Assessment of Symptom Clusters in People With Cancer

Judith A. Paice

The control, and ideally prevention, of symptoms such as pain, depression, and fatigue is dependent on a comprehensive clinical assessment. Furthermore, to advance the science of this field, symptom research requires the use of multidimensional instruments with proven validity and reliability in a cancer population across the lifespan. Studies demonstrate a significant correlation among pain, depression, fatigue, and other symptoms commonly seen throughout the course of cancer. Therefore, multidimensional scales incorporating the most common symptoms would ensure systematic assessment. Optimally, valid and reliable tools that measure symptom clusters would be feasible for use in both clinical and research settings. Currently available instruments that measure symptom clusters include the Edmonton Symptom Assessment Scale, the M.D. Anderson Symptom Inventory, the Memorial Symptom Assessment Scale, the Rotterdam Symptom Checklist, the Symptom Distress Scale, and others. Special populations include cancer patients with advanced disease, where symptom prevalence is expected to increase. Newer tools that attempt to address these populations are the Brief Hospice Inventory and the Hospice Quality of Life Index, appropriate for cancer patients with more advanced disease. Each of these tools has demonstrated utility in measuring symptom severity and quality of life. Few scales have been validated in the measurement of symptom clusters in children, in cognitively impaired adults, or in non-English speaking patients from various cultural backgrounds. The strengths and limitations presented in the clinical and research uses of each these instruments will be presented, as will be areas for future investigation. [J Natl Cancer Inst Monogr 2004;32:98–102]

The control, and ideally prevention, of symptoms common in cancer, such as pain, depression, and fatigue, is dependent on a comprehensive clinical assessment. Furthermore, to advance the science of this field, symptom research requires the use of multidimensional instruments with proven validity and reliability in a cancer population across the lifespan. Studies demonstrate a significant correlation among pain, depression, fatigue, and other symptoms commonly seen throughout the course of cancer. Furthermore, the number of symptoms present may be an indicator of quality of life (1,2). Therefore, multidimensional scales incorporating the most common symptoms, or symptom clusters, would ensure systematic assessment. Symptom clusters have been defined as three or more concurrent symptoms that are related to one another (3). Optimally, valid and reliable tools that measure these symptom clusters would be feasible for use in both clinical and research settings. Moreover, for optimal application, these tools would be valid for use in a variety of age-specific and ethnic populations.

Barriers to the clinical assessment of symptoms are considerable and include lack of awareness, limited time, the subjectivity of cancer-related symptoms, and assumptions that patients will voluntarily report these sensations. Barriers to adequate management of cancer pain, already extensively studied, serve as a guide for understanding obstacles to adequate symptom assessment (4). The use of standardized assessment tools would overcome some of the barriers to adequate symptom assessment by increasing awareness of the importance of measuring these constructs, along with systematically addressing symptoms that affect people with cancer.

Currently, several instruments have been designed to specifically measure symptom clusters, including the Edmonton Symptom Assessment Scale (ESAS), the M.D. Anderson Symptom Inventory (MDASI), the Memorial Symptom Assessment Scale (MSAS), the Rotterdam Symptom Checklist (RSC), the Symptom Distress Scale (SDS), and others. In addition, tools designed to measure broader phenomenon, such as quality of life, often include symptom subscales. One example among many is the Functional Assessment of Cancer Therapy Scale (FACT). Finally, the specific needs of special populations of people with cancer are addressed in a variety of newly developed instruments, notably the Brief Hospice Inventory (BHI) and the Hospice Quality of Life Index (HQLI). This review will address the barriers to symptom assessment, list key principles regarding the measurement of symptoms, and critique instruments currently available for the assessment of symptom clusters in people with cancer.

Barriers to Clinical Assessment of Symptoms

Barriers to the clinical assessment of symptoms are believed to be considerable and can be categorized in a similar fashion to the barriers to adequate cancer pain management (4). Barriers to symptom assessment have not been studied to the degree that cancer pain barriers have been investigated; thus, many of the factors listed are extrapolated from the pain literature as well as from clinical observations of the author (5–7). Barriers on the part of healthcare professionals include the subjectivity of cancer-related symptoms and assumptions that patients will voluntarily report these sensations. Patient-related barriers include many of the same assumptions, particularly that healthcare professionals “know” when the patient experiences these symptoms and that as a result, reporting is not necessary. Furthermore, patients are reluctant to report symptoms because they do not want to be a bother to their physician or family members. Recent studies indicate that patients are reluctant to report pain and other symptoms, as a higher symptom burden may disqualify them from clinical trials (8). Finally, the healthcare system produces barriers, including limits on the time of trained healthcare professionals who confront decreases in staffing in the face of increases in acuity and the lack of tools available for symptom

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SYMPTOM ASSESSMENT: GENERAL PRINCIPLES

In an excellent review, Kroenke (9) posits that because symptom-based research is in its infancy, optimal methods for measuring symptoms have not yet been determined. Currently, symptom detection for research purposes relies on chart review, elicitation by a survey or questionnaire, and spontaneous reporting. Chart reviews typically underestimate symptom prevalence, because symptoms are often unrecorded, and thus, chart reviews are not useful assessment methods in the clinical management of individuals with cancer-related symptoms. There is evidence that in a general population, structured surveys can produce “over-endorsement bias,” a tendency for patients to select large numbers of symptoms from a checklist (10,11), making it difficult for clinicians to prioritize the most distressing concerns. Yet in the cancer arena, hesitancy to report symptoms is common. Therefore, significant concerns about overreporting do not seem to apply to this population. The third method of symptom detection, volunteered, spontaneous reporting, may be optimal in a general population, yet barriers to reporting symptoms in cancer care are significant. The very label used to describe these reports, “chief complaint,” indicates some of the perceptions patients and clinicians hold about these remarks.

Other aspects that should be considered when assessing symptoms include not only the prevalence but also the location, temporal factors (such as onset, periodicity, and duration), severity (including intensity as well as the effect of this severity on overall distress and suffering), and outcomes (including relief, patient satisfaction, and cost) (12–14). Severity scales related to pain assessment have been well studied, including categorical, visual analog, and numeric rating scales (4,15).

Practicality must be considered when selecting an appropriate tool to measure symptom clusters. The ease of completion is particularly important in a cancer population with significant symptom burden, including pain, fatigue, and depression. Tools must be brief, with large print, and should include clear instructions. Because symptoms are subjective, as with pain assessment, the patient is the optimal source of information. However, cognitive impairment resulting from dementia, delirium, or other factors may limit the ability of the patient to respond. When patients are unable to respond, family members are often enlisted as proxies, yet studies suggest that caregivers typically report higher pain and disability (16). Aids to communication include communication boards and assistive devices for the hearing impaired, as well as education of patients, families and professionals to overcome fears, biases, and lack of knowledge (13).

Scales Designed to Measure Symptoms

Several instruments have been designed to specifically measure symptom clusters in people with cancer, including the ESAS, the MDASI, the MSAS, the RSC, the SDS, and others. A critique of their characteristics will aid clinicians and investigators in selecting the optimal tool to meet the assessment needs of their settings, specific populations, and goals of assessment. Instruments selected for this review have at least one published study to support their validity in a population of people with cancer. Because of space limitations, quality-of-life instruments, although often including physical and psychologic symptoms, are not included in this review, except for the few that address special populations.

ESAS. The ESAS consists of nine visual analog scales (using a 10-cm line) that measure pain, activity, nausea, depression, anxiety, drowsiness, lack of appetite, well-being, and shortness of breath (17). A tenth symptom can be added to individualize the scale. The ESAS Distress score is a sum of the nine symptoms. Originally developed to assess symptoms in a palliative care setting, the ESAS has demonstrated validity in palliative care and hospice patients (18) and has been used to measure symptom distress in cancer patients receiving intensive care as well as those being seen by a palliative care consult service (19,20). More recently, the ESAS was found to be valid and reliable in a population of cancer inpatients and outpatients within the Veteran’s Administration (21), although test–retest was better at 2 days than at 1 week. Furthermore, patients required more explanation regarding the use of the ESAS than the MSAS or FACT. Lower functional ability, as measured by Karnofsky performance status, may predict difficulty with completion. The authors of this study found that the visual analog format was more difficult to use than categorical scales (21). These findings were consistent with the results of a study of the use of the ESAS in palliative care patients (22). Furthermore, in a study of the symptom experience of 100 cancer patients treated in a medical intensive care unit, only 50% were able to respond to the ESAS (19). To remedy some of these limitations, the ESAS is currently a combination of visual analog scales supplemented with numeric rating scales (see www.palliative.org for instructions regarding the use of tool).

In addition to its use in clinical practice and research, the ESAS has also been used in quality improvement efforts. The ESAS was used to compare palliative care symptom control across institutions. However, the authors noted that one obstacle to the use of the ESAS as a quality tool was inconsistent documentation of the symptoms within the patients’ charts (23).

MDASI. The MDASI is a list of 13 symptoms rated on an 11-point scale (0–10), with 0 indicating “not present” and 10 meaning “as bad as you can imagine” (24) (www.mdanderson.org/departments/prg). In addition, six interference items are rated using a similar 11-point scale, with 0 meaning “did not interfere” and 10 indicating “interfered completely.” The interference items include general activity, mood, work, relations with other people, walking, and enjoyment of life. The original tool, consisting of 26 symptoms, was tested in a large number of outpatients (n = 640), and inpatients (n = 30) at The University of Texas M.D. Anderson Cancer Center. On the basis of cluster analysis and other statistical measures, the investigators found that 13 symptoms (pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, lack of appetite, drowsy, dry mouth, sad, emesis, bloated, and numbness or tingling) explained 64% of the variance in symptom interference. Fatigue was consistently rated the most severe in both in- and outpatients. Validity was determined using factor analysis and reliability was found to be high, with α values ranging from 0.82 to 0.87 for the symptom items and from 0.91 to 0.94 for the interference items. Regarding clinical utility, most patients completed the form in 5 minutes, and refusal to complete the tool was uncommon at less than 5%. Modules are currently being developed for specific groups of patients, such as those with lung or gastrointestinal...
cancer, as well as those undergoing bone marrow transplantation.

Cleeland and colleagues (8) developed this tool specifically to incorporate new technologies in health care. Using interactive voice response (IVR), patients can be called via the telephone at predetermined times to answer the MDASI using the keys on their touchtone telephone. The information is then communicated to health care professionals, with alerts or prompts for action if a particular symptom is rated as severe. Several intriguing outcomes of this system may include not only improved clinical management of cancer-related symptoms but also a unique strategy for data collection during multicenter clinical trials, or even providing information for quality-improvement efforts within institutions.

**MSAS.** The MSAS measures the prevalence, severity, and distress associated with 32 physical and psychologic symptoms experienced during the prior week (25). Each symptom frequency is rated as occurring “rarely,” “occasionally,” “frequently,” and “almost constantly.” Severity is measured as “mild,” “moderate,” “severe,” and “very severe.” Symptom-related distress is rated using a 5-point Likert scale: “not at all,” “a little bit,” “somewhat,” “quite a bit,” and “very much.” Each symptom score is an average of the three dimensions. The tool consists of physical (MSAS-PHYS) and psychologic (MSAS-PSYCH) subscales, as well as a Global Distress Index (MSAS-GDI). The Global Distress Index is the average of the frequency scores for “feeling sad,” “worrying,” “feeling irritable,” and “feeling anxious,” along with the distress scores for “lack of appetite,” “lack of energy,” “pain,” “feeling drowsy,” “constipation,” and “dry mouth.” The total MSAS (TMSAS) score is the average of the symptom scores for all 32 symptoms. According to the authors, the total MSAS appears to provide information about overall symptom distress, yet the Global Distress Index may be more clinically meaningful because of the high correlation between this measure and quality of life and clinical status (25).

The MSAS has demonstrated validity and reliability in a cancer in- and outpatient population (26). In a study of medical oncology patients at a Veterans Affairs medical center, the number of intense symptoms was found to be highly correlated with decreased Karnofsky performance status and the Functional Assessment Cancer Therapy (FACT-G) Sum Quality-of-Life score (1,26,27). As in other studies of symptom prevalence, lack of energy and pain were most common and were rated as most distressing. Recently, the MSAS was used in a study of seriously ill cancer and noncancer patients, providing preliminary evidence for construct validity and demonstrating the feasibility of the use of this tool in patients near end of life (28). The MSAS also has been revised to measure symptoms in older and younger children (MSAS 7–12 and MSAS 10–18, respectively) (29,30).

**RSC.** The RSC is a 31-item scale specifically designed to measure symptoms experienced by patients undergoing cancer clinical trials (31). Patients are asked to rate symptoms that bothered them using the following descriptors: “not at all,” “a little,” “quite a bit,” and “very much.” As with other instruments employing verbal descriptors, these cues may be difficult for some patients to use, and the length of the tool can be cumbersome for very ill people. Furthermore, the RSC measures distress alone without determining the severity of these symptoms.

**SDS.** The SDS is a 13-item tool that measures the frequency, intensity, and distress associated with 11 symptoms, providing a valid measure of global symptom distress in people with cancer (32). As with other instruments, one possible limitation of this tool is the small number of symptoms measured (33,34).

Each of the above instruments measures different symptoms, although there is a core set of symptoms that are captured by each tool, including pain, fatigue, nausea, depression (feeling sad), drowsiness, lack of appetite, and shortness of breath (Table 1). The ESAS measures severity of each symptom, the MDASI measures severity and functional impairment, and the MSAS evaluates frequency, severity, and the degree to which each symptom causes distress. It is interesting to note that although employing differing instrumentation and methodology, studies using these various tools reveal that fatigue and pain are consistently the most prevalent symptoms (1,24,26,27,35).

**Tools That Incorporate Symptom Measurement**

Health-related quality of life (HRQOL) is a multidimensional construct that includes physical, emotional, social, and other factors (36). Several HRQOL tools have been developed and tested for the cancer population, including the European Organisation for the Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) and the Functional Assessment of Cancer Therapy–General (FACT-G) (www.facit.org) (37). The FACT-G measures quality of life in a cancer population and has been used extensively in clinical trials (38). Consisting of five subscales (functional well-being, physical well-being, social/family well-being, relationship with physician, and emotional well-being) and a total quality-of-life score, the FACT-G has been widely validated in a variety of subjects with numerous malignancies and in quite a few languages (e.g., African languages [Pedi,

### Table 1. Symptoms included within selected instruments

<table>
<thead>
<tr>
<th>Symptom</th>
<th>ESAS</th>
<th>MDASI</th>
<th>MSAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Fatigue</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Nausea</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Activity</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>X</td>
<td>Sad</td>
<td>Feeling sad</td>
</tr>
<tr>
<td>Anxiety</td>
<td>X</td>
<td></td>
<td>Feeling nervous</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>X</td>
<td></td>
<td>Feeling irritable</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Well-being</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Disturbed sleep</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Distress</td>
<td>X</td>
<td></td>
<td>Distress (upset)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Bloated</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbness or tingling</td>
<td>X</td>
<td></td>
<td>Numbness/tingling in hands/feet</td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>X</td>
<td>Problem remembering</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Problems with urination</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweats</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Problems with sexual activity</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Itching</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ESAS = Edmonton Symptom Assessment System, MDASI = M.D. Anderson Symptom Inventory, MSAS = Memorial Symptom Assessment Scale.
Studies incorporating these tools to investigate symptoms in several of these have been adapted for special populations. Assessment is essential to the prevention and management of symptoms common in people with cancer. The length of the scale limits its routine use in a clinical setting when expressly interested in assessing symptoms.

A recently developed tool, the “Distress Thermometer” is a vertical visual analog designed to look like a thermometer, with 0 meaning “no distress” and 10 (at the top of the thermometer) indicating “extreme distress” (www.nccn.org) (43). Accompanying the distress scale is a checklist of various physical, psychologic, practical, family support, and spiritual/religious concerns. In a study of 100 oncology inpatients using the distress thermometer, mean distress scores were 6.3 ± 2.9 (44). These distress scores were negatively correlated with the physical and emotional well-being subscales, as well as the total score, of the FACT-G, providing beginning evidence for the validity of the use of the Distress Thermometer as a global measure of quality of life.

### Special Populations

Special populations include cancer patients with advanced disease, in whom symptom prevalence is expected to increase. Newer tools that attempt to address these populations are the BHI and the HQLI, appropriate for cancer patients with more advanced disease. The BHI assesses outcomes of hospice patients, including physical and psychologic symptoms and patient’s perceptions of hospice care, as well as ratings of their quality of life (45). Each statement is measured using an 11-point scale. A sample of 145 home-based hospice patients completed the surveys on admission, and 20 patient and nurse dyads completed the tool at some time during the first 3 weeks after admission. More than one-third of patients rated fatigue as severe (7 or above). This initial study indicates that the BHI has construct validity (using principal axis factoring techniques) and test–retest reliability (by comparing results obtained at two separate time points).

The HQLI is a 28-item self-report questionnaire designed to assess the overall quality of life of hospice patients. The tool measures three domains: psychophysioligic, functional, and social/spiritual well-being. The HQLI has proven validity and reliability (46). Interestingly, in a recent study of home hospice patients, pain was near the bottom of the list of reported symptoms (47). This is similar to the findings of Guo and colleagues (45) studying the BHI, indicating improved pain management within the hospice setting.

### Conclusion

Assessment is essential to the prevention and management of symptoms common in people with cancer. Symptom research, necessary to promote evidence-based clinical management, requires the use of multidimensional instruments with proven validity and reliability in cancer populations. Several valid and reliable tools have been developed to allow systematic assessment of pain, fatigue, depression, and other symptoms, and several of these have been adapted for special populations. Studies incorporating these tools to investigate symptoms in people with cancer demonstrate similar trends, including a significant prevalence of pain and fatigue. Barriers to adequate symptom assessment persist, and strategies to overcome these obstacles warrant exploration. Furthermore, additional research is needed regarding instruments for symptom assessment in children, in cognitively impaired adults, and in non-English speaking patients from various cultural backgrounds.

As the concept of symptom clusters is more clearly elucidated, symptom-related instruments need to be evaluated for their ability to provide the most valid and reliable data regarding multiple symptoms occurring concurrently. Simple screening strategies require comparisons with more complex assessment techniques for their validity, reliability, and feasibility. Cut points for severity will need to be determined to establish whether a symptom should be included within a cluster. Interventions should be designed to address these clusters, rather than isolated symptoms, to replicate the experiences of people with cancer. Through these efforts, common etiologies of symptom clusters may be explicable. To achieve these ends, valid and reliable symptom cluster assessment tools must be developed and tested, employing current advances in measurement science.

### References


