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Title: Multidimensional measurement of breathlessness - recent advances

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Abstract

Purpose of the review: Breathlessness is a multidimensional sensation for which a range of instruments exists for children, youth and adults, capable or unable to self-report distress with breathing. This review presents developments and applications of multidimensional assessments of breathlessness.

Recent findings: Excluding unidimensional measures and instruments assessing the impact of breathlessness, at least eight psychometrically robust instruments exist which comprehensively assess one or more specific domains of the sensation of breathlessness (intensity, sensory quality, affective distress). These instruments have evolved from modest beginnings (describing breathlessness in various patient cohorts) to a growing use as primary or secondary outcomes in observational, clinical and experimental trials exploring breathlessness mechanisms and intervention effects. For adults and children unable to consciously communicate breathing discomfort, instruments include combinations of physiological and behavioural markers of distress. Non-verbal (graphic scales) have potential use beyond paediatric applications.

Summary: Traditionally, breathlessness has been considered as a 'black box' with unidimensional measures reflecting box size (intensity, unpleasantness). Multidimensional instruments reveal the composition of the black box of breathlessness allowing detailed descriptions of an individual's breathlessness experience, quantification of sensory qualities, affective distress and emotional responses with the potential to capture change over time and treatment effects in each dimension.

Keywords:

Multidimensional breathlessness assessment, dyspnoea

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Introduction

Distress with breathing or dyspnoea is a complex perceptual experience which encompasses both a conscious awareness of the intensity of physical sensations, affective distress and emotional responses. As a symptom, breathlessness is described by the person experiencing this sensation. In situations where a person is unable to communicate, assessments of breathlessness require combinations of physiological and behavioural markers of distress. The sensation of breathlessness exists across a continuum from positive/pleasurable to unpleasant/distressing (dyspnoea) depending on the individual, situation and context. This review focusses upon recent advances in multidimensional assessment of breathlessness as a distressing symptom experience.

What do we mean when we say breathlessness is a multidimensional sensation?

Like pain, breathlessness is not a single generic sensation. Both sensations include different and often co-occuring, types of sensation (sensory qualities) which vary in intensity and contribution to the global experience of unpleasantness/distress. Both sensations provoke emotional responses and motivate avoidance behaviours, which over time, can become habitual resulting in specific activities or environments becoming associated with expectations of breathlessness and anxiety. When acute, pain and breathlessness have more consistent associations with physiological measures. Where these sensations persist beyond expected tissue damage/recovery (chronic pain) or despite optimal medical management (chronic breathlessness [1]), associations with physiological measures, such as pulmonary function are less consistent and subject to wide individual variability [2,3]. The notion that pain is a multidimensional experience which can be described using different sensory qualities (reflecting potential underlying mechanism), severity (intensity), distress (suffering) and impact on daily life (disability/impairment) is well accepted. While multiple afferent information sources inform a conscious appreciation of the sensation of breathlessness, research over the past three decades has confirmed that individuals can discriminate between intensity and distress/unpleasantness of breathlessness, the existence of a range of sensory qualities arising from differing neurophysiological processes (including sensations of work/effort, tightness, air-hunger/unsatisfied inspiration) and varying affective responses contributing to individual distress and consequent disability. [4]

Why measure breathlessness in multiple dimensions?

Unidimensional measures such as visual analogue scales (VAS [5]), numeric rating scales (NRS [6]) and the modified Borg category-ratio scale (mBorg CR [7]), assess the magnitude of the 'black box of breathlessness' but they tell us little about the components contributing to the size of the box and how components contribute in different situations and individuals. Similowski and Serresse (2019)[8**] more eloquently argue that unidimensional assessments of breathlessness intensity -while common -do not have sufficient resolution to capture sensory and affective dimensions which not only vary independently of each other but reflect different neurophysiologic mechanisms and present unique opportunities and targets for therapeutic interventions.

Despite the ubiquity of unidimensional instruments for breathlessness assessment, to quote the VAS godfather (Aitken 1969 pg 989 [7]), these instruments are "….*governed by the rules under which they are made*….." [9]. Concerns continue to be raised over variability of specific wording of instructions, stems and anchors, impact of verbal descriptors within scales and how individuals interpret instructions/concepts (intensity, severity, discomfort, bother) [10]. In addition, while the original developers of these unidimensional measures used 'momentary' ('right now') focal periods, recalled or memory-based assessments of breathlessness (average, worst, peak) over varying periods of time (today, 24 hours, 7-days, 2 weeks) are common. Rarely are these instruments validated for these focal periods and these memory-based recollections of breathlessness may be confounded by cognitive or psychological factors. For example, the 'peak-end ' phenomenon proposes that an individual's recall of an event prioritises the worst or best (peak) part of the experience or closing moments of the episode (end) rather than a cumulative total or average of every moment of the experience. [11,12**]

Recent studies, using pooled data (permitting analysis of larger samples), provide clarity on some of these concerns. Comparing NRS and mBorg scores in people living with chronic breathlessness (n=1048, 10 studies), Johnson et al (2016) [10] identified a responder bias towards mBorg items associated with a verbal descriptor. Using NRS-average and NRS-worst over the past 24 hours (n=561, 3 datasets), Wade et al (2017) [12**] confirmed the existence of a subgroup of both patients (n=21) and carers assessing the patient's breathlessness (n=24), who rated NRS-average higher than NRS-worst over the previous 24 hours. Ekstrom et al (2019) [13*] confirmed that ratings of breathlessness severity and unpleasantness (VAS) (n=256 over eight days) are highly correlated and have similar associations with clinical factors. While this work clarifies factors influencing the shape /size of the black box of breathlessness, it does not (nor was it intended to) illuminate the composition of the box.

Which instruments are available for multidimensional breathlessness assessment?

Instruments, or subsections within instruments, can be classified according to the non-mutually exclusive domains of 1) sensory-perceptual experience (intensity, sensory qualities); 2) affective distress (unpleasantness) and 3) symptom/disease impact or burden. [4] The instruments (n=54) identified by Parshall et al (2012) [4] [Supplemental materials] can be further grouped according to whether they predominantly target sensation of breathlessness (intensity, sensory quality and affective distress n= 8, 15%), predominately target breathlessness impact (functional performance, activity, health status or quality of life n= 29, 54%) or include items for both breathlessness sensation and impact (n= 17, 31%).

Excluding uni-dimensional instruments, there are at least eight instruments available which assess one or more specific domains of the sensation of breathlessness, including two recently developed instruments (Dyspnoea-Amyotrophic Lateral Sclerosis -Scale (DALS-15) [14] and the Intensive Care-Respiratory Distress Observational Scale (IC-RDOS).[15] Table 1 provides a summary of instrument properties.

Multidimensional instruments developed for adults capable of self-report

Multidimensional instruments for assessment of breathlessness include the Dyspnoea -12 (D-12) [16], Multidimensional Dyspnea Profile (MDP) [17], Cancer Dyspnoea Scale (CDS) [18], and the Dyspnoea-ALS-scale (DALS-15) [14]. Three were developed for use in clinical environments (D-12, CDS, DALS-15) with the MDP prospectively designed for both clinical and laboratory-based use [17]. While these instruments share superficial similarities, each of these differ with respect to intended use, original derivation and development process, items and recommended focal period and scoring (See Banzett et al 2015 [17] for further discussion of MDP, D-12, DCS). Table 2 presents a comparison of items between instruments. For both the MDP and D-12, items have been consistently and independently demonstrated to group into two subdomains reflective of specific item wording (sensory qualities and emotional responses respectively [19*, 20]. While factor analysis determined that items within the CDS could be grouped into three relatively independent factors, the developers noted the difficulty of labelling these factors or domains (Sense of effort, Sense of anxiety and Sense of discomfort) based on the wording of the items alone [18]. Independent replication of these CDS subdomains has yielded inconsistent results potentially reflecting cultural/linguistic differences [21,22,23]. Subdomains have not yet been confirmed for the DALS-15 [14].

These relatively recent multidimensional instruments continue to be translated and validated into different languages (Table 1). Studies have described the sensation of breathlessness for hospitalised patients (MDP [24**]; D-12 [25**]) and ambulatory outpatients (COPD (MDP [19*, 20]; D-12 [16,19*,26,27,28]), Asthma (D-12 [29, 30]), pulmonary hypertension (D-12 [31]), interstitial lung disease (D-12 [32]), Amyotrophic Lateral Sclerosis (MDP [33**]; DALS-15 [14]), lung /advanced cancer (D-12 [34]; CDS [18, 21,22,23,35]) and asthma, heart failure or anxiety disorder (D-12 [36]).

Clinically these instruments have been used to describe breathlessness severity as a characteristic of cohorts (CDS [35]), differences between groups (D-12: frailty classifications in people with COPD [37]) and to identify changes in breathless sensation over time (D-12: across 3 months following admission to hospital for acute exacerbation of COPD with greater changes at each time point for physical subdomains (sensory qualities) versus affective subdomains [25**]). There are an increasing number of studies including multidimensional instruments to assess the impact of interventions on the sensation of breathlessness (MDP: before and one month after initiation of non-invasive ventilation in people living with ALS with chronic respiratory failure [33**]; pulmonary rehabilitation with

and without inspiratory muscle training in people with severe /very severe COPD [38]; D-12: cognitive behavioural therapy for people with severe asthma and anxiety/depression [30**]; CDS: oral morphine for cancer related breathlessness [39]).

There is an emerging body of research leveraging these instruments in novel ways or in underexplored contexts. Morelot-Panzini et al (2016) [20] demonstrated that the affective dimension of breathlessness (MDP) could contribute to new forms of COPD phenotyping raising the potential for more personalised interventions. Herigstad et al (2017) [40*] identified and described changes in brain activity in people with COPD following pulmonary rehabilitation related to improvements in overall breathlessness severity (D-12). In laboratory models of breathlessness, sensations assessed by the MDP have been reported to be similar between aerosolised furosemide and saline [41**]. As ratings of sensory quality and emotional responses may not be linearly related to overall breathing discomfort (A1), in sub-analysis Morélot-Panzinia and colleagues also report a means of comparing MDP profiles for equivalent levels of overall breathing discomfort (A1) (i.e identifying individuals with matching A1 levels before and after treatment and comparing sensory quality and emotional responses ratings) [41**]. Under controlled exercise conditions, for people with COPD [42] and interstitial lung disease [43], clarification of when sensations of work/effort change to the more aversive sensation of air hunger inform both mechanisms of exertional breathlessness and implications for exercise training (protocols which delay ventilatory inflection point /preserve inspiratory reserve volume).

One under explored context concerns breathless sensations during hospital admissions for non-critically ill patients, where this symptom is common [44] and has been associated with greater risk of serious adverse events [45]. Using the MDP, Stevens et al (2019) [24**] described the profile, variability and trajectory of breathlessness in general medical-surgical hospitalised patients (n=156) presenting with burdensome breathlessness (≥4/10) on admission. While, noting the wide individual variability, in this study, air hunger (sensory quality) and frustration, anxiety and fear (emotions) were predominant and more than half (57%) of the patients rating breathing discomfort ≥4, confirmed that their level of breathing discomfort was unacceptable.

Minimally important clinical differences (MCID) have been reported for the D-12 (3.5 units) [30**]. While 'cut points' to guide clinical decision-making concerning palliation strategies for breathlessness have been proposed for NRS [46], cut-points specific to multidimensional instruments for breathlessness assessment (beyond rating ≥4/10 breathing discomfort A1 scale MDP [24**], do not appear to be available. While secondary analysis of pooled data sets is evident for unidimensional assessments of breathlessness, similar analyses of data collected via multidimensional instruments to explore commonalities and differences between instruments, sensory qualities, specific conditions and situations, have not yet been reported.

Multidimensional instruments developed for adults unable to self-report

For people unable to self-report or directly communicate distress with breathing due to cognitive impairment or conscious state, the severity of breathlessness may be under recognised resulting in unnecessary suffering or nonspecific over or under management. The challenge in developing instruments to assess distress with breathing in people unable to self-report has been met by elegant approaches which include observing and rating clinical/behavioural signs 1) in participants able to self-report breathlessness; 2) as a response to strategies know to palliative breathlessness in people unable to communicate; or 3) comparing scores between participants capable/incapable of communication. The Respiratory Distress Observation Scale (RDOS) assesses breathlessness intensity and distress through a combination of physiological (heart and respiratory rate, breathing pattern, accessory muscle use, grunting, nasal flaring) and behavioural signs (restless non-purposeful movement, fearful, facial expressions) each scored nominally from 0 to 2 points [47]. Reliability, validity and intensity cut points for guiding clinical decisions have been reported [48,49,50]. The RDOS (Chinese version) has been validated in both conscious and unconscious critically ill patients in respiratory intensive care units [51]. In palliative care patients near end of life but able to communicate (n=122), the RDOS demonstrated moderate to strong correlation with self-reported breathlessness (NRS r=0.702, Dyspnoea verbal descriptor categorical scale r =0.677) and was able to discriminate and predict patients with moderate to severe breathlessness [52].

The intensive care RDOS (IC-RDOS) provides an optimised version of the RDOS developed with patients capable of communicating (n=220) while managed in an intensive care unit [53]. The five item IC-RDOS (heart rate, neck muscle use during inspiration, abdominal paradox, facial expression of fear, and supplemental oxygen) had greater correlation with VAS (r=0.61;95% CI, 0.50 to 0.72 versus r = 0.43; 95% CI, 0.29 to 0.58 respectively) [15]. Secondary analysis of IC-RDOS data for communicative (n=120) and non-communicative patients (n=73) admitted to the ICU units during the same period, indicated that IC-RDOS values did not differ significantly between groups (2.3 range 1.1-3.1 versus 2.4, 2.2-2.7 (p=0.115) respectively) [53].

Instruments developed for infants/paediatric/youth

Numeric scales pose greater cognitive challenges for children under the age of seven, consequently assessments of symptoms such as breathlessness and pain rely upon nonverbal scales or clinical indicators of distress [54,55*]. A number of pain scales have established psychometric properties, including recommended age appropriate cut point scores for intervention/ palliation of pain [54]. Very few instruments for breathlessness assessment in children have sufficient validation or psychometric properties [55*,56,57]. The Dalhousie Dyspnea Scale [58] is comprised of three pictorial scales (1-7) derived from focus group discussions with children (8-16yrs; asthma=6, cystic fibrosis =5, healthy children =14). The three final pictures (determined by consensus amongst investigators) reflect descriptions of 'throat constriction', 'chest tightness' and 'effort, tired or exhaustion' [58] with further validation via histamine bronchoprovocation (n=74 children) [59]. The more recent Dalhousie Dyspnea and Perceived Exertion Scale added one further pictorial scale (leg exertion/fatigue [58]. The Paediatric Dyspnea scale [60] is comprised of pictorial scales reflecting overall wellness/discomfort (faces scale), sensory quality (chest tightness from Dalhouse Dyspnea Scale [56] and a colour coded descriptors scale for breathing difficulty ('No trouble at all to 'Very much trouble')[61].

As pictorial scales rely on scaled graphics (rather than written text/numerals), these may potentially transcend issues of language translations or be of particular use in people (children, youth and adults) with mild cognitive impairment or minimum levels of literacy/numeracy. With the exception of Piasoni et al (2015) [60] who confirmed associations with a small group of children for whom English was not their first language (Italian, n=7), cross language/culture validations of such pictorial scales are uncommon. The Dalhousie Dyspnoea and Exertion scale has recently been validated against the mBorg (CR-10) during maximal cycle exercise in adults with (n=17) and without (n=24) chronic respiratory conditions; with approximately 50:50 split for specific scale preference [60]. Whether or how well these representations of sensory qualities of breathlessness transfer or reflect those commonly reported in adults (sense of work/effort, tightness and unsatisfied inspiration /air hunger) is unknown.

Conclusion

Across paediatric and adult populations, there are psychometrically robust instruments for the multidimensional assessment of breathlessness. Resolution of a number of issues could further progress breathlessness science and the clinical care of people living with breathlessness. These include clarification of: 1) how people (health professionals, patients and informal carers) understand and interpret uni-and multidimensional instruments (cognitive debriefing); 2) which situations and how best to socialise multidimensional instruments for breathlessness assessment throughout our communities; 3) whether cut-points specific to each multidimensional instrument are necessary or useful in guiding clinical decision making; 4) whether psychometric properties of instruments are retained across age groups beyond those for which the instrument was developed and 5) whether it is possible to develop a 'minimum data set' for breathlessness assessment to reduce heterogeneity in future studies and facilitate pooled data analysis. Unidimensional measures provide a blunt measure of the intensity or discomfort of breathing (magnitude of black box of breathlessness). Multidimensional instruments provide a nuanced way of exploring mechanisms contributing to breathlessness experiences and identification of which dimensions of breathlessness might be modifiable through pharmacological and non-pharmacological avenues (reconfigure the size and components of the black box).

Key points:

- For the 'black box' of breathlessness, unidimensional measures provide a measure of box size, but multidimensional instruments assess configuration of components within the box.
- A range of robust instruments exist for the multidimensional assessment of breathlessness (intensity, sensory quality, affective distress) irrespective of a person's ability to self-report.
- Whether multidimensional instruments for assessment of breathlessness developed specifically for adults appropriately reflect the breathless experience and retain their psychometric properties in children (and vice versa) is unknown.
- Whether cut-points specific to each multidimensional instrument will prove useful in guiding clinical decision making is unknown.
- Given the recent and likely future growth in use of multidimensional instruments for assessment of breathlessness in both clinical and research settings, the development of 'minimum data set' for breathlessness assessment would maximise opportunities for pooled data analysis.

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	Dimensions			Instrument properties						
	Sensory perceptual		Affective		Validated conditions/settings		Developer recommended scoring			
Instrument	Intensity	Sensory Quality	Distress	Items N= Scale Score range	Original	Since development	Item	Sub-domain *	Total	Translation available
Multidimensional Dyspnea Profile (MDP) [17]	Y	Y	Y	11 Cont 0-10	Various (ED, laboratory)	COPD (pulm rehab+ usual care) [19,20,38] ALS [33] Inpatients [24]	Y	Y		# English ,Dutch, French, German, Italian, Japanese, Norwegian ,Portuguese, Swedish, Turkish
Dyspnoea-12 [16]	Y	Y	Y	12 Ordinal 0-3	COPD/ILD/CCF (outpatient) [14]	COPD [19,25,26,37,40] Asthma [29,30] Pulm HT [31] ILD [32] Lung cancer [34]		Y	Y	English [16], French [28], Portuguese [26], Italian [27], Swedish [36]
Cancer Dyspnoea Scale [18]	Y	Y	Y	12 Ordinal 1-5	Advanced lung cancer [18]	Advanced lung cancer [22, 23] Advanced cancer [21,35,39]		Y	Y	Japanese [18], English [18], Swedish [23], Vietnamese [22], Hindi [21], Marathi [21]
Dyspnea-ALS-scale [14]	Y	Y	Y	15 Ordinal 0-2	Amyotrophic Lateral Sclerosis [14]				Y	German [14]
Dalhousie Dyspnea Scales [58]	Y	Y		3 Ordinal (graphic) 1-7	Asthma, CF, healthy (8-18yrs) [58]	Histamine challenge [59] Exertional dyspnoea 7-18yrs Asthma, CF, healthy [60] Adults , healthy and resp disease [62]	Y			
Pediatric Dyspnea Scale (PDS) [61]	Y	Y	Y	3 Ordinal (graphic) 1-7	Asthma exac (6-18yrs) [61]		Y			
Respiratory Distress Observation Scale (RDOS) [47]			Y	8 Ordinal 0-2	Respiratory (exertional), acute orthopaedic pain + healthy adults [47] Inpatient palliative care (noncomm)[48]	Able to communicate: Inpatients [49) End of life [50, 52] ICU [15,51]			Y	Chinese [51]
Intensive Care-Respiratory Distress Observational Scale (IC-RDOS) [15, 53]			Y	5 Ordinal 0-1 (±weights)	ICU -able to communicate [15]	ICU- ± able to communicate [15,53)			Y	

*Subdomains: Multidimensional Dyspnea Profile (Immediate Perception, Emotional Response -if single score required developers recommend Affective distress (A1)); Dyspnoea-12 (Physical, Affective); Dyspnea Cancer Scale (Sense of Effort, Sense of Anxiety, Sense of Discomfort)

MAPI Research Trust MDP translations available (https://eprovide.mapi-trust.org/instruments/multidimensional-dyspnea-profile)

Table 1: Summary of multidimensional instruments for assessment of breathlessness.

		Dyspnoea-12 [16]	Multidimensional Dyspnea Profile [17]	Cancer Dyspnea scale (CDS) [18]	Dyspnea-ALS-scale [14]#
		None (0) Mild (1) Moderate (2) Severe (3)	Numeric Rating Scale (0-9) + forced choice sensory quality	Not at all (1) A little (2) Somewhat (3) Considerably (4) Very much (5)	Never (0) On occasion (1) Often (2)
	Affective distress	X	X	X	X
Sensory quality	Rapid, deeply, heavily		X		
	Exhalation/expiration			X	
	Tight, constricted		X	X	
	Work/effort	X	X		
	Unsatisfied inspiration, suffocating, drowning	X	X	X	
	Difficulty catching breath	X			
	Difficulty with Inhalation/inspiration	X		X	
	Short of breath	X		X	X
	Shallow			X	X
	Mental effort or concentration		X		
	Exhausting breathing	X			X
	Upper airways /throat			X	
	Panting			X	
	Breathing may stop			X	
	Breathing difficulty with palpitations /sweating			X	
	Ability to breathe slowly			X	
Affective /Emotional response	Depressed/depression	X	X		X
	Miserable	X			
	Distressing	X			
	Agitation/restless	X			X
	Irritation	X			
	Anxious		X		
	Frustrated		X		
	Angry		X		
	Afraid/fear/threat		X		X
Symptom impact or burden Impact	Breathless at rest/sit quietly				X
	Breathless during exercise				X
	Nocturnal waking due to breathlessness				X
	Breathlessness limits everyday activities				X
	Social isolation due to breathlessness				X
	Breathlessness is a problem for me				X
	Difficult coughing				X
	Breathlessness limits lying flat				X

items informally translated from German and allocated to domains by the authors (MTW & KJ)

Table 2: Multidimensional instruments for assessment of breathlessness in adults capable of self-report: Comparisons of items (simplified from original instruments).