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Measuring dyspnoea – New multidimensional instruments to match our 21st Century understanding

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Introduction

Science and medicine are always limited by our measurement instruments; the study of dyspnoea is limited by the tools we use to measure what patients feel. Whether researching neurophysiological mechanisms in the MRI scanner or trying to understand an individual patient, we need the best tool for the job. We have advanced from measuring dyspnoea as a yes-no item, to the realization that patients can scale the sensation, to the understanding that we can measure more than a single aspect of this complex experience. In this issue, Williams et al [1] have tested two new instruments that attempt to encompass the multidimensional nature of the dyspnoea experience.

It has long been suggested that there are different sensory qualities of breathlessness that may be connected to specific physiological mechanisms, and that breathlessness can give rise to emotional responses such as anxiety [2, 3]. Pieces of the puzzle have accumulated: investigators have used a variety of scales and questionnaires to assess particular aspects of the dyspnoea experience, different sensory qualities of dyspnoea [4–6] and particular emotional responses [7, 8]. The emerging picture led to the development of the most widely cited **definition of dyspnoea**: *"a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity… distinct mechanisms and afferent pathways are reliably associated with different sensory qualities (notably work/effort, tightness, and air hunger/unsatisfied inspiration) [that] most often do not occur in isolation [and] vary in their unpleasantness and in their emotional and behavioral significance"* [9–11]. This definition made it clear that dyspnoea is a multidimensional experience. Yet, there was no comprehensive, validated instrument that encompassed the multidimensional nature of dyspnoea. Now there are two multidimensional instruments: the Dyspnoea 12 (D-12) and the Multidimensional Dyspnea Profile (MDP). In this issue, Williams et al present the first independent comparison of D-12 and MDP to each other and to a number of established measures. Their assessment will be valuable for all those seeking to use or interpret these new patient-reported outcome measures.

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One of the conceptual breakthroughs in pain research was the idea that there are multiple dimensions of pain, proposed many decades ago, and refined more recently with scaling approaches [12–14]. The seminal multidimensional pain instrument, the McGill Pain Questionnaire (MPQ)[15], has been cited 3662 times. The multidimensional model is now considered essential to ‘state of the art’ pain science and clinical management. Multidimensional measures are strongly recommended for outcome measures of pain management in clinical trials [16], are very widely used in assessing pain in patients [17], and are widely used in basic pain research. Multidimensional tools have revealed phenomena invisible to unidimensional scales; for instance, they have shown different profiles of pain in different categories of patients [18], and have shown that sensory and affective dimensions can respond differentially to treatment [19–21]. The main elements of the multidimensional pain model are the sensory quality, sensory intensity, unpleasantness, and emotional impact; other elements included location and temporal properties. Ronald Melzack, originator of the MPQ and of the gate control theory of pain neurophysiology, made this point in recent reflections: “As I look back, I realize that my fascination with pain descriptors as a reflection of the multiple dimensions of pain perception had a powerful impact on my thoughts on the neural basis of pain”[22].

A similar multidimensional model may be applied to dyspnoea – separable sensory qualities (e.g., the sense of needing more air, the sense of excessive work of breathing, the tightness of asthma) and emotional outcomes (e.g., anxiety, depression, fear) have been described separately in various studies of dyspnoea. The new instruments are attempts to bring these ideas together. The idea that dyspnoea is not a unitary sensation underlies both instruments, leading to some strong common aspects of their performance. But there are underlying differences in design approach that result in important differences in performance and suitability for particular applications.

Common ideas, different design philosophies

The design specification for the D-12 was based on a clinical need expressed by the senior clinical author of the D-12, who stipulated that the instrument should provide a single global score that includes the affective dimension, is applicable to a variety of patient groups, and is quick and easy to complete by patients waiting to be seen in clinic. Development of this instrument was prompted by unease that some dyspneic patients could be under- or over-medicated based on unidimensional scales that ignored the affective aspect of dyspnea. To meet these criteria, 81 respiratory and emotion descriptors were compiled from published reports of the language of dyspnoea; these were presented to a large cohort comprising outpatients with interstitial or obstructive lung disease or congestive heart failure. A core set of 12 descriptors was identified using hierarchical methods to remove the least discriminating items and using Rasch analysis to exclude those items with the poorest fit to breathlessness severity [23]. The authors have published accounts of the background and development of the D-12 [23, 24].

The design specification for the MDP was to provide a better characterization of the complex dyspnoea experience that would be useful in both laboratory and clinical research – in part so that we could understand the connection between research and clinical dyspnoea.

Items derived from both patients and laboratory subjects were chosen so that each of the sensory qualities of dyspnoea known to the authors was represented by a single item. Subjects first rate the overall breathing “discomfort” or “unpleasantness”, then rate the “intensity” of individual sensory descriptors. The difference between intensity and unpleasantness is explained to the subject using the “radio analogy”, which makes a distinction between how loud (intense) and how disagreeable (unpleasant) a sound is. Synonymous sensory descriptors were combined into five sensation categories on the basis of previous clustering and principle components analyses [5, 6, 25]. A measurement model for pain [13, 14] formed the overall conceptual structure [26], and a list of negative emotions was adopted from that model. The MDP items were not intended to be summed, but rather to provide a more complex profile. If needed, a single item, overall breathing discomfort/unpleasantness (termed A1), provides an overall score, and closely parallels the ATS core definition of dyspnoea. A summary of MDP features, background evidence, and guidance for use is available [27].

Although the MDP and D-12 have a similar number of individual items (11 vs 12), the item content is somewhat different, and the end use of the items is substantially different – these differences have been summarized previously [27].

Then an interesting thing happened. The developers of each instrument, applying principle component analysis to validation cohort data, found that both the D-12 and the MDP can be analyzed as 2 components. In the case of the MDP, items meant to be individual were found to ‘hang together’. Likewise, in the case of the D-12, the 12 items meant to be lumped naturally split into two divisions. These divisions in both instruments appear to represent similar aspects of dyspnoea – immediate sensory phenomena and emotional responses. An important finding of Williams et al is that the scores of the “Emotional Domain” of the MDP are well correlated across subjects with scores of the “Affective Dimension” of the D-12; likewise, the “Immediate Perception” domain of the MDP is well correlated with the “Sensory Dimension” of the D-12. This finding is strong support for the underlying concepts – instruments developed using diverging methods came together because the multidimensional model is valid, in common with established pain perception models [26, 28].

Another important finding in the Williams paper is that both the MDP and the D-12 are flexible enough to be used with time frames not originally tested – both showed good performance when used to assess two-week recalled dyspnoea, and for assessing current dyspnoea during a clinical exercise test. (The two-week time frame had already been tested for the MDP [29]) Although ease of use was not formally measured, a personal communication from Dr Williams informs us that both instruments were readily understood by patients. The D-12 did have a time advantage on initial administration, Williams et al estimated that the D-12 required only 2–3 minutes, compared to 3–4 minutes for the MDP; subsequent administrations of both instruments were estimated to require only 1–2 minutes. Both MDP and D-12 required less time than other instruments used in the same study (e.g., Hospital Anxiety & Depression Scale, Chronic Respiratory Questionnaire, and Mahler et alia’s 15-descriptor list)

How shall we decide whether these new instruments measure what we want to know?

Concurrent validity (i.e., whether the results of the new instrument track the results of older, widely accepted instruments) is a conventional method of assessing new psychometric instruments. Williams et al compared appropriately chosen elements of the D-12 and MDP with familiar measures such as the Medical Research Council Breathlessness Questionnaire, Visual Analog Scales, and CRQ in a large sample of COPD patients. The correlations are sufficiently strong to support "concurrent validity". One older instrument, the MRC Breathlessness Questionnaire, is of particular note. As one of the oldest instruments, the MRC has been used in many studies. Although it has its flaws, the MRC has shown great strength in predicting mortality, perhaps the 'hardest' outcome possible [30, 31]. Concurrent validity is reassuring, but it is not the whole answer. If the new instruments really represent a novel approach that takes account of hitherto neglected domains of the dyspnoea experience, they must diverge from existing instruments.

Which instrument should you use?

The D-12 and the MDP are not the same. One or the other may be more suitable for your study. The two authors of this review are members of the development teams for the two instruments. Although we agree on the major concepts, each of us has arguments in favor of our own instrument:

Why chose the MDP? (Author RBB). In Williams's study, The MDP outperformed the D-12 in comparisons with existing instruments in both time frames, although neither instrument had an overwhelming advantage. Williams et al showed that the MDP correlated better than the D-12 with other instruments when analyzed as two components or as a single score, and report that in their cohort of patients the MDP "appeared to more completely capture the most salient sensations and emotions". However, the MDP has an additional advantage not addressed by the analyses done by Williams et al: the MDP has been designed and tested for individual item analysis. The items have been balanced, so that each concept appears once; the items include all known respiratory sensations, not just those that contributed strongly to total score in the test populations. The MDP also contains a forced-choice panel that uses the patient's own judgment to sharpen the distinctions between respiratory sensations. Thus, the MDP is the best instrument to use when you want to determine what particular sensation or emotion (e.g., air hunger vs tightness, anxiety vs depression) is present in a patient or is affected by a particular therapy. For more descriptive studies, the MDP will provide a profile characterizing the sensory and emotional experience (e.g., to compare laboratory models to clinical dyspnoea). I see no reason not to choose the MDP for most studies that require a multidimensional instrument.

The MDP has been used in a few studies both for validation and for discovery [29, 32–41]. A convenient graphical representation of results is shown in reference [41]

Why chose the D-12? (Author SHM). The development approach for the D-12 produced a unique instrument that was fit for the purpose it was intended – use in the clinic with a wide

variety of patients. The D-12 is fast and easy to complete: (i) Williams et al estimate a 1 minute advantage in completing the D-12 compared to the MDP on first presentation. This may be an advantage, for instance, in the busy clinic environment where an overall score of dyspnoea is needed without complex analysis of individual items. (ii) In the original validation of the D-12 (Study 2 in reference [23]) 53 COPD patients scored ‘ease of completion’, ‘ease of understanding’ and ‘helpfulness’; the median response to each question was 9 or 9.5 out of 10. In our laboratory, seven of ten healthy volunteers undergoing tests of experimentally induced dyspnoea, indicated that they preferred to complete the D12 as compared to the MDP (unpublished data). I speculate that profoundly affected breathless patients are likely to require more assistance with completing the MDP, which could run a greater risk of the assisting person influencing patient selections.

The reliability of the D-12 has been confirmed in patients with a variety of diseases such as COPD [23], Asthma [42], ILD [43], pulmonary hypertension [44], heart failure [23], lung cancer [45] and bronchiectasis/tuberculosis [46].

Relationship of the new to the old

There are many instruments that have been used to assess dyspnoea [47, 48], and many of them will continue to be useful. Commonly used clinical dyspnoea assessments often do not ask the patient to report what he feels. Rather they ask multiple questions to determine what activities make the patient feel breathless (e.g., the MRC [49]), or what activities the patient cannot do because of dyspnoea (e.g., the BDI-TDI [50]). These instruments have proven quite useful in prognostication, but the data are not directly comparable to either one-dimensional or multidimensional scales in which the patient rates her experience. The new scales do not obsolete these measures; for instance, simple unidimensional measures may be the best compromise if a data point is required every 20 seconds during an exercise test, or when dyspnea is documented at frequent intervals in busy clinical settings; e.g., the nurses at RBB’s home institution use a single-scale assessment to document dyspnoea every shift on every patient [51]. The MDP and the D-12 do not inherently specify the level of exertion, therefore scales comprising levels of exertion that cause dyspnoea will also continue to be useful. One might even imagine a combination of approaches for more complete investigation, in which levels of exertion causing dyspnoea are first determined, then the nature of the dyspnoea is further explored with multidimensional instruments.

Conclusions

Both the MDP and D-12 strive to take account of complexities in the dyspnoea experience – but are they worth the trouble? Theoretically they should do a better job than previous unidimensional instruments [26]. But are they really an advance in practice? Is one summary number integrating 12 affective and sensory items (D-12) better than one number provided by the patient, in which the patient himself integrates the experience? Do separate scores from 11 different items (MDP) describe the dyspn0ea experience better than one number provided by the patient? Do two dimension scores (MDP and D-12 analyzed as 2-component) describe dyspnoea better than one number provided by the patient?

The real test of the new instruments will be whether they improve our understanding. For instance – do they predict mortality better, are they more sensitive to therapeutic intervention, do they help us understand mechanism better, and do they help us translate laboratory studies to clinical practice better than existing instruments? The answers to these questions will only emerge as the new instruments are used in real studies.

Dyspnoea is a leading symptom of cardiovascular and pulmonary disease, neuromuscular disorders, obesity, metabolic disease, and advanced cancer. Persistent dyspnoea is a source of suffering and can become the foremost concern irrespective of the causes and mechanisms (for instance in emergency departments, in intensive care units [52], or in palliative care settings [53]). Dyspnoea is important in diagnosis and can predict outcomes. It is thus an important patient-reported outcome in this era of patient centered care. But which instrument is the right tool to measure dyspnoea? Each investigator will need to make that decision – no tool suits all jobs. More sophisticated multidimensional measurement may help understand individual problem patients, and is likely to advance our understanding of dyspnoea mechanisms, epidemiology, and symptom management. The good news is that two tools encompassing the multidimensional experience of dyspnoea are now available and have now been tested and compared by an independent lab. Versions of both are available in several languages*. It's up to you to choose the right one for your study.

* English and French versions of the MDP are available through this journal as open access (http://erj.ersjournals.com/content/45/6/1681). Translations in French localized to France, Belgium and Canada, in Swedish, Dutch, Flemish, German, and English localized to UK are available from MAPI Research Trust free or at nominal cost for academic use (https://eprovide.mapi-trust.org/instruments/multidimensional-dyspnea-profile#languages). Future translations will be coordinated through MAPI Trust. The original UK English D-12 appears in the appendix of the open access publication in Thorax (http://thorax.bmj.com/content/65/1/21.full.pdf) and has been translated and validated for use in, Korean [46], and Arabic [54]. Contact the authors or MAPI for information on new translations.

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Take home message

Developers of the D-12 and MDP add context to Williams et alia's evaluation of these instruments.