

**Brief Report****Personalized Goal for Dyspnea and Clinical Response in Advanced Cancer Patients**

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**Abstract**

**Background.** The clinical response after comprehensive symptom management is difficult to determine in terms of a clinically important difference. Moreover, therapies should try to reach the threshold perceived by the individual patient for the determination of a favorable response to a treatment.

**Measures.** The Edmonton Symptom Assessment Score (ESAS) was measured at admission (T0), and seven days after starting palliative care (T7). Patient Global Impression and Goal Response after one week of palliative care and its relation with the Personalized Dyspnea Goal were measured at T7.

**Intervention.** Patients admitted to palliative care units underwent a comprehensive symptom assessment by a specialist palliative care team. At T0, patients were asked about their Personalized Dyspnea Intensity Goal on ESAS. One week later (T7), after a comprehensive palliative care treatment, Personalized Dyspnea Intensity Goals were measured again. Patients were considered to have achieved a Patient Dyspnea Goal Response if dyspnea intensity (measured at T7) was equal or less than their expected Personalized Dyspnea Intensity Goal. At the same interval (T7), Patient Global Impression (improvement or deterioration) was measured.

**Outcomes.** 279 patients were analyzed in this study. The mean Personalized Dyspnea Intensity Goal at T0 and T7 were 0.97 (SD 1.3), and 0.71 (SD 2.1), respectively. 263 patients (94.2%) indicated a Personalized Dyspnea Intensity Goal of  $\leq 3$  as a target at T0. Patients perceived a bit better, a better improvement, and a much better improvement with a mean decrease in dyspnea intensity of -2.1, -3.5, and -4.3 points on the dyspnea intensity scale, respectively. In 60 patients (21.5%), dyspnea intensity did not change, and in 4.7%, dyspnea intensity worsened. Patients perceived a Minimal Clinically Important Difference (little worse) with a mean increase in dyspnea intensity of 0.10, and they perceived a worse with a mean increase of 1.7 points. Higher dyspnea intensity at T0 and lower dyspnea intensity at T7 were independently related to Patient Global Impression. At T7, 93 (33.3%) patients achieved their Personalized Goal Response, based on Personalized Dyspnea Intensity. Patient Dyspnea Goal Response was associated with Memorial Delirium Assessment Scale score and Personalized Dyspnea Intensity Goal at T0, and inversely associated with dyspnea intensity at T0 and T7, and lower Karnofsky level. For Patient Dyspnea Goal Response, no significant differences among categories of dyspnea intensity were found ( $P > 0.05$ ).

**Conclusion.** Patient Dyspnea Goal Response and Patient Global Impression seem to be relevant for evaluating the effects of a comprehensive management of symptoms, including dyspnea, assisting decision making process. Some factors may be implicated in determining the individual target and clinical response. A personalized symptom goal may translate in terms of

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therapeutic intervention, according to the achievement of the patients' expectations. High values of dyspnea intensity, a lower Karnofsky level, as well as high level of Dyspnea Intensity Goal (that is less patients' expectations) favor the achievement of the target. *J Pain Symptom Manage* 2019;57:79–85. © 2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

### Key Words

Advanced cancer, dyspnea, symptom assessment, palliative care, personalized symptom goal, global impression of change

## Introduction

Patients with chronic dyspnea represent a clinical challenge. As dyspnea is multifactorial and subjective, assessment and outcome measurement are difficult. As inadequate assessment is a relevant barrier for an appropriate management, dyspnea assessment is of paramount importance.<sup>1</sup> Currently, symptom assessment reported by the patient also is the gold standard to evaluate clinical response. The Edmonton Symptom Assessment System (ESAS) is the most common tool used to assess both physical and psychological symptoms and includes multiple unidimensional numeric rating scales that range from 0 (no symptom) to 10 (worse possible).<sup>2,3</sup> This tool has some important limitations because of its subjectivity; patients may individually interpret the scale, expressing symptom intensity with significant variations.

The clinical response after a comprehensive symptom management is started is also difficult to determine in terms of a clinically important difference. Minimal clinically important difference has been reported to be the smallest amount of change required to impact the patient's feeling of improvement or deterioration of a certain symptom. For dyspnea, minimal clinical intensity difference has been the subject of recent research and corresponds to the change in intensity the patient can perceive as improvement or deterioration. Different tools have been variably considered as methods to assess minimal clinical intensity difference, including the distribution method, based on fractionations of SD or standard error<sup>5</sup> and the use of anchors, such as changes of intensity categories of well-being,<sup>6</sup> the magnitude of change in the patient-reported outcome, or the optimal balance between sensitivity and specificity. Considering the need to evaluate the individual variations in assessing scales or numbers, the use of the Patient Global Impression also has been suggested; this is a validated global rating-of-change scale that assesses patients' subjective response based on the individual feeling of improvement or deterioration, after administering a particular treatment.<sup>7,8</sup>

Therapies should try to reach the threshold perceived by the individual patient for the determination of a favorable response to a treatment. To explore

this concept, a Personalized Dyspnea Goal has been recently introduced as an assessment tool to tailor symptom management, providing a therapeutic "target" that is simple, and individual.<sup>7,8</sup> The Personalized Dyspnea Goal Response has also been defined and is the achievement of the individual desired Patient Dyspnea Goal; it, too, is practical and meaningful. The factors associated with Personalized Dyspnea Goal, Patient Global Impression, and Patient Dyspnea Goal Response have not been examined. Previous studies have variably assessed these points for some symptoms, especially for pain.<sup>6–9</sup> The aim of this study was to characterize the Patient Dyspnea Goal and Patient Dyspnea Goal Response, and Patients Global Impression after 1 week of a comprehensive symptom management in advanced cancer patients admitted to palliative care units. The secondary aim was to find possible factors influencing the clinical responses assessed as Patient Dyspnea Goal Response and Patient Global Impression.

## Methods

This is a secondary analysis of a large international study.<sup>10</sup> The aim of this study was to characterize the Patient Global Impression after one week of palliative care and its relation with the Personalized Dyspnea Goal in advanced cancer patients admitted to a palliative care unit. The secondary outcome was to find possible factors influencing these outcomes. The original study was conducted in accordance with the amended Declaration of Helsinki. Local institutional review boards at all participating centers approved the protocol, and written informed consent was obtained from all patients. Patients were admitted to palliative care units.

## Participants

All patients underwent a comprehensive symptom assessment by a specialist palliative care team. Age  $\geq 18$  years and a diagnosis of advanced cancer were the inclusion criteria, whereas exclusion criteria were no dyspnea, a life expectancy of less than 14 days, and a significant level of cognitive failure, corresponding to a score of  $\geq 13$  in the Memorial Delirium Assessment Scale (MDAS).<sup>11</sup>

### Data Collection

Age, gender, condition, education level, primary diagnosis, and Karnofsky performance status were recorded. The intensity of symptoms included in the ESAS (pain, fatigue, nausea, depression, anxiety, drowsiness, dyspnea, appetite, feelings of well-being, and sleep) were measured at admission (T0), and seven days after starting palliative care (T7). ESAS is a well-validated self-reported tool assessing the intensity of most common psychological and physical symptoms; it is responsive to changes produced by therapeutic intervention. ESAS uses a numeric rating scale for each symptom from 0 (no symptom) to 10 (worst intensity) over the past 24 hours.<sup>2,3</sup>

At T0, patients were asked about their Personalized Dyspnea Intensity Goal. The question was “At what level would you feel comfortable with dyspnea?” using the 0–10 numeric rating scale used for ESAS.<sup>8</sup> Comprehensive palliative care treatment was started according to patients’ needs and local policy. One week later (T7), the ESAS and the Personalized Dyspnea Intensity Goal were measured again to detect changes after a palliative care intervention. Patients were considered to have achieved a Patient Dyspnea Goal Response if their follow-up intensity (measured at T7) was equal to or less than their expected Personalized Dyspnea Intensity Goal. At the same interval (T7), Patient Global Impression (improvement or deterioration) was measured according to the following scale: 3 = much better, 2 = better, 1 = a bit better, 0 = the same, –1 a little worse, –2 worse, –3 much worse. This global response has been used as an anchor for a clinically significant change of symptom intensity,<sup>7,8</sup> and the minimal clinically important difference was calculated by evaluating the Patient Global Impression of improvement or deterioration at T7 (bit better or a little worse, respectively).

### Statistical Analysis

Descriptive statistics (means [ $\pm$ SD] for continuous data, and proportions for categorical data) were summarized for sociodemographics, clinical characteristics, disease, and self-management data. Frequency analysis was performed using the Pearson’s chi-square test and Fisher exact test, as needed. The paired samples Student’s t-test was used to compare mean patient characteristic changes and their corresponding SD with 95% CIs, with Type I error set at 5%. For paired differences between dyspnea grading (no severe/severe) at different time intervals, McNemar’s test was performed. Patient Global Impression was categorized into three classes: deterioration (–1, –2, and –3), no change (=0), improvement (+1, +2, +3). The univariate analysis of variance was performed to evaluate difference between patient

clinical characteristics, and post hoc analysis with the Bonferroni test was used to determine whether there were pairwise differences. Multivariate logistic regression analysis was performed on the significant variables at analysis of variance to examine the correlation between patient characteristics (independent variables), and Patient Global Impression groups (dependent variable). Pearson correlation analysis was conducted to examine the association between Patient Dyspnea Global Response and patient clinical variables. Data were analyzed by IBM SPSS Software 22 version (IBM Corp., Armonk, NY). All *P*-values were two sided, and *P* < 0.05 was considered statistically significant.

### Results

Eight hundred seventy-six patients meet the inclusion criteria and were taken into consideration in the original study. Five hundred eighty-five patients had no dyspnea and 12 patients did not have assessment at T7. Thus, 279 patients were analyzed in this study.

Patients’ characteristics are presented in [Table 1](#).

The mean age was 68.2 (SD 11.1) years, 141 patients (50.5%) were males, and the mean Karnofsky level was 51.1 (SD 12.2). The mean MDAS value was 4.4 (SD = 3.4), with 76 patients (27.2%) having an MDAS of 7–12 at T0.

The mean intensities of dyspnea at T0 and T7 were 4.9 (SD 2.3) and 2.8 (SD 2.3), respectively, with a mean difference of 2.1 (SD 2.2) points (*P* < 0.0005). Seventy-seven (27.6%) and 22 patients (7.9%) reported severe intensity in dyspnea ( $\geq 7/10$ ), at T0 and T7, respectively. The difference was highly significant (*P* < 0.0005, McNemar test).

#### Patient Dyspnea Goal

Most patients (*n* = 263, 94.2%) indicated a Personalized Dyspnea Intensity Goal of  $\leq 3$  as a target at T0. The mean values of Personalized Dyspnea Intensity Goal at T0 and T7 were 0.97 (SD 1.3) and 0.71 (SD 2.1), respectively ( $\Delta$  –0.27; SD 2.1). Thus, the Personalized Dyspnea Intensity Goal significantly changed after one week (*P* = 0.039).

#### Patient Global Impression

Data regarding Patient Global Impression are presented in [Table 2](#). Patients perceived a minimal clinically important difference (a bit better) with a mean decrease in dyspnea intensity of –2.1. A better improvement and a much better improvement corresponded to a mean change of –3.5 and –4.3 points on the dyspnea intensity scale, respectively. In 60 patients (21.5%), dyspnea intensity did not change. In a minority of patients (13; 4.7%), dyspnea intensity worsened. Patients perceived a minimal clinically important difference

Table 1  
Characteristics of Patients

	No. of Patients (%)
Age (yrs)	
Mean	68.2 (11.1)
Range	35–92
Gender	
Male	141 (50.5)
Female	138 (49.5)
Karnofsky Performance Status	
Mean	51.1 (12.2)
Range	5–100
Primary tumor	
Gastrointestinal	32 (11.5)
Lung	127 (45.5)
Breast	28 (10.0)
Prostate	7 (2.5)
Urological	11 (3.9)
Gynecological	21 (7.5)
Head-neck	12 (4.3)
Hematological	7 (2.5)
Liver	5 (1.8)
Pancreas	13 (4.7)
Others	16 (5.7)
Education	
Illiterate	4 (1.4)
Primary	88 (31.5)
Secondary	73 (26.2)
Tertiary or undergraduate	83 (29.7)
Degree	29 (10.4)
	Two missing
House situation	
Alone	41 (14.7)
Partner	124 (44.4)
Partner and sons	64 (22.9)
Sons	32 (11.52)
Nursing home	1 (0.4)
Others	14 (5.0)
	Three missing

(little worse) with a mean increase in dyspnea intensity of 0.10 (SD 1.3), and they perceived a worse with a mean increase of 1.7 (SD 2.9) points.

In the univariate analyses, Personalized Dyspnea Intensity Goal at T0 and at T7 and age were related to Patient Global Impression, categorized into three classes (no change, 1 = improvement (+1, +2 or +3), 2 = deterioration (−1, −2, or −3) (Table 3). In the multiple logistic regression analysis, higher dyspnea intensity at T0 and lower dyspnea intensity at T7 were independently related to Patient Global Impression (Table 4).

#### Personalized Dyspnea Goal Response

At T7, 93 (33.3%) patients achieved their target, based on the Personalized Dyspnea Intensity Goal

(i.e., Personalized Dyspnea Goal Response). Factors related to Personalized Dyspnea Goal Response were associated with the MDAS score and Patient Dyspnea Goal at T0 and were inversely associated with dyspnea intensity at T0 and T7, and lower Karnofsky level (Table 5).

Patients with higher dyspnea intensity at T0 achieved a favorable Patient Global Impression ( $P < 0.0005$ ), even when the target, based on Patient Dyspnea Goal (i.e., Personalized Dyspnea Goal Response), was not achieved. For Personalized Dyspnea Goal Response, no significant differences among categories of dyspnea intensity were found ( $P > 0.05$ ) (Table 6).

#### Discussion

The analysis gathered from an international multi-center study with a large number of patients provided interesting data that could help physicians in personalizing the management of dyspnea, focusing on how much patients would like to improve their level of dyspnea and how physicians may be able to achieve their target. Intensity of dyspnea significantly improved after one week of comprehensive palliative care treatment. Patients were able to perceive a minimal improvement of dyspnea with a change of two points in dyspnea intensity.

#### Patient Dyspnea Intensity Goal

The Personalized Dyspnea Intensity Goal provides relevant insights for the interpretation of the numerical scale 0–10. Although some cutoffs have been reported for mild, moderate, and severe intensity, not all patients interpret the scale similarly.<sup>12</sup> The use of a Personalized Dyspnea Intensity Goal has obvious clinical implications, suggesting a reasonable individual target. For example, some patients may be comfortable even with an intensity of 6 or more. The percentage of patients who reach their target could be more important than the average change in dyspnea intensity. Most patients indicated a Personalized Dyspnea Intensity Goal of  $\leq 3$ , as reported in previous studies, where a median of 2 was found for dyspnea.<sup>7</sup> Of interest, the Personalized Dyspnea Intensity Goal further decreased after one week, as patients would have even more expectations after they had an improvement in dyspnea or after achieving their

Table 2  
Minimal Clinical Difference According to Patient Global Impression After Comprehensive Symptom Management

	Patient Global Impression						
	Much Better	Better	A Bit Better	The Same	A Little Worse	Worse	Much Worse
Dyspnea							
N	23	44	89	105	10	6	2
Mean (SD)	−4.3 (1.6)	−3.5 (1.9)	−2.1 (1.5)	−1.5 (2.2)	0.10 (1.3)	1.7 (2.9)	0

Table 3  
ANOVA Analysis

Variables	N	Patient Global Impression			P
		No Change	Improvement	Deterioration	
		105	156	18	
Age	Mean (SD)	65.8 (12.0)	69.3 (10.6)	72.9 (7.8)	0.007 1 vs. 0, <i>P</i> = 0.035 2 vs. 0, <i>P</i> = 0.033
Karnofsky Dyspnea T0	Mean (SD)	51.7 (12.1)	50.8 (12.2)	51.2 (13.1)	0.816
	Mean (SD)	3.9 (2.3)	5.4 (2.1)	5.7 (2.4)	<0.0005 1 vs. 0, <i>P</i> < 0.0005 2 vs. 0, <i>P</i> = 0.004
Dyspnea T7	Mean (SD)	2.4 (2.3)	2.6 (1.9)	6.3 (2.2)	<0.0005 2 vs. 0, <i>P</i> < 0.0005 2 vs. 1, <i>P</i> < 0.0005
MDAS	Mean (SD)	4.6 (3.5)	4.3 (3.5)	3.9 (3.1)	0.641
Patient Dyspnea Intensity Goal T0	Mean (SD)	0.4 (0.8)	1.3 (1.4)	1.0 (1.6)	<0.0005
	Mean (SD)	0.4 (0.9)	0.9 (2.7)	1.2 (2.4)	1 vs. 0, <i>P</i> < 0.0005 0.137

ANOVA = analysis of variance; MDAS = Memorial Delirium Assessment Scale.  
Patient Global Impression was categorized into three classes: no change, improvement, deterioration.

initial target. This observation was similarly found for pain, in contrast with other studies in which expectations did not change after symptom management.<sup>10</sup> This could be explained by the undetermined follow-up visits, mainly two to three weeks, in an outpatient setting in comparison with an inpatient acute setting.<sup>7,9</sup>

*Patient Global Impression*

The Patient Global Impression for dyspnea was positive in the majority of patients, with 156 (55%) of them reporting an improvement in dyspnea intensity. This could be explained by the decrease in dyspnea intensity measured with ESAS after a comprehensive management by experienced palliative care physicians. Seven days are a meaningful period to reach a symptom stabilization in patients admitted to a setting like a palliative care unit, where symptom management is more intensive.<sup>13</sup> Patients perceived a minimally clinically important difference with a decrease in dyspnea intensity of about two points,

whereas a better improvement and a much better improvement required a decrease in pain intensity of about 3.5 and 4.3 points, respectively.

The factors principally related to improvements of Patient Global Impression for dyspnea have never been explored. We found that the higher the dyspnea

Table 5  
Factors Associated With Patient Dyspnea Goal Response

	Patient Dyspnea Goal Response
Age	
Pearson correlation	-0.071
<i>P</i> (two-tailed)	0.235
<i>N</i>	279
Gender	
Pearson correlation	0.061
<i>P</i> (two-tailed)	0.314
<i>N</i>	279
MDAS	
Pearson correlation	0.128
<i>P</i> (two-tailed)	0.036
<i>N</i>	267
Karnofsky	
Pearson correlation	-0.132
<i>P</i> (two-tailed)	0.029
<i>N</i>	276
Dyspnea T0	
Pearson correlation	-0.271
<i>P</i> (two-tailed)	<0.0005
<i>N</i>	279
Patient Dyspnea Goal T0	
Pearson correlation	0.330
<i>P</i> (two-tailed)	<0.0005
<i>N</i>	279
Dyspnea T7	
Pearson correlation	-0.832
<i>P</i> (two-tailed)	<0.0005
<i>N</i>	279
Patient Dyspnea Goal T7	
Pearson correlation	-0.104
<i>P</i> (two-tailed)	0.082
<i>N</i>	279

Table 4

Patient Global Impression

Patient Global Impression	OR	OR (95% CI)	<i>P</i>
No change			
Dyspnea T0	1.98	1.10–3.60	0.024
Dyspnea T7	0.29	0.16–0.53	<0.0005
Age	0.93	0.87–0.99	0.041
Patient Dyspnea Goal T0	0.75	0.45–1.24	0.265
Improvement			
Dyspnea T0	2.91	1.60–5.30	<0.0005
Dyspnea T7	0.22	0.12–0.41	<0.0005
Age	0.96	0.90–1.03	0.294
Patient Dyspnea Goal T0	1.31	0.82–2.09	0.255

OR = odds ratio.  
Multiple logistic regression in reference to category of deterioration.

Table 6  
Patient Dyspnea Goal Response and Patient Global Impression, According to the Categories of Dyspnea Intensity Measured at T0

Dyspnea T0	Mild (n, %) 91	Moderate (n, %) 111	Severe (n, %) 77	Total 279
Patient Dyspnea Goal Response	35 (38.5%)	38 (34.2%) <sup>a</sup>	20 (25.9%)	93
Patient Global Impression (≥1)	32 (35.2%)	69 (62.2%) <sup>a</sup>	55 (71.4%) <sup>a</sup>	156 <sup>a</sup>

<sup>a</sup>*P* < 0.0005 compared to mild dyspnea intensity.

intensity, the better the Patient Global Impression, although not all patients achieved their target, as expressed by Patient Dyspnea Goal Response (which was determined by the achievement of the expected Patient Dyspnea Goal). It is likely that patients perceive a more evident feeling of improvement when passing to a lower dyspnea intensity in a short time (more than halving dyspnea intensity, with about two points of difference). Similarly, a higher Personalized Dyspnea Intensity Goal was also independently associated with a better Patient Global Impression, possibly because the expected target, measured by the initial Personalized Dyspnea Intensity Goal, is easier to be reached with a little change in dyspnea intensity. Similar findings were reported in a previous study, where patients with higher baseline symptoms intensity, including dyspnea, were more likely to achieve a response, based on minimal clinically important difference criteria.<sup>7</sup> Thus, patients who would be satisfied with a relatively high level of dyspnea intensity will be more likely to achieve better satisfaction. For example, in this study, a Personalized Dyspnea Intensity Goal ≥4 was found in 16 patients (5.7%). This group of patients possibly required only minimal changes of dyspnea intensity to improve their condition in terms of Patient Global Impression. On the other hand, the finding that a low level of dyspnea intensity at T7 was associated with a better Patient Global Impression is consequential to an adequate symptom management. Such data resemble the outcomes observed with the personalized concept for pain.

Few studies have assessed these aspects of dyspnea. In an outpatient setting, dyspnea intensity significantly decreased of 0.27 points, but only 19% of patients had an improvement of dyspnea, according to Patient Global Impression.<sup>8</sup> Many studies performed in non-cancer patients with progressive diseases reported a minimal clinically important difference of 5–18 mm (from small to large change) on a Visual Analogue Scale or one point on the numerical scale.<sup>4,7,14–16</sup> A reduction of 9 mm represented a change that patients considered significant enough, in differentiating one intervention over another.<sup>7</sup> In these studies, the minimal clinically important difference was calculated using the distribution-based approach, according to Cohen' guidelines for interpreting small, moderate, and large effect sizes, and/or the anchor-based method from analysis of pooled data of patients

included in randomized controlled trials. Moreover, these studies have been performed in chronic non-cancer diseases. In this study, performed in advanced cancer patients admitted to a palliative care unit, however, Patient Global Impression was used to differentiate the levels of improvement or deterioration. This method represents an individual judgment which is the basis of a personalized symptom goal.<sup>7,8</sup>

#### *Patient Personalized Dyspnea Goal Response*

Patients with higher levels of symptom intensity or a lower Karnofsky level were more likely to achieve a Personalized Dyspnea Goal Response, allowing them to reach expected level of intensity (the Personalized Dyspnea Intensity Goal). A smaller improvement in dyspnea intensity was needed to reach the target predetermined by patients. This finding reflects the observation reported previously regarding Patient Global Impression. On the other hand, it is likely that patients with a lower Karnofsky status may have less expectations reporting a more positive outcome after a palliative care treatment. This aspect deserves specific studies. In a previous study, the percentages of patients who achieved Patient Dyspnea Goal Response were 56% and 64% at the first and second visits, respectively. However, patients who had a lower baseline symptom intensity were more likely to achieve that response.<sup>7</sup> This is in contrast with the findings of the present study, possibly because of the differences in the variable times of follow-up visits and the outpatient setting.

This study has some limitations. Data were gathered from a large number of patients recruited in palliative care units where symptom assessment and therapeutic changes are intensive to achieve a clinical improvement in a short time. Thus, these data cannot be generalized to other settings, such as outpatients or home care patients. In this study, a Patient Global Impression scale was used to test minimal clinically important difference, that is, the way patients perceive a clinical change. This tool proved to be easy and repeatable for patients, although other external criteria could be added. Finally, this study did not take into account the phenomenon of episodic breathlessness, which could influence the evaluation of persistent dyspnea. Further data should help differentiate this phenomenon with appropriate methods.

## Conclusion

Patient Personalized Dyspnea Intensity Goal and Patient Global Impression seem to be relevant for patients' assessment and decision-making process, translating in terms of therapeutic intervention, according to the achievement of the patient's expectations (e.g., the achievement of the patient's Personalized Goal Response). Some factors may influence both the Personalized Dyspnea Intensity Goal and the clinical response, assessed by Patient Global Impression and Personalized Dyspnea Goal Response. Further investigation should confirm data in other palliative care settings or in other noncancer advanced diseases.

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## References

1. Wysham NG, Miriovsky BJ, Currow DC, et al. Practical dyspnea assessment: relationship between the 0-10 numerical rating scale and the four-level categorical verbal descriptor scale of dyspnea intensity. *J Pain Symptom Manage* 2015;50:480–487.
2. Hui D, Bruera E. The Edmonton Symptom Assessment System 25 years later: past, present, and future developments. *J Pain Symptom Manage* 2017;53:630–664.
3. Chang VT, Hwang SS, Feurman M. Validation of the Edmonton Symptom Assessment Scale. *Cancer* 2000;88:2164–2171.
4. Oxberry SG, Bland JM, Clark AL, Cleland JG, Johnson MJ. Minimally clinically important difference in chronic breathlessness: every little helps. *Am Heart J* 2012;164:229–235.
5. Lydick E, Epstein R. Interpretation of quality of life changes. *Qual Life Res* 1993;2:221–226.
6. Bedart G, Zeng L, Zhang L, et al. Minimal clinically important differences in the Edmonton Symptom Assessment System in patients with advanced cancer. *J Pain Symptom Manage* 2013;46:192–200.
7. Hui D, Park M, Shamieh O, et al. Personalized symptom goals and response in patients with advanced cancer. *Cancer* 2016;122:1774–1781.
8. Hui D, Shamieh O, Paiva CE, et al. Minimal clinically important differences in the Edmonton Symptom Assessment Scale in cancer patients: a prospective, multicenter study. *Cancer* 2015;121:3027–3035.
9. Dalal S, Hui D, Nguyen L, et al. Achievement of personalized pain goal in cancer patients referred to a supportive care clinic at a comprehensive cancer center. *Cancer* 2012;118:3869–3877.
10. Mercadante S, Adile C, Lanzetta G, et al. Personalized symptom goals and patient global impression on clinical changes in advanced cancer patients. *Oncologist* 2018. In press.
11. Breitbart W, Rosenfeld B, Roth A, et al. The Memorial Delirium Assessment Scale. *J Pain Symptom Manage* 1997;13:128–137.
12. Oldenmenger WH, de Raaf PJ, de Klerk C, van der Rijt CC. Cut points on 0-10 numeric rating scales for symptoms included in the Edmonton Symptom Assessment Scale in cancer patients: a systematic review. *J Pain Symptom Manage* 2013;45:1083–1089.
13. Mercadante S, Adile C, Caruselli A, et al. The palliative-supportive care unit in a comprehensive cancer center as crossroad for patients' oncological pathway. *PLoS One* 2016;11:e015730.
14. Abernethy AP, Currow DC, Frith P, et al. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. *BMJ* 2003;327:523–528.
15. Currow DC, McDonald C, Oaten S, et al. Once-daily opioids for chronic dyspnea: a dose increment and pharmacovigilance study. *J Pain Symptom Manage* 2011;42:388–399.
16. Oxberry SG, Torgerson DJ, Bland JM, et al. Short-term opioids for breathlessness in stable chronic heart failure: a randomized controlled trial. *Eur J Heart Fail* 2011;13:1006–1012.