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I. Dyspnoea mechanisms, assessment, prevalence and clinical importance

An Official Thoracic Society Statement: Update on the mechanism, assessment and management of dyspnea

Authors: Parshall MB et al
Comments: This consensus statement updates and advances the previous 1999 statement and provides a comprehensive overview of the current understanding of neurophysiological mechanisms underpinning the multidimensional sensation of dyspnoea, assessment options and recommendations for management. Dyspnoea is not a generic, single sensation of being “short of breath” but as explained in this statement, a perceptual experience akin to the experience of pain which can only be described by the person experiencing it (self-report of symptoms) rather than those observing signs of respiratory distress. Dyspnoea arises from a complex interaction of physiological, psychological, social, and environmental factors and as a multidimensional experience, is comprised of different sensory qualities (e.g. work/effort, tightness, air hunger) which may occur together but can vary in their perceived unpleasantness and emotional and behavioural consequences. Key points raised in this statement include the recognition that different sensory qualities are underpinned by discrete physiological mechanisms, that central processing of dyspnoea involves similar cortico-limbic structures as those required for processing of pain, that dyspnoea should be assessed with explicit reporting of which domains are assessed (what the breathless sensations feel like to the patient (sensory–perceptual experience), how distressing the sensation feels (affective distress) or how the breathless sensation impacts or affects the individual (e.g. functional ability, quality of life –see Table E1 in supplementary online material) and provides a broad range of future research recommendations.

Prevalence of dyspnoea differs between countries

Authors: Grønseth R et al
URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4143752/pdf/emss-59950.pdf
Comments: Using cross sectional survey data from general population based samples (at least 300 men and 300 women aged ≥ 40 years), across 15 countries, amongst other measures, 9,484 participants completed the modified Medical Research Council scale (mMRC) for breathlessness (impact of breathlessness on functional performance / activity). In this cohort, approximately 25% were obese, 45% were never smokers and a diagnosis of asthma (11%) or COPD, chronic bronchitis/emphysema (1-2%) was reported by the minority of participants. Across the cohort, 27% reported dyspnoea (inclusive of mMRC grades 1 to 4) with prevalence differing between countries ranging from highest estimates; Turkey (48.5%), USA (47.7%), South Africa (42.3%), Philippines (41.3%), Poland (35.91%), Australia (27.2%), UK (25.4%), Canada (24.1%), Iceland (22.6%), Austria (17.9%), Germany (13.7%), Norway (13.3%), Sweden (12.3%), India (11.7%) and China (8.1%) (estimates from Figure 1 us-
Geo1graphic location significantly predicted dyspnoea even after adjustment for socioeconomic variables, comorbidities and lung function. Dyspnoea was more common in women and more likely when forced vital capacity fell below 60% predicted which raises the possibility that smaller absolute lung volumes (women, socio-economic deprivation) may play a role in susceptibility to breathlessness. While the mMRC is almost ubiquitous in studies of dyspnoea, the authors note two pivotal limitations of this instrument with respect to assessing dyspnoea; 1) the instrument assesses the presence of activity-related breathlessness, but the respondent is not required to indicate whether or not the sensation is distressing; 2) the statements assume the activity is part of everyday life (hurrying on the level or up a slight hill, walking 100 meters/yards). This study confirms that the prevalence of dyspnoea in the general population differs between geographic locations, may affect greater than 25% of the population in specific countries, even in the absence of chronic conditions and while the usual covariates were strongly associated, these only explained 13% of dyspnoea variance. The value of population level data allows identification of groups of greater risk.

**Dyspnoea is an independent predictor of mortality**

**Authors:** Pesola GR and Ahsan H.


**Comments:** This systematic review included ten longitudinal/cohort studies (minimum sample size >500) where analysis was controlled for age, smoking and lung function, to explore whether presence of dyspnoea (exposure at baseline) predicted mortality (outcome). These ten studies included a total of 48,353 participants, a median study duration of 15.5 years (range 6 to 43 years) with presence of activity-related breathlessness at enrolment in the study assessed by mMRC (or similar statements). In all ten studies, breathlessness predicted mortality with point estimates by odds ratio, rate ratio or hazard ratios for participants reporting breathlessness (compared to those reporting no breathlessness) ranging from 1.2 to 2.9 fold greater mortality over time. Notably where breathlessness resolved after the baseline assessment, the risk of mortality was similar to the general population. The authors emphasize that persistent or chronic breathlessness is an “independent predictor of all cause (six studies) and cardiovascular disease (four studies) mortality after controlling for age, smoking and lung function” (pg 8). Chronic breathlessness or dyspnoea, especially if occurring during low level physical activities may be misinterpreted as a benign, corollary symptom common to a range of chronic conditions or part of normal aging and consequently not assessed or prioritised in management. This study highlights the independent association between chronic breathlessness and mortality and the need to thoroughly evaluate and remediate this sensation.
### Proactive identification and management of chronic refractory breathlessness has ethical and potentially, legal implications

**Authors:** Currow DC, Abernethy AP, Ko DN.
**Reference:** Thorax 2014; 69:393-394
**URL:** [doi:10.1136/thoraxjnli-2013-204701](https://doi.org/10.1136/thoraxjnli-2013-204701)

**Comments:** Chronic refractory breathlessness is the breathlessness that exists at rest or with minor exertion and persists despite optimal treatment of underlying causes. A degree of clinical inertia surrounds refractory breathlessness as this symptom may be perceived by both patients and clinicians as an inevitable part of chronic illness and/or aging. In this short opinion piece, Currow and colleagues eloquently present a case for obligatory assessment and management of this symptom where it is identified in patients. This case is made on three foundations: 1) As a number of evidence-based professional body statements provide unambiguous advice concerning the use of low dose, titrated sustained release morphine for the reduction of refractory breathlessness in individual patients where disease-modifying therapies have been exhausted, failure to assess and manage refractory breathlessness in such an individual could be considered sub-standard medical care and potentially, a breach of duty of care and negligence; 2) such inaction could also be considered to breach the principles of modern bioethics; 3) and, in the same way that adequate pain control through access to pain relief is considered a basic human right, symptomatic treatment of refractory breathlessness should be considered in the same light. This opinion piece presents an a case for clear case for equivalence of prioritising identification and proactive management of pain and refractory breathlessness.

### Assessing multidimensional aspects of dyspnoea

**Authors:** Williams MT, John D, Frith P.
**Reference:** Eur Respir J 2016
**URL:** [http://erj.ersjournals.com/content/early/2016/12/19/13993003.00773-2016](http://erj.ersjournals.com/content/early/2016/12/19/13993003.00773-2016)

**Comments:** While measurement of breathlessness has previously focussed on unidimensional scales (visual analogue or numeric rating) and/or functional impact, our understanding has shifted to recognise the affective distress, sensory qualities and emotional responses of this experience. In this paper, two assessment tools developed to reflect these aspects of the experience of breathlessness were directly compared in a clinical sample of patients (n=84) with moderate to severe COPD. The Dyspnoea-12 (D-12) and Multidimensional Dyspnoea Profile (MDP) were used to report on (a) breathlessness experienced in daily life and (b) breathlessness experienced at the end of a six minute walk test. Scores were compared with other dyspnoea measures (e.g. volunteered descriptors, visual analogue scales for unpleasantness and intensity) and clinical measures (e.g. lung function, exercise tolerance, anxiety and depression). The authors found that single-scores for the D-12 (total) and MDP (MDP-A1 unpleasantness) and item group scores (subdomains) showed broadly equivalent properties in terms of convergent, discriminative and concurrent validity. In this sample, MDP items matched volunteer descriptors more closely than did D-12 items in sensory qualities (feeling of chest tightness/constriction) and emotional responses (afraid/frightening). The paper highlights differ-
ences between the two instruments (e.g. rationale, development, items, and instructions) and provides valuable reference data for the D-12 and MDP in a clinical COPD population reported for both daily life and at end-exercise.

II. Comprehensive management of dyspnoea

People with advanced disease report a range of self-management strategies to cope with episodic breathlessness – many of which were no/low cost and required minimal resources

Authors: Simon ST et al
Reference: J Pain Symptom Manage. 2016;52(2):228-34
Comments: In their own words, what helps people with chronic breathlessness to cope with this troublesome symptom? Simon and colleagues interviewed 51 people with advanced disease: severe COPD, chronic heart failure, lung cancer and motor neuron disease to explore this question. The most common strategy (reported by 96%) to relieve breathlessness was to avoid or adapt their activity: predominantly physical activity but also talking and interacting. Sixty-eight percent of participants reported a physical strategy to cope with breathlessness such as breathing techniques or changes to body position, while 61 percent described a cognitive strategy such as calming, concentrating, distracting or self-talk. Air movement, fresh air and oxygen (the latter mostly in people receiving long-term oxygen therapy), medications (mostly inhaled bronchodilators and rarely morphine) and environmental strategies (warmth or coolness, chewing or drinking) completed the picture. The consumer perspective provided by this paper is a key compliment to evidence-based interventions for breathlessness. It reminds clinicians that management strategies must be individualised; what is effective in a randomised controlled trial may not benefit a specific patient. It also reminds us to see the patient’s perspective when as a clinician we advocate the benefit of an intervention with strong research evidence, such as exercise-based pulmonary rehabilitation, which may conflict with patient's strategies for managing their breathlessness.

Five minutes exposure to a hand-held fan provided over 30 minutes relief of breathlessness for over 50% of people with refractory breathlessness at rest

Authors: Booth S et al.
URL: http://journals.sagepub.com/doi/pdf/10.1177/0269216315607180
Comments: In this observational, feasibility study, Booth and colleagues confirm the benefits of a simple, low resource and cost, universally applicable intervention to relieve the sensation of breathlessness. Thirty–one people experiencing refractory breathlessness while
sitting at rest, used a hand-held fan for five minutes at a distance of 15-30cm to deliver air movement across their face (areas innervated by second and third branches of the trigeminal nerve). Breathlessness intensity was assessed before and after the exposure to intervention using visual analogue scale (VAS) and numeric rating scale (NRS) with a five point “relief of breathlessness” scale completed immediately post intervention. Participants indicating an appreciable reduction in breathlessness (≥25% reduction in baseline VAS/NRS score or reduction of 10 mm/1 point) were assessed 30 minutes post intervention and then every 10 minutes until breathlessness scores returned to baseline or plateaued. Approximately half the sample experienced a reduction of moderate effect size in breathlessness intensity immediately after five minutes of the intervention (VAS n=17/31, NRS n=19/31). For those responding to the intervention, the median estimated duration of effect for VAS was 75 minutes (95% CI: 2.8 -147.2) and NRS was 35 minutes (95% CI: 20 to 49.3). This study highlights the beneficial effect of a simple, low cost intervention for relief of breathlessness in people with refractory breathlessness at rest. In addition, it provides pragmatic recommendations for the conduct of feasibility /pilot protocols for studies investigating interventions for breathlessness relief and much needed interpretations for the minimal important clinical differences for VAS/NRS when used to assess breathlessness intensity.

**Activity-related breathlessness in COPD; support for efficacy of bronchodilators and, in selected patients, low dose oral opioids**

**Authors:** O'Donnell DE. et al  
**Reference:** Expert Review of Respiratory Medicine 2016; 10:823-834  
**URL:** [http://dx.doi.org/10.1080/17476348.2016.1182867](http://dx.doi.org/10.1080/17476348.2016.1182867)  
**Comments:** This review links current neurobiological understandings of activity-related breathlessness with pharmacological strategies to address this symptom. The effectiveness of pharmacotherapy directed toward three mechanisms is reviewed. Firstly, optimisation of respiratory mechanics through long-acting bronchodilator medication (LABA, LAMA and LABA/LAMA combinations) has resulted in clinically and statistically meaningful improvements in exercise tolerance and breathlessness. Secondly, central drive to breathe and central perception of the affective dimensions of breathlessness may be reduced by low-dose opioids in selected patients with severe disease. Reported adverse effects of low-dose opioids were mostly reversible and transient and included constipation, nausea and vomiting but not respiratory depression or hypoventilation. Thirdly, pharmacotherapy has potential to reduce the affective dimension of breathlessness. Low-dose opioids also address this mechanism; while benzodiazepines were found not to be superior to placebo in improving breathlessness in a systematic review. Ability to measure the affective aspect of breathlessness and its response to treatments such as anxiolytics is highlighted as an opportunity for future research.

**More on dyspnoea in Respirology:**


A predominantly home based, multidisciplinary Breathlessness Intervention Service (BIS) combining non-pharmacological and pharmacological strategies provided relief from breathlessness distress in people with advanced cancer

Authors: Farquhar MC et al.
Reference: Trials 2016 17:185

Authors: Farquhar MC et al.
Reference: BMC Medicine 2014, 12:194
URL: https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-014-0194-2

Comments: Over the last 13 years the Cambridge Breathlessness Intervention Service (BIS) has been developed, piloted and now evaluated in a randomised controlled trial with two sub-protocols (one for people with advanced cancer and one for people with advanced non-malignant disease). This complex, multidisciplinary intervention combines non-pharmacological and pharmacological strategies for breathlessness management in a largely home-based environment, delivered over 2 weeks (cancer) or 4 weeks (non-malignant disease). In their 2016 paper Farquhar and colleagues describe outcomes for patients with advanced non-malignant conditions, and compare findings with those previously reported in people with advanced cancer (Farquhar et al 2014). The primary study outcome was score on a 0 to 10 numeric rating scale for patient distress due to breathlessness at end-intervention (2 or 4 weeks depending on sub-protocol). In people with advanced cancer, distress due to breathlessness reduced significantly as a result of the BIS compared with control (−1.29; 95% CI −2.57 to −0.005; p = 0.049). In people with advanced non-malignant disease there was no significant difference in the BIS group on this outcome compared with control; both study arms had reduced distress at the end of 4 weeks (intervention by 2.22 points and control by 1.56 points). Analysis of qualitative data (interview transcripts) indicated that the BIS made a positive difference for 92% (non-malignant disease) to 94% (cancer) of participants. Participants in the non-malignant sub-protocol had worse breathlessness and associated distress, poorer quality of life and worse anxiety and depression at baseline than participants with cancer. The reassuring role of the BIS was highly valued by people with non-malignant disease, who also reported perceived benefit from the data collection interviews (which occurred in both control and intervention arms). This highlights the longevity of suffering with breathlessness in those with advanced non-malignant lung disease, and the therapeutic value of being listened to with empathy. The contrasting trajectories and impacts of breathlessness and related distress in the two patient groups suggest different aspects of the intervention may be more relevant to each. These two studies strengthen existing evidence from other BIS-type models that show benefits for patients with advanced malignant and non-malignant disease and point the way to further tailoring and implementation of such services.
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