

NIH Public Access

Author Manuscript

J Pain Symptom Manage. Author manuscript; available in PMC 2015 April 01

Published in final edited form as:

J Pain Symptom Manage. 2014 April; 47(4): 697–709. doi:10.1016/j.jpainsymman.2013.05.017.

Differences in the Symptom Experience of Older Oncology Outpatients

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Abstract

Context—The relatively low number of older patients in cancer trials limits knowledge of how older adults experience symptoms associated with cancer and its treatment.

Objectives—This study evaluated for differences in the symptom experience across four older age groups (60–64, 65–69, 70–74, 75 years of age).

Methods—Demographic, clinical, and symptom data from 330 patients >60 years of age who participated in one Australian and two U.S. studies were evaluated. The Memorial Symptom Assessment Scale (MSAS) was used to evaluate the occurrence, severity, frequency, and distress of 32 symptoms commonly associated with cancer and its treatment.

Results—On average, regardless of age group, patients reported 10 concurrent symptoms. The most prevalent symptoms were physical in nature. Worrying was the most common psychological symptom. For 28 (87.5%) of the 32 MSAS symptoms, no age-related differences were found in symptom occurrence rates. For symptom severity ratings, an age-related trend was found for difficulty swallowing. As age increased, severity of difficulty swallowing decreased. For symptom frequency, age-related trends were found for feeling irritable and diarrhea, with both decreasing in frequency as age increased. For symptom distress, age-related trends were found for lack of energy, shortness of breath, feeling bloated, and difficulty swallowing. As age increased, these symptoms received lower average distress ratings.

Disclosures

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The authors declare no conflicts of interest.

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Conclusion—Additional research is warranted to examine how age differences in symptom experience are influenced by treatment differences, aging-related changes in biological or psychological processes, or age-related response shift.

Keywords

geriatric oncology; symptoms; symptom assessment; cancer; symptom distress; multiple concurrent symptoms

Introduction

Among adults ages 60 to 85, cancer is the leading cause of death in both men and women.¹ From 2005 to 2009, adults 65 and older accounted for 53% of all new cancer diagnoses and 69% of cancer-related deaths.² As the older population grows and the number of older adults with cancer grows concomitantly, studies are needed that focus specifically on older patients' responses to cancer treatment. These responses are likely to be heterogeneous, given the variations in health status that are observed with age.³

Despite the high incidence of and mortality associated with cancer in older adults, only onethird of participants in National Cancer Institute trials were 65 years of age or older.^{4,5} This recruitment bias limits our knowledge of how older adults respond to cancer treatment. In turn, this knowledge deficit limits the ability of clinicians to tailor treatments for older adults with cancer.^{6,7}

Similar to younger adults, older adults with solid tumors may experience a broad range of physical and psychological symptoms. However, findings on differences in symptom occurrence rates, as well as ratings of symptom severity and distress between older and younger oncology patients, are inconsistent. In some studies, older patients report higher symptom occurrence rates,⁸ whereas in other studies the rates are lower.^{9,10} Given the paucity of research on age-related differences in the symptom experience of oncology patients, recent work from our research team evaluated for differences in symptom occurrence, severity, frequency and distress between older and younger oncology patients using the Memorial Symptom Assessment Scale (MSAS).¹¹ After controlling for significant covariates, patients 60 years of age and older endorsed significantly lower occurrence rates for 15 of 32 MSAS symptoms. Moreover, these older adults reported lower severity ratings for six symptoms, lower frequency ratings for four symptoms, and lower distress ratings for 14 symptoms. Eight of eleven symptoms with the highest occurrence rates (i.e., lack of energy, pain, feeling drowsy, difficulty sleeping, dry mouth, difficulty concentrating, worrying, feeling irritable) were the same in the older and younger age groups.

Whereas additional research is warranted to explain these age-related differences in various dimensions of the symptom experience, an equally important consideration is whether specific age groups across older adults report differences in symptom occurrence, severity, frequency, and distress associated with cancer and its treatment. Only two studies were identified that compared symptom experiences across older age groups.^{12,13}

In the first study, which evaluated the influence of age on symptom distress of older adults following cancer surgery,¹² patients were divided into three age categories (i.e., 65 to 69 [n=147], 70 to 74 [n=108], 75 and older [n=71]) and symptom distress was measured using the Symptom Distress Scale.¹⁴ Although overall symptom distress decreased over time, a significant age group by time interaction was identified. Patients 75 years of age and older reported higher symptom distress scores over the six months of the study compared with patients between 65 and 69 years of age.

In the second study of patients newly diagnosed with gastrointestinal cancer (n=337),¹³ agerelated differences in patients' symptom experiences pre- and post-treatment were evaluated using the Rotterdam Symptom Checklist. In this study, younger patients' (i.e., 58 to 74 years of age) psychological distress and overall quality of life improved from pre- to posttreatment. In contrast, older patients (75 years of age and older) reported no changes in symptom distress over time. However, a comprehensive evaluation of differences in symptom experiences among older age groups was not reported.

Neither of these studies provides detailed information on age-related differences in multiple dimensions of the symptom experience in older patients with cancer.^{12,13} Therefore, given the paucity of information on the symptom experience of older oncology patients and the limitations of the previous studies,^{12,13} the purposes of this study, in a relatively large sample of older oncology patients (n=330), were to evaluate for differences in symptom occurrence rates, as well as ratings of symptom severity, frequency, and distress across four older age groups (i.e., 60–64, 65–69, 70–74, and 75 years of age).

Methods

Study Samples

Demographic, clinical, and symptom data from one Australian study (Symptom Clusters) and two U.S. studies (Fatigue, Pain, and Sleep Study [FPS Study];^{15,16} and Symptom Prevalence Study) were combined to conduct this analysis.¹¹ All three studies enrolled patients who were receiving active treatment for their cancer. This paper analyzed data from patients 60 years of age or older (n=330).

Symptom Clusters Study—This was a prospective, longitudinal study designed to identify symptom clusters and their effects on physical and psychological functioning of patients with metastatic disease. Data were collected from patients using an interview-administered survey at the time of diagnosis or progression of metastatic disease and again at two months and four months. Data from the first assessment were used in these analyses.

Patients were recruited consecutively from two major tertiary referral hospitals in Australia: the Royal Brisbane and Women's Hospital and Peter MacCallum Cancer Centre (Melbourne). Patients were eligible to participate if they were adults (18 years of age or older) who could read, write, and understand English; had no cognitive limitations; had a primary cancer of breast, lung, colon/rectum, prostate, upper gastrointestinal tract, or ovaries; and were diagnosed with metastatic disease in the past month or had clinical evidence of progressive metastatic disease. Patients were excluded if they had local

recurrence, but no evidence of metastatic disease; had a prognosis of less than four months as determined by their clinician; or had physical or cognitive impairments that precluded participation in the 20-minute survey. The study was approved by the Ethics Committees of Queensland University of Technology and of the two participating hospitals.

Research staff worked with clinical staff to identify potentially eligible patients, using a standard screening assessment sheet. All patients provided written consent prior to completing the study questionnaires. Of 306 patients approached, 218 patients were recruited (71.2% response rate). One hundred thirty-one patients were 60 years of age. Reasons for non-participation included: clinician's assessment that patients were not well enough to participate (27.9%), prognosis of less than four months (22%), limited English (18.7%), patient was participating in another study (18.4%), and patient was physically or cognitively unable to participate (13%). The questionnaire was completed during a 20-minute face-to-face interview conducted by trained interviewers with nursing or psychology backgrounds. Clinical and demographic data were obtained from medical record reviews.

Fatigue, Pain, and Sleep Study—The FPS Study was a longitudinal study that evaluated symptoms in patients with breast, prostate, lung, or brain cancer undergoing primary or adjuvant radiation therapy (RT).^{15,16} Patients were recruited from two RT departments located in a comprehensive cancer center and a community-based oncology program at the time of the patient's simulation visit. Patients were eligible to participate if they: were 18 years of age; were scheduled to receive primary or adjuvant RT; were able to read, write, and understand English; gave written informed consent; and had a Karnofsky Performance Status (KPS) score of 60. Patients were excluded if they had: metastatic disease, more than one cancer diagnosis, or a diagnosed sleep disorder.

A total of 472 patients were approached and 185 consented to participate (response rate of 39.2%). Ninety-five patients were 60 years of age. The primary reasons for refusal were being overwhelmed or too busy. The study was approved by the Committee on Human Research at the University of California, San Francisco (UCSF) and at the second site. At the time of the simulation visit (i.e., approximately one week prior to the initiation of RT), patients were approached by a research nurse to discuss participation in the study. After obtaining written informed consent, patients completed the study questionnaires. In addition, medical records were reviewed for disease and treatment information. Data from the first assessment were used in these analyses.

Symptom Prevalence Study—The Symptom Prevalence Study was a descriptive, crosssectional study that used self-report questionnaires to obtain information from a convenience sample of oncology outpatients. Patients were recruited from four outpatient settings in northern California, including a university-based comprehensive cancer center, a Veterans Affairs facility, and two community-based outpatient clinics. Patients were eligible to participate if they were 18 years of age; were able to read, write, and understand English; gave written, informed consent; had KPS scores of 50; and were receiving active cancer treatment.

A total of 310 patients were approached and 206 consented to participate (response rate of 66.5%). One hundred four patients were 60 years of age. The primary reasons for refusal were that a patient was too ill to participate (80%), too busy (15%), or not interested in the research study (5%). Patients who agreed to participate provided written informed consent and were given a copy of the questionnaire booklet. They completed the study questionnaires in their home and returned them to the research office using a postage paid envelope. The study was approved by the Committee on Human Research at UCSF and at each of the study sites.

Instruments

Demographic and Clinical Characteristics—Demographic information on age, gender, marital status, and living arrangements were obtained at enrollment. Because of differences in the educational systems in Australia and the U.S., data on education were recoded into a dichotomous variable (i.e., no post high school vs. post high school education). In addition, patients' medical records were reviewed for cancer diagnosis, presence of metastatic disease, and current treatment regimens (i.e., none, chemotherapy [CTX], RT, both CTX and RT).

In the Australian study, patients' functional status was rated by their clinicians using the Eastern Cooperative Oncology Group (ECOG) Performance Status score, which ranges from 0 (fully active) to 4 (disabled).¹⁷ In the U.S. studies, patients rated their functional status using the KPS scale, which ranged from 30 ("I feel severely disabled and need to be hospitalized") to 100 ("I feel normal; I have no complaints or symptoms"). The KPS scale is widely used to evaluate functional status in patients with cancer and has well-established validity and reliability. Based on the recommendations of Verger and colleagues,¹⁸ KPS scores were converted to ECOG scores for use in subsequent analyses.

Memorial Symptom Assessment Scale (MSAS)—All three studies used the MSAS to evaluate the occurrence, severity, frequency, and distress of 32 symptoms commonly associated with cancer and its treatment.¹⁹ The MSAS is a self-report questionnaire designed to measure the multidimensional experience of symptoms. Using the MSAS, patients were asked to indicate whether or not they had experienced each symptom in the past week (i.e., symptom occurrence). If they had experienced the symptom, they were asked to rate its frequency of occurrence, severity, and distress. Symptom frequency was evaluated using a 4-point Likert scale (i.e., 1=rarely, 2=occasionally, 3=frequently, 4=almost constantly). Symptom severity was measured using a 4-point Likert scale (i.e., 1=slight, 2=moderate, 3=severe, 4=very severe). Symptom distress was measured using a 5-point Likert scale (i.e., 0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, 4=very much).

Three subscale scores (i.e., Global Distress Index, physical [MSAS PHYSICAL], psychological [MSAS PSYCH]) and a total MSAS score were calculated. The Global Distress Index is an overall measure of symptom distress. It is the average of the frequency of four psychological symptoms (i.e., feeling sad, worrying, feeling irritable, feeling nervous) and the distress of six physical symptoms (i.e., lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth). The MSAS PHYSICAL subscale is the

average of the distress associated with 12 symptoms (i.e., lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, dizziness). The MSAS PSYCH subscale is the average of the frequency associated with six symptoms (i.e., worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, difficulty concentrating). The reliability and validity of the MSAS are well established in studies of oncology inpatients and outpatients.^{19,20} In this older sample, Cronbach's alphas for the MSAS PHYSICAL subscale, MSAS PSYCH subscale, the Global Distress Index, and total MSAS score were 0.82, 0.77, 0.83, and 0.87, respectively.

Statistical Analysis

The three data sets were combined and data were analyzed using SPSS v. 19 (SPSS Inc., Chicao, IL) and STATA/SE v. 12 (StataCorp LP, College Station, TX). Descriptive statistics, means, and standard deviations (SD) for quantitative variables and frequencies and percentages for categorical variables were calculated to describe various patient characteristics. Mean ratings of severity, frequency, and distress were calculated for those patients who reported the symptom. Patients were separated into four age groups: 60 to 64 (n=78), 65–69 (n=94), 70 to 74 (n=76) and 75 (n=82). Multinomial logistic regression was used to examine the differences across the four age groups in categorical demographic and clinical characteristics. These analyses accounted for the ordinal nature of the four age groups in the ordinal ECOG Performance Status variable.

Significant differences, across the four age groups, in the occurrence rates for each symptom were evaluated using binary logistic regression analyses, in which age group was treated as an ordinal predictor variable. To examine for differences, across the four age groups, in the severity, frequency and distress ratings of each symptom, ordinal logistic regression was used, with age group treated as an ordinal predictor variable. Significant differences across the four age groups in the MSAS subscale and total scores were evaluated with linear regression analyses. Odds ratios (OR) and their 95% confidence intervals (CI) are reported for all of the logistic regression analyses. Based on the recommendations of Rothman,²¹ adjustments were not made for missing data. A *P*-value of <0.05 was considered statistically significant.

Results

Differences in Demographic and Clinical Characteristics Across the Older Age Groups

Among the three studies, no differences were found in the mean age of the patients (Symptom Clusters Study = 70.1 (± 6.9) years, FPS Study = 69.3 (± 6.1) years, Symptom Prevalence Study = 70.9 (± 6.2) years; F (2,237) = 1.54, P = 0.216). As shown in Table 1, the distribution of the four age groups did not differ by study ($X^2 = 5.19$, P = 0.519). In addition, no significant differences were found in any demographic or clinical characteristics across the four age groups.

Differences in Symptom Occurrence Rates Across the Older Age Groups

The symptom occurrence rates for each of the MSAS symptoms within each age group are listed in Table 2. Across the four age groups, significant differences in occurrence rates were found for four symptoms (i.e., problems with sexual interest, lack of appetite, dizziness, swelling of arms or legs). As age increased, a decreasing linear trend was found for the occurrence of problems with sexual interest. In contrast, as age increased, an increasing linear trend was found for the occurrence of lack of appetite, dizziness, and swelling of arms or legs.

Differences in Symptom Severity Ratings Across the Older Age Groups

Differences in symptom severity ratings across the older age groups are summarized in Table 3. Across the 32 MSAS symptoms, difficulty swallowing was the only symptom with significant age-related differences in severity ratings. As age increased, a decreasing linear trend was observed for difficulty swallowing.

Differences in Symptom Frequency Ratings Across the Older Age Groups

Differences in symptom frequency ratings across the older age groups are summarized in Table 4. Across the 32 MSAS symptoms, the only symptoms with significant age-related differences in frequency ratings were feeling irritable and diarrhea. As age increased, a decreasing linear trend was observed for both symptoms.

Differences in Symptom Distress Ratings Across the Older Age Groups

Differences in symptom distress ratings across the older age groups are summarized in Table 5. Across the 32 MSAS symptoms, distress ratings differed across the older age groups for: lack of energy, shortness of breath, feeling bloated, and difficulty swallowing. As age increased, a decreasing linear trend was observed for all four symptoms.

Differences in MSAS Subscale and Total Scores Across the Older Age Groups

As shown in Table 6, no significant differences were found across the older age groups in total number of symptoms, MSAS PSYCH or PHYSICAL subscale scores, MSAS Global Distress Index, and MSAS total scores.

Differences in Rankings of Occurrence Rates and Ratings of Severity, Frequency, and Distress Across the Older Age Groups

Table 7 provides rankings of the symptoms with the highest occurrence rates as well as highest severity, frequency, and distress ratings across the four older age groups. Pain had the highest rate of occurrence for those in the 60–64 age group (66.7%). However, lack of energy was the most commonly occurring symptom in the other three age groups. Two other commonly occurring symptoms among all four age groups were feeling drowsy and difficulty sleeping. Except for the oldest age group (75), problems with sexual interest had the highest severity rating. For the 65 to <70 and 70 to <75 age groups, problems with sexual interest rating differed across the four older age groups.

Discussion

This study provides an in-depth evaluation of the symptom experience of older oncology patients. The use of a detailed symptom assessment tool enabled characterization of multiple dimensions of the symptom experience (i.e., occurrence, severity, frequency, distress). It is one of the first studies to comprehensively assess symptom experiences of older cancer patients with a variety of cancer types in different stages of treatment. Although the sample was heterogeneous in terms of diagnoses and treatments, the most common cancer diagnoses in this study (i.e., breast, prostate, lung) are representative of older oncology patients.

Consistent with previous reports,^{12,22} the overall number of symptoms was high, with older adults reporting an average of ten concurrent symptoms. Across the four older age groups, few age-related trends were found in symptom occurrence rates for 28 (87.5%) of the 32 MSAS symptoms. However, as age increased, occurrence rates for problems with sexual interest decreased. This finding is consistent with our previous report,¹¹ which found lower occurrence rates for problems with sexual interest in older compared with younger oncology patients. In contrast, as age increased, higher occurrence rates were reported for lack of appetite, dizziness, and swelling of arms or legs. These findings are notable because in our previous analysis,¹¹ occurrence rates for these symptoms did not differ between the commonly employed dichotomy of "older and younger" age groups and emphasizes the need to evaluate older adults' symptom experiences in more detail.

Lower occurrence rates for problems with sexual interest with increasing age may reflect lower rates of sexual activity in this age group. Increased occurrence rates with increased age for swelling of arms or legs may reflect higher rates of heart failure and venous stasis disease that occur with aging.²³ Likewise, higher occurrence rates for dizziness in the older age groups may reflect comorbid cardiovascular conditions, medication effects or increased risks for volume depletion with increased age. In this study, comorbidity was not evaluated systematically, so whether these symptoms correlated with higher rates of cardiac or vascular disease cannot be confirmed. An alternative explanation for the increased swelling in the older age groups may relate to differences in the treatments they received. Additional research is warranted to evaluate both the inter-relationships between common symptoms associated with cancer and other chronic medical conditions, and the potential effect of cancer treatment duration and intensity on symptoms in older adults.

For the patients who reported a symptom, the majority of the symptom *severity* ratings were in the slight to moderate range. For symptom *frequency*, age-related trends were found only for feeling irritable and diarrhea, with both of these symptoms decreasing in frequency as age increased. For symptom *distress*, age-related trends were found for only four symptoms (i.e., lack of energy, shortness of breath, feeling bloated, difficulty swallowing), with these symptoms receiving lower average distress ratings as age increased.

Findings regarding relatively lower rates of symptom distress for several symptoms in the older versus younger older adults add to the scant literature on symptom distress within the older population.^{12,13,24,25} Lower levels of symptom distress may reflect a lower subjective perception of bother from these symptoms. Alternatively, the lower rates of distress may

reflect a more "fit" and less frail older adult population that would be more likely to receive cancer treatment and participate in a research study.^{6,26} These findings underscore the need to examine the full range of potential predictors of symptom distress in older adults, beyond age alone. Inclusion of more detailed assessments of fitness and frailty will likely shed greater light on the symptom experiences of older adults.

For the most part, few significant differences were found in symptom experience across the older age groups. What is driving this relative lack of age-related differences is unclear. Further research will be required to understand whether the observed symptom experience of older adults is because: 1) older patients may receive lower doses of CTX or RT; 2) age-related shifts in biological and/or psychological processes may affect the occurrence and severity of these common symptoms; and/or 3) older adults may experience an age-related "response shift" that influences the perception of symptoms. It is worth exploring these hypotheses further in light of the present findings. Several studies have noted undertreatment of various cancer types in the elderly.^{27–30} As detailed information on types and doses of CTX and RT were not available in the present study, additional research is warranted to evaluate how age differences in symptom experiences are influenced by various treatment regimens.

Finally, it is important to note that this sample of older adults was highly functional. Specifically, 67.1% of those patients aged 75 years and 74.4% of those aged 60 to <65 had an ECOG Performance Status of "fully active" or "ambulatory, light work." Higher functional status among older adults who enroll in cancer clinical trials was noted by others to be a factor that limits the generalizability of study findings to all older adults.⁶ Thus, the present findings must be viewed in light of the possibility that these patients, although representative of the most common cancer diagnoses in older adults, may not be fully representative of older adults who are diagnosed with cancer or receive cancer treatment. On the other hand, it is possible that more functional patients are more likely to be offered treatment. Therefore, the present sample may be representative of older adults who receive cancer treatment.

Several limitations need to be acknowledged. Combining data from three studies limited the analyses to those characteristics collected in all three studies. Details on the doses of CTX and RT received by these patients were not collected for these studies. Measures of comorbidity, functional status, or geriatric syndromes specifically developed for and validated in older adults (e.g., geriatric assessment, frailty³¹) were not used, which limits our ability to examine predictors of the various symptom dimensions.

Nevertheless, this study provides important descriptive findings regarding symptoms in older cancer patients and can be used to generate testable hypotheses for future research. Future research should include measures of comorbidity to better ascertain the relationship between symptom burden and comorbidity in these older cancer patients.³² In addition, use of appropriate functional measures, as well as careful assessments of the full range of geriatric syndromes,^{6,33,34} will help the field develop a more detailed picture of the symptom experience of older cancer patients.

Findings from this study provide valuable information to guide clinical practice and research. Across the four symptom dimensions, the most common, severe, frequent, and distressing symptoms were similar for all four age groups in this older adult population. What differs is the magnitude estimation for each dimension, with older persons reporting lower rates of occurrence, severity, frequency, and distress for most symptoms. Because the age-related differences in symptom severity, frequency, and distress scores were small, additional research, within and across these age groups, will assist in determining the impact of each dimension of the symptom experience on functional status and quality of life.

Acknowledgments

This collaborative project was funded by a grant from Atlantic Philanthropies and a Queensland University of Technology Institute of Health and Biomedical Innovation Human Health and Wellbeing Collaborative Grant Scheme 2010. The Symptoms Cluster Study was funded under a Palliative Care National Health and Medical Research Council grant. The Fatigue Pain, and Sleep Study was funded by the National Institute of Nursing Research (NR04835).

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Characteristic	60 to <65 $n = 78$ (23.6%)	65 to <70 $n = 94$ (28.6%)	70 to $<75 \ n = 76 \ (23.0\%)$	75 <i>n</i> = 82 (24.8%)	Statistics
Age, yrs, mean (SD)	62.1 (1.6)	67.3 (1.5)	72.4 (1.3)	78.8 (3.2)	
Age range, yrs	60 to 64	65 to 69	70 to 74	75 to 86	
	%	%	%	%	
Study project Fatigue, Pain, and Sleep	37.2	28.7	26.3	23.2	
Symptom Prevalence	24.4	34.0	34.2	32.9	NS
Symptom Clusters	38.5	37.2	39.5	43.9	
Gender, female	41.0	41.5	43.4	41.5	NS
Lives alone	28.6	27.2	28.9	28.4	NS
Married/partnered	64.1	64.5	64.0	62.2	NS
Education – Post high school	53.9	54.3	58.1	55.7	NS
Diagnosis					
Breast	28.2	23.4	21.1	14.6	
Prostate	38.5	32.7	34.2	41.5	NS
Lung	10.3	12.8	22.4	13.4	
Other	23.1	26.6	22.4	30.5	
Metastasis	22.4	30.4	43.4	34.1	NS
Treatment					
None	12.8	16.1	14.5	25.6	
Only radiation	52.6	50.5	52.6	50.0	NS
Only chemotherapy	24.4	25.8	25.0	22.0	
Both	10.3	7.5	7.9	2.4	
ECOG Performance Status					

Characteristic	60 to <65 $n = 78$ (23.6%)	65 to <70 $n = 94$ (28.6%)	60 to <65 $n = 78$ (23.6%) 65 to <70 $n = 94$ (28.6%) 70 to <75 $n = 76$ (23.0%) 75 $n = 82$ (24.8%) Statistics	75 <i>n</i> = 82 (24.8%)	Statistics
Fully active	30.8	26.1	24.3	22.8	
Ambulatory, light work	43.6	48.9	44.6	44.3	
Ambulatory, mobile >50%	19.2	20.7	20.3	20.3	NS
Ambulatory mobile <50%	6.4	4.3	8.1	12.7	
Disabled	0.0	0.0	2.7	0.0	

SD = standard deviation; ECOG = Eastern Cooperative Oncology Group.

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Table 2

Age Groups
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Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal Ag	Ordinal Age Four Levels
	%	%	%	%	OR	CI
Pain	66.7	50.0	59.2	53.7	0.89	0.73, 1.09
Lack of energy	66.7	66.0	76.3	68.3	1.07	0.87, 1.33
Feeling drowsy	52.6	52.1	57.9	52.4	1.02	0.84, 1.24
Difficulty sleeping	50.0	43.6	50.0	36.6	0.87	0.72, 1.06
Difficulty concentrating	42.3	36.2	43.4	26.8	0.84	0.69, 1.03
Worrying	37.2	27.7	40.8	24.4	0.89	0.72, 1.10
Dry mouth	37.2	44.7	50.0	36.6	1.01	0.83, 1.23
Sweats	35.9	31.9	36.8	20.7	0.82	0.67, 1.02
Constipation	34.6	23.4	32.9	34.1	1.05	0.85, 1.29
Feeling irritable	34.6	33.0	35.5	25.6	0.89	0.72, 1.10
Numbness/tingling in hands/feet	33.3	23.4	27.6	30.5	0.99	0.79, 1.22
Problems with urination	33.3	36.2	36.8	37.8	1.06	0.87, 1.30
Feeling sad	32.1	30.9	34.2	28.0	0.96	0.78, 1.19
Cough	30.8	39.4	34.2	36.6	1.05	0.86, 1.29
Changes in the way food tastes	28.2	30.9	27.6	32.9	1.05	0.85, 1.30
Problems with sexual interest	28.2	28.7	25.0	7.3	0.67 b	0.52, .85
Shortness of breath	28.2	34.0	38.2	28.0	1.01	0.82, 1.25
Changes in skin	26.9	21.3	17.1	15.9	0.79	0.62, 1.02
Nausea	24.4	24.5	31.6	23.2	1.02	0.81, 1.27
I don't look like myself	24.4	19.1	19.7	20.7	0.94	0.74, 1.20
Feeling nervous	24.4	25.5	35.5	22.0	1.01	0.81, 1.26
Weight loss	23.1	21.3	28.9	19.5	0.98	0.78, 1.24
Lack of appetite	23.1	26.6	39.5	34.1	1.24 <i>a</i>	1.00, 1.54
Feeling bloated	21.8	19.1	22.4	13.4	0.87	0.67, 1.11
Diarrhea	20.5	18.1	26.3	23.2	1.10	0.87, 1.40

Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal Ag	Ordinal Age Four Levels
	%	%	%	%	OR	CI
Hair loss	15.4	24.5	15.8	17.1	<i>L</i> 6.0	0.75, 1.25
Dizziness	15.4	1.91	22.4	28.0	1.28 <i>a</i>	1.01, 1.64
Itching	14.1	23.4	31.6	23.2	1.21	0.96, 1.53
Difficulty swallowing	12.8	13.8	17.1	17.1	1.13	0.86, 1.49
Mouth sores	10.3	<i>1</i> .4	19.7	14.6	1.26	0.94, 1.70
Vomiting	10.3	10.6	10.5	12.2	1.06	0.78, 1.45
Swelling of arms or legs	<i>T.</i> 7	17.0	21.1	19.5	1.33 <i>a</i>	1.02, 1.74

OR = odds ratio; CI = confidence interval.

 $^{a}_{P < 0.05}$, $^{b}_{P < 0.01}$. **NIH-PA Author Manuscript**

Table 3

Ritchie et al.

Differences in Symptom SEVERITY Ratings Across the Four Older Age Groups

Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal Ag	Ordinal Age Four Levels
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	OR	CI
Pain	2.2 (0.8)	2.0 (0.9)	2.1 (0.9)	2.3 (0.8)	1.09	0.87, 1.38
Lack of energy	2.3 (1.0)	2.1 (0.7)	2.1 (0.9)	2.1 (0.8)	0.86	0.68, 1.09
Feeling drowsy	1.8 (0.7)	1.9(0.7)	1.8 (0.7)	1.7 (0.7)	0.89	0.69, 1.17
Difficulty sleeping	2.1 (0.8)	2.3 (0.7)	2.2 (0.7)	2.2 (0.7)	1.07	0.80, 1.43
Difficulty concentrating	1.8 (0.9)	1.5 (0.7)	1.4 (0.6)	1.8 (0.5)	1.01	0.73, 1.41
Worrying	(0.0)	1.6(0.6)	1.9(0.7)	1.7 (0.9)	06.0	0.64, 1.28
Dry mouth	1.9(0.9)	1.8 (0.9)	1.9(0.9)	1.9(0.9)	1.04	0.78, 1.40
Sweats	2.0 (0.7)	1.8(0.8)	1.9(0.9)	1.7 (0.6)	0.76	0.54, 1.08
Constipation	2.0 (1.0)	2.2 (0.8)	2.4 (1.1)	2.2 (0.8)	1.11	0.81, 1.52
Feeling irritable	1.8 (0.6)	1.5 (0.6)	1.8 (0.8)	1.6 (0.6)	0.91	0.63, 1.29
Numbness/tingling in hands/feet	2.0 (0.8)	2.0 (1.0)	1.8 (0.9)	1.7 (0.8)	0.79	0.57, 1.10
Problems with urination	2.0 (0.8)	1.9(0.9)	2.1 (0.8)	2.1 (0.8)	1.19	0.86, 1.65
Feeling sad	1.9(1.0)	1.4 (0.5)	1.7 (0.6)	1.7 (0.8)	1.03	0.72, 1.48
Cough	1.9(0.9)	1.7(0.8)	1.7 (0.8)	1.8 (0.7)	0.97	0.71, 1.33
Changes in the way food tastes	2.0 (0.8)	1.9(0.8)	2.1 (0.9)	1.8 (0.9)	0.89	0.63, 1.26
Problems with sexual interest	2.8 (1.3)	2.7 (1.0)	2.9 (1.0)	2.0 (1.3)	0.81	0.50, 1.31
Shortness of breath	2.0 (1.0)	2.1 (0.9)	1.9(0.8)	1.9 (1.0)	0.91	0.64, 1.29
Changes in skin	2.0 (1.0)	1.8(0.7)	1.7 (1.1)	1.9 (0.8)	0.90	0.59, 1.38
Nausea	2.2 (0.9)	1.6(0.7)	1.6(0.8)	2.0 (0.8)	.85	0.59, 1.24
I don't look like myself	2.1 (0.9)	1.4(0.6)	1.9(0.8)	1.9(0.9)	0.91	0.61, 1.36
Feeling nervous	1.8(1.1)	1.7(0.7)	1.8 (0.6)	1.8 (0.9)	1.14	0.77, 1.71
Weight loss	1.6(0.9)	1.4 (0.5)	1.8 (0.9)	1.8 (0.7)	1.38	0.89, 2.14
Lack of appetite	2.0 (0.8)	2.0 (0.8)	2.1 (0.9)	1.9(0.8)	0.93	0.65, 1.32
Feeling bloated	2.1 (1.0)	1.9(0.7)	1.6 (0.5)	1.6(0.7)	0.64	0.39, 1.05
Diarrhea	2.3 (0.9)	1.7 (0.7)	1.4 (0.5)	1.9 (0.6)	0.72	0.46, 1.10
Hair loss	2.2 (1.3)	2.4 (1.1)	1.8 (0.9)	2.9 (1.2)	1.32	0.81, 2.14

Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal Ag	Ordinal Age Four Levels
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	OR	CI
Dizziness	1.3 (0.5)	1.5 (0.7)	1.4 (0.5)	1.6 (0.8)	1.17	0.76, 1.83
Itching	2.2 (1.2)	1.8 (0.8)	1.5 (0.6)	1.8 (0.8)	0.84	0.54, 1.31
Difficulty swallowing	2.3 (0.7)	1.7 (0.9)	1.8 (0.6)	1.4 (0.7)	0.48 <i>a</i>	0.27, 0.84
Mouth sores	1.8 (1.2)	1.6 (0.9)	1.6 (0.8)	1.5 (0.7)	0.93	0.51, 1.70
Vomiting	2.0 (0.5)	1.6 (0.7)	1.5 (0.6)	1.9 (0.9)	88.0	0.49, 1.58
Swelling of arms or legs	2.0 (0.6)	2.1 (0.9)	2.0 (0.9)	2.1 (0.9)	1.01	0.61, 1.67

SD = standard deviation; OR = odds ratio; CI = confidence interval.

Severity ratings: 1 = slight, 2 = moderate, 3 = severe, 4 = very severe for patients who reported the occurrence of a symptom.

 $^{a}P < 0.05.$

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Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal A _§	Ordinal Age Four Levels
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	NO	CI
Pain	2.7 (1.0)	2.4 (1.0)	2.6 (1.1)	2.7 (0.9)	1.03	0.82, 1.29
Lack of energy	2.9 (1.0)	2.6 (1.1)	2.8 (1.0)	2.7 (0.9)	0.95	0.77, 1.18
Feeling drowsy	2.3 (0.8)	2.3 (0.8)	2.6 (0.9)	2.2 (0.8)	0.99	0.77, 1.28
Difficulty sleeping	2.5 (0.8)	2.8 (0.8)	2.4 (0.9)	2.9 (1.0)	1.15	0.87, 1.52
Difficulty concentrating	2.2 (0.8)	2.1 (1.0)	2.1 (0.9)	2.0 (0.7)	0.91	0.67, 1.24
Worrying	2.5 (0.9)	2.1 (1.0)	1.9 (0.8)	2.4 (1.0)	0.83	0.59, 1.16
Dry mouth	2.5 (1.1)	2.3 (1.0)	2.5 (0.9)	2.6 (1.0)	1.13	0.85, 1.51
Sweats	2.5 (0.8)	2.0 (0.9)	2.1 (0.9)	2.2 (1.1)	62.0	0.56, 1.11
Constipation	2.4 (0.8)	2.6 (0.9)	2.4 (1.2)	2.3 (1.0)	68.0	0.66, 1.21
Feeling irritable	2.1 (0.7)	1.9 (0.6)	1.9(0.9)	1.7 (0.7)	0.70 a	0.49, 0.99
Numbness/tingling in hands/feet	2.9 (1.1)	2.9 (1.0)	2.6 (1.4)	2.4 (1.0)	0.75	0.55, 1.02
Problems with urination	2.6 (0.9)	2.4 (0.9)	2.6 (1.0)	2.8 (0.9)	1.26	0.93, 1.71
Feeling sad	2.4 (1.0)	1.7 (0.7)	2.1 (0.9)	2.2 (0.9)	1.00	0.72, 1.39
Cough	2.4 (0.9)	2.0 (0.9)	2.0 (0.9)	2.1 (0.9)	0.87	0.64, 1.18
Changes in the way food tastes	2.7 (1.2)	2.4 (0.9)	2.7 (1.1)	2.7 (1.1)	1.08	0.78, 1.50
Problems with sexual interest	2.9 (1.3)	3.0 (1.0)	3.0 (1.1)	2.3 (1.4)	0.86	0.54, 1.37
Shortness of breath	2.3 (1.1)	2.4 (1.1)	2.3 (1.2)	2.4 (0.9)	1.07	0.77, 1.47
Changes in skin	2.6 (1.2)	2.4 (1.1)	2.5 (1.3)	2.8 (1.1)	1.11	0.75, 1.64
Nausea	2.4 (1.0)	1.9(1.1)	1.7 (0.6)	2.0 (0.8)	0.81	0.56, 1.17
I don't look like myself	2.8 (1.0)	2.1 (1.1)	2.6 (1.1)	2.7 (1.1)	0.98	0.68, 1.41
Feeling nervous	2.2 (1.0)	1.7 (0.8)	1.9(0.9)	1.9(1.0)	0.85	0.59, 1.24
Weight loss	2.0 (1.0)	1.7 (0.8)	2.2 (1.0)	2.0 (1.0)	1.14	0.77, 1.69
Lack of appetite	2.7 (0.9)	2.6 (1.0)	2.6 (1.2)	2.7 (1.2)	1.02	0.74, 1.41
Feeling bloated	2.4 (1.0)	1.9 (0.8)	2.2 (1.1)	1.7 (0.6)	0.75	0.48, 1.16
Diarrhea	2.4 (.08)	1.7 (0.5)	1.8 (0.7)	1.7 (0.7)	0.62 <i>a</i>	0.40, 0.94

Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal A	Ordinal Age Four Levels
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	OR	CI
Hair loss	2.5 (1.3)	2.8 (1.3)	2.8 (1.1)	3.3 (1.0)	1.37	0.88, 2.14
Dizziness	1.8 (0.7)	1.8 (0.8)	1.8 (0.8)	1.8 (0.9)	1.02	0.68, 1.53
Itching	2.3 (1.1)	2.3 (0.8)	1.9 (0.8)	2.5 (1.0)	1.03	0.68, 1.57
Difficulty swallowing	2.7 (0.7)	2.0 (1.1)	2.1 (1.0)	1.9 (1.1)	0.66	0.41, 1.05
Mouth sores	1.6 (1.1)	1.7 (1.1)	2.5 (1.2)	1.9 (1.3)	1.24	0.72, 2.14
Vomiting	2.3 (0.9)	1.4 (0.5)	2.1 (0.7)	1.6 (0.7)	0.76	0.44, 1.32
Swelling of arms or legs	2.5 (1.0)	2.8 (1.3)	2.8 (1.3)	2.7 (1.3)	1.06	0.66, 1.69

SD = standard deviation; OR = odds ratio; CI = confidence interval.

Frequency ratings: 1=rarely, 2=occasionally, 3=frequently, 4=almost constantly for patients who reported the occurrence of a symptom.

 $^{a}P < 0.05.$

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Symptom	60 to <65	65 to <70	70 to <75	75	Ordinal A§	Ordinal Age Four Levels
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	OR	CI
Pain	1.7 (1.2)	1.7 (1.2)	1.7 (1.2)	1.7 (1.1)	1.00	0.80, 1.25
Lack of energy	1.9 (1.3)	1.7 (1.2)	1.6(1.1)	1.3 (1.3)	$0.73 \ b$	0.59, 0.91
Feeling drowsy	(1.1)	1.2 (1.2)	1.3 (1.3)	0.8(1.1)	0.95	0.74, 1.22
Difficulty sleeping	1.7 (1.2)	1.9(1.0)	1.5 (1.2)	1.5 (1.3)	0.86	0.65, 1.13
Difficulty concentrating	1.4 (1.2)	1.3 (1.0)	1.2 (1.2)	1.5(1.0)	1.00	0.74, 1.35
Worrying	1.8 (1.1)	1.4 (0.8)	1.3 (0.8)	1.3 (0.9)	0.71	0.50, 1.00
Dry mouth	1.0(1.1)	1.0 (1.2)	1.2 (1.2)	1.0 (1.2)	1.03	0.77, 1.38
Sweats	1.4(1.0)	1.4(1.0)	1.4 (1.2)	0.8 (0.9)	0.74	0.52, 1.05
Constipation	1.6 (1.3)	2.1 (1.2)	2.0 (1.6)	1.7 (1.6)	1.01	0.74, 1.37
Feeling irritable	1.3 (1.1)	1.2 (0.8)	1.6(1.1)	1.1 (0.9)	0.98	0.69, 1.40
Numbness/tingling in hands/feet	1.6 (1.2)	1.2 (1.2)	1.1 (1.2)	1.1 (1.3)	0.76	0.55, 1.05
Problems with urination	1.8 (1.1)	1.5 (1.1)	1.9 (1.3)	1.8 (1.2)	1.10	0.81, 1.50
Feeling sad	1.7 (1.1)	1.1 (0.8)	1.4(1.0)	1.5(1.0)	1.00	0.71, 1.40
Cough	1.4 (1.3)	1.1 (1.1)	0.8 (1.2)	1.0 (1.2)	0.80	0.58, 1.09
Changes in the way food tastes	1.5 (1.2)	1.0(1.0)	1.6 (1.2)	0.8(0.9)	0.78	0.56, 1.10
Problems with sexual interest	2.1 (1.5)	2.1 (1.4)	2.2 (1.5)	1.0(0.9)	0.80	0.51, 1.25
Shortness of breath	1.6 (1.3)	1.8 (1.2)	1.4 (1.2)	1.0 (1.2)	0.70 <i>a</i>	0.50, 0.98
Changes in skin	1.3 (1.4)	1.4 (1.3)	1.2 (1.3)	1.0(1.3)	0.86	0.57, 1.30
Nausea	1.8 (1.4)	1.2 (1.1)	1.1 (1.4)	1.5 (1.5)	0.83	0.58, 1.20
I don't look like myself	1.7 (1.3)	0.8(0.9)	1.2 (1.3)	0.8~(0.8)	0.69	0.46, 1.01
Feeling nervous	1.7 (1.3)	1.0(0.9)	1.4(1.0)	1.3 (1.3)	0.91	0.63, 1.33
Weight loss	0.7 (1.2)	0.7 (0.7)	1.2 (1.2)	0.5 (1.2)	0.95	0.62, 1.46
Lack of appetite	1.4 (1.3)	1.3 (1.0)	1.3 (1.2)	1.1 (1.3)	0.82	0.58, 1.16
Feeling bloated	1.7 (0.8)	1.7 (1.1)	0.6 (0.8)	0.9 (0.6)	$0.47 \ b$	0.29, 0.76
Diarrhea	1.9 (1.2)	1.2 (1.0)	0.8(1.0)	1.4 (0.9)	0.75	0.50, 1.13

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	Mean (SD)	Mean (SD)	Mean (SD) Mean (SD) Mean (SD)	Mean (SD)	NO	CI
Hair loss	1.3 (1.4)	1.1 (1.3)	1.3 (1.5)	1.7 (1.7)	1.15	0.72, 1.85
Dizziness	1.4 (0.8)	1.4(1.1)	1.1 (0.8)	1.1 (1.4)	0.72	0.47, 1.09
Itching	1.6 (1.5)	1.4 (1.2)	1.4 (1.2)	1.3 (1.0)	0.94	0.62, 1.42
Difficulty swallowing	2.3 (1.1)	1.5 (1.0)	1.9 (1.3)	1.0 (1.1)	0.55 a	0.33, 0.92
Mouth sores	1.0 (1.4)	1.2 (1.1)	1.2 (0.9)	1.1 (1.1)	1.15	0.65, 2.03
Vomiting	1.8 (1.2)	1.1 (0.8)	1.2 (1.8)	1.6 (1.7)	0.85	0.48, 1.51
Swelling of arms or legs	1.5 (1.4)	1.6 (1.4)	1.5 (1.4) 1.6 (1.4) 1.5 (1.4)	1.7 (1.2)	1.05	0.64, 1.71

SD = standard deviation; OR = odds ratio; CI = confidence interval.

Distress Ratings: 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much for patients who reported the occurrence of a symptom.

 $^{a}_{P<0.05}$, $^{b}_{P<0.01.}$

Table 6

Older Age Groups	
Scores Across the Four	
Differences in MSAS Summary	

MSAS Scores	60 to <65	60 to <65 65 to <70	70 to <75	75	Statistics
	Mean (SD)	Mean (SD)	Mean (SD) Mean (SD) Mean (SD) Mean (SD)	Mean (SD)	
Total number of symptoms	9.5 (6.4)	9.2 (7.1)	10.7 (7.1)	8.8 (6.3)	SN
MSAS PSYCH Subscale score	0.8 (0.9)	0.6 (0.6)	0.8 (0.7)	0.5 (0.7)	SN
MSAS PHYSICAL Subscale score	0.7 (0.6)	0.6 (0.6)	0.8 (0.6)	0.7 (0.6)	SN
MSAS Global Distress Index	(8.0) 0.0	0.7 (0.6)	(2.0) (0.0)	0.7 (0.7)	SN
MSAS Total score	0.6 (0.5)	0.6(0.4)	0.7 (0.5)	0.5 (0.4)	SN

MSAS = Memorial Symptom Assessment Scale; SD = standard deviation.

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Table 7

Differences in Rankings of Symptoms With the Highest Occurrence, Severity, Frequency, and Distress Ratings Across the Four Older Age Groups

60 to <65		65 to <70		70 to <75		75	
			OCCURRENCE RATINGS	ERATINGS			
Symptom	%	Symptom	%	Symptom	%	Symptom	%
Pain	66.7	Lack of energy	66.0	Lack of energy	76.3	Lack of energy	68.3
Lack of energy	66.7	Feeling drowsy	52.1	Pain	59.2	Pain	53.7
Feeling drowsy	52.6	Pain	50.0	Feeling drowsy	57.9	Feeling drowsy	52.4
Difficulty sleeping	50.0	Dry mouth	44.7	Difficulty sleeping	50.0	Problems with urination	37.8
Difficulty concentrating	42.3	Difficulty sleeping	43.6	Dry mouth	50.0	Difficulty sleeping	36.6
		SI	SEVERITY RATINGS (1 to 4)	INGS (1 to 4)			
Symptom	Mean score	Symptom	Mean score	Symptom	Mean score	Symptom	Mean score
Problems with sexual interest	2.8	Problems with sexual interest	2.7	Problems with sexual interest	2.9	Hair loss	2.9
Lack of energy	2.3	Hair loss	2.4	Constipation	2.4	Pain	2.3
Diarrhea	2.3	Difficulty sleeping	2.3	Difficulty sleeping	2.2	Difficulty sleeping	2.2
Difficulty swallowing	2.3	Constipation	2.2	Pain	2.1	Constipation	2.2
Pain	2.2	Lack of energy	2.1	Lack of energy	2.1	Lack of energy	2.1
Nausea	2.2	Shortness of breath	2.1	Problems with urination	2.1	Problems with urination	2.1
Hair loss	2.2	Swelling	2.1	Changes in the way food tastes	2.1	Swelling of the arms or legs	2.1
Itching	2.2			Lack of appetite	2.1		
		FRI	EQUENCY RA	FREQUENCY RATINGS (1 to 4)			
Symptom	Mean score	Symptom	Mean score	Symptom	Mean score	Symptom	Mean score
Lack of energy	2.9	Problems with sexual interest	3.0	Problems with sexual interest	3.0	Hair loss	3.3
Numbness/tingling in hands/feet	2.9	Numbness/tingling in hands/feet	2.9	Lack of energy	2.8	Difficulty sleeping	2.9
Problems with sexual interest	2.9	Difficulty sleeping	2.8	Hair loss	2.8	Problems with urination	2.8
I don't look like myself	2.8	Hair loss	2.8	Swelling of arms or legs	2.8	Changes in skin	2.8
Pain	2.7	Swelling of arms or legs	2.8	Changes in the way food tastes	2.7	Pain	2.7
Changes in the way food tastes	2.7					Lack of energy	2.7
Lack of appetite	2.7					Changes in the way food tastes	2.7
Difficulty swallowing	2.7					I don't look like myself	2.7

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60 to <65		65 to <70		70 to <75		75	
						Lack of appetite	2.7
						Swelling of arms or legs	2.7
		D	DISTRESS RATINGS (0 to 4)	INGS (0 to 4)			
Symptom	Mean score	Symptom	Mean score	Symptom	Mean score	Symptom	Mean score
Difficulty swallowing	2.3	Constipation	2.1	Problems with sexual interest	2.2	Problems with urination	1.8
Problems with sexual interest	2.1	Problems with sexual interest	2.1	Constipation	2.0	Pain	1.7
Lack of energy	1.9	Difficulty sleeping	1.9	Problems with urination	1.9	Constipation	1.7
Diarrhea	1.9	Shortness of breath	1.8	Difficulty swallowing	1.9	Hair loss	1.7
Worrying	1.8	Pain	1.7	Pain	1.7	Swelling of arms or legs	1.7
Problems with urination	1.8	Lack of energy	1.7				
Nausea	1.8	Feeling bloated	1.7				
Vomiting	1.8						