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A Review of the Prevalence and Impact of Multiple Symptoms in Oncology Patients

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Abstract

Findings from several studies suggest that oncology patients undergoing active treatment experience multiple symptoms and that these symptoms can have a negative effect on patient outcomes. However, no systematic review has summarized the findings from studies that assessed multiple symptoms in these patients. Therefore, the purposes of this review were to: 1) compare and contrast the characteristics of the three most commonly used instruments to measure multiple symptoms; 2) summarize the prevalence rates for multiple symptoms in studies of oncology patients receiving active treatment; 3) describe the relationships among selected demographic, disease, and treatment characteristics and multiple symptoms; and 4) describe the relationships between the occurrence of multiple symptoms and patient outcomes (i.e., functional status, quality of life). Only 18 studies were found that met the inclusion criteria for this review. The majority of the studies were cross-sectional with sample sizes that ranged from 26 to 527. Approximately 40% of patients experienced more than one symptom. However, little is known about the relationships between demographic and clinical characteristics and the occurrence of multiple symptoms. Findings from this review suggest that the occurrence of multiple symptoms is associated with decreased functional status and quality of life. However, given the large number of oncology patients who undergo active treatment each year, additional research is warranted on the prevalence and impact of multiple symptoms. Only when this descriptive research is completed with homogenous samples of patients in terms of cancer diagnoses and treatments can intervention studies for multiple symptoms be developed and tested.

Keywords

Multiple symptoms; symptom clusters; patient outcomes; symptom assessment; symptom prevalence; outpatient oncology

Introduction

Patients with cancer can undergo a variety of treatments (e.g., surgery, radiation (RT), chemotherapy (CTX), hormonal therapy), either singly or in combination. While these treatments improve survival, they can produce a variety of symptoms. In fact, findings from

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several studies suggest that patients receiving active treatment (1,2) experience multiple symptoms simultaneously. For example, in one of the first studies of multiple symptoms (3), women with ovarian cancer reported an average of 10.2 symptoms (range of 0 to 25 concurrent symptoms). More recently, Donovan and colleagues (4) found that 74% of women who received CTX for ovarian cancer reported 13.4 concurrent symptoms.

When these symptoms are not managed effectively, they can cause interruptions or cessation of cancer treatment (5) or decrease patients' level of adherence with a treatment regimen (6–12). In addition, unrelieved symptoms can have a negative impact on patients' functional status, mood, and quality of life (QOL) (5,13–16).

Given the negative outcomes associated with multiple symptoms, it seems prudent that clinicians and researchers should evaluate the prevalence and impact of multiple symptoms in oncology patients undergoing active treatment. These types of evaluations could be used to guide the development and testing of interventions for multiple symptoms. However, no systematic review has summarized the findings from studies that evaluated multiple symptoms in oncology patients receiving active treatment. Therefore, the purposes of this review were to: 1) compare and contrast the characteristics of the three most commonly used instruments to measure multiple symptoms; 2) summarize the prevalence rates for multiple symptoms in studies of oncology patients receiving active treatment; 3) describe the relationships among selected demographic, disease, and treatment characteristics and multiple symptoms; and 4) describe the relationships between the occurrence of multiple symptoms and patient outcomes (i.e., functional status, QOL).

Search Methods

For this review, systematic electronic searches of MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PsycINFO databases were performed. The searches were restricted to adults with cancer and English language articles. The search terms used were symptom, multiple symptoms, cancer, cancer treatment, QOL, and symptom assessment instruments. The searches were limited to the years 1990 through 2007 because no studies of multiple symptoms in oncology patients were published prior to 1990.

Studies were included if they: evaluated the prevalence of multiple (greater than one) symptoms; used one of three valid and reliable instruments (i.e., the Symptom Distress Scale (SDS) (17), the M. D. Anderson Symptom Inventory (MDASI) (18), the Memorial Symptom Assessment Scale (MSAS) (19)) to evaluate multiple symptoms; and included adult oncology patients who were receiving active treatment in inpatient or outpatient settings. Studies were excluded if they: evaluated multiple symptoms in patients who were receiving palliative or hospice care; measured the side effects of treatment; and/or used QOL instruments or symptom specific instruments to measure multiple symptoms.

The retrieved studies were reviewed by the first author (J-EK) initially to determine if they met the inclusion and exclusion criteria. Then the reference lists of selected studies were manually searched to identify any additional studies. Based on the search parameters, 76 abstracts were identified for this review. A total of 69 studies addressed some aspect of multiple symptoms. Fifty-one abstracts were eliminated because they used instruments without established validity and reliability (i.e., Canberra Symptom Score Card, Chemotherapy Symptom Assessment Scale, a Computerized Symptom Assessment Instrument, Pain and Symptom Assessment Record, Symptom Experience Scale, the Symptom Monitor, the Symptom Reporting Tool, the modified Edmonton Symptom Assessment System (ESAS), the MSAS Modified for family caregivers). Therefore, 18 studies of multiple symptoms met the prespecified inclusion/exclusion criteria (see Table 1).

Comparison of the Characteristics of Three Instruments Used To Measure Multiple Symptoms

Rationale for the Choice of the Three Instruments Included in This Review

The ideal instrument to measure multiple symptoms should include those symptoms that occur frequently and are most distressing to patients. In addition, it should be relatively short, easy for patients with limited educational backgrounds to understand, and applicable for both clinical practice and research (5,18). Ideally, the instrument should be available in multiple languages.

Several instruments are available to measure multiple symptoms including the ESAS (20,21), the MDASI (18), the MSAS (19), the Oncology Treatment Toxicity Assessment Tool (OTTA) (2), the Rotterdam Symptom Checklist (RSCL) (22), the SDS (17,23), and the Worthing Chemotherapy Questionnaire (24). All of these instruments are comprehensive and have good psychometric properties. For this review, the ESAS, RSCL, OTTA, and the Worthing Chemotherapy Questionnaire were excluded for a number of reasons. The ESAS was designed to assess symptoms in palliative care patients. The RSCL was designed to assess symptoms in cancer patients who participated in a clinical trial. Both the OTTA and the Worthing Chemotherapy Questionnaire assess treatment-related side effects.

It should be noted that several symptom specific instruments and QOL scales can be used to evaluate the presence and severity of a single symptom or pairs of symptoms such as fatigue (e.g., Piper Fatigue Scale (25)), depression and anxiety (e.g., Hospital Anxiety and Depression Scale (26)), and nausea and vomiting (e.g., Rhodes Index of Nausea and Vomiting, (27)). While symptom-specific scales provide valuable information on the multiple dimensions of a single symptom and many QOL instruments contain items that evaluate multiple symptoms often as part of physical and psychological subscales, they capture different aspects of the symptom experience compared to valid and reliable instruments that were designed to capture the occurrence, severity, and/or distress of multiple concurrent symptoms in patients undergoing active cancer treatment. In addition, most of the multidimensional QOL instruments contain only a limited number of common symptoms (19). Therefore, in this review, only those studies that used one of three symptom inventories (i.e., SDS, MDASI, MSAS) were reviewed because they are valid and reliable measures that provide information about a large number of physical and psychological symptoms that are assessed concurrently. The psychometric properties of these three instruments are summarized in Table 2.

M.D. Anderson Symptom Inventory

The MDASI was developed by the Pain Research Group at the University of Texas M. D. Anderson Cancer Center (18). The original tool included 26 symptoms. However, 13 items (i.e., not able to get things done, weak, worrying, nervous, irritable, sick, constipation, attention, bloated, cough, diarrhea, mouth sores, bleeding) were deleted because they were deemed redundant or had low prevalence rates in oncology patients. The MDASI measures the severity of 10 physical symptoms (i.e., pain, fatigue (tiredness), disturbed sleep, dry mouth, lack of appetite, nausea, vomiting, drowsy, shortness of breath, numbness or tingling), three psychological symptoms (i.e., problem with remembering things, feeling sad, distress), and six interference items (i.e., general activity, mood, work, relations with other people, walking, enjoyment of life).

Each symptom is rated on an 11-point numeric rating scale (NRS) with 0 indicating “not present” and 10 indicating “as bad as you can imagine.” Each symptom on the MDASI is rated at its worst in the past 24 hours. Six interference items that describe how much all of the symptoms interfere with common activities are rated using an 11-point NRS (i.e., 0 “does not

interfere to 10 “interferes completely”). Of note, the final 13 symptoms explained 64% of the variance in symptom interference. Validity of the MDASI was determined using factor analysis and internal reliabilities ranged from 0.82 to 0.87 for the symptom items and from 0.91 to 0.94 for the interference items (18).

Memorial Symptom Assessment Scale

The MSAS is a self-report instrument that measures, using Likert scales, the severity (1 (mild) to 4 (very severe)), frequency (1 (rarely) to 4 (almost constantly)), and distress (0 (not at all) to 4 (very much)) of 26 physical and 6 psychological symptoms (i.e., difficulty concentrating, feeling sad, worrying, feeling nervous, feeling irritable, and “I don’t look like myself”) in cancer patients during the previous seven days (19). It provides multidimensional information about a large number of symptoms that are experienced by oncology patients. Twenty-four symptoms are evaluated in terms of all three dimensions (i.e., severity, frequency, distress), and eight symptoms (i.e., mouth sores, change in the way food tastes, weight loss, constipation, hair loss, swelling of arms or legs, changes in skin, “I don’t look like myself”) are evaluated for only severity and distress.

The MSAS is scored into physical and psychological subscales as well as a Global Distress Index (GDI). The GDI is made up of four prevalent psychological symptoms (i.e., feeling sad, worrying, feeling irritable, feeling nervous) and six prevalent physical symptoms (i.e., lack of energy, dry mouth, lack of appetite, pain, constipation, feeling drowsy). The GDI provides a measure of global symptom distress.

The physical symptom subscale score (MSAS-PHYS) is the average of the frequency, severity, and distress of the 12 most prevalent physical symptoms. The psychological symptom subscale score (MSAS-PSYCH) is the average of the frequency, severity, and distress of the six most prevalent psychological symptoms. The total MSAS (TMSAS) score is the average of the three symptom scores for all 32 symptoms. The MSAS has demonstrated validity and reliability in patients with cancer (19,21). Concurrent validity of the MSAS was demonstrated through a strong positive correlation with the Functional Living Index for Cancer (FLIC) QOL measure and with the Karnofsky Performance Status (KPS) Score (19). Construct validity was determined through comparisons of MSAS scores among different cancer diagnoses. Discriminant validity was determined by comparing the MSAS scores of inpatients and outpatients (19).

Symptom Distress Scale

The SDS is a measure of symptom distress defined as “the degree of discomfort from specific symptoms being experienced as reported by the patient” (17). It provides a measure of the severity of symptom distress and was one of the first valid and reliable instruments developed for symptom assessment in oncology patients. This 13-item self-report instrument assesses the level of symptom distress for 13 symptoms (i.e., pain, fatigue, insomnia, lack of appetite, nausea, bowel dysfunction, shortness of breath, coughing, poor activity, difficulty with concentration, mood, altered appearance, poor outlook). In addition, the frequency of occurrence of pain and nausea are reported separately.

Each item is scored on a 5-point Likert scale (i.e., 1 = the least amount of distress associated with a symptom to 5 = extreme distress associated with a symptom) that measures the distress associated with each symptom at that moment or for that day. Items rated ≥ 3 indicate serious distress. A total score is obtained by summing the scores for the 13 items and can range from 13 (little distress) to 65 (severe symptom distress). A total score of ≥ 25 indicates moderate distress and a score of ≥ 33 indicates severe distress that requires immediate intervention (23). The SDS has demonstrated acceptable internal consistency (Cronbach $\alpha > 0.80$) and test-

retest reliability in patients with lung cancer (28) as well as content, construct, and criterion validity.

Comparisons Among the Three Symptom Assessment Instruments

The specific symptoms that are measured by each of these instruments were summarized in Table 3. While these three instruments purport to measure “common” symptoms in oncology patients, the number as well as the specific symptoms that are assessed vary across the three instruments. Only eight symptoms (i.e., pain, fatigue, difficulty sleeping, lack of appetite, nausea, shortness of breath, difficulty with concentration, mood/sad) are measured by all three instruments.

Another difference among these three instruments is the aspect of the symptom experience that is assessed. The SDS focuses on the distress associated with each symptom, which is suggested to be a proxy for symptom severity. While the MDASI measures the severity of each symptom individually, interference is assessed for all of the symptoms collectively. In contrast, the MSAS measures frequency, severity, and distress for each symptom. However, the MDASI and the MSAS measure symptom severity using different scales. In addition, the instructions for the MDASI ask patients to rate symptoms at their worst, while the MSAS asks for ratings of average symptom severity.

Although both the SDS and the MSAS measure symptom distress, it is assessed using different scales (i.e., a 1 to 5 scale on the SDS versus a 0 to 4 scale on the MSAS). Another difference is that the timeframe for symptom assessment varies across the three instruments (i.e., SDS and MDASI = “at that moment or on that particular day;” MSAS = “past week”).

The SDS and the MDASI take 5 to 10 minutes to complete. No information is available on how long it takes to complete the MSAS. The psychometric properties of these three instruments are well established. Factor analysis of the MSAS and MDASI confirmed the factor structure of these instruments (18,19). The Cronbach’s alphas for the three instruments are comparable (see Table 2).

All three instruments were developed in the United States. The SDS and the MDASI have been translated and validated in several languages. Translations of the SDS are available in Dutch, Italian, Spanish, Swedish, Korean, and Taiwanese. The MDASI has been translated into Chinese, Korean, Japanese, Greek, Russian, and Filipino. No information was found on translations of the MSAS.

Summary of the Prevalence of Multiple Symptoms

Table 1 provides a summary of the 18 studies that evaluated multiple symptoms in adult oncology patients receiving active treatment. Of these 18 studies, six (37%) used the SDS (29–34), seven (39%) used the MDASI (4,18,35–39), and five (28%) used the MSAS (3,19, 21,40,41).

Characteristics of These Studies

Sixteen studies (89%) used a cross-sectional design, while only two (11%) were longitudinal. Prospective data were collected in all of the cross-sectional studies. One of the longitudinal studies (33) used a prospective design and assessed multiple symptoms and symptom distress at the initiation of treatment, and one and two months later. The other longitudinal study (34) evaluated multiple symptoms at the start of treatment and again at three and six months. Both of these longitudinal studies used the SDS to describe the patterns of symptom distress in patients with lung cancer.

Characteristics of the Study Samples

Sample sizes for the 18 studies varied widely and ranged from 26 (33) to 527 participants (18). Five studies (28%) had sample sizes of less than 100 (29,30,32,33,40). The remaining 13 studies (72%) had sample sizes that ranged from 117 to 527. All of these studies recruited convenience samples from multiple sites.

The mean age of the participants was 59.1 with a range from 47.0 to 66.9 years. About 78% of the studies ($n=14$) enrolled both genders and overall 52% of the participants were male. Four studies measured symptoms only in women with lung or ovarian cancer (3,4,30,42).

Approximately, 44% of the studies ($n=8$) were conducted in United States (3,4,18,19,21,29,30,34). Across these eight studies, the majority (73%) of the participants were Caucasian (range 63% to 94%). Of the remaining 10 studies, three were done in Canada (31,32,40), two in China (36,41), one in Sweden (33), one in Japan (35), one in Russia (37), one in the Philippines (38), and one in Taiwan (39).

Fifty percent of the studies ($n=9$) collected data from heterogeneous samples of patients with a variety of cancer diagnoses (18,19,21,31,35,37,38–40). Regarding the site of cancer, four studies (22%) assessed symptoms only in patients with lung cancer (30,32–34), two (11%) assessed patients with ovarian cancer (3,4), and one (6%) assessed patients with gastrointestinal cancers (41). One study (6%) failed to provide information on cancer diagnosis (29).

Among the six studies that assessed multiple symptoms using the SDS, four studies evaluated patients with lung cancer (30,32–34), one assessed a heterogeneous sample (31), and one failed to describe the patients' cancer diagnoses (29). In the seven studies that used the MDASI, five recruited patients with a variety of cancer diagnoses (18,35,37–39), one recruited only patients with ovarian cancer (4), and one recruited only patients with lung cancer (36). Of the five studies that used the MSAS, one study assessed patients with prostate, colon, breast, and ovarian cancers (19), one assessed patients with ovarian cancer (3), one with gastrointestinal cancers (41), and two evaluated heterogeneous samples (21,40).

The patients' stage of disease varied across these studies. Four studies (29,33,40,41) did not provide any information on stage of disease, while three (19,21,35) found that the presence of metastatic disease was associated with an increased number of symptoms. Across the remaining 11 studies, 52% of the patients (range 12% to 87%) had stage III-IV disease. In sixteen studies, patients were receiving active treatment with CTX, RT, biotherapy, surgery, or a combination of treatments. No information on the specific treatments was provided in two studies (19,33).

Symptom Prevalence in Oncology Patients Receiving Active Treatment

Table 4 provides a summary of the prevalence rates for the various symptoms in each of the studies as well as a mean prevalence rate across these studies. Symptom prevalence rates ranged from 11% for sore mouth to 62% for fatigue. The ten most prevalent symptoms across the 18 studies were fatigue (62%), worrying (54%), feeling nervous (45%), dry mouth (42%), insomnia (41%), feeling sad/mood (39%), feeling irritable (37%), pain (36%), drowsiness (36%), and distress (34%). The prevalence rates for these 10 symptoms ranged from 34% to 62%. Across the 18 studies, 40% to 61% of patients experienced more than one symptom (30,36) and 22% to 30% of patients experienced more than five concurrent symptoms (18,36,37).

Relationships Among Select Characteristics and Multiple Symptoms

Relationships Among Demographic Characteristics and Symptom Severity/Distress

The relationships among a variety of demographic characteristics and the type of symptom experienced were examined in only four studies (19,21,31,41). However, the findings from these studies are inconsistent. Only two studies evaluated for age differences in the severity of symptom distress. In one study (31), age was weakly correlated with symptoms distress ($r = -0.11$, $P < 0.02$) and younger patients tended to have higher levels of symptom distress than older patients. In contrast, Yan and Sellick (41) found that patients in their older age group (≥ 70 years) reported higher symptom distress scores than those in their younger age group (< 40 years).

In addition to age, gender differences in symptom distress (31) and symptom prevalence (19) were evaluated in only two studies. In one study that used the SDS (31), women reported higher symptom distress scores than men ($P < 0.041$). In another study that used the MSAS (19), no gender differences were found in any of the symptom prevalence rates.

Relationships Among Disease Characteristics and Treatments and Symptom Severity/Distress

The relationships between site and stage of cancer and symptom severity and distress were evaluated in five studies (21,30,31,36,41). In one study (31), patients with lung cancer had higher symptom distress scores than either women with breast cancer or males with genitourinary cancer. In a study of Chinese patients (36), fatigue and sleep disturbance were the most common symptoms in patients with breast and lung cancer, whereas fatigue and lack of appetite were the most common symptoms in patients with gastrointestinal cancer. In another study of symptoms, psychological distress, and QOL in Chinese patients with newly diagnosed gastrointestinal cancer (41), patients with liver cancer had higher symptom frequency, severity, and distress scores than patients with all other gastrointestinal cancer diagnoses. Findings across these three studies suggest that patients with recurrent (30), metastatic (21), or advanced stage of disease (31) reported the most severe and distressing symptoms.

The type of cancer treatment appeared to influence the prevalence and severity of multiple symptoms. However, of the 18 studies, only three evaluated the prevalence of symptoms and symptom severity/distress in relationship to type of cancer treatment (29,30,34). In a study that compared mean SDS scores of patients who received CTX versus RT (29), patients who received CTX reported higher SDS scores especially for tiredness and poor appearance compared to those who received RT. In another study (30), patients who received CTX reported higher symptom distress scores than patients who underwent surgery. More recently, the prevalence of distressing symptoms was evaluated in patients who received a variety of treatments for lung cancer (34). At entry into the study, the three most distressing symptoms for patients with surgery were pain, fatigue, and insomnia; for patients with RT they were fatigue, lack of appetite, and nausea; for patients with CTX they were fatigue, insomnia, and lack of appetite; and for patients with combined treatments they were fatigue, pain, and insomnia. Patients who received only RT reported a significantly higher number of symptoms across time compared to the other three groups.

Symptom prevalence rates appear to differ based on the settings of care. Findings from two studies (3,19) found that inpatients reported a higher number of symptoms than outpatients. The mean number of symptoms for inpatients with ovarian cancer was 11.2 (range of 1 to 25) compared to 7.4 for outpatients (range of 0 to 16, (3)). In another study (19), the mean number of symptoms for inpatients with various cancers was 13.5 compared to 9.7 for outpatients.

Relationship Between Multiple Symptoms and Outcomes

The relationships between symptoms and functional status and QOL were examined in only five (28%) of the 18 studies (19,21,30,31,41). Two studies examined the relationships between the number of symptoms, symptom distress, and functional status (19,30). In a study of symptom distress and functional status in women with lung cancer (30), as symptom distress increased, functional status decreased. The other study (19) reported that the higher the number of symptoms, the poorer the patients' functional status. Patients with KPS scores of ≤ 80 reported 14.8 symptoms while patients with KPS scores of > 80 reported only 9.2 symptoms ($P < 0.0001$).

Four studies found that patients who reported a larger number of symptoms or symptom distress had poorer QOL scores (19,21,30,41). Sarna (30) reported that higher levels of symptom distress in women with lung cancer were significantly correlated with decreases in both the physical and psychological dimensions of QOL. In another study of patients newly diagnosed with gastrointestinal cancers (41), those who reported lower levels of symptoms distress reported higher QOL scores.

Findings from two studies that used the MSAS (19,21) suggest that a higher number of symptoms was strongly correlated with poorer QOL. In one study of 243 adults with various types of cancer (19), significant negative correlations were found between the number of symptoms and patients' overall QOL ($r = -0.67$, $P < 0.0001$). In addition, higher symptom distress scores were associated with increased psychological distress. Another study (21) confirmed that a higher number of symptoms was associated with a poorer QOL. Finally, two studies (31,34) found that symptom distress at diagnosis was a significant predictor of symptom distress over time, as well as decreased functional status, poorer QOL, and decreased survival. Cooley et al. (34) reported that baseline symptom distress predicted nine distressing symptoms at three months and seven distressing symptoms at six months in 117 patients with newly diagnosed lung cancer.

Summary and Conclusions

This review is the first to evaluate the prevalence of, as well as the factors associated with, the occurrence of multiple symptoms in adult oncology patients undergoing active treatment. Findings from a limited number of studies suggest that the prevalence rates for multiple symptoms are relatively high. Across 18 studies, more than 50% of oncology patients reported experiencing fatigue and worry. Of note, fatigue was the most prevalent symptom across the 18 studies. In addition, findings from these studies suggest that multiple symptoms are associated with decreases in functional status and QOL. The occurrence of multiple symptoms may be related to the disease itself, active treatment, sequelae of treatment, or comorbid conditions. Finally, the experience of multiple symptoms is associated with higher levels of symptom distress.

Several limitations across these studies must be noted. First, of the 18 studies, 89% were descriptive and cross-sectional. Therefore, little is known about how multiple symptoms change across the course of a patient's treatment trajectory. Longitudinal studies are needed to describe the trajectories of multiple symptoms in oncology patients undergoing active treatment. Without these descriptive, longitudinal studies, it will be difficult to plan intervention studies to manage multiple symptoms.

Second, all of the studies in this review used convenience samples which limit the generalizability of the study findings. In addition, the majority of the patients were Caucasian. Future research should evaluate the prevalence and severity of multiple symptoms in more ethnically diverse samples because some data suggest that differences in symptom severity and

distress do occur across ethnic groups (43–45). Third, relationships between various patient and disease characteristics and multiple symptoms warrant additional investigation since only a few studies have examined this aspect.

Perhaps one of the major areas that needs to be addressed in future studies of multiple symptoms is which symptoms should be included in any comprehensive symptom inventory. The number of symptoms in the three instruments included in this review range from 13 to 32 symptoms and only eight of these symptoms are common across instruments. However, it is not clear if any of these instrument's list of symptoms is comprehensive and appropriate for all cancer diagnoses and treatments. As equally important question that warrants consideration is what symptom dimensions (i.e., severity, frequency, and/or distress) should be assessed to capture the patient's experience of multiple symptoms.

Clinical experience suggests that cancer and its treatment is marked by the occurrence of multiple symptoms that influence the patient's ability to continue usual activities and enjoy life. However, a very limited number of studies have attempted to measure the prevalence and impact of multiple symptoms in patients with cancer. The gaps in knowledge identified in this review warrant additional research. That said, within the past five years, the concept of a symptom cluster has emerged as an important area in symptom management research (46–48). However, this concept is still in its infancy and warrants additional concept clarification and refinements in its methodology and approaches (49). Therefore, at the present time studies of multiple symptoms need to continue particularly in samples of patients with homogeneous cancer diagnoses and cancer treatments. These types of studies will guide the development of intervention studies as well as symptom cluster research.

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Table 1
Summary of the Studies of Multiple Symptoms in Adult Oncology Patients

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
Chang et al. (2000)	<i>n</i> =240	Cross-sectional	Median number of symptoms was 8.
To assess symptom prevalence and symptom intensity and their relationship to quality of life	Age: 65.4 years	MSAS	Most prevalent symptoms were lack of energy (62%), pain (59%), dry mouth (54%), shortness of breath (50%), and difficulty sleeping (45%).
	Female: 4%		Patients with moderate pain had a median of 11 symptoms.
	Ethnicity: 63% white	FACT-G	Patients with moderate fatigue had a median of 13 symptoms.
	Various cancers	BPI	Patients with metastatic disease experienced more severe and distressing symptoms.
	Stage: 69% metastasis		Patients with moderate pain and fatigue experienced nausea, shortness of breath, and lack of appetite.
	Treatment: no specific information		Number of symptoms positively correlated with extent of disease. The prevalence of weight loss, shortness of breath, constipation, problem with sexual interest, and difficulty with swallowing was higher for inpatients than outpatients. The higher the number of symptoms the lower the patients' QOL.
Chen & Tseng (2006)	<i>n</i> =151	Cross-sectional	Mean number of concurrent symptoms was 8.3.
To understand which cancer-related symptoms clustered together	Age: 50 years (range:18–79)	MDASI	Most prevalent symptoms were dry mouth (84.1%), fatigue (82.1%), lack of appetite (76.2%), pain (72.8%), and disturbed sleep (72.2%).
	Female: 40%	HADS-D	Five most severe symptoms were fatigue, dry mouth, distress, disturbed sleep, lack of appetite, and pain.
	Ethnicity: 100%	KPS	Symptoms interfered most often with working, enjoyment of life, and general activity.
To test the conceptual meanings of the revealed symptom clusters	Taiwanese		
	Various cancers		
	Stage: 50% stage III–IV		
	Treatment: 48.3% CTX		
Cleeland et al. (2000)	<i>n</i> = 527 inpatients and outpatients	Cross-sectional	Most prevalent symptoms in the moderate to severe range were fatigue (59%), not able to get things done (51%), weakness (50%), worrying (43%), disturbed

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
To develop the M.D. Anderson Symptom Inventory	Age: 55 years	MDASI	sleep (41%), dry mouth (37%), and pain (34%).
	Female: 55%	ECOG-PS	Over 25% of the patients experienced 18 symptoms at moderate or severe levels.
	Ethnicity: not reported		The two symptoms that contributed the most to interference were fatigue and sadness.
	Various cancers Stage: 29% metastasis Treatment: 56% CTX, 23% biotherapy		Patients who received CTX reported a higher level of nausea, lack of appetite, and emesis compared to patients who did not receive cancer treatment.
Cooley et al. (2003)	<i>n</i> =117	Longitudinal	At T1, the five most distressing symptoms were fatigue (64%), frequent pain (56%), insomnia (49%), lack of appetite (43%), and severity of pain (37%). The prevalence of these symptoms decreased over time.
To describe the most distressing symptoms in adults newly diagnosed with lung cancer	Age: 64.7 years (42–84)	T1 at baseline, T2 at 3 months, and T3 at 6 months	Adults with lung cancer experienced an average of 4 highly distressing symptoms at entry into study and this number decreased to 3 at 3 and 6 months.
	Female: 46%		At T1, patients who received RT reported a higher mean number of symptoms than those who received CTX or combined therapy.
	Ethnicity: 91% white		Mean number of distressing symptoms varied significantly among treatment groups at T1 but not at T2 and T3.
To describe the prevalence of symptoms in adults receiving treatment for lung cancer	Lung cancer	SDS	The mean number of highly distressing symptoms decreased over time in the combined treatment groups as compared to the other treatment groups.
To examine changes in symptom prevalence in adults receiving treatment for lung cancer over time	Stage: 86% early and regional, 12% advanced stage		Patient and clinical characteristics did not predict distressing symptoms consistently.
To identify patient and clinical characteristics related to symptom distress	Treatment: 7% CTX, 11% RT, 38% surgery, 44% combined therapy		Symptom distress at T1 was the best predictor of symptom distress at T2 and T3.
Degner & Sloan (1995)	<i>n</i> =434 outpatients	Cross-sectional	Level of symptoms distress in ambulatory patients was low.
To describe levels of symptom distress in a	Age: 59.3 years (range: 45–73)	SDS	The mean symptom distress score was 23.0 (range of 13 to 50).

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
general ambulatory population	Female: 48%		Lung cancer patients had the highest levels of symptom distress scores.
	Ethnicity: Canadian		The most distressing symptoms were fatigue (39%), insomnia (31%), pain frequency (24%), pain intensity (19%), and poor outlook (24%).
To describe the factors associated with symptom distress	Various cancers		Women and patients with advanced disease reported higher levels of symptom distress.
	Stage: 29% early, 34% advanced stage		Older patients had less symptom distress than younger patients.
	Treatment: 34% CTX, 63% RT, 49% surgery		Higher symptom distress at baseline predicted shorter survival.
Donovan et al. (2005)	<i>n</i> =279	Cross-sectional	Mean number of concurrent symptoms was 12. These symptoms were in the moderate to severe range.
To describe the symptom experiences of women with ovarian cancer	Age=55.5 years (range: 22–91)	MDASI-modified to include symptoms specific to ovarian cancer (22 symptoms)	Five “most noticed” symptoms in the past week were fatigue (59%), bowel disturbances (37%), pain (27%), neuropathy (26%), and abdominal bloating (25%).
	Female:100%		Five most severe symptoms were fatigue, bowel disturbances, sleep disturbances, memory problems, and peripheral neuropathy.
	Ethnicity: 94% white		Mean severity of symptoms identified as noticed most was 7.
To describe the extent to which women and clinicians communicate about symptoms	Ovarian cancer	SRQ	61% of the patients had discussed their most noticed symptom with a clinician in the past month.
	Stage: 81% stage III–IV		50% of the patients reported receiving symptom management recommendations from clinicians.
	Treatment: 57% CTX, 10% RT		76% of the patients identified at least one coping strategy to manage their most noticed symptom.
To evaluate whether communication was associated with patients’ confidence in managing symptoms		A single question designed to measure discussion of symptoms and adherence to treatment recommendations	
		Daily Coping Inventory	
Holmes (1990)	<i>n</i> =51	Cross-sectional	The most distressing symptoms were tiredness (59%), appearance (51%), concentration (43%), mood (43%), and pain (37%) in both patients with CTX and RT.

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
To identify any differences in the degree of symptom distress between patients undergoing CTX and RT	22 (43%) with CTX and 29 (57%) with RT		The common causes of distress in patients with CTX were tiredness (64%), difficulty with concentration and mood (55%), altered appearance (55%), poor activity (36%), and pain (27.3%).
	No information provided about demographic and clinical characteristics	SDS based on a linear analogue self assessment (LASA) (0–100 mm)	The common causes of distress in patients with RT were tiredness (55%), altered appearance (48%), pain (45%), constipation (41%), and poor appetite (38%). The mean SDS score for patients on CTX (746.5) was higher than for patients on RT (710.0).
Ivonava et al. (2005) To develop and validate a Russian-language version of the MDASI-R	<i>n</i> =226 inpatients and outpatients	Cross-sectional	Most prevalent moderate to severe symptoms were fatigue (94%), sleep disturbances (59%), pain (53%), sadness (35%), and poor appetite (24%).
	Age: 61 years (range: 18–92)	MDASI	53% of the sample reported one to four symptoms at moderate to severe levels.
	Female: 62%	SF-36	22% of the sample had five or more moderate to severe symptoms.
	Ethnicity: 100% Russian		Of those who reported severe symptoms, 48% reported at least one symptom and 37% reported one to three symptoms.
	Various cancers		Fatigue, pain, and sleep disturbance were prevalent symptoms in patients with solid tumors and hematologic malignancies.
	Stage: 87% stage III–IV		The prevalence rates for poor appetite, distress, and sadness were significantly greater in patients with solid tumors compared to hematologic malignancies. SOB and difficulty remembering were more common in patients with hematologic cancers.
Treatment: 40% CTX, 38% RT, 15% surgery		Patients on CTX reported more severe fatigue, SOB, difficulty remembering, drowsiness, and poor appetite than those who received RT. Symptoms interfered most with work and general activity followed by mood, enjoyment of life, and walking.	
Lobchuk et al. (1997)	<i>n</i> =41	Cross-sectional	Most distressing symptoms for patients were fatigue (65%), cough (57%), shortness of breath (42%), pain frequency (31%), poorer outlook (30%), and insomnia (30%).

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
To describe differences between family caregivers' interpretations of symptom distress and patients' perceptions of symptom distress	Age: 65 years (range: 40–80)	SDS	Most distressing symptoms for family caregivers were fatigue (70%), poorer outlook (55%), cough (55%), insomnia (45%), and frequent pain (40%).
	Female: 32%	MMSE	The average global SDS score for patients was 27.8 and for family caregivers was 31.3.
	Ethnicity: Canadian	KPS	Family caregivers tended to rate the patients' degree of distress as slightly more severe than the patients for all symptoms except difficulty with concentration.
	Lung cancer Stage: 74% stage III–IV Treatment: 29% CTX, 10% RT		
Lobchuk & Degner (2002) To compare patient and family caregiver perceptual congruence on symptom experience	<i>n</i> =98 outpatients	Cross-sectional	Mean number of patient reported symptoms was 11.4.
	Age: 64.7 years (range: 35–86)	MSAS	Mean number of family caregiver reported symptoms was 14.1.
	Female: 61%		Both patients and family caregivers reported that the most highly prevalent physical symptoms were lack of energy, pain, and feeling drowsy. Worrying was the most prevalent psychological symptom.
	Ethnicity: Canadian		Most frequently occurring, severe, and distressing symptom as reported by both patients and family caregivers was lack of energy.
	Various cancers		Family caregivers tended to over-report symptom distress.
	Treatment: 42% CTX, 10% RT, and 51% none		Patient and family caregiver reports of physical symptoms were more highly correlated than their reports of psychological symptoms.
Okuyama et al. (2003) To examine the validity and reliability of the Japanese version of the MDASI	<i>n</i> =252 outpatients	Cross-sectional	Most common symptoms at the moderate to severe level were fatigue (36%), drowsiness (33%), distress (31%), dry mouth(29%), and disturbed sleep (26%).
	Age: 62.5 years	MDASI	Over 30% of the patients experienced 3 symptoms at moderate or severe levels.
	Female: 42%		The two symptoms that contributed the most to symptom interference were fatigue and sadness.

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
	Ethnicity: 100% Japanese Various cancers Stage: 50% metastasis Treatment: 22% CTX, 2% RT	EORTC POMS	
Portenoy, Kornblith, et al. (1994) To evaluate the prevalence, characteristics, and impact of pain and other symptoms in patients with ovarian cancer	<i>n</i> =151 inpatients and outpatients Age: 54 years (range: 23–86) Female: 100% Ethnicity: 92% white Ovarian cancer Stage: 82% stage III–IV Treatment: 87% CTX	Cross-sectional MSAS Comprehensive pain questionnaire Rand Mental Health Inventory FLIC KPS	Mean number of symptoms per patient was 10.2. Inpatients experienced a mean of 11.2 symptoms whereas outpatients experienced a mean of 7.4 symptoms. Most prevalent symptoms were pain (62%), lack of energy(68%), psychological distress (worrying =72%, feeling sad=64%, feeling nervous=62%), and insomnia (57%). Most severe symptoms were worrying, lack of energy, pain, feeling sad, and difficulty sleeping. Most frequent symptoms were lack of energy, worrying, pain, difficulty sleeping, and feeling nervous. Most distressing symptoms were lack of energy, worrying, pain, feeling sad, and difficulty sleeping. Most severe, frequent, and distressing symptoms were worrying, lack of energy, and pain.
Portenoy, Thaler, et al. (1994) To evaluate the validity of the MSAS in a heterogeneous population of cancer patients	<i>n</i> =243 inpatients and outpatients Age: 55.5 years (range: 23–86) Female: 61% Ethnicity: no information	Cross-sectional MSAS Memorial Pain Assessment Card Revised Rand Mental Health Inventory	Mean number of symptoms was 11.5. Inpatients reported a mean of 13.5 symptoms, whereas outpatients reported a mean of 9.7. Most prevalent symptoms were lack of energy (74%), worrying (71%), feeling sad (65%), pain (64%), feeling nervous (61%), drowsiness (60%), dry mouth (54%), and difficulty sleeping (52%). No significant differences in overall symptom prevalence by age, gender, tumor type, or extent of disease. Proportion of patients who reported a high level of symptom distress was always lower than the proportion of patients who reported the symptom as severe or frequent.

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
	Prostate, colon, breast, or ovarian cancer	FLIC	A higher number of symptoms was associated with more psychological distress ($r = -0.37$) and poorer quality of life ($r = -0.67$).
	Stage: 28% local disease, 56% metastasis	SDS	
	Treatment: no specific information	KPS	
Sama (1993)	$n=69$	Cross-sectional	Most distressing symptoms were fatigue (57%), pain (29%), insomnia (25%), poor outlook (23%), and appetite disruption (19%).
To explore and describe symptom distress and its correlates in women with lung cancer	Age: 61 years (range: 50–72)	SDS	61% of women experienced more than one distressing symptom.
	Gender: 100% female	KPS	41% of patients with fatigue experienced pain and 31% of patients with fatigue experienced insomnia.
	Ethnicity: 86% white	CARES-SF	23% of women reported four or more symptoms.
	Lung cancer		Higher symptom distress was associated with lower QOL ($r=0.72$) and poorer functional status ($r=0.71$).
	Stage: 68% limited disease, 32% distant disease		Presence of respiratory disease, previous CTX, recurrent disease, and absence of previous surgery were associated with higher levels of symptom distress.
	Treatment: 43% CTX, 9% RT, 4% combination treatment		Age, treatment status, and site of metastasis were not associated with a higher level of symptom distress.
Tishelman, Degner, & Bryan (2000)	$n=26$ patients at T1, 15 patients at T2, and 8 patients at T3	Longitudinal study	SDS score was 2.02 at T1, 1.9 at T2, and 2.0 at T3.
		Over three times (T1: after first contact with unit, then 1 (T2) and 2 months later (T3))	Most distressing symptoms were fatigue (69%), poor outlook (54%), shortness of breath (50%), insomnia (46%), and frequent pain (40%).
To explore the differences between patients' perceived importance of symptoms and patients' rated symptom intensity	Age: 66.9 (T1), 64.5 (T2), and 66.0 years (T3)		At T1, T2, and T3, shortness of breathing, pain, and insomnia were rated as severe.
	Female: 50%		At T1, fatigue, poor outlook, and insomnia were the most severe symptoms, whereas poor outlook, shortness of breath, and pain were the most distressing symptoms.

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
	Ethnicity:100% Swedish	SDS	Patients weighted the importance of symptoms differently than they weighted their intensity.
	Lung cancer Stage: no information Treatment: no specific information	Thurstone Scale	
Wang et al. (2004)	<i>n</i> =249 inpatients	Cross-sectional	Most severe symptoms were fatigue, sleep disturbance, distress, pain, and poor appetite.
To establish and validate a Chinese version of the MDASI	Age: 51 years (range: 18–77)	MDASI	About 40% of patients reported severe symptoms and at least 2 symptoms were severe.
	Female: 54%	MOS 36-SF	Fatigue and sleep disturbance were the most severe symptoms for patients with breast and lung cancer whereas fatigue and lack of appetite were the most severe symptoms for patients with GI cancer.
	Ethnicity: 100% Chinese	ECOG-PS	At least 30% of patients with lung cancer reported 7 symptoms as being moderate to severe symptoms whereas those with GI and breast cancer reported 4 to 5 symptoms as severe.
	Various cancers		Fatigue, sadness, drowsiness, and lack of appetite were significant predictors of and accounted for 49% of the variance in interference.
To examine the severity of symptoms caused by the most common cancers in China	Stage: 50% stage III–IV		The highest level of symptom interference was for work, enjoyment of life, and mood.
	Treatment: 35% CTX, 12% RT, 21% surgery, 22% combined treatment		
Wang et al. (2006)	<i>n</i> =206 inpatients and outpatients	Cross-sectional	The top five moderate to severe symptoms were problem with remembering (43%), fatigue (40%), drowsiness (35%), sadness (31%), and numbness (31%).
To test the validity and reliability of a Filipino version of the MDASI	Age: 47 years (range: 18–76)	MDASI	62% of patients rated a single or multiple symptoms as severe.
	Female: 68%		44% of patients rated at least two symptoms as severe.
To examine the prevalence and severity of cancer symptoms and their impact on Filipino patients' daily functioning	Ethnicity: 100% Filipino		Fatigue, sadness, distress, and pain were significant predictors of symptom interference.
	Various cancers		

Author Purpose	Sample Characteristics	Design Instruments	Major Findings
	Stage: 65% stage III–IV, 18% Metastasis Treatment: 32% CTX, 28% RT, 29% surgery		
Yan & Sellick (2004)	<i>n</i> =146 outpatients	Cross-sectional	The mean number of symptoms was 5.
To describe symptoms, psychological distress, social support, and quality of life of Chinese patients with newly diagnosed gastrointestinal cancer	Age: 55 years (range: 17–93)	MSAS	The most prevalent symptoms were fatigue (63%), pain (42%), weight loss (41%), dry mouth (38%), and lack of appetite (36%).
	Female: 24%	SAI	The most frequent symptoms were fatigue, vomiting, shortness of breath, lack of appetite, nausea, and pain.
	Ethnicity: 100% Chinese	BDI-SF	The most severe symptoms were change in the way food tastes, insomnia, hair loss, fatigue, and weight loss.
	Esophagus, stomach, liver, pancreas, and colorectal cancer	SSQ	The most distressing symptoms were insomnia, change in the way food tastes, hair loss, fatigue, and shortness of breath.
	Stage: no information	CARES-SF (HRQoL)	Patients over 70 years of age and with liver cancer reported more symptom distress.
	Treatment: 56% surgery, 14% CTX, 16% RT	VAS (GQoL)	Patients younger than 40 years of age had higher depression and anxiety than those 70 years of age or older. Depression (29%) and symptom distress (12%) accounted for the largest amount of variance HRQOL.

BDI-SF = Beck Depression Inventory-Short Form; CARE-SF = Cancer Rehabilitation Evaluation System-Short Form; CTX = Chemotherapy; ECOG-PS = Eastern Cooperative Oncology Group Performance Status; EORTC = European Organization for-Research and Treatment of Cancer; FLIC = Functional Living Index Cancer; GI = Gastrointestinal; HRQOL = Health Related Quality of Life; KPS = Karnofsky Performance Status Scale; MDASI = M. D. Anderson Symptom Inventory; MMSE = Mini-Mental State Examination; MSAS = Memorial Symptom Assessment Scale; MOS 36-SF = Medical Outcome Survey-Short Form; POMS = Profile of Mood States; RT = Radiation Therapy; SAI = Spielberger State Anxiety Inventory; SDS = Symptom Distress Scale; SF-36 = Short Form Health Survey; SOB = Shortness of Breath; SRQ = Symptom Representation Questionnaire; SSQ = Social Support Questionnaire; VAS = Visual Analogue Scale.

Table 2
 Characteristics and Psychometric Properties of Instruments Used to Measure Multiple Symptoms in Adults with Cancer

Instrument	Number of Items and Dimensions Measured	Dimensions	Scale	Reliability	Validity	Number of studies
MDASI	13 symptoms severity items 6 interference items	Physical Psychological	11-point numeric rating scale	Internal consistency(Cronbach alpha=0.82-0.91)	Content Construct	7
	-Severity -Level of interference with function		Intensity = 0 (not present) to 10 (as bad as you can imagine) Interference = 0 (does not interfere) to 10 (interferes completely)			
MSAS	32 items	Physical Psychological	4- and 5-point Likert scales	Internal consistency(Cronbach alpha =0.83-0.85)	Content Construct	5
	-Frequency -Severity -Distress		Severity and frequency = 1 (slight/rarely) to 4 (very severe/almost constantly) Distress = 0 (not at all) to 4 (very much)			
SDS	13 items	Physical Psychological	5-point Likert scales	Internal consistency (Cronbach alpha =0.82)	Criterion Content Construct	6
	-Distress		Distress = 1 (the least amount of distress) to 5 (extreme distress)	Test-retest		

MDASI=M. D. Anderson Symptom Inventory; MSAS=Memorial Symptom Assessment Scale; SDS=Symptom Distress Scale.

Table 3
Comparison of the Symptoms Evaluated Using Three Multiple Item Symptom Instruments

M. D. Anderson Symptom Inventory 13 symptoms	Memorial Symptom Assessment Scale 32 symptoms	Symptom Distress Scale 13 symptoms
<i>Physical symptoms</i>		
Pain	Pain	Pain severity/frequency
Fatigue	Lack of energy	Fatigue
Disturbed sleep	Difficulty sleeping	Insomnia
Dry mouth	Dry mouth	
	Mouth sores	
	Change in the way food tastes	
	Difficulty of swallowing	
Lack of appetite	Lack of appetite	Lack of appetite
	Weight loss	
Nausea	Nausea	Nausea severity/frequency
Vomiting	Vomiting	
		Bowel dysfunction
	Diarrhea	
	Constipation	
Drowsy (sleepy)	Feeling drowsy	
Shortness of breath	Shortness of breath	Shortness of breath
	Cough	Coughing
	Feeling bloated	
Numbness or tingling	Numbness/tingling in hands or feet	
	Itching	
	Dizziness	
		Poor activity
	Hair loss	
	Problem with sexual interest or activity	
	Problems with urination	
	Sweats	
	Swelling of arms or legs	
	Changes in skin	
<i>Psychological symptoms</i>		
Problem with remembering things	Difficulty concentrating	Difficulty with concentration
Feeling sad	Feeling sad	Mood
	Worrying	
	Feeling nervous	
	Feeling irritable	
Distress (upset)		
	"I don't look like myself"	Altered appearance

M. D. Anderson Symptom Inventory 13 symptoms	Memorial Symptom Assessment Scale 32 symptoms	Symptom Distress Scale 13 symptoms
		Poor outlook

Table 4
Prevalence Rates for Physical and Psychological Symptoms Across the Various Studies

Physical Symptoms	Holmes (1991) <i>n</i> =51 patients 43% chemotherapy, 57% RT SDS-11 symptoms	Sarna (1993) <i>n</i> =69 women with lung cancer 43% chemotherapy SDS	Degner & Sloan (1995) <i>n</i> =434 newly lung cancer 34% chemotherapy, 63% RT SDS	Lobchuk et al. (1997) <i>n</i> =37 with lung cancer 29% chemotherapy, 10% RT SDS	Tishelman & Degner (2000) <i>n</i> =26 patients with lung cancer SDS
Pain severity ¹ and frequency ¹ Pain ^{2,3}	37.3%	17.4% (S)/28.8 (F)	18.7% (S)/23.5% (F)	28% (S)/32% (F)	30.8% (S)/40% (F)
Fatigue or Tiredness ^{1,2} Lack of energy ³	58.8% (T)	56.5%	38.9%	70%	69.2%
Insomnia ¹ Difficulty sleeping ^{2,3}	23.5%	24.6%	30.9%	31%	46.2%
Dry mouth ^{2,3}					
Sore mouth ³					
Taste change ³					
Lack of appetite ^{1,2,3}	33.3%	18.8%	18%	29%	34.6%
Weight loss ³					
Nausea severity ¹ and frequency ¹ Nausea ^{2,3}	13.7%	13% (S)/10.1% (F)	12.2% (S)/7.4% (F)	20% (S)/20% (F)	
Vomiting ^{2,3}					
Bowel dysfunction ¹	29.4%	8.6%	18.4%	25%	23.1%
Diarrhea ³	9.8%				
Constipation ¹	29.4%				
Drowsiness ^{2,3}					
SOB ^{1,2,3}		15.9%	9%	41%	50%
Coughing ^{1,3}		17.4%	13.4%	58%	26.9%
Feeling bloated ³					
Numbness/Tingling ^{2,3}					
Itching ³					
Dizziness ³					
Psychological Symptoms					
Concentration ^{1,2,3}	43.1%		9.7%	21%	
Feeling sad ^{2,3} /Mood ¹	43.1%				
Worrying ³					
Feeling nervous ³					
Feeling irritable ³					

Physical Symptoms	Holmes (1991) ¹ <i>n</i> =51 patients 43% chemotherapy, 57% RT, <i>SDS-II</i> symptoms	Sarna (1993) ² <i>n</i> =69 women with lung cancer 43% chemotherapy, <i>SDS</i>	Degner & Sloan (1995) ³ <i>n</i> =434 newly lung cancer 34% chemotherapy, 63% RT, <i>SDS</i>	Lobchuk et al. (1997) ⁴ <i>n</i> =37 with lung cancer 29% chemotherapy, 10% RT, <i>SDS</i>	Tishelman & Degner (2000) ⁵ <i>n</i> =26 patients with lung cancer <i>SDS</i>
Distress ^{2,3}					
Altered appearance ¹	50.9%	10.1%	19.6%	28%	34.6%
Poor outlook ¹		23.1%	23.5%	31%	53.8%
Physical Symptoms	Cooley et al. (2003) ⁶ <i>n</i> =117 with lung cancer 7% chemotherapy, 11% RT, & 38% surgery, <i>SDS</i>	Cleeland et al. (2000) ⁷ <i>n</i> =527 with various cancer 56% chemotherapy, 23% biotherapy, <i>MDASI</i>	Okuyama et al. (2003) ⁸ <i>n</i> =252 with various cancer 22% chemotherapy, 2% RT, & 2% surgery, <i>MDASI</i>	Wong et al. (2004) ⁹ <i>n</i> =51 with lung cancer 35% chemotherapy, 12% RT, 21% surgery, <i>MDASI</i>	Ivanova et al. (2005) ¹⁰ <i>n</i> =226 with various cancer 40% chemotherapy, 38% RT, 15% surgery, <i>MDASI</i>
Pain severity ¹ and frequency ¹ Pain 2,3	37% (S); 56% (F)	34%	23%	25%	53%
Fatigue or Tiredness ^{1,2} Lack of energy ³	64%	59%	36%	38%	90%
Insomnia ¹ Difficulty sleeping ^{2,3}	49%	41%	26%	33%	81%
Dry mouth ^{2,3}		37%	29%	16%	22%
Sore mouth ³		15%			
Taste change ³					
Lack of appetite ^{1,2,3}	43%	39%	27%	22%	24%
Weight loss ³				14%	
Nausea severity ¹ and frequency ¹ Nausea ^{2,3}		19%	13%	7%	9%
Vomiting ^{2,3}		11%	15%		1%
Bowel dysfunction ¹					
Diarrhea ³		14%			
Constipation ¹		32%		12%	
Drowsiness ^{2,3}		41%	33		18%
SOB ^{1,2,3}		26%	23%	22%	17%
Coughing ^{1,3}		18%			
Feeling bloated ³		23%		9%	
Numbness/Tingling ^{2,3}		29%	24%		11%
Itching ³					
Dizziness ³					
Psychological symptoms					

Physical Symptoms	Holmes (1991) <i>n</i> =51 patients 43% chemotherapy, 57% RT SDS-II symptoms	Sarna (1993) <i>n</i> =69 women with lung cancer 43% chemotherapy SDS	Degner & Sloan (1995) <i>n</i> =434 newly lung cancer 34% chemotherapy, 63% RT SDS	Lobchuk et al. (1997) <i>n</i> =37 with lung cancer 29% chemotherapy, 10% RT SDS	Tishelman & Degner (2000) <i>n</i> =26 patients with lung cancer SDS
Concentration ^{1,2,3}		23%	15%	7%	15%
Feeling sad ^{2,3} /Mood ¹		32%	29%	17%	35%
Worrying ³		43%			
Feeling nervous ³		34%			
Feeling irritable ³		33%			
Distress ^{2,3}		42%	31%	20%	9%
Altered appearance ¹					
Poor outlook ¹					
Physical Symptoms	Donovan et al (2005) <i>n</i>=279 women with ovarian cancer 57% chemotherapy, 10% RT MDASI	Chen & Tseng (2006) <i>n</i>=151 with various cancer 50% chemotherapy MDASI	Wang et al. (2006)<i>n</i>=206 with various cancer 32% chemotherapy MDASI	Portenoy et al. (1994) <i>n</i>=151 with ovarian cancer 87% chemotherapy MSAS	Portenoy et al. (1994) <i>n</i>=243 with various cancer MSAS
Pain severity ¹ and frequency ¹ /Pain ^{2,3}	27%	72.8%	30.0%	61.8%	64.0%
Fatigue or Tiredness ^{1,2} Lack of energy ³	59%	82.1%	40.0%	68.6%	73.7%
Insomnia ¹ Difficulty sleeping ^{2,3}	14%	72.2%	27.0%	57.3%	52.3%
Dry mouth ^{2,3}		84.1%	29.0%	45.6%	54.4%
Sore mouth ³				8.1%	12.4%
Taste change ³				25.7%	35.4%
Lack of appetite ^{1,2,3}	2%	76.2%	26.0%	28.4%	44.4%
Weight loss ³	2%			18.5%	27.1%
Nausea severity ¹ and frequency ¹ Nausea ^{2,3}	9%	52.3%	20.4%	35.6%	44.2%
Vomiting ^{2,3}	4%	45.0%	5.8%	13.3%	20.6%
Bowel dysfunction ¹	37%			28.6%	34.7%
Diarrhea ³				20.8%	23.5%
Constipation ¹				28.6%	34.7%
Drowsiness ^{2,3}	5%	65.6%	35.4%	45.3%	59.8%
SOB ^{1,2,3}	7%	44.4%	14.1%	18.7%	23.5%
Coughing ^{1,3}				25.3%	28.6%
Feeling bloated ³	25%			34.7%	37.2%

	Holmes (1991) <i>n</i> =51 patients 43% chemotherapy, 57% RT SDS-II symptoms	Sarna (1993) <i>n</i> =69 women with lung cancer 43% chemotherapy SDS	Degner & Sloan (1995) <i>n</i> =434 newly lung cancer 34% chemotherapy, 63% RT SDS	Lobchuk et al. (1997) <i>n</i> =37 with lung cancer 29% chemotherapy, 10% RT SDS	Tishelman & Degner (2000) <i>n</i> =26 patients with lung cancer SDS
Physical Symptoms					
Numbness/Tingling ^{2,3}	26%	49.0%	30.6%	42.7%	37.2%
Itching ³				22.3%	27.1%
Dizziness ³	0%			16.2%	23.6%
Psychological symptoms					
Concentration ^{1,2,3}	4%	55.0%	43.2%	34.7%	40.5%
Feeling sad ^{2,3} /Mood ¹	9%	60.9%	31.0%	63.8%	65.0%
Worrying ³				71.7%	70.7%
Feeling nervous ³				61.5%	61.3%
Feeling irritable ³				45.9%	47.0%
Distress ^{2,3}		72.2%	21.8%		
Altered appearance ¹					
Poor outlook ¹					
Physical Symptoms	Chang et al. (2000) <i>n</i> =240 with various cancer No treatment information MSAS	Lobchuk & Degner (2002) <i>n</i> =98 with various cancer 42% chemotherapy, 10% RT MSAS	Yan & Sellick (2004) <i>n</i> =146 newly diagnosed GII cancer 56% surgery, 14% chemotherapy, 16% RT MSAS	<i>Mean Prevalence Rate for Each Symptom Across the 18 Studies 40% (S)/36% (F)</i>	
Pain severity ¹ and frequency ¹ Pain ^{2,3}	59%	51%	42%		
Fatigue or Tiredness ^{1,2} Lack of energy ³	62%	60.2%	63%		62%
Insomnia ¹ Difficulty sleeping ^{2,3}	45%	39.2%	25%		41%
Dry mouth ^{2,3}	54%	37.8%	38.4%		42%
Sore mouth ³		10.2%			11%
Taste change ³		18.4%	11.6%		23%
Lack of appetite ^{1,2,3}	29%	36.7%	35.6%		32%
Wt loss ³	33%	10.2%	42%		22%
Nausea severity ¹ and frequency ¹ Nausea ^{2,3}		19.4%	17.1%		21% (S)/13% (F)
Vomiting ^{2,3}		9.2%	11%		13%
Bowel dysfunction ¹		21.4%	15.1%		24%
Diarrhea ³		11.2%	19.2%		16%

Physical Symptoms	Holmes (1991) ¹ n=51 patients 43% chemotherapy, 57% RT SDS-II symptoms	Sarna (1993) ² n=69 women with lung cancer 43% chemotherapy SDS	Degner & Sloan (1995) ³ n=434 newly lung cancer 34% chemotherapy, 63% RT SDS	Lobchuk et al. (1997) ⁴ n=37 with lung cancer 29% chemotherapy, 10% RT SDS	Tishelman & Degner (2000) ⁵ n=26 patients with lung cancer SDS
Constipation ¹		21.4%	15.1%		27%
Drowsiness ^{2,3}	44%	49.9%	13.7%		36%
SOB ^{1,2,3}	50%	29.6%/	15.8%		26%
Coughing ^{1,3}	33%	25.5%	15.8%		26%
Feeling bloated ³		24.5%			29%
Numbness/Tingling ^{2,3}		26.5%			29%
Itching ³		22.4%	18.5%		23%
Dizziness ³		10.2%	29.5%		20%
Psychological symptoms					
Concentration ^{1,2,3}		15.3%			25%
Feeling sad ^{2,3} /Mood ¹		35.7%			39%
Worrying ³	40%	41.8%			54%
Feeling nervous ³	37%	29.6%			45%
Feeling irritable ³	28%	33.7%			37%
Distress ^{2,3}					34%
Altered appearance ¹					29%
Poor outlook ¹					33%

F = frequency; GIT = gastrointestinal; MDASI² = M. D. Anderson Symptom Inventory; MSAS³ = Memorial Symptom Assessment Scale; RT = radiation therapy; S = severity; SDS¹ = Symptom Distress Scale; SOB = shortness of breath.