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Prevalence and severity of differing dimensions of breathlessness among elderly males in the population

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Tweetable abstract

This first epidemiological study of multi-dimensional breathlessness shows that unpleasant, physical, affective, and emotional experiences of breathlessness are common among elderly males and were strongly associated with mMRC ≥ 3 .

ABSTRACT

Breathlessness is common in the general population. Existing data were obtained primarily with the uni-dimensional modified Medical Research Council (mMRC) breathlessness scale that does not assess intensities of unpleasantness nor physical, emotional, and affective dimensions. The aim of this research was to determine the prevalence and intensity of these dimensions of breathlessness in elderly males and any associations with their duration, change over time, and mMRC grade.

We conducted a population-based, cross-sectional study of 73-year-old males in a county in southern Sweden. Breathlessness was self-reported at one time-point using a postal survey including the Dyspnoea-12 (D-12), the Multidimensional Dyspnoea profile (MDP), and the mMRC. Presence of an increased dimension score was defined as a score \geq minimal clinically important difference for each dimension scale. Association with mMRC, recalled change since age 65, and duration of breathlessness were analysed with linear regression.

Among 907 men, an increased dimension score was present in 17% (D-12 total score), 33% (MDP A1 unpleasantness), 19% (D-12 physical), 17% (MDP immediate perception), 10% (D-12 affective), and 17% (MDP emotional response). The unpleasantness and affective dimensions were strongly associated with mMRC ≥ 3 . Higher MDP and D-12 scores were associated with worsening of breathlessness since age 65, and higher MDP A1 unpleasantness was associated with breathlessness of less than one year duration.

Increased scores of several dimensions of breathlessness are prevalent in 73-year-old males and are positively correlated with mMRC scores, worsening of breathlessness after age 65, and duration of less than one year.

INTRODUCTION

Breathlessness is prevalent in the general population [1, 2] and is a dominant symptom of cardio-respiratory disease [2]. Approximately 10–25% of the middle-aged and older population experience breathlessness in their daily activities [2, 3]. Chronic breathlessness is persistent and disabling even after optimal treatment of underlying condition(s) [4]. It is an independent risk factor for morbidity and mortality among older adults [5] and is associated with reduced physical capacity, anxiety and depression, and impaired health-related quality of life [6-8].

Breathlessness is defined by the American Thoracic Society as “a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity” [9]. Breathlessness should therefore be seen as a multi-dimensional condition, comprising overall intensity, intensity of sensory qualities such as air hunger and chest tightness, level of unpleasantness and discomfort, with emotional responses such as fear and anxiety, and impacts on physical activity and function [6]. Research from the past decade has shown that different physiological conditions lead to differences in qualitative breathlessness experience, and these experiences may be relevant when assessing causes and symptomatic treatment of breathlessness [9]. The goal of developing new therapies for the alleviation of symptomatic chronic breathlessness requires knowledge of the prevalence of the known dimensions of breathlessness, as well as how these are related to the duration of the symptom and changes over time.

Previous epidemiological studies [10-12] have assessed the prevalence of breathlessness chiefly through the use of the modified Medical Research Council (mMRC) breathlessness scale [9, 13]. The mMRC scale is a uni-dimensional, ordinal scale assessing the degree of

exertion before breathlessness limits the person. It is scored from zero to four but does not assess the intensity or severity of symptoms *per se* or their affective and emotional impacts [9]. To measure multiple dimensions of breathlessness, Dyspnoea-12 (D-12) [14] and Multidimensional Dyspnoea profile [15] (MDP) are frequently used [16], both of which can summarise scores relating to specific dimensions of breathlessness. A common definition of clinically relevant breathlessness in population studies is an mMRC score ≥ 2 [17]. When using instruments which summarise domain scores in population studies, a common threshold to define a clinically relevant increased score often do not exist. Minimal clinically important differences (MCID) have emerged as a method of establishing a threshold at which a change in a symptom score becomes clinically relevant for the individual, which can be used as a treatment outcome in clinical trials. Recent studies have defined MCIDs for the D-12 and MDP [18, 19], but the MCID scores have not been used as a threshold for defining clinically relevant increased breathlessness in population studies before. The prevalence of dimensions of breathlessness and their intensities in the older population are unknown, as is their impact on physical limitations, how these change over time and their duration.

The primary aim of this study was to describe the prevalence of the dimensions of breathlessness and their intensities among elderly males measured using the D-12 and MDP. We also analysed these dimensions of breathlessness in relation to the mMRC score, duration of the symptom, and self-reported change since the age of 65.

METHODS

Study design and participants

Older males from Blekinge, Sweden were recruited in 2010 to the longitudinal VAScular and Chronic Obstructive Lung disease (VASCOL) study [20]. In 2019, when participants were approximately 73 years old, a postal survey focusing on breathlessness was sent to

participants with a known address. Data collection and the VASCOL study has been described [20]. Inclusion criteria for the present study were participants in the 2019 VASCOL study that completed the D-12, MDP, and mMRC breathlessness scales and responded to additional questions about the unpleasantness of breathlessness, its duration, and any changes over time.

Ethical considerations

The study was approved by the Swedish Ethical Review Authority (ref. 2019-00134). Written informed consent was obtained from all participants.

Assessments

Self-reported questionnaire data included height, weight, smoking history, and physician-diagnosed condition(s) which were categorised as lung disease (chronic obstructive pulmonary disease (COPD), asthma, tuberculosis, sleep apnoea, or other lung disease), cardiovascular disease (myocardial infarction, angina, atrial fibrillation, heart failure, valvular disease, bypass, aortic aneurysm, carotid artery stenosis, stroke), and diabetes.

Breathlessness was self-reported using the D-12, MDP, and mMRC instruments, with the focal period *during the past two weeks*. The D-12 tool consists of 12 items with descriptors of breathlessness. The physical dimension scale has a maximum score of 21, and the affective dimension scale has a maximum of 15 [14] for a possible total score of 36. The MDP consists of 11 items divided into three scales: A1 *unpleasantness* (range 0–10), *immediate perception* (range 0–60), and *emotional response* (range 0–50). Higher scores indicate increased severity. This study used validated Swedish versions of the D-12 and MDP [21, 22]. The mMRC version used in this study was translated from Mahler and Wells (1988) [23]. The D-12 total scores were imputed for 20 participants as recommended in the original paper [14]. No other

imputations were made. The participants were asked to grade the level of unpleasantness or troublesome breathlessness as none, mild, moderate, or severe. Recalled change in breathlessness since age 65 was measured with a seven-point ordinal Global Impression of Change (GIC) scale: very much better (1), much better (2), minimally better (3), no difference (4), minimally worse (5), much worse (6), or very much worse (7). Responses were categorised as better (1–3), no different (4), or worse (5–7). The participants were also asked to state how long they had experienced breathlessness in the number of years, less than one year, or “I do not remember”. The duration was categorised as <1 year, 1–5 years, or >5 years.

The prevalence of clinically relevant increased breathlessness dimension scores were reported by a score \geq MCID for each scale of D-12 and MDP. The MCID scores of the MDP and D-12 scales used in this study has been defined by previous studies [18, 19]. As an example, the MCID for the D-12 total (range 0-36) is a score of 2.83. MCID is usually used in treatment studies for defining a clinically significant change on a symptom scale, in comparison to a statistically significant change. Use of MCID increases comparability between scales. Hence reporting the prevalence of an increased breathlessness dimension score using the MCID of D-12 and MDP can be considered as a valuable complement to reporting crude scores.

Statistical analysis

Characteristics of the participants and the prevalence of score \geq MCID and non-zero scores of the D-12 and MDP dimension scales were tabulated using descriptive statistics. The percentage of participants with mMRC \geq 1 and scores \geq MCID of D-12 and MDP, as well as mMRC \geq 1 and non-zero scores of D-12 and MDP scales were tabulated. The mean of the MDP item-scores among participants reporting scores \geq MCID of *MDP A1 unpleasantness* were plotted. Differences in the D-12 and MDP dimension scales among the total study population relative

to mMRC score (each mMRC score 1–4 separately compared to the reference mMRC of 0), perceived change in breathlessness since age 65 (*worse* or *no difference* compared to the reference *better*), and duration of breathlessness (<1 year or >5 years compared to the reference 1–5 years) were analysed using linear regression. Beta coefficients and 95% confidence intervals (CI) were presented in forest plots. To facilitate comparison between dimension scales of different ranges, the beta coefficient as a percentage of the scale's range was also presented in the forest plots. For example, an MDP A1 beta coefficient of two will represent 20% of its range, since the maximum score of MDP A1 is ten. The D-12 and MDP dimension scale medians and interquartile ranges (IQR) of each category of mMRC, as well as the duration of and change in breathlessness, are presented in boxplots for comparison of linear regression estimates. In the linear regressions and boxplots including change and duration of breathlessness, participants who had not experienced breathlessness after the age of 65 years were excluded, as indicated by reporting mMRC grade 0 and that their breathlessness was unchanged since age 65. Statistical analysis was conducted with R 4.0.2 (R Foundation for Statistical Computing, Austria).

RESULTS

Patient characteristics

Of the 1193 men invited, 907 (76%) participated. Mean BMI was 27.1 (\pm 3.8) and mean years of smoking was 9.5 (16.2). At least one respiratory disease was reported by 17%, and at least one cardiovascular disease by 37% (table 1).

Prevalence of increased breathlessness dimension scores

The prevalence of an increased breathlessness dimension score \geq MCID was 17% based on the D-12 total, and 33% based on the MDP A1 unpleasantness. The prevalence of an increased breathlessness dimension scale with non-zero scores was 29% based on the D-12 total, and 33% based on the MDP A1 unpleasantness (table 3). The prevalence of scores \geq MCID and non-zero scores of all D-12 and MDP dimension scales are show in Table 3. The mean intensities of MDP item scores in participants reporting an MDP A1 unpleasantness score \geq MCID are shown Figure 1.

Associations with mMRC, and duration and change of breathlessness

Higher D-12 and MDP estimates were associated with higher mMRC scores with the reported unpleasantness and affective dimensions markedly greater in participants with mMRC \geq 3 scores (Figures 2, 3, 4), as well as with the reported change category *worse* (Figures 2, 3, [Supplemental Materials Figure S1](#)). Higher D-12 and MDP scores were associated with breathlessness of less than one year duration. The MDP A1 unpleasantness dimension was markedly increased in participants experiencing breathlessness of less than one year duration. The D-12 and MDP ratings were slightly higher in participants experiencing breathlessness for more than five years (Figures 2, 3). The median D-12 and MDP total scores were lower in participants experiencing breathlessness of less than one year duration. ([Supplemental Materials figure S2](#)). Overall, there were larger differences in-between the MDP subdomain scores compared to in-between the D-12 subdomain scores (Figures 2, 3).

DISCUSSION

This is the first epidemiological study of breathlessness from a multi-dimensional perspective in a sample from the general population. Multiple impacts and experiences of breathlessness were common in the studied elderly male population. A score \geq MCID by MDP A1 was reported by approximately one third of the subjects completing the MDP scales, while score \geq MCID as indicated by the D-12 total, D-12 physical, and MDP emotional response were present in approximately 20%. In the studied population, breathlessness was not dominated by a single dimension but included multiple dimensions that impact overall well-being. Level of perceived dimensions of breathlessness increased stepwise in relation to increasing mMRC scores. Unpleasant and affective dimensions (consequences of physical limitations due to breathlessness) increased in people with mMRC \geq 3.

Among the patients reporting a score \geq MCID by MDP A1, the mean values are similar across the MDP sensory qualities and emotional response scores which is similar to a study of patients admitted to hospital and reporting breathing discomfort [24]. However, our results differed from a study of COPD patients [25] that reported greater differences across MDP mean values in comparison to our study. Our study and that of hospitalised patients [24] included participants with multiple health conditions, possibly explaining the greater similarities across the MDP scores. This suggests that the profile may be disease-dependant, and supports previous research showing that qualitative experiences of breathlessness differ with pathophysiological mechanisms [9].

This study is the first evaluating the relationship between manifestations of breathlessness and mMRC scores at a population level. The MDP A1 and D-12 affective scales correlated with mMRC 3, suggesting the unpleasant and affective dimensions of breathlessness are worse in

subjects in whom minimal exertion induces breathlessness. The severity of all dimension scales of breathlessness in individuals with an mMRC score ≥ 3 suggests that focus in clinical practice should be on patients' experiences of breathlessness and not only on limits to activity, as previously suggested [26]. This is especially true if the aim is to improve patient overall well-being by treating symptoms of severe breathlessness. Some participants reported increased breathlessness dimension scores not detected by the mMRC as seen in Figure 4 and reinforced in the lower overlap percentages in Table 3. This further suggests that the mMRC only evaluates some aspects of breathlessness given that it is uni-dimensional. The mMRC is shorter and more suitable than the D-12 and MDP as a screening tool in clinical practice. However, the D-12 and MDP can be used as additional tools for evaluate individuals with an mMRC score ≥ 2 .

Our findings suggest that the breathlessness dimension scores may take the form of a U-shaped curve related to its duration. The severity was lower in the group experiencing breathlessness for one to five years, compared to the groups experiencing breathlessness for less than one year or five years or more. People affected by breathlessness may adapt and learn to cope with the symptoms over time. This relates to the Hutchinson et al. [26] concept of "breathing space," which suggests that personal limitations depend on how the individual is engaged in coping with and seeking help for breathlessness, along with the health care professional's responsiveness [26]. This finding of a U-shaped relationship between the breathlessness dimension scores and its duration is also mirrored by a previously reported U-shaped relationship between breathlessness and quality of life; postulated to be due to a similar mechanism of adaptation over time [27, 28].

This study included the largest sample to date of participants reporting breathlessness-related data using validated instruments. The population characteristics were similar to those of the age-matched male general population in Sweden [20]. The prevalence of non-zero scores was

higher compared to scores \geq MCID. Using scores \geq MCID to report prevalence of increased breathlessness dimensions could be seen as a strength as it reports experiences that are of clinical relevance to the participant as opposed to non-zero scores. MCID can therefore be seen as less “noisy” than non-zero scores as MCID can filter out temporary worsening. Also, the MCID simplifies the comparison between scales of different ranges, which was very important in this study. However, this is the first use of MCID as a threshold to define the prevalence of clinically relevant dimension scores of breathlessness, and the validity of this approach is therefore uncertain. The usage of MCID in population studies of breathlessness and other symptoms needs to be further evaluated in future studies, for example by exploring the association to future health events and mortality. The linear regression models used in this study should be seen as robust, as the results were reinforced by the calculated medians, which showed a similar pattern in most analyses.

The study was restricted to 73-year-old males, effectively eliminating sex- or age-related bias in the analyses. However, the findings may not be generalisable to females and other age groups. The VASCOL study is an ongoing study and is planning to recruit females and younger age groups in the next follow-up [20]. The prevalence of COPD and asthma was slightly lower than previously reported among males and females of the same age [29, 30]. The prevalence of breathlessness as established by mMRC among males was similar to that found in previous studies, but the prevalence of breathlessness indicated by mMRC has been shown to be higher among females [31]. Another limitation is that the duration of, and change in, breathlessness was not based on objective data, but on recall, as breathlessness was not measured among the participants at the age of 65 years. Among other symptoms the highest and final experienced intensity has been shown to be what the individual recalls, the so called “peak-end-rule”[32]. If the same is true with breathlessness, this could impact the result in our study to overestimate the breathlessness intensities, especially as the final

experiences of breathlessness among the participants might be more severe at the age of 73 than 65. However, the knowledge of recalled breathlessness is lacking and needs to be further investigated [32]. Breathlessness can also be avoided by the individual until the symptom gets sufficiently severe to interfere with the basic instrumental activities of daily living, as suggested previously [9]. We used a postal survey to examine recalled breathlessness in the past two weeks, and not breathlessness during a standardised recalled activity. This will lead to a systematic (and unquantifiable) underestimate of the prevalence of increased breathlessness dimensions in our study. We did not explore how breathlessness dimension scores differs between conditions and how individual items relates with duration. Future studies should therefore explore breathlessness profiles on item level in relation to conditions and duration. Follow-up studies within the VASCOL study are planned to measure and validate the change and duration of multiple dimensions of breathlessness longitudinally.

CONCLUSIONS

This study demonstrates that multiple increased dimension scores of breathlessness are common in a population of elderly males. More severe impacts are associated with higher mMRC score, with worsening breathlessness after 65 years and with duration less than one year. Increased breathlessness is a public health issue in elderly males with high prevalence of increased dimension scores and unpleasantness manifestations. Increased awareness of the multiple aspects of the condition could enhance the health of older men affected by severe breathlessness.

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TABLES

TABLE 1 Characteristics of 907 men aged 73 years.

Variable (non-missing observations)	Value
Age years	73.2 (0.67)
Body mass index, kg/m ² (n=895)	27.1 (3.8)
Smoking status (n=892)	
Daily	41 (6%)
Sometimes	11 (1%)
Former smoker	530 (59%)
Never smoker	310 (35%)
Pack-years of smoking (ever smokers) (n=522)	9.1 (6.08 – 18.2)*
Respiratory disease (n=861)	143 (17%)
Asthma	47 (5%)
COPD	32 (4%)
Sleep apnoea	79 (9%)
Tuberculosis	3 (1%)
Cardiovascular disease (n = 861)	318 (37%)
Angina pectoris	62 (7%)
Atrial fibrillation	135 (16%)
Carotid artery stenosis	24 (3%)
Heart failure	35 (4%)
Myocardial infarction	79 (9%)
Stroke	66 (8%)
Valvular heart disease	43 (5%)
Diabetes mellitus	146 (17%)

Data are means (SD), or frequency (percentage), *medians (1st and 3rd quartile). COPD =

Chronic obstructive pulmonary disease.

TABLE 2 Distribution of breathlessness scores in 907 men aged 73 years

Item (Non missing observations)	Mean (SD) or Frequency (%)
Dyspnoea-12 scales	
Total (n = 858)	1.62 (4.0)
Physical (n = 846)	1.08 (2.5)
Affective (n = 850)	0.54 (1.7)
Multidimensional Dyspnea Profile scales	
A1 unpleasantness (n=830)	0.71 (1.4)
Immediate perception (n=721)	2.62 (6.4)
Emotional response (n=809)	1.77 (5.1)
mMRC (n=880)	
0	606 (67%)
1	120 (13%)
2	71 (8%)
3	44 (5%)
4	39 (4%)
Breathlessness severity (n=844)	
None	555 (66%)
Mild	186 (22%)
Moderate	98 (12%)
Severe	5 (1%)
Recalled change in breathlessness since age 65 years (n=900)	
Better	97 (11%)

No difference	543 (60%)
Worse	260 (29%)

Recalled duration of experienced

breathlessness (n = 167)

Less than one year	48 (29%)
One to five years	72 (43%)
More than five years	47 (28%)

Data are means(SD) or frequency (percentage). A higher score on D-12 or MDP scales signify worse breathlessness. Recalled change in breathlessness since age 65 years was measured through global impression of change (GIC). mMRC = Medical Research Council breathlessness scale.

TABLE 3 Prevalence and distribution of breathlessness based on D-12 and MDP.

	Dyspnoea-12 scales			Multidimensional Dyspnoea profile scales		
	<i>Total (0–36)</i>	<i>Physical (0–21)</i>	<i>Affective (0–15)</i>	<i>A1 unpleasantness (0–10)</i>	<i>Immediate Perception (0–60)</i>	<i>Emotional Response (0–50)</i>
Score > 0, n (%)	249 (29)	244 (29)	119 (14)	271 (33)	285 (40)	194 (24)
mMRC \geq 1 and Score > 0, n (%)	162 (19)	160 (19)	93(11)	169 (21)	157 (22)	106 (13)
Mean	5.6 (5.9)	3.7 (3.5)	3.8 (3)	2.2 (1.6)	6.6 (8.7)	7.4 (8.2)
Median	3 (1–8)	2 (1–5)	3 (1–5)	2 (1–3)	3 (1–8)	4 (2–9)
Score \geq MCID, n (%) *	144 (17)	162 (19)	89 (10)	271 (33)	120 (17)	134 (17)
mMRC \geq 1 and score \geq MCID, n (%)	114 (14)	119 (14)	71 (9)	169 (21)	80 (11)	80 (10)
Mean	8.7 (6.1)	5.1 (3.5)	4.8 (2.9)	2.2 (1.6)	13.2 (10.3)	10 (8.7)
Median	7 (4–11)	4 (2–7)	4 (3–6)	2 (1–3)	9 (6–16)	6.5 (4–14)

Data are presented as mean(SD), median (1st and 3rd quartile), or frequency (percentage). A higher score on D-12 or MDP scales signify worse breathlessness. *MCID values used for stratification were based on previous research[18] as follows: D-12, total =

2.83; physical subdomain = 1.81; affective subdomain = 1.07. MDP A1 = 0.82; MDP immediate perception = 4.63, MDP emotional response = 2.37. MCID = minimal clinically important difference.

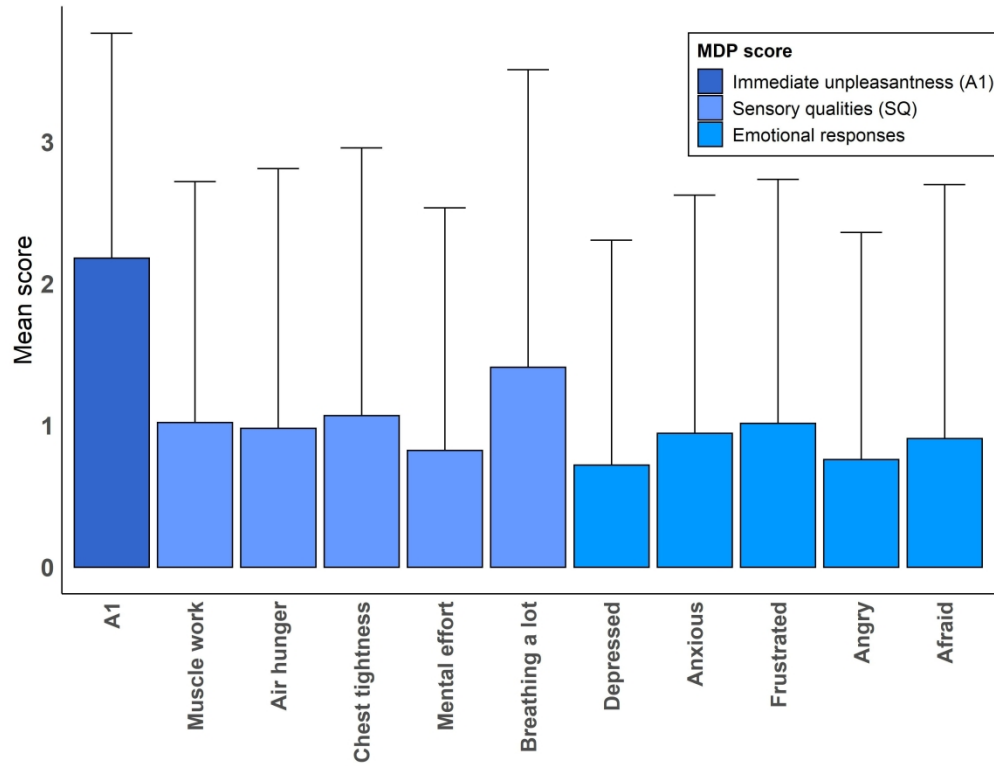


FIGURE 1 Dyspnoea profiles among 271 men experiencing unpleasant breathlessness. Intensity of MDP A1 unpleasantness, sensory qualities, and emotional response. Participants with an MDP A1 unpleasantness score > minimal clinically important difference (MCID). Standard deviation is marked by the error bars. MDP = Multidimensional Dyspnea Profile,

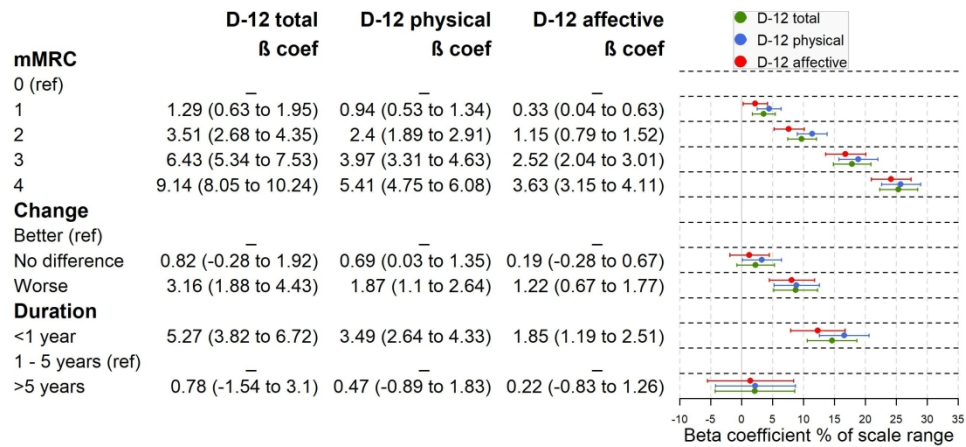


FIGURE 2 Dyspnoea-12 scales relative to mMRC score, duration of and of breathlessness. Table shows beta coefficients (CI) from simple linear regression. To facilitate comparison between scales of different ranges, the points represent the beta coefficient percentage of scale range with 95 % CI. β coef = Beta coefficient, D-12 = Dyspnoea-12, mMRC = modified Medical Research Council breathlessness scale; ref = reference.

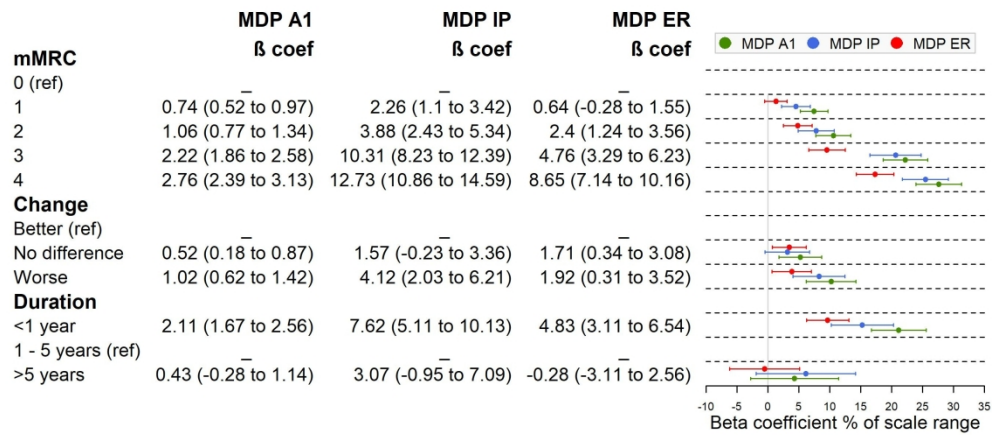


FIGURE 3 MDP scales relative to mMRC score and duration and change of breathlessness. Table shows beta coefficients (CI) from simple linear regression. To facilitate comparison between scales of different ranges, the points represent the coefficients percentage of scale range with 95 % CI. β coef = Beta coefficient, ER = emotional response, MDP = Multidimensional Dyspnea Profile, mMRC = modified Medical Research Council breathlessness scale, IP = immediate perception, ref = reference.

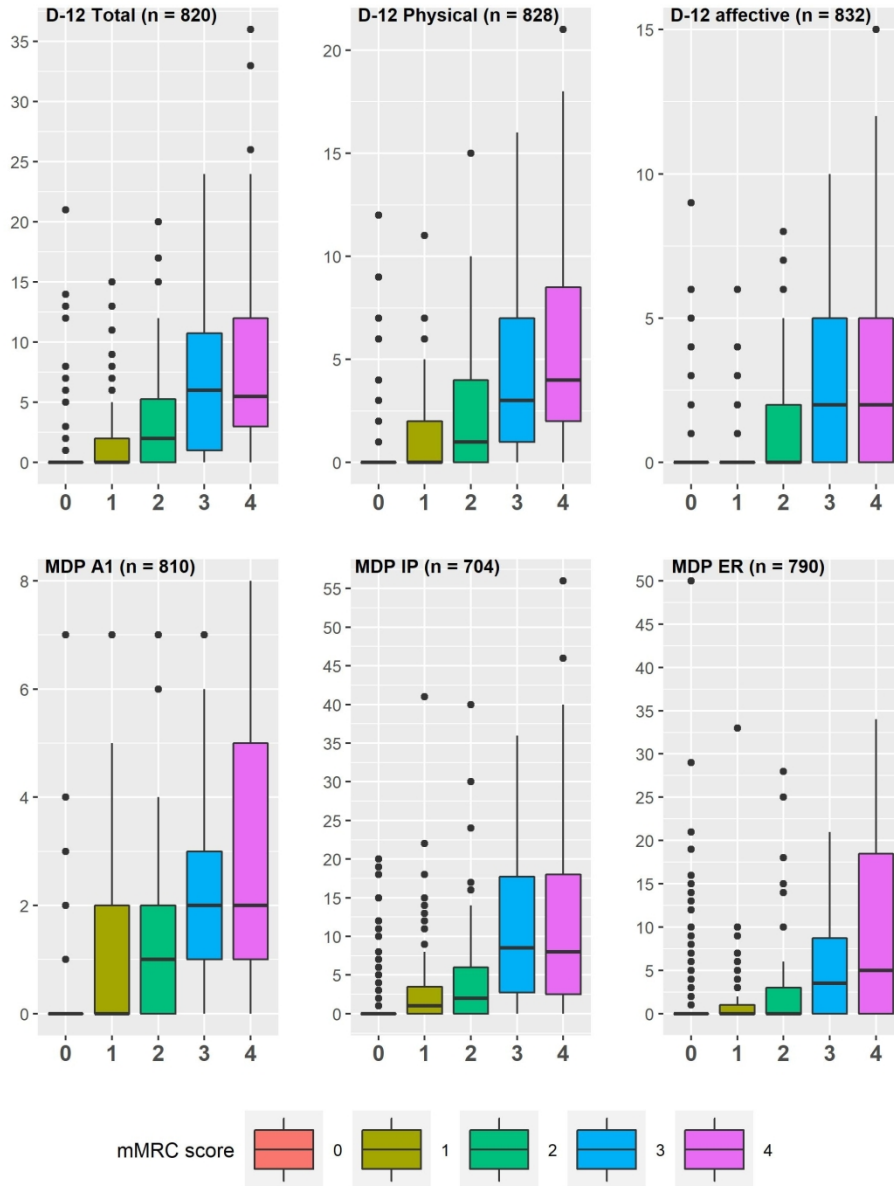


FIGURE 4. Median scores of D-12 and MDP relative to mMRC categories in 73-year-old males. Whiskers represent IQR times 1.5 with outliers represented by dots. D-12 = Dyspnoea-12, ER = emotional response; MDP = Multidimensional Dyspnea Profile; mMRC = Medical Research Council breathlessness scale; IP = immediate perception.

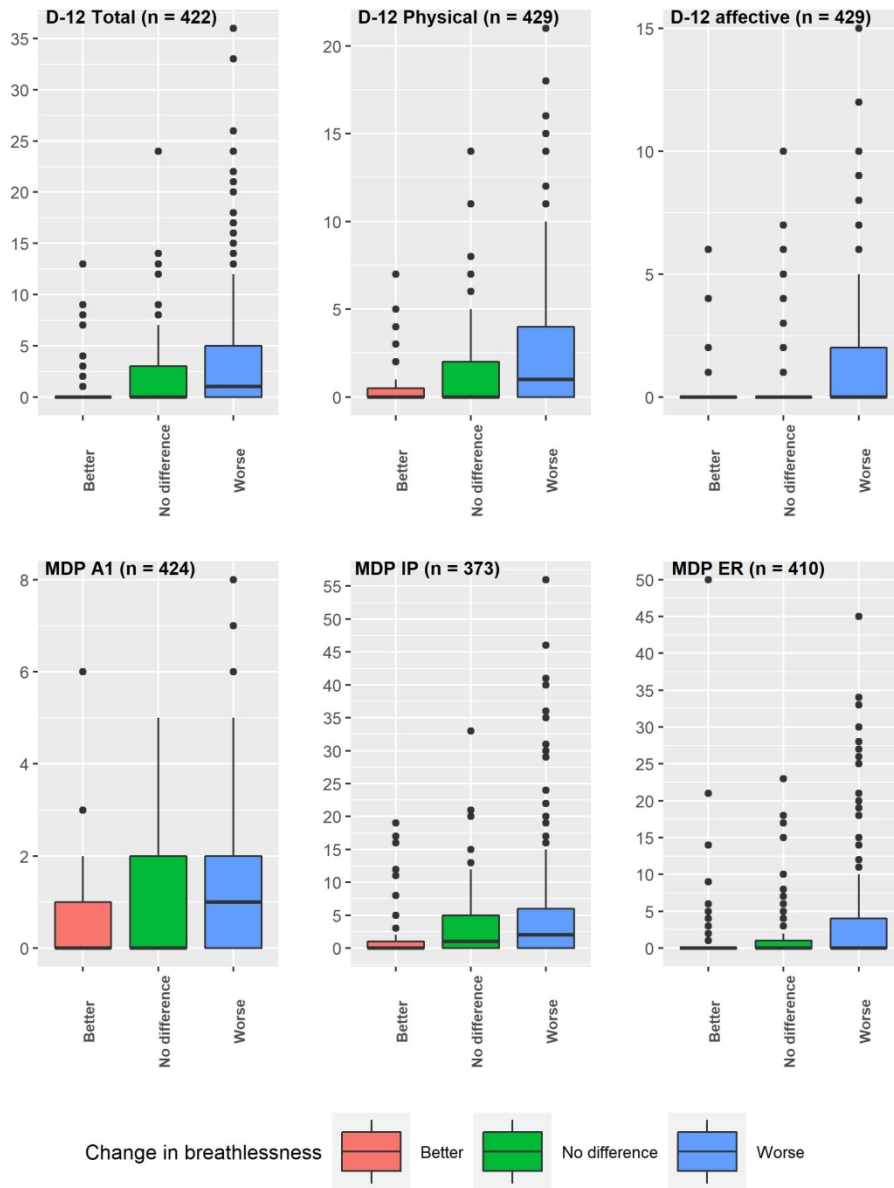


FIGURE S1. Median score of D-12 and MDP relative to experience of change in breathlessness categories in 73-year-old males with available data experiencing breathlessness since age 65 years. Whiskers represent IQR times 1.5. D-12 = Dyspnoea-12, ER = emotional response; MDP = Multidimensional Dyspnea Profile.

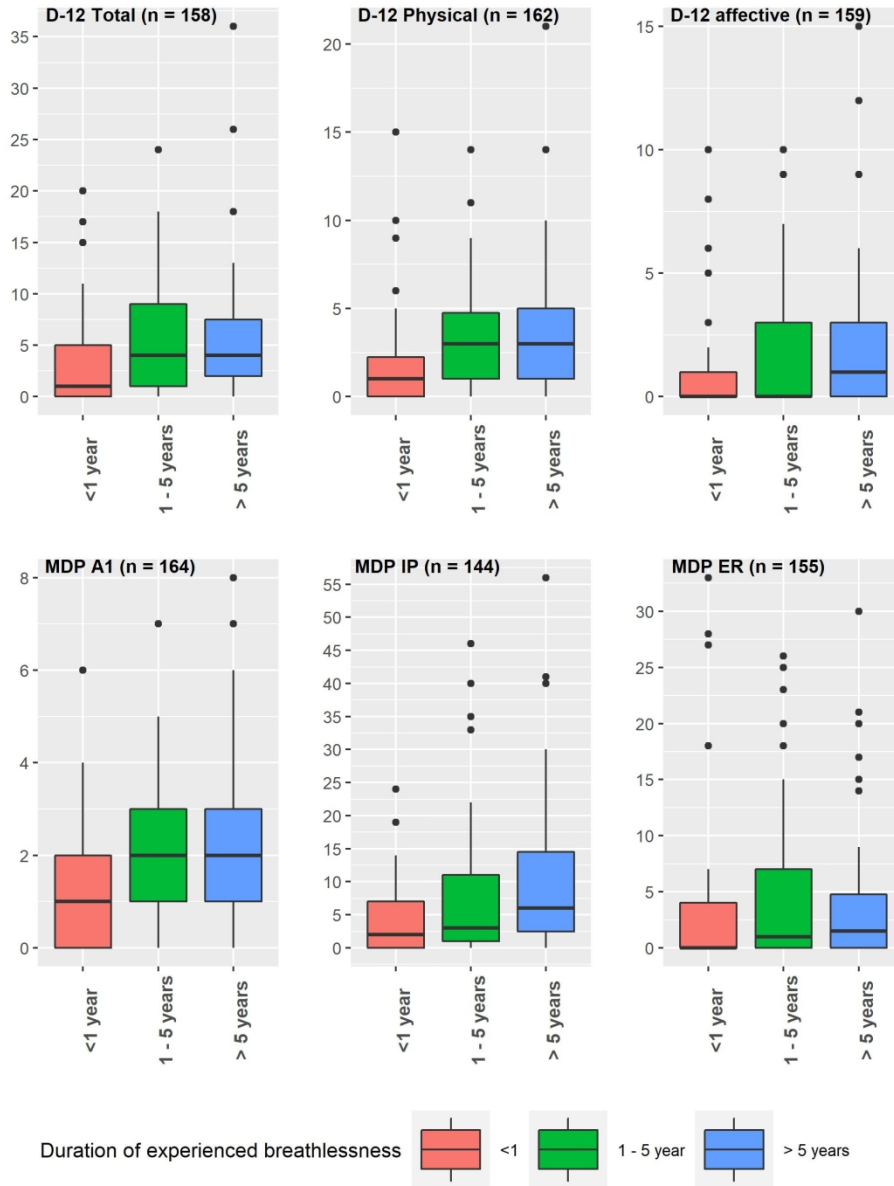


FIGURE S2 Median score of D-12 and MDP in duration of breathlessness categories in 73-year-old males with available data experiencing breathlessness since age 65 years. Whiskers represent IQR times 1.5 with outliers represented by dots. D-12 = Dyspnoea-12, ER = emotional response; MDP = Multidimensional Dyspnea Profile.