

Managing breathlessness: a palliative care approach

Chloe Chin, Sara Booth

Department of Palliative Medicine, Addenbrookes Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Correspondence to

Dr Chloe Chin, Department of Palliative Medicine, Cambridge University Hospitals NHS Foundation Trust, Addenbrookes Hospital, Box 63, Elsworth House, Hills Road, Cambridge CB2 0QQ, UK; chloe.chin@addenbrookes.nhs.uk

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ABSTRACT

Breathlessness is an important and common symptom globally, affecting patients with a variety of malignant and non-malignant diseases. It causes considerable suffering to patients and also their families, and is a significant cost to healthcare systems. Optimal management of the symptom should therefore be of interest and importance to a wide range of clinicians. Best practice in the management of breathlessness consists of both non-pharmacological and pharmacological interventions as evidenced by recent randomised controlled trials of multidisciplinary breathlessness support services. As well as providing evidence for integration of early palliative care into respiratory services, these revealed that patient distress due to breathlessness can be significantly reduced and better outcomes can be achieved at lower cost than standard care.

many of these will be precipitated by breathlessness.⁵ One to four per cent of primary care encounters are also related to breathlessness.³ Although trajectories of breathlessness vary depending on the underlying aetiology, as disease advances, the prevalence and intensity of breathlessness increases with up to 78% of patients with lung cancer, 88% of those with congestive heart failure and 95% of patients with chronic obstructive pulmonary disease (COPD) experiencing breathlessness at the end of their lives.^{3–6} Prevalence also increases with age: a large Australian study reports breathlessness prevalence at 6.7% in those under 35 years, 9.8% in those aged 50–64 years and 16.9% in those aged above 65 years.⁷

This article summarises the available evidence on the aetiology and clinical management of breathlessness in advanced disease to help clinicians improve their care of this highly symptomatic group.

INTRODUCTION

Breathlessness, or dyspnoea, is an unpleasant sensation defined as “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity.”¹ These include work of breathing, chest tightness and air hunger or unsatisfied inspiration.¹ As well as varying in intensity, they also vary in their unpleasantness, emotional and behavioural significance.¹ Breathlessness arises from interactions between multiple physiological, psychological, social and environmental factors, and it is imperative to appreciate that the sensation of breathlessness is primarily derived from the brain and can only be perceived by the person experiencing it.²

An important and common symptom globally, breathlessness affects patients with a spectrum of malignant and non-malignant diseases and with varying trajectories. Some experience breathlessness for a short time as they approach the end of their life, others with chronic disease live with this troubling symptom for many years. Therefore, the ability to manage the symptom optimally should be of crucial importance to clinicians from a wide range of specialities.

RELEVANCE

Although prevalence is variably reported, up to 16.4% of people experience breathlessness at any one time.³ In the UK, it is a frequent cause of unplanned attendance at hospital, with up to 25% of accident and emergency admissions due to breathlessness, and similar figures are noted for the USA.^{3–4} Therefore, breathlessness is a significant burden on individuals and healthcare systems. Emergency admissions due to respiratory disease cost the UK approximately £834.6 million and

IMPACT OF BREATHLESSNESS

Breathlessness is a cause of considerable suffering: breathlessness is described as ‘very distressing’ by an estimated 60% of patients with lung cancer.³ The anxiety and distress in both those experiencing the symptom and their carers lead to poor quality of life and can cause crises leading to emergency admissions. Approximately 10 patients with breathlessness per single general practitioner are reported to have anxiety, leading to an 8.65% prevalence rate of breathlessness and anxiety.⁸ Results from the recent Living with Breathlessness study in patients with advanced COPD in the UK also corroborate this demonstrating Hospital Anxiety and Depression Scale scores that were higher than population norms.⁹ It has been reported that for each person with chronic disease and a comorbid mental health problem, their total healthcare costs raise by 45% and highlight the importance of effective management of this symptom.³

Increasingly, correlations with mortality are being recognised, with the presence of breathlessness being found to predict clinical course more effectively than other commonly measured parameters such as forced expiratory volume in one second, and in a variety of diseases such as COPD and heart failure.^{10–13} One study has shown that breathlessness severity correlates statistically significantly with 5-year survival rate for patients with COPD.¹⁰ Another large study in heart failure patients with breathlessness showed that greater severity of baseline breathlessness was associated with mortality and readmission.¹¹ The link with mortality indicates that optimal management of breathlessness is important for patient outcomes, as well as symptom control, and has led to calls for clinicians to consider measuring breathlessness routinely.¹⁴



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AETIOLOGY AND PATHOPHYSIOLOGY

A range of clinical conditions comprising respiratory, cardiovascular, psychological and systemic disorders contribute to breathlessness (table 1).

Understanding the central perception of breathlessness is pivotal to managing the symptom effectively. Sensory information from the respiratory system is relayed to the brainstem respiratory centres in the cerebral cortex, which produce the unpleasant sensations that accompany breathlessness (figure 1).¹⁵ Functional imaging has allowed identification of areas in the brain that are active in the sensation of breathlessness, including the insular cortex, anterior cingulate cortex and amygdala.¹⁶ These areas are thought to participate in awareness of homeostatic threats, generating emotional and behavioural responses, which explain the importance of psychological influences on breathlessness perception.¹⁷

ASSESSMENT

Good management of breathlessness requires thorough holistic assessment with a careful history and medical examination; identifying any reversible causes of breathlessness (such as infection, effusion, pulmonary embolism or anaemia) should be an initial priority before focusing on symptom relief.

Gaining an idea of the patient's rating of their symptom severity, levels of associated anxiety and distress, understanding of the reason for their breathlessness, their fears and its impact on their life is imperative. Although physical impairments exist and contribute to breathlessness, psychological aspects play a significant part in genesis of the symptom and this biopsychosocial context needs consideration when treating patients. Establishing the kind of breathlessness being experienced by the patient is also important. Breathlessness may be continuous, experienced all the time, at rest or with minimal exertion, or episodic. Episodic breathlessness is characterised by a severe worsening of breathlessness intensity or unpleasantness beyond

usual fluctuations in the patient's perception. Episodes may be both predictable and unpredictable, may be time-limited and may occur intermittently, with or without underlying continuous breathlessness.¹⁸

Traditionally, emphasis has been on searching for pathology in the lungs, heart or neuromuscular systems, and diagnostic testing occurs afterwards to identify the precise nature of the disorder. However, breathlessness itself must be directly measured, which is difficult given the wide patient variability in experience of the symptom. Clinicians have been shown to underestimate breathlessness and the multidimensional nature of breathlessness makes assessment of the various types of respiratory discomfort and development of robust assessment tools challenging.¹⁹ To date, several validated scales, questionnaires and physical tests assessing different components of breathlessness exist, all with advantages and disadvantages. However, it is becoming increasingly recognised that an assessment of the emotional component of breathlessness is imperative because it is influenced by psychological processes, and it is likely that affective states contribute to the perceived severity of breathlessness.^{1 20} The Multidimensional Dyspnoea Profile is an example of an instrument designed to measure both sensory and affective components of breathlessness and using this in clinical research could improve management of the symptom.^{21 22} An alternative questionnaire being used in clinical practice is the Dyspnoea-12, which also provides a global score of breathlessness severity applicable to a variety of diseases, and incorporates both physical and affective aspects.²³ These two tools contrast with others such as the often used modified Medical Research Council (MRC) breathlessness scale, which solely concentrates on measurement of functional limitation due to breathlessness, and should be considered as insufficient measures of the symptom when used in isolation.²⁴

MANAGEMENT

Two recently published randomised controlled trials (RCTs) have emphasised the importance of multidisciplinary breathlessness support services in the management of breathlessness.^{25 26} The first study showed that the interventions of a Breathlessness Intervention Service (BIS) significantly reduced distress due to breathlessness and increased confidence in managing breathlessness in patients with advanced cancer.²⁵ A BIS comprises of a multidisciplinary complex intervention underpinned by a palliative care approach and uses evidence-based non-pharmacological and pharmacological interventions to support patients with advanced disease. Patients also had better outcomes for breathlessness at lower cost than standard care.²⁵ The second RCT showed that a breathlessness support service improved breathlessness mastery in patients with a variety of advanced diseases and provided evidence to support the early integration of palliative care into respiratory services.²⁶

The 'Breathing, Thinking, Functioning' model used by the Cambridge BIS (CBIS) introduces three aspects of the vicious cycle of breathlessness: inefficient breathing, feelings of anxiety and distress and muscle deconditioning, which are interlinked and perpetuate each other if unhelpful emotions or behaviours develop.¹⁵ CBIS uses this model to target different components of the complex intervention (figure 2) and evidence for their effectiveness will be detailed below.

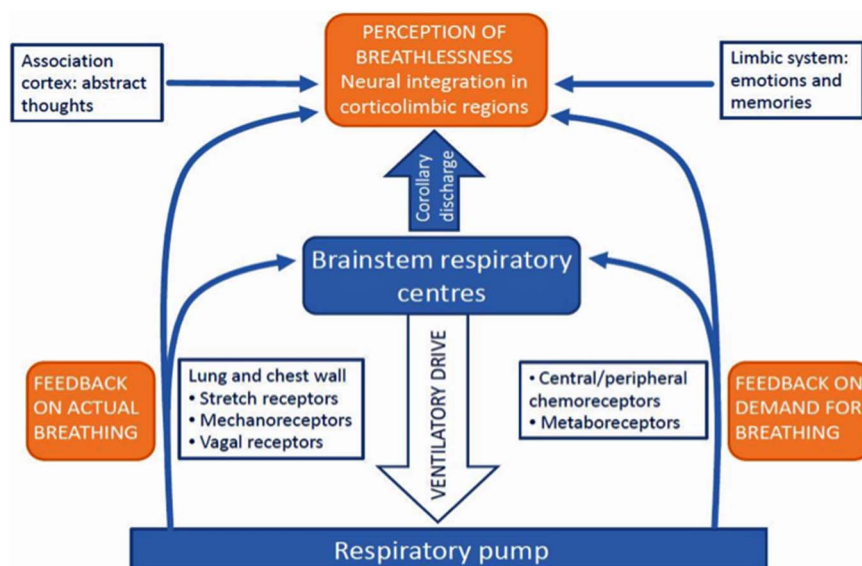
NON-PHARMACOLOGICAL

Various non-pharmacological management strategies exist that encourage exercise and aim to reverse muscle deconditioning, helping to maximise mechanical function of the chest wall and

Table 1 Causes of breathlessness

Respiratory	Pneumonia Collapse Pulmonary embolism Interstitial lung disease Obstructive airways disease Pleural effusion Malignancy ► Primary or secondary ► Lymphangitis carcinomatosa ► Mesothelioma
Cardiovascular	Congestive cardiac failure Arrhythmias Pericardial effusion Pulmonary hypertension
Musculoskeletal	Respiratory muscle weakness (eg, motor neurone disease) Diaphragmatic weakness Chest wall deformities (eg, kyphoscoliosis)
Pressure effects	Lymphadenopathy Superior vena cava obstruction Ascites
Systemic	Sepsis Anaemia Uraemia Cachexia Obesity Sarcoidosis
Psychological	Anxiety Depression

Figure 1 Pathophysiology of breathlessness.¹⁵



efficiency of skeletal muscles.¹⁵ They often form part of complex, non-pharmacological breathlessness interventions. A 2008 Cochrane review, currently being updated, of non-pharmacological interventions for breathlessness in advanced malignant and non-malignant disease demonstrated high strength evidence for neuro-electrical muscle stimulation and chest wall vibration; however, these can be impractical to implement.²⁷ Other important non-pharmacological strategies will be discussed in more detail below.

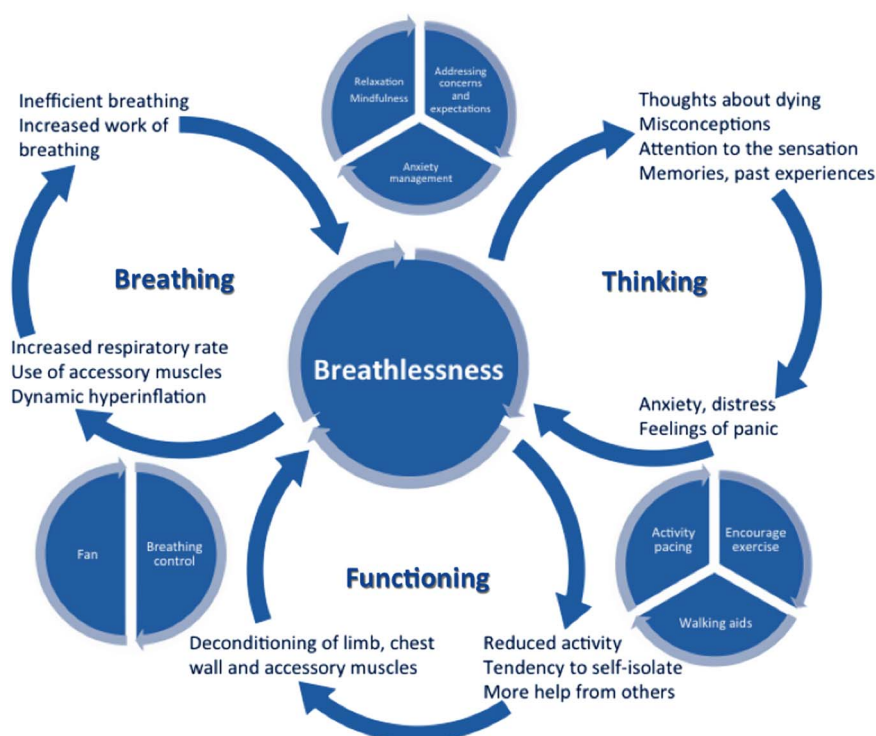
Fan

The handheld fan is a simple, cheap, portable piece of equipment that provides relief from the symptom whatever the aetiology. Its mechanism of action is possibly linked to the diving reflex, via stimulation of facial and nasopharyngeal receptors, which trigger events in the brain that allow animals to stay

under water without breathing for extended periods.²⁸ In this way, the perception of breathlessness is reduced and it provides some understanding as to why patients often describe the need to sit or stand by an open window to improve their symptoms. Evidence supporting the use of the fan included a randomised, crossover trial, which showed that the handheld fan blowing air across the nose and face reduced the sensation of breathlessness in patients compared with directing the airflow to their leg.²⁹ Additionally, the recently published mixed-methods RCT evaluating CBIS, of which the fan is an important component of, showed that the intervention as a whole was effective and cost-effective.²⁵

Evidence suggests that *how* the fan is provided to patients is also important—some patients received handheld fans from clinicians, but identified that the way CBIS delivered the intervention was different as they provided explanation as to how

Figure 2 The 'Breathing, Thinking, Functioning' model and non-pharmacological strategies for breathlessness. Adapted from Booth *et al.*¹⁵



and when to use the fan, and how it might work, legitimising what might appear to be an ineffective intervention.²³ Therefore, offering a fan should include a brief scientific explanation of the mechanisms thought to underlie its effectiveness, instruction and demonstration of its optimal use. The fan should be held 15–20 cm from the face, and airflow directed at the nose and mouth (trigeminal area). Patients usually notice an effect very quickly and should be advised to keep the fan close to hand. They should also be encouraged to use the fan to help them stay in control rather than waiting for a breathlessness attack to worsen.¹⁵

Cognitive-behavioural and self-management techniques

The relationship between breathlessness and anxiety is now well appreciated with functional neuroimaging of patients with breathlessness highlighting areas of the brain, such as the amygdala, involved in emotional processing.^{16 17} Strategies to break the cognitive-behavioural cycle of breathlessness and anxiety form part of complex non-pharmacological interventions for the symptom. A simple cognitive approach would include identifying triggers to patients' anxiety and learning how to overcome them, as well as helping patients to challenge unhelpful thoughts, relaxation exercises, mindfulness and distraction techniques are all useful. A RCT of 222 patients with COPD with examining the effectiveness of a cognitive-behavioural manual and self-management strategies versus information booklets showed a reduction in emergency department visits and hospital admissions at 12 months, and improved breathlessness, anxiety and depression at 6 months in the group allocated to receive the manual.³⁰ Manuals such as this may be useful as maintenance therapy for patients by empowering them to have mastery over the symptom.

A recently updated Cochrane review has also evaluated whether self-management interventions in COPD led to improved health outcomes and reduced health service usage. Improvement in breathlessness was an outcome examined in 3 of the 29 studies and, although graded as low quality evidence, individuals who participated in self-management were found to have reduced levels of breathlessness as measured by the modified MRC scale.³¹

Pulmonary rehabilitation

Another recently updated Cochrane review has evaluated pulmonary rehabilitation versus usual care on health-related quality of life measures, and functional and maximal exercise capacity in patients with COPD.³² Sixty-five RCTs involving 3822 participants were reviewed and showed that pulmonary rehabilitation improved breathlessness as measured by the Chronic Respiratory Questionnaire. The effect was statistically significant and larger than the minimal clinically important difference of 0.5 (0.79, 95% CI 0.47 to 0.95). Pulmonary rehabilitation, part of which consists of exercise and strength training of muscles in both upper and lower limbs, has a grade A evidence basis and is recommended by the joint British Thoracic Society and Association of Chartered Physiotherapists in Respiratory Care (BTS/ACPRC) guidelines for all patients with COPD.³³

Breathing techniques

A Cochrane review in 2012 examined whether breathing exercises, such as pursed-lip breathing, diaphragmatic breathing and yoga-based breathing techniques, which focussed on exhalation, had beneficial effects on breathlessness, exercise capacity and health-related quality of life in patients with COPD.³⁴ Sixteen studies with 1233 patients were included, but they were

Table 2 Joint BTS/ACPRC guidelines on breathing techniques

Breathing technique	Mechanism of action
1 Breathing control to encourage patients to bring back their breathing to an efficient pattern. (Also endorsed by NICE in lung cancer.)	Deters hyperventilation by encouraging appropriate tidal volume, promotes efficient use of breathing muscles, promotes even distribution of inhaled air by encouraging smooth laminar air flow.
2 Pursed-lip breathing during exertion	Increases expiratory airway pressure and maintaining airway patency, thus improving expiratory airflow and reducing dynamic hyperinflation.
3 Exhalation on effort ('blow as you go')	Focuses on out-breath and facilitates recovery breathing.
4 Relaxed, slow, deep breathing	Reduces respiratory rate and aids recovery, facilitates more effective ventilation, can be relaxing and calming.
5 Paced breathing	Maintains control and reduces dyspnoea during exertion.

BTS/ACPRC, British Thoracic Society and Association of Chartered Physiotherapists in Respiratory Care; NICE, National Institute for Health and Care Excellence.

generally of low quality and the effects on breathlessness and quality of life were inconsistent across trials, which suggests that further high-quality, adequately sized trials are needed in this area. Functional exercise capacity did improve with breathing exercises over 4–15 weeks compared with no intervention and outcomes were similar across all the techniques examined.

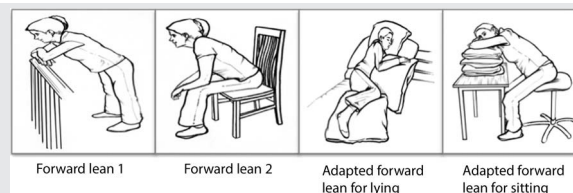
The strategies suggested to alleviate breathlessness in patients with COPD by the joint BTS/ACPRC guidelines are outlined in table 2.³³

Breathing techniques require regular practice to be effective when the patient is breathless and it is important to ensure that patients and their carers understand this.

Positioning and energy conservation

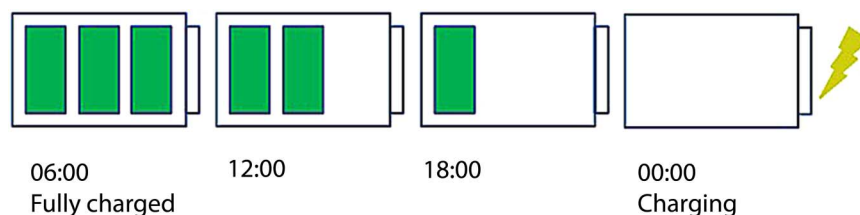
Specific positions are taught in conjunction with breathing exercises and use of the handheld fan. However, often they are instinctively taken up by patients with breathlessness. Box 1 shows the joint BTS/ACPRC guidance for relieving breathlessness.

Box 1 Joint British Thoracic Society and Association of Chartered Physiotherapists in Respiratory Care (BTS/ACPRC) guidance on positioning to relieve breathlessness^{33 35}



- ▶ Passive fixation of the shoulder girdle by bracing the upper limbs, for example, placing hands on hips, to assist ventilatory muscle efficiency.
- ▶ Forward lean sitting which domes the diaphragm leading to improved force generation and ventilator capacity.
- ▶ Adaptation of forward lean for standing or lying if sitting is not possible.

Figure 3 Activity pacing and energy conservation.³⁵ Patients should ensure that all available energy is not being expended unnecessarily on basic every day tasks, or on trying to complete tasks too quickly, leaving no energy to engage in other activities or exercise.³⁵ Using an analogy such as a jug or battery full of energy for each day, which needs to be replenished by rest, can help patients think about how they want to expend their limited amount of energy.



Forward lean and upper limb bracing can be combined effectively. The guidelines also suggest assessing the patient for walking aids such as a rollator frame, and teaching energy conservation techniques to reduce breathlessness during activities of daily living.³³ Energy conservation (figure 3) aims to use the body in the most efficient way possible and involves adapting activities, activity pacing and prioritisation of activities, which are important to the individual. Patients are encouraged to set realistic, achievable goals and plan ahead and it is a core component of effective self-management of breathlessness.³⁵

PHARMACOLOGICAL

Opioids

Opioids have the largest evidence base for the management of breathlessness of various aetiologies. A systematic review in 2002 showed that oral and parenteral opioids had a positive effect on the sensation of breathlessness and a subsequent RCT by Abernethy *et al*³⁶ in 2003 showed that sustained-release oral morphine at low dosage (20 mg) provided significant symptomatic improvement in refractory breathlessness.³⁷ Constipation was a notable side effect, and other patients withdrew from the study due to vomiting or sedation. However, these can be anticipated and managed. The concern of significant respiratory depression is unfounded, with a recently published systematic review finding no serious adverse effects in patients with advanced COPD given opioids for breathlessness.^{36–39} Additionally, a recent study of 2249 patients with COPD starting long-term oxygen therapy in Sweden confirmed that opioids at low dose (<30 mg oral morphine equivalents per day) were not associated with increased admissions or deaths and would be safe for symptom reduction in severe respiratory disease.⁴⁰

Optimal dosing regimens for opioids are still being researched. A phase II dose increment study of 83 patients with a variety of clinical conditions in 2011 found that 10 mg of sustained-release oral morphine a day was a safe and effective dose for most people who responded, and benefit was maintained for one in three people at 3 months.⁴¹ More than 90% of patients responded to 20 mg or less daily.⁴¹ CBIS prefers to use a slow up-titration regimen (figure 4) and aims to find the lowest effective opioid dose.³⁵ This approach develops the patient's confidence by minimising side effects and reassures other clinicians involved in the patient's care who may be less accustomed to prescribing opioids in this situation.

Benzodiazepines

Benzodiazepines are often prescribed for relief of breathlessness in advanced diseases, and in combination with opioids. However, a Cochrane review of their efficacy in relieving breathlessness in advanced disease identified just seven trials and did not show beneficial effect of benzodiazepines for relief of

breathlessness in patients with advanced cancer and COPD.⁴² Additionally, no significant effect could be observed in the prevention of breakthrough breathlessness in patients with cancer.⁴² A recent prospective study on the safety of benzodiazepines and opioids showed that use of benzodiazepines was not associated with increased admission, but there was a dose-response trend associated with mortality.⁴⁰ However, low-dose opioids (<30 mg oral morphine equivalent per day) concurrently with benzodiazepines were not associated with increased admissions or mortality.⁴⁰ Although this study could not ascribe causality, benzodiazepines should not be used as first-line treatment for breathlessness.

Oxygen

It has been clearly demonstrated that oxygen therapy improves survival in hypoxaemic patients with COPD and is needed for management of conditions such as interstitial lung disease.⁴³ However, oxygen is often used for the palliation of breathlessness even in people who are not hypoxaemic and evidence does not support its use in relief of breathlessness: neither a meta-analysis of people with cancer, nor a phase III double-blind RCT showed any improvement in breathlessness using oxygen

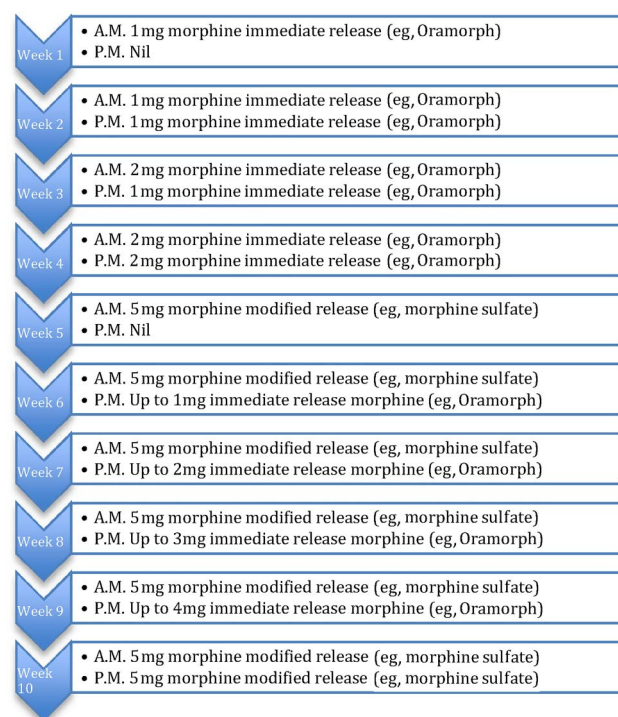


Figure 4 Opioid up-titration regimen.³⁵

Box 2 Patients with breathlessness in their last days of life³⁵

Involvement of specialist palliative care team (community/inpatient) and close liaison with primary care services to ensure best quality care.

Syringe pump containing:

- ▶ Diamorphine 5–10 mg/24 h (if opioid naïve). Consider 2.5 mg in elderly/frail.
- ▶ Midazolam 5–10 mg/24 h, rising to 30 mg if needed, for sedation.
- ▶ Haloperidol 3–10 mg/24 h, for nausea.
If levomepromazine needed for nausea, try once-daily subcutaneous injection 6.25–12.5 mg.

over air.^{44 45} A Cochrane review in 2011 did show that oxygen can relieve breathlessness in mildly and non-hypoxaemic patients with COPD, but significant heterogeneity between studies means firm evidence to support use of oxygen is still lacking.⁴⁶ Additionally, a more recent small study reaffirmed that there was no additional symptomatic benefit from routine oxygen in the last hours or days of life, but approximately 10% of patients did use oxygen to relieve distress from dyspnoea.⁴⁷ There may be a role for oxygen in certain subgroups of patients once other approaches have been optimised, and in these cases individual clinical assessment is warranted, but certainly routine use of oxygen for palliation of breathlessness is not indicated (box 2).

CURRENT GUIDELINES

The BTS has recently published updated guidance on home oxygen use in adults, in which palliative oxygen therapy (POT) relieves the sensation of refractory persistent breathlessness in advanced or life-limiting illness.⁴⁸

In light of the evidence statements (table 3), the BTS recommends that patients with cancer or end-stage cardiorespiratory disease who are experiencing intractable breathlessness should not receive POT, if they are non-hypoxaemic or have mild levels of hypoxaemia above current long term oxygen therapy thresholds ($\text{SpO}_2 \geq 92\%$) (grade A).⁴⁸ Patients should be assessed for a trial of opioids, and also for a trial of non-pharmacological treatments including fan therapy (grade A and D, respectively).⁴⁸ They suggest that it is good practice for POT to be considered, on an individual basis, by specialist teams for breathlessness unresponsive to all other modalities of treatment. Its effects on symptom reduction and improved quality of life should also be formally assessed.⁴⁸

Table 3 Evidence statements for palliative oxygen therapy⁴⁸

Evidence statements	Evidence level
Oxygenation measurements do <i>not</i> correlate well with subjective experience of breathlessness.	2+
Patients with hypoxaemia do <i>not</i> experience significant difference in symptoms between air and POT despite oxygen saturations improving with oxygen.	2+
Patients with no hypoxaemia or mild hypoxaemia who do not qualify for LTOT do <i>not</i> experience symptomatic benefit with POT versus air.	1+++
Opioids are significantly better than POT in reducing the intensity of dyspnoea.	1+

LTOT, long term oxygen therapy; POT, palliative oxygen therapy.

The joint BTS/ACPRC guidelines have already been mentioned, which provide advice regarding non-pharmacological strategies to manage breathlessness, particularly in patients with COPD, and National Institute for Health and Care Excellence (NICE) in England's lung cancer guidance suggests non-drug interventions based on psychosocial support, coping mechanisms and breathing control should be considered as palliative measures for breathlessness.^{33 49} Importantly, NICE recommend that the non-pharmacological interventions should be delivered by a multidisciplinary team, coordinated by a professional with an interest in breathlessness and expertise in the techniques, and that this support should be accessible by patients in all care settings, not necessarily just in specialist breathlessness clinics.⁴⁹

NHS Scotland and the Scottish Partnership for Palliative Care have published an accessible and concise guidance on breathlessness in palliative care.⁵⁰ Additionally, NICE Clinical Knowledge Summaries have evidence-based step-by-step guidance on management of breathlessness in palliative cancer care.⁵¹ There are also Breathlessness IMPRESS Tips for clinicians from the Primary Care Respiratory Society UK and BTS.⁵² Finally, there is of course, the American Thoracic Society statement, which provides an update on the mechanisms, assessment and management of breathlessness.¹

AREAS OF CONTROVERSY

A now withdrawn Cochrane review in 2012 did not find any evidence to support the use of nebulised opioids for palliation of breathlessness among the nine studies it examined.⁵³ However, a small study of patients with breathlessness secondary to mustard gas exposure did find benefit from once-daily nebulised morphine without significant adverse effects.⁵⁴ Another recently published systematic review showed some effect of nebulised opioids on breathlessness, but these effects were inconsistent and the evidences were of low quality.⁵⁸ Further investigation of this route of delivery of opioids continues and an updated Cochrane review on opioids for the palliation of breathlessness is expected this year.

FUTURE RESEARCH QUESTIONS

Many areas of breathlessness research are still to be fully understood and it lags behind other symptoms such as pain. However, at a meeting of the Breathlessness Research Interest Group in Cambridge, UK, considerable research activity elucidating the underlying mechanisms and experiences of the symptom, novel assessments and treatments and development of services to adequately meet the needs of patients with breathlessness and their carers was demonstrated.⁵⁵ Future research will address our understanding of the neurophysiological basis of breathlessness, and neuroimaging studies will pave the way forward with new imaging modalities and exploration of new areas of significance in the brain.⁵⁶

There is growing appreciation that symptoms do not exist in isolation, and breathlessness is often experienced in conjunction with cough and fatigue, forming a respiratory distress symptom cluster that can impact significantly on a patient's quality of life.⁵⁷ Symptom cluster exploration is a developing area of research with current studies examining whether complex interventions can have a positive impact on the entire cluster in certain diseases. Future research efforts will, like optimal management of the symptom, need to become more integrative and collaborative. Interdisciplinary programmes of research such as the Wellcome Trust-funded Life of Breath project, which combines a medical humanities approach with clinical research to

explore the phenomenology of breathing and breathlessness, are now emerging. Clearly, it will be exciting to see what the many future dimensions of breathlessness research hold.

Main messages

- ▶ Breathlessness is a cause of considerable suffering to patients, their families and a cost to healthcare systems for often futile medical strategies.
- ▶ Optimal management of breathlessness consists of both non-pharmacological and pharmacological interventions as evidenced by recent randomised controlled trials (RCTs) of multidisciplinary breathlessness support services.
- ▶ Low-dose opioids are safe to use to alleviate the sensation of breathlessness.

Current research questions

- ▶ Can new neuroimaging modalities elucidate more of the neurophysiological basis of breathlessness?
- ▶ Breathlessness is often experienced with other respiratory symptoms. Can complex interventions target these symptom clusters to impact positively on patients' quality of life?
- ▶ The RCT evaluation of Cambridge Breathlessness Intervention Service revealed that the way in which interventions are delivered is integral to their success. This may be related to the placebo or context effect. Can we understand this further in order to determine the skills breathlessness service practitioners need to develop, across all healthcare settings?

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Self assessment questions

Please answer true (T) or false (F) to the below statements.

1. Breathlessness is a sensation that arises from interactions between multiple physiological, psychological, social and environmental factors.
2. Benzodiazepines should be used as first-line pharmacological treatment for breathlessness.
3. A handheld fan should be provided to patients with explanation as to how and when to use it, and how it might work.
4. Respiratory depression is a common adverse event when using opioids to manage breathlessness.
5. The amygdala is one of the areas activated in the brain when a patient feels breathless and its role in awareness of homeostatic threats helps explain some of the emotional and behavioural responses patients with breathlessness exhibit.

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Competing interests None declared.

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Answers

1. (T); 2. (F); 3. (T); 4. (F); 5.(T)