently put evidence into practice. The results indicate that there are multiple reasons for why nurses do not use the latest evidence. Firstly, that research is difficult to understand, overwhelming in the amount published and secondly that they feel they don't have the expertise to interpret the quality of the evidence. If we could put even a little of what we know about symptom management into practice we would improve patient experience.

This Euro PEP has been developed as a partnership with the Oncology Nursing Society and funded by the European Commission as part of the European Action Against Cancer. Many people have contributed to the development and expert review of these documents, both in Europe and in the USA. EONS thanks their dedication and great efforts.

This documentation provides you with a concise summary of the evidence, a synthesis of patient assessments, a summary of evidence based interventions, and expert opinions to help guide you in the interpretation of European standards along with the references and source material. You may wish to adapt the guidance for your own work setting, but the PEPs gives you the confidence that these topics were reviewed in 2012 through a rigorous process by some of the leading experts and practitioners in the field.

On behalf of the review team we are confident that this information, coupled with your efforts and commitment to improve your practice, will help you achieve better, patient-centered outcomes based on scientific evidence.

We wish you great success!

Sara Faithfull Chair EPAAC Project

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Putting Evidence into Practice (PEP) resources (evidence syntheses and weight of evidence categorization) are the work of the Oncology Nursing Society (ONS). Because translations from English may not always be accurate or precise, ONS disclaims any responsibility for inaccuracies in words or meaning that may occur as a result of the translation.

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Introduction to the Sections



Quick view

The quick view provides very brief summary from the ONS PEP resources. A full copy of this is provided in the course documentation. ONS PEP information for this topic and description of the categories of evidence can be accessed at http://www.ons.org.



Expert opinion

Expert Opinion: low-risk interventions that are (1) consistent with sound clinical practice, (2) suggested by an expert in a peer-reviewed publication (journal or book chapter), and (3) for which limited evidence exists. An expert is an individual with peer-reviewed journal publications in the domain of interest.



Assessment tools

In general, no single tool measures all of the elements of a symptom. The choice of tool depends on the purpose of the assessment as well as the level of clinician and patient burden.

Most symptoms are a subjective experience, thus self-report is the most reliable assessment method.



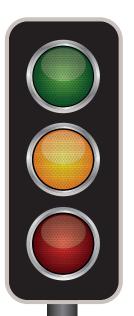
Definitions

Within the documentation various terms may need further explanation which through better understanding, could improve the outcomes of chosen interventions. The following definitions are tailored to the content of the respective PEP document.

How to use this guide

- Review the Euro PEP resources and consider the applicability in your own practice and your patient situation.
- Do a thorough patient assessment of the relevant clinical problem(s). Examples of measurement tools are provided by the evidence-based measurement summaries, located on the individual PEP topic pages.
- Identify interventions with the highest category of evidence and integrate them into the plan of care. Consider the patient's preferences, lifestyle, and the cost and availability of the interventions.
- Evaluate and document the patient's response to the interventions.
 If indicated, consider implementing other interventions supported by a high level of evidence.
- Educate patients that their care is based on the best available evidence.
- The Weight of Evidence Table (traffic light) provides information about how the evidence was weighed.

Adapted for Euro PEP Resources from www.ons.org/Research/PEP



Green = Go!

The evidence supports the consideration of these interventions in practice.

Yellow = Caution!

There is not sufficient evidence to say whether these interventions are effective or not.

Red = Stop!

The evidence indicates that these interventions are either ineffective or may cause harm.

Recommended for practice

Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, metaanalysis, or systematic reviews, and for which expectation of harm is small compared to the benefits.

Likely to be Effective

Interventions for which effectiveness has been demonstrated from a single rigorously conducted controlled trial, consistent supportive evidence form well -designed controlled trials using small samples, or guidelines developed from evidence and supported by expert opinion.

Benefits Balanced with Harm

Interventions for which clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.

Effectiveness Not Established

Interventions for which insufficient or conflicting data or data of inadequate quality currently exist, with no clear indication of harm.

Effectiveness Unlikely

Interventions for which lack of effectiveness has been demonstrated by negative evidence from a single rigorously conducted controlled trial, consistent negative evidence from well-designed controlled trials using small samples, or guidelines developed from evidence and supported by expert opinion.

Not Recommended for Practice

Interventions for which lack of effectiveness or harmfulness has been demonstrated by strong evidence from rigorously conducted studies, meta-analyses, or systematic reviews, or interventions where the costs, burden, or harm associated with the intervention exceed anticipated benefit.

Dyspnea Quick View

Definition and Incidence:

Dyspnea is breathing discomfort of various intensities. Although subjective, the experience features distinct sensations with multiple physiologic, psycological, social and environmental etiologies that in turn can cause secondary physiologic and behavioral responses. At cancer diagnosis, dyspnea is estimated to occur in 15-55 % of patients, and up to 18-79% during the last week of life.



Recommended for practice

• Immediate-release opioids (oral and parenteral)

Likely to be Effective

There are no interventions as of May 2012.

Benefits Balanced with Harm

There are no interventions as of May 2012.

Effectiveness Not Established

- Nebulized opiods
- Extended release morphine
- Nebulized Lignocaine (Lidocaine)
- Nebulized Furosemide
- Anxyiolytics
- Transmucosal fentanyl
- Fan
- Acupuncture
- Psychoeducation
- Non pharmacologic interventions: (PEP EFFECTIVENESS NOT ESTABLISHED)

Effectiveness Unlikely

 Palliative oxygen (in patients not hypoxic or otherwise do not meet criteria for oxygen use)

Not Recommended for Practice

There are no interventions as of May 2012.

Expert Opinion

Low-risk interventions that are:

- consistent with sound clinical practice
- suggested by an expert in a peer-reviewed publication (journal or book chapter) and
- for which limited evidence exists.

An expert is an individual who has authored articles published in a peer-reviewed journal in the domain of interest.

Although limited evidence exists, the following supportive interventions in patient experiencing cancer-related* dyspnea have been suggested.

Depending on the grade of dyspnea (NYHA I-IV)

Grade I-II

- Educate patients to recognize physical activities that precipitate dyspnea.
- Educate patients about breathing exercise such as diaphragmatic breathing, altering breathing rhythm and pursed lip breathing.
 Early consulting with physiotherapy etc.



Grade III

- Consider the use of assistive devices, such as wheelchair to decrease physical activities that precipitate dyspnea.
- Reorganisation of living areas e.g sitting possibilities e.g. in the bath/shower, utensils at reach in the kitchen etc.
- Adapting clothes for ease of dressing e.g. Velcro shoe bands.
- Use upright positioning that affords patient optimal lung capacity, especially with a coexisting diagnosis of chronic obstructive pulmonary disease.
- Employ interventions such as cognitive behavioural techniques to decrease the anticipatory component associated with dyspnea. (Dudgeon 2002)

Grade IV

For the dying patient experiencing dyspnea, consider the previous measures and possibly include:

- Reduce excessive secretions with scopolamine, or atropine.
- Implement oxygen therapy, if subjective report of relief.
- Implement mouth care to reduce dryness as often as comfortable
- Reduce length of conversation time.
- Discontinue fluid support, consider low-dose diuretics if fluid overload may be contributing factor.
- Institute sedation as needed.

^{*} Some suggestions have been based on interventions used for patients with non-cancer related dyspnea, but originate from peer-reviewed publications.

Assessment Tools

No single tool measures all of the dimensions of dyspnea. The choice of tool depends on the purpose of the assessment as well as the level of patient burden.

Numeric Rating Scale for Dyspnea

On a scale from 0 to 10, indicate how much shortness of breath you have had in the past week where 0 = no shortness of breath and 10 = shortness of breath as the worst possible. Circle the number.

0 1 2 3 4 5 6 7 8 9 10

No shortness of breath Worst possible

Note. From "Dyspnea" (p. 671), by A. Gift and A. Hoffman in M.E. Langhorne, J.S. Fulton, and S.E. Otto (Eds.), Oncology Nursing (5th ed.), 2007, St. Louis, MO: Elsevier Mosby. Copyright 2007 by Elsevier Mosby. Reprinted with permission.



Classification of Dyspnea according to the New York Heart Association

NYHA Class	Symptoms
I	No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
II limitation	Mild symptoms (mild shortness of breath and/or angina) and slight during ordinary activity.
III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m). Comfortable only at rest.
IV	Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

Dyspnea Definition List

Acupuncture

A method of producing analgesia or altering the function of a body system by inserting fine, wirethin needles (about the diameter of a strand of hair) into acupoints along a specific meridian on the body. The insertion of the needles may cause momentary discomfort. The needles are twirled or energized electronically or are warmed and left in place for approximately 20–30 minutes. (Tipton, McDaniel, Barbour, Johnson, LeRoy, Kayne, et.al,2005)

Dihydrocodeine

Also called DHC, is a synthetic opioid analgesic used for postoperative (moderate to moderately severe) pain, cough, and severe dyspnea. In the United States, it is available only as a combination pill with acetaminophen and caffeine. (Wikipedia, 2007)

Diamorphine

A semisynthetic opioid also known as heroin. It is available by prescription as diamorphine in the United Kingdom; it is illegal in the United States. (Wikipedia, 2007)

Dyspnea

"Dyspnea is a term used to characterize a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social and environmental factors, and may induce secondary physiological and behavioral responses." (p. 322 American Thoracic Society, 1999)

Heliox 28

A gas mixture that has a low density and the potential for reducing the work of breathing and improving alveolar ventilation when replacing nitrogen in air. It is 72% helium and 28% oxygen. (Ahmedzai, Laude, Roberson, Troy & Vora, 2004)

Hospital Anxiety and Depression Scale

A self-screening questionnaire for depression and anxiety from the United Kingdom. The scale contains 14 questions, seven for anxiety and seven for depression. (Bredin, Corner, Krishnasamy, Plant, Bailey & A'Hern, 1996; Zigmond & Snaith, 1983)



Lignocaine

Lignocaine is the former British Approved Name for lidocaine, a common local anesthetic and antiarrhythmic drug. (Wikipedia, 2007)

Medical Air

A gas mixture of 78.9% nitrogen and 21.1% oxygen. (Ahmedzai, Laude, Roberson, Troy & Vora, 2004)

Modified Borg Scale

Vertical 0 to 10+ item scale with words describing degrees of perceived exertion anchored to numbers. (Borg, 1982)

Nebulized Therapy or Aerosol Therapy

An aerosol is a suspension of fine liquid or solid particles dispersed in a gas or solution. Aerosol medication is inhaled as a fine mist deposited on the respiratory tract as a form of topical pulmonary treatment". (p. 625 McKenry & Salerno, 1992)

Oxygen-Enriched Air

Gas mixture of 72% nitrogen and 28% oxygen. (Ahmedzai, Laude, Roberson, Troy & Vora, 2004)

Oxygen Saturation

Measure of the degree to which oxygen is bound to hemoglobin, usually measured by a pulse oximeter, given as a percentage calculated by dividing the maximum oxygen capacity into the actual oxygen content and multiplying by 100. (McKenry & Salerno, 1992)

Visual Analog Scale (VAS)

Visual Analog Scale (VAS): 1100 mm line (either vertical or horizontal) with anchors at either end to indicate extremes of the sensation. Measuring the distance from the bottom of an original, noncopied scale (or left if it is horizontal) to the level indicated by the subject is the VAS score. Duplicating or copying a scale may alter the 100 mm length, so it is important to be precise with construction of the VAS line. (Gift, 1986)

World Health Organization Performance Status Scale

A scale of 0-4 that rates performance status, with 0 being normal activity and 4 being completely disabled. (Bredin, Corner, Krishnasamy, Plant, Bailey & A'Hern, 1996)

References

Ahmedzai, S.H., Laude, E., Robertson, A., Troy, G., & Vora, V. (2004). A double blind, randomized, controlled phase II trial of heliox28 gas mixture in lung cancer patients with dyspnoea on exertion. British Journal of Cancer, 90(2), 366–371.

Allard, P., Lamontagne, C., Bernard, P., & Tremblay, C. (1999). How effective are supplementary doses of opioids for dyspnea in terminally ill cancer patients? A randomized continuous sequential clinical trial. Journal of Pain and Symptom Management, 17(4), 256–265.

Bausewein, C., Booth, S., Gysels, M., & Higginson, I. (2008). Nonpharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. Cochrane Database of Systematic Reviews (Online), (2)(2), CD005623.doi:10.1002/14651858.CD005623.pub2.

Ben-Aharon, I., Gafter-Gvili, A., Paul, M., Leibovici, L., & Stemmer, S. M. (2008). Interventions for alleviating cancer-related dyspnea: a systematic review. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, 26(14), 2396-2404. doi:10.1200/JCO.2007.15.5796.

Benitez-Rosario, M.A., Martin, A.S., & Feria, M. (2005). Oral transmucosal fentanyl citrate in the management of dyspnea crises in cancer patients. Journal of Pain and Symptom Management, 30(5), 395–397.

Booth, S., Kelly, M.J., Cox, N.P., Adams, L., & Guz, A. (1996). Does oxygen help dyspnea in patients with cancer? American Journal of Respiratory and Critical Care Medicine, 153(5), 1515–1518.

Booth, S., Moosavi, S. H., & Higginson, I. J. (2008). The etiology and management of intractable breathlessness in patients with advanced cancer: a systematic review of pharmacological therapy. Nature Clinical Practice. Oncology, 5(2), 90-100. doi:10.1038/ncponc1034.

Bredin, M., Corner, J., Krishnasamy, M., Plant, H., Bailey, C., & A'Hern, R. (1999). Multicentre randomised controlled trial of nursing intervention for breathlessness in patients with lung cancer. BMJ, 318(7188), 901–904.

Boyd, K.J., & Kelly, M. (1997). Oral morphine as symptomatic treatment of dyspnoea in patients with advanced cancer. Palliative Medicine, 11(4), 277–281.

Bruera, E., de Stoutz, N., Velasco-Leiva, A., Schoeller, T., & Hanson, J. (1993). Effects of oxygen on dyspnoea in hypoxaemic terminal-cancer patients. Lancet, 342(8862), 13–14.

Bruera, E., Sweeney, C., Willey, J., Palmer, J.L., Strasser, F., Morice, R.C., et al. (2003). Randomized controlled trial of

supplemental oxygen versus air in cancer patients with dyspnea. Palliative Medicine, 17(8), 659–663.

Bruera, E., Sala, R., Spruyt, O., Palmer, J.L., Zhang, T., & Willey, J. (2005). Nebulized versus subcutaneous morphine for patients with cancer dyspnea: A preliminary study. Journal of Pain and Symptom Management, 29(6), 613–618.

Bruera, E., Macmillan, K., Pither, J., & MacDonald, R.N. (1990). Effects of morphine on the dyspnea of terminal cancer patients. Journal of Pain and Symptom Management, 5(6), 341–344.

Charles, M.A., Reymond, L., & Israel, F. (2008). Relief of incident dyspnea in palliative cancer patients: A pilot, randomized, controlled trial comparing nebulized hydromorphone, systemic hydromorphone, and nebulized saline. Journal of Pain and Symptom Management, 36(1), 29–38.

Charles, M. A., Reymond, L., & Israel, F. (2008). Relief of incident dyspnea in palliative cancer patients: a pilot, randomized, controlled trial comparing nebulized hydromorphone, systemic hydromorphone, and nebulized saline. Journal of Pain and Symptom Management, 36(1), 29-38. doi:10.1016/j.jpainsymman.2007.08.016.

Clemens, K.E., & Klaschik, E. (2007). Symptomatic therapy of dyspnea with strong opioids and its effect on ventilation in palliative care patients. Journal of Pain and Symptom Management, 33(4), 473–481.

Clemens, K. E., & Klaschik, E. (2008). Effect of hydromorphone on ventilation in palliative care patients with dyspnea. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer, 16(1), 93-99. doi:10.1007/s00520-007-0310-3.

Clemens, K. E., Quednau, I., & Klaschik, E. (2009). Use of oxygen and opioids in the palliation of dyspnoea in hypoxic and non-hypoxic palliative care patients: a prospective study. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer, 17(4), 367-377. doi:10.1007/s00520-008-0479-0.

Connors, S., Graham, S., & Peel, T. (2007). An evaluation of a physiotherapy led non-pharmacological breathlessness programme for patients with intrathoracic malignancy. Palliative Medicine, 21(4), 285–287.

Corner, J., Plant, H., A'Hern, R., & Bailey, C. (1996). Non-pharmacological intervention for breathlessness in lung cancer. Palliative Medicine, 10(4), 299–305.



Coyne, P.J., Viswanathan, R., & Smith, T.J. (2002). Nebulized fentanyl citrate improves patients' perception of breathing, respiratory rate, and oxygen saturation in dyspnea. Journal of Pain and Symptom Management, 23(2), 157–160.

Cranston, J. M., Crockett, A., & Currow, D. (2008). Oxygen therapy for dyspnoea in adults. Cochrane Database of Systematic Reviews (Online), (3)(3), CD004769. doi:10.1002/14651858.CD004769.pub2.

Currow, D. C., Agar, M., Smith, J., & Abernethy, A. P. (2009). Does palliative home oxygen improve dyspnoea? A consecutive cohort study. Palliative Medicine, 23(4), 309-316. doi:10.1177/0269216309104058.

Filshie, J., Penn, K., Ashley, S., & Davis, C.L. (1996). Acupuncture for the relief of cancer-related breathlessness. Palliative Medicine, 10(2), 145–150.

Galbraith, S., Fagan, P., Perkins, P., Lynch, A., & Booth, S. (2010). Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial. Journal of Pain and Symptom Management, 39(5), 831-838. doi:10.1016/j.jpainsymman.2009.09.024.

Jennings, A.L., Davies, A.N., Higgins, J.P., Gibbs, J.S., & Broadley, K.E. (2002). A systematic review of the use of opioids in the management of dyspnoea. Thorax, 57(11), 939–944.

Kohara, H., Ueoka, H., Maeda, T., Takeyama, H., Saito, R., Shima, Y., et al. (2003). Effect of nebulized furosemide in terminally ill cancer patients with dyspnea. Journal of Pain and Symptom Management, 26(4), 962–967.

Mazzocato, C., Buclin, T., & Rapin, C.H. (1999). The effects of morphine on dyspnea and ventilatory function in elderly patients with advanced cancer: A randomized double-blind controlled trial. Annals of Oncology, 10(12), 1511–1514.

Navigante, A.H., Cerchietti, L.C., Castro, M.A., Lutteral, M.A., & Cabalar, M.E. (2006). Midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer. Journal of Pain and Symptom Management, 31(1), 38–47.

Navigante, A. H., Castro, M. A., & Cerchietti, L. C. (2010). Morphine versus midazolam as upfront therapy to control dyspnea perception in cancer patients while its underlying cause is sought or treated. Journal of Pain and Symptom Management, 39(5), 820-830. doi:10.1016/j.jpainsymman.2009.10.003.

Qaseem, A., Snow, V., Shekelle, P., Casey, D. E., Jr, Cross, J. T., Jr, Owens, D. K., Shekelle, P. (2008). Evidence-based interventions to improve the palliative care of pain, dyspnea, and

depression at the end of life: a clinical practice guideline from the American College of Physicians. Annals of Internal Medicine, 148(2), 141-146.

Quigley, C., Joel, S., Patel, N., Baksh, A., & Slevin, M. (2002). A phase I/II study of nebulized morphine-6-glucuronide in patients with cancer-related breathlessness. Journal of Pain and Symptom Management, 23(1), 7–9.

Rietjens, J. A., van Zuylen, L., van Veluw, H., van der Wijk, L., van der Heide, A., & van der Rijt, C. C. (2008). Palliative sedation in a specialized unit for acute palliative care in a cancer hospital: comparing patients dying with and without palliative sedation. Journal of Pain and Symptom Management, 36(3), 228-234. doi:10.1016/j.jpainsymman.2007.10.014.

Shimoyama, N., & Shimoyama, M. (2002). Nebulized furosemide as a novel treatment for dyspnea in terminal cancer patients. Journal of Pain and Symptom Management, 23(1), 73–76.

Simon, S. T., & Bausewein, C. (2009). Management of refractory breathlessness in patients with advanced cancer. Wiener Medizinische Wochenschrift (1946), 159(23-24), 591-598. doi:10.1007/s10354-009-0728-y.

Simon, S. T., Higginson, I. J., Booth, S., Harding, R., & Bausewein, C. (2010). Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults. Cochrane Database of Systematic Reviews (Online), (1)(1), CD007354. doi:10.1002/14651858.CD007354.pub2.

Tanaka, K., Shima, Y., Kakinuma, R., Kubota, K., Ohe, Y., Hojo, F., et al. (1999). Effect of nebulized morphine in cancer patients with dyspnea: A pilot study. Japanese Journal of Clinical Oncology, 29(12), 600–603.

Uronis, H. E., & Abernethy, A. P. (2008). Oxygen for relief of dyspnea: what is the evidence? Current Opinion in Supportive and Palliative Care, 2(2), 89-94. doi:10.1097/SPC.0b013e3282ff0f5d.

Uronis, H. E., Currow, D. C., McCrory, D. C., Samsa, G. P., & Abernethy, A. P. (2008). Oxygen for relief of dyspnoea in mildly- or non-hypoxaemic patients with cancer: a systematic review and meta-analysis. British Journal of Cancer, 98(2), 294-299. doi:10.1038/sj.bjc.6604161.

Vickers, A.J., Feinstein, M.B., Deng, G.E., & Cassileth, B.R. (2005, August 18). Acupuncture for dyspnea in advanced cancer: A randomized, placebo-controlled pilot trial [ISRCTN89462491]. BMC Palliative Care, 4, 5.

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Viola, R., Kiteley, C., Lloyd, N. S., Mackay, J. A., Wilson, J., Wong, R. K., & Supportive Care Guidelines Group of the Cancer Care Ontario Program in Evidence-Based Care. (2008). The management of dyspnea in cancer patients: a systematic review. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer, 16(4), 329-337. doi:10.1007/s00520-007-0389-6.

Wiese, C. H., Barrels, U. E., Graf, B. M., & Hanekop, G. G. (2009). Out-of-hospital opioid therapy of palliative care patients with "acute dyspnoea": a retrospective multicenter investigation. Journal of Opioid Management, 5(2), 115-122.

Wilcock, A., Corcoran, R., & Tattersfield, A.E. (1994). Safety and efficacy of nebulized lignocaine in patients with cancer and breathlessness. Palliative Medicine, 8(1), 35–38.

Wilcock, A., Walton, A., Manderson, C., Feathers, L., El Khoury, B., Lewis, M., Tattersfield, A. (2008). Randomised, placebo controlled trial of nebulised furosemide for breathlessness in patients with cancer. Thorax, 63(10), 872-875. doi:10.1136/thx.2007.091538.

Zeppetella, G. (1997). Nebulized morphine in the palliation of dyspnoea. Palliative Medicine, 11(4), 267–275.

Zhao, I., & Yates, P. (2008). Non-pharmacological interventions for breathlessness management in patients with lung cancer: a systematic review. Palliative Medicine, 22(6), 693-701. doi:10.1177/0269216308095024.

