

*Review Article*

# The Edmonton Symptom Assessment System 25 Years Later: Past, Present, and Future Developments



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**Abstract**

**Context.** Routine symptom assessment represents the cornerstone of symptom management. Edmonton Symptom Assessment System (ESAS) is one of the first quantitative symptom assessment batteries that allows for simple and rapid documentation of multiple patient-reported symptoms at the same time.

**Objectives.** To discuss the historical development of ESAS, its current uses in different settings, and future developments.

**Methods.** Narrative review.

**Results.** Since its development in 1991, ESAS has been psychometrically validated and translated into over 20 languages. We will discuss the variations, advantages, and limitations with ESAS. From the clinical perspective, ESAS is now commonly used for symptom screening and longitudinal monitoring in patients seen by palliative care, oncology, nephrology, and other disciplines in both inpatient and outpatient settings. From the research perspective, ESAS has offered important insights into the nature of symptom trajectory, symptom clusters, and symptom modulators. Furthermore, multiple clinical studies have incorporated ESAS as a study outcome and documented the impact of various interventions on symptom burden. On the horizon, multiple groups are actively investigating further refinements to ESAS, such as incorporating it in electronic health records, using ESAS as a trigger for palliative care referral, and coupling ESAS with personalized symptom goals to optimize symptom response assessment.

**Conclusion.** ESAS has evolved over the past 25 years to become an important symptom assessment instrument in both clinical practice and research. Future efforts are needed to standardize this tool and explore its full potential to support symptom management. *J Pain Symptom Manage* 2017;53:630–643. © 2016 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

**Key Words***Clinical trial, dyspnea, fatigue, surveys and questionnaires, symptom assessment, personalized medicine, neoplasms, pain, palliative care*

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**Introduction**

Patients with advanced diseases experience significant symptom burden from the time of diagnosis, which often increases in intensity over time.<sup>1,2</sup> In cross-sectional studies, the average cancer patient reports 8–12 symptoms, with fatigue, pain, anorexia, cachexia, dyspnea, anxiety, and depression being particularly common.<sup>3–5</sup> These symptoms are often multidimensional in nature, and can negatively impact patients' quality of life and function while increasing caregiver burden.<sup>6</sup>

Over the past decades, the specialty of palliative care has acquired substantial expertise in symptom management.<sup>7</sup> One of the most critical aspects of symptom management is routine symptom assessment and reassessment with patient reported outcomes (PROs)—which allows symptoms to be recognized, diagnosed, treated, and monitored over time. Theoretical frameworks such as the symptom expression pathway have formed the basis for multidimensional symptom management guided by patient-reported outcomes instead of clinician-based assessments.<sup>8</sup> The symptom transduction cascade illustrates why

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patients often present with multiple symptoms at the same time, and support the need for symptom assessment batteries that document multiple symptoms.<sup>9</sup>

The Edmonton Symptom Assessment System (ESAS) represents one of the first symptom batteries in palliative care, and has since been validated by multiple groups, translated into over 20 languages, and adopted in both clinical practice and research to support symptom assessment in many centers worldwide. The year 2016 marks the 25th anniversary of ESAS. In this review, we shall examine the historical development of ESAS, its current uses in different settings, and future developments of this tool.

## Past Developments

### Derivation

ESAS was initially developed by Bruera et al.<sup>10</sup> as a clinical tool to document the symptom burden in patients with advanced cancer admitted to a palliative care unit. The initial version consisted of eight horizontal 0–100 mm visual analog scales (VASs) assessing pain, activity, nausea, depression, anxiety, drowsiness, appetite, and sensation of well-being. A ninth VAS was added to document “a less frequent symptom that might be important for a given patient.” ESAS was completed by patients, relatives and/or nurses twice daily at 10 AM and 6 PM. Although not explicitly stated, the original version was intended to examine symptom intensity at the moment of assessment. The investigators proposed a symptom distress score (SDS) based on the total score of eight symptoms (range 0–800). Among the 101 consecutive patients admitted to the palliative care unit in Edmonton, the mean SDS was 410 on Day 1 and 362 on Day 5. The authors concluded that ESAS was a “simple and useful method for the regular assessment of symptom distress in the palliative care setting.”<sup>10</sup>

### Validation and Modifications

ESAS has been validated by multiple research groups. In 1993, Bruera et al.<sup>11</sup> found that ESAS had good test-retest reliability among 34 hospitalized patients, and correlated with Support Team Assessment Schedule. Philip et al.<sup>12</sup> assessed the validity of a slightly modified version of ESAS assessing symptoms “now,” in which “activity” was replaced with “weakness” in 80 patients with cancer from Australia. ESAS had satisfactory to good correlation with Brief Pain Inventory and Rotterdam Symptom Checklist, with weighted kappas between 0.46 and 0.61. In a prospective study involving 240 cancer patients from the U.S., Chang et al.<sup>13</sup> reported ESAS (nine items, VAS) to have good internal reliability (Cronbach  $\alpha$  0.79), test-retest reliability (Spearman correlation coefficient 0.86 on Day 2 and 0.45 on Day 7) and convergent validity (correlation coefficient 0.85 with Functional

Assessment of Cancer Therapy [FACT] pain, 0.83 with Memorial Symptom Assessment Scale [MSAS] pain, 0.56 with Brief Pain Inventory [BPI] worst pain). The psychometric validation of ESAS has been reviewed in detail by others.<sup>14,15</sup> More recently, several investigators have also examined ESAS’s predictive validity. Specifically, higher ESAS symptom burden was associated with more emergency room visits in the next seven days and a shorter survival.<sup>16–18</sup>

Over the years, ESAS has evolved from VASs to 11-point numeric rating scales (NRSs) ranging from 0 (no symptom) to 10 (worst possible). NRS was easier to complete and report, and the findings generally corresponded with VAS.<sup>19</sup> The items were also revised: “activity” was replaced with “tiredness/fatigue”; “shortness of breath” was added as a standard item; and “constipation,” “insomnia,” “spiritual distress,” “financial distress,” and several other symptoms have been proposed as additional items for assessment.<sup>20–22</sup> When ESAS was used daily, the time frame of assessment was modified to examine the average symptom intensity over the past 24 hours instead of “now” to better capture the fluctuating nature of many symptoms.<sup>23</sup>

Several studies have examined patients’ perception of ESAS and highlighted opportunities for improvement. In a prospective study of 60 patients seen at an outpatient palliative care clinic, Garyali et al.<sup>23</sup> found that the items of appetite and sleep were sometimes misinterpreted, resulting in reversed scoring. Watanabe et al.<sup>24</sup> conducted a think-aloud study asking 20 patients about their perception of ESAS, and reported that some patients had difficulty in understanding the terms depression, anxiety, appetite, and well-being, whereas others found it challenging to distinguish between tiredness and drowsiness.

These findings led to the proposal of a revised ESAS (ESAS-r) NRS consisting of nine core symptoms (pain, tiredness, nausea, depression, anxious, drowsiness, appetite, feeling of well-being, and shortness of breath) and an optional 10th symptom.<sup>25</sup> Specifically, ESAS-r (1) stated the time frame of symptom assessment as “now,” (2) added brief explanations for tiredness (“lack of energy”), drowsiness (“feeling sleepy”), depression (“feeling sad”), anxiety (“feeling nervous”), and well-being (“how you feel overall”), (3) changed “appetite” to “lack of appetite,” (4) adjusted the order of symptoms, (5) removed the horizontal line over the numbers and shaded alternate items in gray for readability, and (6) suggested constipation as the 10th item. A study comparing the two versions of ESAS in 160 cancer patients reported that ESAS-r was easier to understand ( $P = 0.008$ ).<sup>25</sup> More recently, Hannon et al.<sup>20</sup> assessed the validity of the original versus revised version of ESAS with constipation and sleep added (ESAS-CS) among 202 ambulatory patients with advanced cancer. Both NRSs were found

to be reliable and valid. A greater proportion of patients found the wording in ESAS-r-CS to be easier to understand than ESAS-CS (44% vs. 11%), but more preferred the 24 hours time frame in ESAS-CS over “right now” in ESAS-r-CS (53% vs. 21%).

To date, many permutations of ESAS exist. The version used by the Supportive Care team at MD Anderson Cancer Center is shown in Fig. 1. It consists of 10 items with “sleep” replacing “other symptom,” and asks about the average symptom intensity over the past 24 hours.

### Translation

ESAS has been translated professionally by Mapi Research Trust into over 20 languages and is freely available (Table 1). Multiple research groups have further validated ESAS both linguistically and psychometrically in Chinese,<sup>28</sup> Flemish,<sup>26</sup> French,<sup>29</sup> German,<sup>30</sup> Icelandic,<sup>31</sup> Italian,<sup>32</sup> Japanese,<sup>33</sup> Korean,<sup>34</sup> Portuguese,<sup>27</sup> Spanish,<sup>36</sup> Thai,<sup>37</sup> and Turkish.<sup>38</sup> An Arabic variation of ESAS is also available.<sup>35</sup>

### Score Interpretation

Some investigators have examined how the 0–10 was interpreted by patients. Specifically, what cutoffs within the 0–10 NRS represent none, mild, moderate, and

severe symptom burden? In a prospective study involving 400 cancer patients, Selby et al.<sup>39</sup> reported that 7 was the optimal cutoff for severe pain, depression, anxiety, drowsiness, appetite, and well-being, 8 was the optimal cutoff for severe fatigue, and 6 was the optimal cutoff for dyspnea. Oldenmenger conducted a systematic review of cutoffs for ESAS NRS. Among 18 studies, the cutoffs for moderate symptom intensity was generally between 4 and 5, and the cutoffs for severe symptom burden varied between 7 and 8.<sup>40</sup> A recent study found similar cutoffs for moderate (i.e., 3–4) and severe symptoms (i.e., 5–7) for the Japanese version of ESAS-r, despite differences in culture, language and patient populations.<sup>41</sup> In summary, ESAS scores of 0, 1–3, 4–6, and 7–10 are generally considered as none, mild, moderate, and severe in clinical practice,<sup>42</sup> although there may be significant variations in how the individual patient interprets the scores.<sup>43</sup>

### Responsiveness and Minimal Clinically Important Difference (MCID)

Another aspect of ESAS relates to its responsiveness to change and what is the smallest magnitude of change that is clinically significant. Hui et al.<sup>44</sup> conducted a prospective multicenter study specifically designed to identify the MCID for each of the 10 ESAS symptoms. Seven

Date: \_\_\_\_\_ Time: \_\_\_\_\_

**Please circle the number that best describes your average symptom over the past 24 hours:**

No Pain	0 1 2 3 4 5 6 7 8 9 10	Worst Pain
No Fatigue	0 1 2 3 4 5 6 7 8 9 10	Worst Fatigue
No Nausea	0 1 2 3 4 5 6 7 8 9 10	Worst Nausea
No Depressed	0 1 2 3 4 5 6 7 8 9 10	Worst Depression
Not Anxiety	0 1 2 3 4 5 6 7 8 9 10	Worst Anxiety
No Drowsiness	0 1 2 3 4 5 6 7 8 9 10	Worst Drowsiness
No Shortness of Breath	0 1 2 3 4 5 6 7 8 9 10	Worst Shortness of Breath
Best Appetite	0 1 2 3 4 5 6 7 8 9 10	Worst Possible
Best Feeling or Well Being	0 1 2 3 4 5 6 7 8 9 10	Worst Feeling of Well Being
Best Sleep	0 1 2 3 4 5 6 7 8 9 10	Worst Sleep

Completed by:  Patient  Family

Assessed by (Signature/Credentials/ID# Date/ Time) \_\_\_\_\_

Print / Stamp Name: \_\_\_\_\_

Fig. 1. Edmonton Symptom Assessment System. The current version used at MD Anderson Cancer Center uses 24 hours as the time frame anchor for the 0–10 numeric rating scales.

Table 1  
Language Availability for the Edmonton Symptom Assessment System

Country	Language	Psychometrically Validated in Language (Reference)	Linguistically Validated by Mapi Research Institute
Argentina	Spanish	—	✓
Australia	English	12	✓
Belgium	Flemish	26	—
Brazil	Portuguese	27	✓
China	Chinese	28	✓
Canada	English	10,11	✓
	French	—	✓
Denmark	Danish	—	✓
France	French	29	✓
Germany	German	30	✓
Hungary	Hungarian	—	✓
Iceland	Icelandic	31	—
Israel	Hebrew	—	✓
	Russian	—	✓
	Arabic	—	✓
Italy	Italian	32	✓
Japan	Japanese	33	✓
Korea	Korean	34	—
The Netherlands	Dutch	—	✓
New Zealand	English	—	✓
Portugal	Portuguese	—	✓
Poland	Polish	—	✓
Russia	Russian	—	✓
Saudi Arabia	Arabic	35	—
South Africa	English	—	✓
	Afrikaans	—	✓
Spain	Spanish	36	✓
Sweden	Swedish	—	✓
Thailand	Thai	37	—
Turkey	Turkish	38	✓
United Kingdom	English	—	✓
United States	English	13	✓
	Spanish	—	✓

hundred ninety-six patients with cancer were enrolled from six centers. Patients were asked about their average ESAS symptom intensity over the past 24 hours at the first clinic visit and then a subsequent visit

approximately three weeks later. They were also asked to provide the global assessment of change (better, same, or worse) for each symptom which was used as an anchor for MCID determination. The area under

Table 2  
Minimal Clinically Important Differences for ESAS Individual Items and Total Scores<sup>44,45</sup>

Symptom	Improvement			Deterioration		
	Optimal Cutoff <sup>a</sup>	Sensitivity	Specificity	Optimal Cutoff <sup>a</sup>	Sensitivity	Specificity
Pain	≥+1	0.727	0.739	≤-1	0.731	0.849
Fatigue	≥+1	0.727	0.694	≤-1	0.733	0.805
Nausea	≥+1	0.593	0.841	≤-1	0.856	0.851
Depression	≥+1	0.639	0.758	≤-1	0.780	0.813
Anxiety	≥+1	0.681	0.711	≤-1	0.595	0.805
Drowsiness	≥+1	0.599	0.732	≤-1	0.728	0.733
Appetite	≥+1	0.673	0.765	≤-1	0.790	0.765
Well-being	≥+1	0.664	0.689	≤-1	0.642	0.743
Dyspnea	≥+1	0.658	0.743	≤-1	0.722	0.842
Sleep	≥+1	0.728	0.693	≤-1	0.677	0.765
Physical score <sup>b</sup>	≥+3	0.630	0.697	≤-4	0.598	0.804
Emotional score <sup>c</sup>	≥+2	0.585	0.742	≤-1	0.611	0.752
Total SDS <sup>d</sup>	≥+3	0.683	0.622	≤-4	0.590	0.776

ESAS = Edmonton Symptom Assessment System; SDS = symptom distress score.

<sup>a</sup>The optimal cutoff for sensitivity and specificity was determined based on the Youden J method and top left method. A positive value indicates improvement, whereas a negative value indicates deterioration.

<sup>b</sup>Combined score based on ESAS pain, fatigue, nausea, drowsiness, appetite, and dyspnea. The total ranges from 0 to 60, with a higher score indicating higher physical symptom burden.

<sup>c</sup>Combined score based on ESAS anxiety and depression. The total ranges from 0 to 20, with a higher score indicating higher emotional symptom burden.

<sup>d</sup>Combined score based on ESAS physical score, ESAS emotional score, and ESAS well-being. The total ranges from 0 to 90, with a higher score indicating higher total symptom burden.

the receiver-operating characteristic curves ranged between 0.70 and 0.87, suggesting that ESAS had good discrimination for symptom change.<sup>44</sup> Interestingly, a change of one point was found to be the optimal cutoff for both improvement and deterioration for all the 10 symptoms using a sensitivity-specificity approach (Table 2). This finding was consistent with additional analyses using other anchor-based and distribution-based approaches in the same data set. A retrospective analysis using change in ESAS well-being categories as an anchor also found similar magnitude of change to be the MCID.<sup>46,47</sup>

### ESAS Physical, Emotional, and Total SDS

A SDS was proposed by Bruera et al. by adding the eight VASs in the original ESAS (total score 0–800). Since then, ESAS has undergone significant modifications, although most versions of ESAS retain six physical symptoms (pain, tiredness, nausea, drowsiness, appetite, and shortness of breath), two emotional symptoms (depression and anxiety), and one global item (well-being). This led some investigators to propose the ESAS physical score (total of six physical symptoms, score range 0–60), ESAS emotional score (total of two emotional symptoms, score range 0–60), and ESAS total SDS (physical score + emotional score + well-being).<sup>48</sup> Indeed, the ESAS physical and emotional symptoms form two separate groups in cluster analysis.<sup>49,50</sup> Furthermore, higher ESAS physical and total SDSs were associated with shortened survival.<sup>51</sup>

A recent study identified the MCID cutoffs for symptom improvement was  $\geq +3/60$ ,  $\geq +2/20$ , and  $\geq +3/90$  for ESAS physical, emotional, and total SDSs, respectively, and  $\leq -4/60$ ,  $\leq -1/20$ , and  $\leq -4/90$  for deterioration.<sup>45</sup>

### Present Applications

The ability of ESAS to quantify multiple symptoms efficiently and systematically has revolutionized

symptom assessment in both clinical practice and research, resulting in its widespread adoption. The advantages and limitations of ESAS are shown in Table 3. ESAS is currently used for symptom screening and monitoring in different palliative care settings, including inpatients,<sup>52–54</sup> outpatients,<sup>55–58</sup> and home care.<sup>17</sup> Within other branches of oncology, ESAS has been used by medical oncologists,<sup>59,60</sup> radiation oncologists,<sup>61</sup> surgical oncologists,<sup>62,63</sup> and gynecological oncologists.<sup>64,65</sup> Outside of oncology, ESAS has also been adopted for symptom assessment in patients with kidney diseases,<sup>66,67</sup> heart failure,<sup>68,69</sup> pulmonary disorders,<sup>70</sup> hepatic diseases,<sup>71</sup> and sickle cell anemia.<sup>72</sup>

### Clinical Applications: Symptom Screening

In the clinical setting, ESAS is most often used to identify patients' unmet needs by systematic screening. Since 2006, Cancer Care Ontario has adopted the ESAS for routine symptom assessment in a province-wide Palliative Care Integration Project.<sup>73–75</sup> Patients rated their symptom intensity using the ESAS at ambulatory clinics at 14 Regional Cancer Centers. Data were predominantly captured electronically using Interactive Symptom Assessment and Collection (ISAAC) with touch-screen kiosks.<sup>60</sup> In 2014, two million symptom data points had been captured from 280,000 patients. The target symptom screening rate was 70%. Over 28,000 patients providing their symptom rating using ESAS each month.<sup>75</sup> A patient satisfaction survey involving 3660 patients in Ontario reported that a vast majority of patients (92%) agreed that the ESAS was important "as it helped their healthcare team to know their symptoms and severity."<sup>76</sup>

Routine collection of symptom data needs to be coupled with clinician endorsement and proper action plan to have a meaningful impact on patient care (Fig. 2). In a survey of 40 physicians from a single center in Ottawa, the respondents found ESAS to be

Table 3  
Strengths and Limitations of the ESAS

Strengths	Limitations
<ul style="list-style-type: none"> <li>• Pragmatic patient-centered symptom assessment tool that is easy to administer, interpret, and report</li> <li>• The assessment of 10 symptoms at the same time allows for symptom clusters to be identified</li> <li>• Can be completed rapidly (&lt;1 minute)</li> <li>• Currently used by many clinical and research groups worldwide, allowing for benchmarking</li> <li>• Face validity</li> <li>• Psychometrically validated by multiple groups</li> <li>• Available into &gt;20 languages</li> <li>• The responsiveness and minimal clinically important differences have been identified</li> <li>• Available in many different languages</li> <li>• Free of charge</li> </ul>	<ul style="list-style-type: none"> <li>• Unidimensional scales that assess only symptom intensity</li> <li>• Different versions of ESAS are currently used with different time anchors and number of items, making it sometimes difficult to compare or combine results</li> <li>• Few validation studies in noncancer populations</li> <li>• Some items (e.g., well-being) are not well defined</li> </ul>

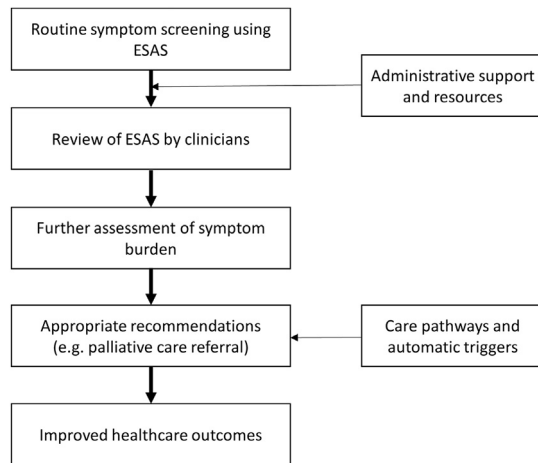


Fig. 2. Use of ESAS to trigger palliative care referral. Routine symptom assessment needs to be endorsed by clinicians and coupled with action plans to improve clinical outcomes. A recent international consensus identified severe symptom distress as a criterion for palliative care referral, although this threshold may need to be refined at each institution.<sup>77</sup> ESAS = Edmonton Symptom Assessment System.

helpful and should be completed at every visit.<sup>78</sup> A subsequent survey of 2806 oncology professionals in Ontario (response rate 38%) also found that a majority of physicians (67%) and nurses (85%) perceived ESAS to be a useful starting point to assess patients' symptoms.<sup>76</sup> Seventy-nine percent of physicians reported that they reviewed the ESAS scores at visits either "always" or "often.". However, a separate chart audit found that only 29% of patients with moderate-to-severe pain and 6% of patients with moderate-to-severe dyspnea had clinical actions documented in the chart, suggesting the need to strengthen the downstream actions from symptom screening through clinician education, resource allocation, and care pathways.<sup>42</sup> We shall discuss the use of ESAS as an automatic trigger later in this manuscript.

#### *Clinical Applications: Longitudinal Symptom Monitoring*

Because symptoms often fluctuate over time, it is important to follow patients longitudinally and document their symptom improvement and/or deterioration.<sup>79</sup> As such, ESAS can be administered at every clinic visit to capture symptom changes. In a study that included 1612 patients with cancer seen at an outpatient palliative care clinic reported the change in symptom scores by baseline symptom intensity (absent/mild NRS  $\leq 3$  vs. moderate/severe NRS  $\geq 4$ ). The average symptom intensity worsened among patients with absent/mild baseline symptom intensity ( $-3.04$  to  $0.12$ ), but generally improved among those with moderate/severe intensity ( $-0.2$  to  $3.86$ ). Overall, between 52% and 74% of patients with moderate/severe

symptoms reported an improvement. This study highlights the fluctuating nature of symptom intensity, which is related to disease trajectory, effectiveness of symptom management strategies, and variations in symptom expression. It further illustrates why it is important to document baseline symptoms even in patients who have low symptom burden because they are likely to experience concerns in the future.<sup>55</sup>

#### *Research Applications: Symptom Trajectory*

Cummings et al.<sup>80</sup> conducted a bibliometric analysis of ESAS between 1991 and 2006, and documented the rapid uptake of this tool in the global literature, particularly in general medicine and oncology journals. By facilitating the documentation of multiple symptoms systematically, longitudinally, and universally, ESAS has contributed to advancing multiple aspects of symptom research, including symptom trajectory, symptom clusters, symptom modulators, and interventions for symptom management.<sup>49,50,81–85</sup>

As mentioned above, Ontario has a rich and growing data set of over four million ESAS scores, providing some unique insights into symptom trajectory. Seow et al.<sup>81</sup> documented the intensity of nine ESAS symptoms in the last six months of life. Fatigue, appetite, drowsiness, shortness of breath, and well-being worsened over time, whereas nausea, depression, anxiety, and pain remained mostly stable. Jia et al.<sup>82</sup> recently reported the use of Markov Multistate Models to examine the symptom trajectory in patients with cancer. A total of 280,000 assessments were collected among 55,883 patients. They reported that fatigue and well-being deteriorated rapidly over time.

#### *Research Applications: Symptom Cluster Studies*

The assessment of multiple symptoms at the same time has allowed researchers to gain insights into symptom clusters. Symptoms often have similar etiology (e.g., inflammation), modulators (e.g., alcoholism), and may contribute to each other (e.g., dyspnea may worsen anxiety and vice versa). Multiple investigators have examined symptom clusters within ESAS. In the outpatient palliative care setting, two main symptom clusters had been identified (physical and emotional).<sup>49,50</sup> Chen et al.<sup>86</sup> examined symptom clusters among 1296 patients with advanced cancer seen at palliative radiation oncology clinics using three statistical approaches (i.e., principal component analysis, hierarchical cluster analysis, and exploratory factor analysis). Depression and anxiety consistently formed a cluster, whereas fatigue, drowsiness, and dyspnea formed another cluster. Using a version of ESAS that included 22 different items, Jimenez et al.<sup>87</sup> reported four clusters (cognitive impairment, agitation, and urinary incontinence; anxiety, depression, and insomnia; anorexia, weight loss, and tiredness; and nausea and vomiting) among 437

hospitalized patients with advanced cancer. The variations in symptom clusters among different studies is likely related to differences in statistical techniques, patient populations, and ESAS versions.<sup>88</sup> Further studies are needed to better understand the evolving nature of symptom clusters. More recently, ESAS has also been used to assess symptom clusters among patients with advanced heart failure.<sup>89</sup>

#### Research Applications: Symptom Modulators

The examination of ESAS symptoms with other factors enabled the identification of various symptom modulators—variables that are consistently associated with the expression of one or more symptoms. For example, Parsons et al.<sup>90</sup> identified that a history of alcoholism (assessed based on Cut down-Annoyed-Guilty-Eye opener [CAGE] questionnaire positivity) was associated with elevated symptom expression in multiple ESAS items. Similarly, a history of smoking

correlated with an increased expression of multiple symptoms.<sup>83,84</sup> Spiritual distress, depression, and anxiety were also found to be important modulators of symptom expression.<sup>91,92</sup> These insights into symptom modulators have substantial implications for symptom management. For example, a patient with high pain expression, severe depression, and spiritual distress would mandate concurrent interdisciplinary management of his emotional and spiritual concerns rather than continual escalation of opioid doses.<sup>8</sup>

#### Research Applications: Assessing the Effect of Various Symptom Control Interventions

Because symptoms are often associated with each other, interventions targeting one symptom may also impact others. Over the years, ESAS has been incorporated as an outcome to assess symptom response in multiple observational studies, open-label studies, and randomized controlled trials.<sup>93–102</sup> This has facilitated

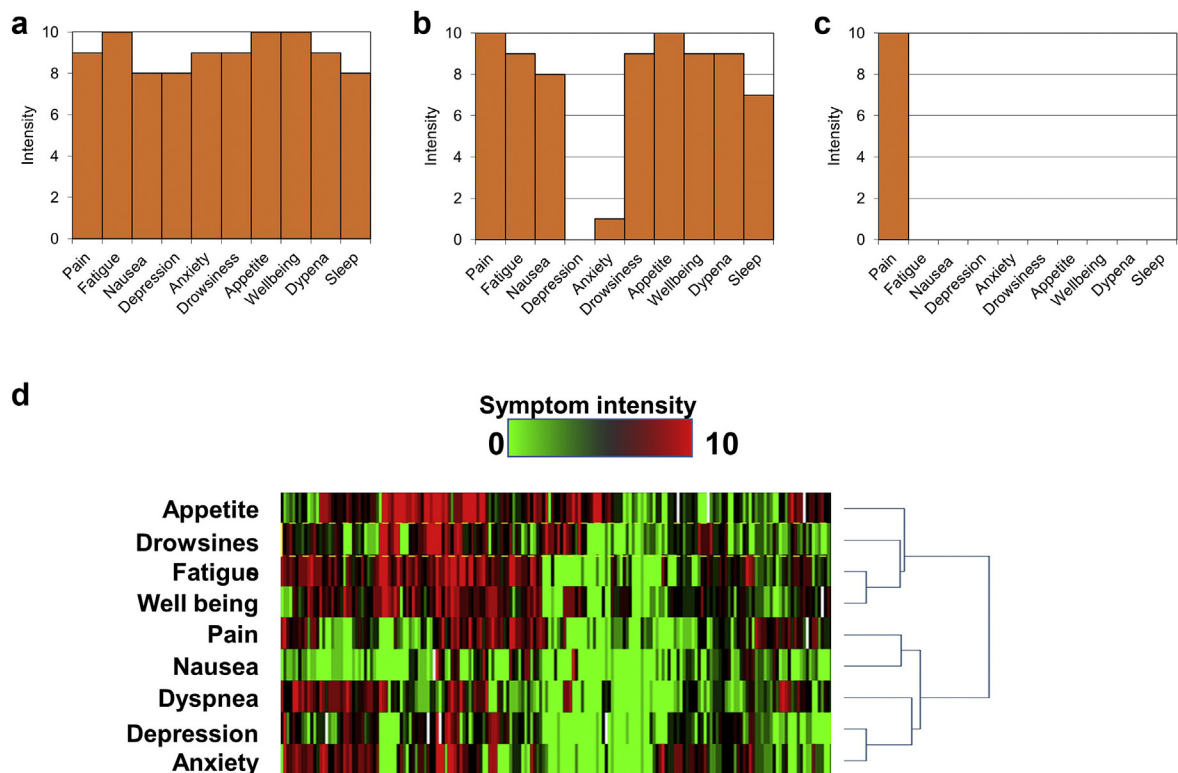


Fig. 3. ESAS displays. ESAS can be graphically displayed, and the pattern of symptom expression can be highly informative. (a) Globally elevated symptom expression—this pattern may suggest the presence of symptom modulators such as depression or anxiety. These modulators would need to be properly addressed as part of the symptom management plan. (b) U-shape distribution—some patients may under-report their level of anxiety and depression, although they may be contributing to their high physical symptom expression. These patients may benefit from assessment of their emotional status even if they do not report any. (c) Solitary pain—some patients have very high pain expression, but no other associated symptoms, which is atypical. The clinician may want to carefully characterize the patient's pain history and ensure safe opioid use. (d) ESAS symptom expression array—each column represents one ESAS assessment for an individual patient, each row represents one ESAS symptom, and the color represents symptom intensity (green = none, red = worst). This novel display may be generated by a computer program to illustrate the ESAS symptoms for multiple patients at the same time, or for the same patient over time. The example here displays ESAS scores on admission for patients at an acute palliative care unit. Symptom clusters can be clearly detected (fatigue, appetite, drowsiness). Nausea had low expression. The expression of dyspnea was also associated with anxiety. ESAS = Edmonton Symptom Assessment System.

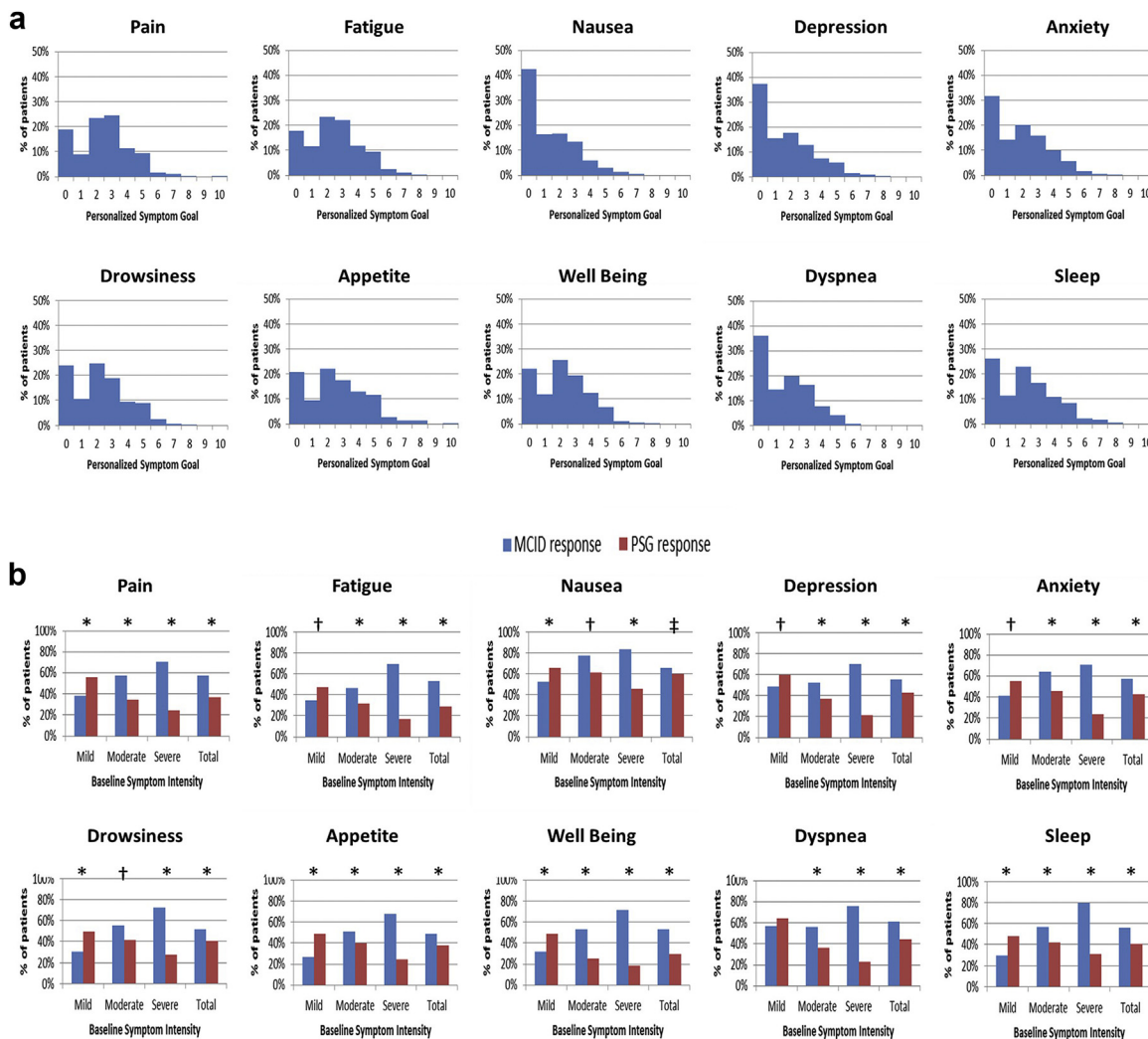


Fig. 4. Symptom response criteria. (a) Distribution of PSG for 10 symptoms. Most patients reported a PSG of three or less. (b) Response rates differences by baseline symptom intensity and response criteria. We plotted the response rates by two criteria (MCID and PSG) according to baseline symptom intensity (i.e., mild 1–3, moderate 4–6, and severe 7–10). Using the MCID criteria, patients with higher baseline symptom intensity were more likely to achieve a response and vice versa; in contrast, the personalized symptom response criteria resulted in the opposite conclusion. *P*-values were computed based on the McNemar test (\**P* < 0.0001, †*P* < 0.001, ‡*P* < 0.05). Reprinted with permissions from the American Cancer Society.<sup>43</sup> MCID = minimal clinically important difference; PSG = personalized symptom goal.

the documentation of the treatment effect on multiple symptoms simultaneously. For example, in double-blind, randomized controlled trial of dexamethasone for cancer-related fatigue, ESAS-dyspnea as one of the secondary outcomes and showed a trend toward improvement with dexamethasone.<sup>103</sup> More recently, a separate randomized placebo-controlled trial that incorporated ESAS dyspnea as the primary outcome confirmed this observation.<sup>104</sup>

Several investigators have also used total ESAS scores to examine the effect of specialty palliative care versus usual oncologic care on symptom burden. In a single-blinded cluster randomized trial, Zimmermann et al.<sup>105</sup> found that timely involvement of palliative care was associated with symptom improvement,

whereas the symptoms worsened in the usual care group, with a statistically significant difference between the two study arms at four months. Based on an MCID of three points for total symptom distress, this magnitude could be considered to be clinically significant.<sup>45</sup> Bakitas et al.<sup>106</sup> also examined the effect of a nurse-led palliative care program, although there was an improvement in quality of life and depression, ESAS total burden did not change significantly.

### Future Developments

As ESAS continues to be used by a growing number of clinics, hospitals, jurisdictions, and countries, multiple groups are actively examining how ESAS can be



applied to further augment clinical practice and research. We shall discuss standardization and further validation of ESAS, incorporation of ESAS in the electronic health records, the use of ESAS to trigger clinical actions, and the use of personalized symptom goals (PSGs) to individualize symptom assessment.

#### *Standardization and Further Validation*

As highlighted in Table 3, there are several barriers to the use of ESAS. Going forward, it would be ideal to standardize ESAS item description and layout to facilitate combination and comparison of data across studies. Although symptom intensity over the past 24 hours is associated with symptom intensity “now,” there are important differences given that symptom burden fluctuates over time. ESAS “now” may be particularly useful to assess interventions with a rapid onset (i.e., effect of intravenous opioids on dyspnea “now”), whereas ESAS “24 hours” may be more suited for everyday clinical practice. At a minimum, investigators should consistently report which version of ESAS they are using in the publications and clearly state the time frame anchor. Further efforts are also needed to standardize the administration of ESAS to optimize accuracy.<sup>107</sup> As in many aspects of palliative care, precise definitions for specific terms are needed.<sup>108–110</sup> ESAS-r has contributed to improving the clarity for several items. However, some terms such as depression and well-being may benefit from further research to examine their construct validity.<sup>111–113</sup> Further studies to compare the use of ESAS to other PROs would also be useful.

#### *Incorporation of ESAS in Electronic Medical Records*

In the era of information technology, patient-reported outcomes are increasingly being captured, stored, and displayed electronically. As mentioned above, Ontario has been systematically collecting ESAS via kiosks.<sup>75</sup> Several groups have also published their experience capturing ESAS using mobile device or computer.<sup>114,115</sup> Strasser et al.<sup>116</sup> reported a cluster randomized controlled trial comparing provision of symptom data to oncologists immediately after electronic symptom assessment versus no provision of data. The intervention arm was associated with a statistically and clinically significant improvement in ESAS SDS (reduction of 5.4 points vs. worsening by 2.1 points,  $P = 0.003$ ).

Electronic data capture has some advantages, including reduced missing data during the data entry process, the ease of completing the questionnaires at home, the possibility for computerized adaptive testing, rapid data access while minimizing the need for data entry manually, immediate display and scoring, and the ability to incorporate patient alerts and automatic triggers.<sup>114,117</sup> However, there are some barriers to

implementation, including the upfront cost of building a system for data entry, storage, display, integration, and protection and the financial burden for maintaining and updating, lack of familiarity with electronic interface among some patients and health care professionals, the training required, the need to address security concerns, and the need to build a system that can be incorporated into the clinical work flow. Although the advantages of incorporating ESAS and other health outcomes electronically outweigh the disadvantages, each institution would need to customize this process individually.

Electronic data capture could also facilitate data display and interpretation. ESAS can be plotted graphically using bar graphs, with some specific patterns that may augment symptom assessment (Fig. 3a–c). More recently, our group has piloted the use of symptom expression arrays to display the individual data for large number of patients (Fig. 3d).

#### *Use of ESAS to Trigger Clinical Actions*

ESAS is increasingly used to trigger specific clinical actions, such as referral to a palliative care team (Fig. 2).<sup>118</sup> The American College of Surgeons Commission on Cancer mandates distress screening as a criterion for accreditation.<sup>119</sup> ESAS has been proposed as tool for such purpose.<sup>120</sup> In a systematic review of the literature to characterize referral criteria to outpatient palliative care for patients with cancer, 13 of 21 included studies specified symptom distress as a reason for referral.<sup>121</sup> Among these studies, ESAS was the most commonly used symptom assessment scale, with seven of the nine studies that reported the use of a validated scale using ESAS.<sup>64,101,122–126</sup> However, only one study stated a symptom intensity cutoff of  $\geq 6/10$  was needed to trigger a referral.<sup>123</sup>

More recently, 60 international experts reached consensus on 11 major criteria for outpatient palliative care referral for patients with advanced cancer, in which fulfillment of any one major criteria is sufficient to initiate a referral. The level of agreement was highest for severe physical distress (i.e., NRS  $\geq 7/10$ , agreement 100%) and severe emotion distress (i.e., NRS  $\geq 7/10$ , agreement 97%).<sup>77</sup> These ESAS cutoffs may vary somewhat at each institution by the resource availability of specialty palliative care and the level of interest among oncologists to provide basic symptom management.<sup>124,127</sup> Importantly, any automatic referral should complement rather than override clinician judgment. Future studies should determine what proportion of patients who fulfill these criteria,<sup>118</sup> how patients, families, and clinicians perceive the use of ESAS to trigger a referral, and whether it would improve health care outcomes compared with clinician-based referral alone.<sup>128</sup>

ESAS may also trigger clinical actions other than a palliative care referral. Dhiliwal et al.<sup>129</sup> described the use of ESAS to triage patients for the intensity of home-based palliative care visits. Among the 506 patients included, 6% had high symptom burden (any ESAS  $\geq 7$ ), 21% had moderate burden (any ESAS 4–6), and 73% had low symptom burden (ESAS scores 0–3). These three groups were seen within an average of 2.6, 7, and 10.5 working days of referral. Comparing with data a year ago, implementation of this triaging system was associated with a decrease in hospital deaths (19% vs. 27%).

### Personalized Symptom Goals

Although 0, 1–3, 4–6, and 7–10 points on a scale of 0–10 generally correspond to none, mild, moderate, and severe symptom burden, there is significant variation in how each patient interprets the scale. For example, one patient may consider a pain score of 6/10 to be agonizing, whereas another may consider this to be her baseline and appears to be comfortable. Furthermore, a change in one point (i.e., MCID of ESAS) may or may not be representative of a meaningful change for the individual patient.

PSG represents an innovative approach to address these issues. By asking patients “Using the same 0–10 scale, at what level of (specific symptom) would you feel comfortable?” clinicians can better appreciate how each patient interprets the NRS, while establishing an individualized treatment target at the same time.<sup>130</sup> Our research group conducted a multicenter study involving 728 patients with advanced cancer seen at palliative care clinics.<sup>43</sup> A majority reported a PSG of three or less for each ESAS symptom (Fig. 4a). The median PSG was one for nausea; two for depression, anxiety, drowsiness, well-being, dyspnea, and sleep; and three for pain, fatigue, and appetite. Between 33% and 73% of patients achieved their PSG by the second palliative care clinic visit. PSG also addresses a concern with the MCID criterion to assess response—that patients with higher symptom intensity were more likely to achieve a response, when many patients who “responded” continue to have suboptimal symptom control above their PSG (Fig. 4b). PSG may be applied in clinical practice (e.g., one assessment at consultation) or research studies to personalize the symptom treatment goal.

### Summary

Over 25 years, ESAS has evolved to become one of the most commonly used PROs for symptom assessment in palliative care, oncology, and beyond. ESAS has been psychometrically validated, translated into multiple languages, and is freely available. By

enabling rapid, pragmatic assessment of multiple symptoms simultaneously, ESAS is used extensively in the clinical setting for symptom screening and monitoring worldwide. As one of the first symptom batteries ever developed, ESAS has also transformed the symptom research paradigm, contributing to major insights into symptom prevalence, trajectory, clusters, modulators, and interventions. Active work is ongoing to help standardize the administration of ESAS, integrate it into electronic health records, link it to clinical actions, and couple it to PSGs.

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