Minimal clinically important differences for Dyspnea-12 and MDP scores are similar at 2 weeks and 6 months: follow-up of a longitudinal clinical study

To the Editor:

Chronic breathlessness is a dominating symptom that restricts daily life for many people with cardiorespiratory disease [1]. Different dimensions of the symptom, such as the intensity, sensory qualities and emotional responses, can be assessed using the instruments Dyspnea-12 (D-12) [2] and the Multidimensional Dyspnea Profile (MDP) [3], which share similarities in the underlying constructs of what is measured [4] and have emerged as widely used instruments for multi-dimensional measurement of breathlessness.

D-12 and MDP are responsive to change and feasible to use as endpoints in clinical trials [5]. We recently published minimal clinically important differences (MCID) of the instruments in cardiorespiratory disease [5]. Data on MCIDs are fundamentally important to be able to evaluate the clinical significance of a change in breathlessness or a treatment effect. A recommended method to determine the MCID is to evaluate the mean change from the baseline score (over a time period) in people who experienced a clinically significant change in another relevant measure (anchor), compared to those who did not experience such a change [6]. However, a limitation in breathlessness research is that most datasets only have short-term data.

There is a need for longer-term trials of breathlessness, but MCIDs for D-12 and MDP to date have only been evaluated for up to a 2-week period [5]. No study has reported MCIDs for MDP scores for individual sensory qualities (descriptors) and emotional responses. It is not known if MCIDs, which are used to evaluate and compare effects, are stable or differ between short-term (2 weeks) and longer follow-up (such as 6 months). This knowledge is essential to be able to validly design, interpret and compare breathlessness trials of different durations.

We performed 6 months follow-up of a longitudinal validation study of the Swedish versions of D-12 and MDP, which was previously used to determine MCIDs at 2 weeks [5]. We included a total of 182 outpatients with cardiorespiratory disease (25% had COPD, 21% asthma, 29% heart failure and 19% idiopathic pulmonary fibrosis), who reported having breathlessness in their daily lives for the past 2 weeks or longer. They completed D-12 and MDP at a baseline clinical visit, and using a postal questionnaire at about 2 weeks (n=162 responses; 89%) and 6 months (n=145; 80%). The actual times to follow-up were 14 days (interquartile range 14–18 days) and 6 months (interquartile range 5.4–7.2 months). The order of D-12 and MDP was randomised and the order was then the same at each time point for that participant, to facilitate unbiased comparison between the instruments. The focus period for the participants' breathlessness ratings was "the last 2 weeks" [5].

Minimal clinically important differences were evaluated using an anchor-based method [6] as detailed elsewhere [5]: the MCID was estimated using linear regression as the mean change for each breathlessness score for one unit change on the Global Impression of Change (GIC) scale. The GIC is a seven point scale of the change in breathlessness from baseline (1: "very much better"; 2: "much better"; 3: "minimally better"; 4: "no change"; 5: "minimally worse"; 6: "much worse"; 7: "very much worse") [7]. Mean differences in the breathlessness scores were similar between the different steps across the GIC scale [5].

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This paper reports minimal clinically important differences (MCIDs) for measuring different aspects of breathlessness using the instruments D-12 and MDP at long-term follow-up (6 months), which were similar to MCIDs at short-term (2 week) assessment https://bit.ly/36r8BnK

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The MCIDs were also quantified using distributional methods [6], defining a minimal to small effect size as a change of 0.25 standard deviations of the breathlessness score at each time point. MCIDs were evaluated for all summary and sub-scores at 2 weeks and 6 months, respectively. Estimates were reported with 95% confidence intervals. Statistical analyses were conducted using the software package Matlab R2018b (Mathworks, Natick, MA, USA).

At 6 months, each tool had similar MCID scores to those measured at 2 weeks, as shown in table 1. The proportions of patients with worse/similar/improved breathlessness were 22/48/30% at 2 weeks and 32/25/43% at 6 months. The MCIDs were similar, with overlapping confidence intervals, when analysed using the anchor- and distribution-based methods, which support the validity of the estimates.

This study provides several novel findings. Firstly, it supports that the MCIDs of the instruments are stable when assessing changes in breathlessness over 2 weeks and 6 months, demonstrating that the same MCIDs can be used to evaluate and compare findings using these instruments across time periods. These MCIDs

TABLE 1 Minimal clinically important differences (MCIDs) in the Dyspnea-12 and the Multidimensional Dyspnea Profile (MDP) assessed at 2 weeks and 6 months

	MCID			
	Anchor-based: mean (95% CI)		Distribution-based: small effect size	
	2 weeks	6 months	2 weeks	6 months
Dyspnea-12				
Total	2.8 (2.0–3.7) n=133	2.9 (2.0–3.7) n=120	2.3 n=167	2.6 n=132
Physical	1.8 (1.3–2.3) n=142	1.9 (1.3–2.4) n=128	1.3 n=174	1.5 n=137
Affective	1.1 (0.6–1.5) n=144	1.1 (0.7–1.5) n=129	1.1 n=174	1.1 n=134
MDP				
A1 unpleasantness	0.8 (0.6–1.1) n=149	0.8 (0.6–1.1) n=132	0.7 n=157	0.7 n=137
Perception subdomain	4.6 (3.2–6.1) n= 123	5.1 (3.6–6.6) n=102	3.7 n=146	4.0 n=114
Emotional subdomain	2.4 (1.1–3.6) n=142	2.9 (1.6–4.2) n=125	3.3 n=158	3.2 n=129
Sensory qualities (descriptors)				
Muscle work or effort	0.8 (0.5–1.1) n=145	0.8 (0.6–1.1) n=123	0.7 n=158	0.7 n=128
Air hunger	0.7 (0.4–1.0) n=145	0.7 (0.4–1.0) n=127	0.8 n=158	0.8 n=132
Chest tightness	0.8 (0.5–1.1) n=146	0.9 (0.6–1.2) n=128	0.8 n=159	0.8 n=131
Mental effort	0.6 (0.3–1.0) n=142	0.6 (0.3–0.9) n=120	0.8 n=157	0.8 n=127
Breathing a lot	0.7 (0.3–1.1) n=140	0.9 (0.5–1.3) n=122	0.8 n=155	0.8 n=128
Emotional responses				
Depression	0.4 (0.1–0.7) n=151	0.3 (0.0–0.6) n=132	0.8 n=161	0.6 n=135
Anxiety	0.6 (0.3–0.9) n=150	0.7 (0.4–1.0) n=135	0.8 n=162	0.7 n=137
Frustration	0.4 (0.1–0.8) n=150	0.7 (0.4–1.0) n=129	0.8 n=159	0.8 n=132
Anger	0.3 (0.0–0.7) n=148	0.5 (0.2–0.9) n=129	0.8 n=159	0.8 n=134
Fright	0.5 (0.2–0.9) n=151	0.7 (0.4–1.1) n=129	0.8 n=160	0.8 n=133

MCIDs were estimated for change from baseline in each breathlessness score at 2 weeks and 6 months, respectively. A small effect size was defined as a change of 0.25 standard deviations of the score at each time point.

are also useful for sample size estimation in planning breathlessness trials. Secondly, this is the first comparison of short-term and longer-term use of the MDP and D-12. The findings are consistent with recently reported MCIDs for uni-dimensional scales of breathlessness intensity and unpleasantness for different recall periods (current and best, worst and average over the past 24 h) [8, 9]. Thirdly, we report the first MCIDs for the intensity of individual sensory quality descriptors and emotional responses of breathlessness. We show that a change of 0.8 points is likely to be clinically significant both for overall unpleasantness (MDP A1 score) and across different sensations such as work/effort or air hunger, and that an even smaller difference can be clinically important for emotional responses such as anxiety, frustration or fright, which are likely to affect the person's wellbeing and behaviour.

A strength of this study was the inclusion of a clinical cohort of patients with various forms of chronic cardiorespiratory disease and breathlessness in daily life, with longitudinal analysis of validated instruments and a high response rate at follow-up. Data collection was similar at the follow-up time points and MCIDs were estimated using both anchor-based and distribution-based methods. A limitation is that participants were too few to evaluate MCIDs for specific diagnostic groups. The present findings pertain to changes in breathlessness over time, and further data from randomised controlled trials would be valuable. Interventional trials are required to assess the MCIDs of the D-12 and MDP in response to an intervention. Further research is also needed on multi-dimensional measurement during even longer follow-up and on the impact of different aspects of breathlessness on the person's quality of life and function. Multi-dimensional measurements are important, given the complexity of the lived experiences of breathlessness, which impacts important domains (including physical, psychological, social and sexual) of the person affected [10].

In conclusion, we report the first long-term follow-up MCIDs for multi-dimensional breathlessness instruments D-12 and MDP. The MCIDs were similar to those at short-term follow-up (2 weeks). These findings inform trial design, evaluation of treatment effects in longer-term studies and comparisons between trials of different durations in chronic breathlessness.

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