



Published in final edited form as:

Pain. 2016 April ; 157(4): 892–900. doi:10.1097/j.pain.0000000000000456.

Differences in Demographic, Clinical, and Symptom Characteristics and Quality of Life Outcomes Among Oncology Patients with Different Types of Pain

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Abstract

The purposes of this study, in oncology outpatients receiving chemotherapy (CTX, n=926), were to: describe the occurrence of different types of pain (i.e., no pain, only non-cancer pain (NCP), only cancer pain (CP), or both CP and NCP) and evaluate for differences in demographic, clinical, and symptom characteristics, and quality of life (QOL) among the four groups. Patients completed self-report questionnaires on demographic and symptom characteristics and QOL. Patients who had pain were asked to indicate if it was or was not related to their cancer or its treatment. Medical records were reviewed for information on cancer and its treatments. In this study, 72.5% of the patients reported pain. Of the 671 who reported pain, 21.5% reported only NCP, 37.0% only CP, and 41.5% both CP and NCP. Across the three pain groups, worst pain scores were in the moderate to severe range. Compared to the no pain group, patients with both CP and NCP were significantly younger, more likely to be female, have a higher level of comorbidity and a poorer functional status. In addition, these patients reported: higher levels of depression, anxiety, fatigue, and sleep disturbance; lower levels of energy and attentional function; and poorer QOL. Patients with only NCP were significantly older than the other three groups. The most common comorbidities in the NCP group were back pain, hypertension, osteoarthritis, and depression. Unrelieved CP and NCP continue to be significant problems. Oncology outpatients need to be assessed for both CP and NCP conditions.

Keywords

cancer pain; non-cancer pain; pain prevalence; chemotherapy; fatigue; depression; anxiety; sleep disturbance; quality of life

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Conflict of interest: The authors have no conflicts of interest to disclose.

INTRODUCTION

Pain is one of the most prevalent and distressing symptoms for cancer patients. Over 30 years ago, Bonica attempted to evaluate the worldwide prevalence of cancer pain.¹³ In this survey that evaluated pain in 15 countries, the mean pain prevalence rate across various stages of cancer was 50%. Since that publication,¹³ a number of organizations,^{43,62,70} have disseminated guidelines to improve cancer pain management. Despite the increased attention to this problem, three systematic reviews have documented the ongoing problem of unrelieved cancer pain.^{29,40,88} In a 2007 meta-analysis that focused on the prevalence of cancer pain,⁸⁸ pooled prevalence rates were: 33% in patients after curative treatment; 59% in patients undergoing active treatment; and 64% in patients with advanced cancer. Of note, across these three groups, 33% of the patients rated their pain as moderate or severe.

The other two systematic reviews were focused on the undertreatment of cancer pain.^{29,40} In a 2008 review of studies that used the Pain Management Index score²⁷ to estimate the undertreatment of cancer pain,²⁹ the authors concluded that 43% of oncology patients were undertreated (range 8% to 82%). In an update of this review,⁴⁰ an additional 20 articles were evaluated. Over a six year period, cancer pain management improved by 25%.

Notably absent from these reviews was a systematic evaluation of the types of pain that oncology outpatients experience while undergoing cancer treatment. A fundamental principle of effective pain management is to determine the cause of the pain. This type of evaluation is particularly important given the increased number of older adults with^{6,22,46} and the increased number of comorbid conditions^{77,79} in patients with cancer. However, no studies were identified that evaluated the prevalence of non-cancer pain (NCP), cancer pain (CP), and both CP and NCP in patients undergoing cancer treatment.

An equally important consideration in the evaluation of the pain experience of oncology patients is its association with other common symptoms. Several studies have documented that pain can co-occur with fatigue,^{4,80} sleep disturbance,^{4,51,80} anxiety,^{4,51,80} and depression^{4,42,51,80} in oncology patients undergoing chemotherapy (CTX). However, none of these studies documented the severity of these symptoms in oncology patients with different types of pain.

The identification of risk factors associated with different types of pain and the impact of different types of pain on patients' quality of life (QOL) will assist clinicians to perform more comprehensive pain assessments. Given the paucity of information on the occurrence of pain, its association with other common symptoms, and its impact on QOL, the purposes of this study, in a sample of oncology outpatients receiving CTX (n=926), were to describe the occurrence of different types of pain (i.e., no pain, only NCP, only CP, or both CP and NCP) and to evaluate for differences in demographic, clinical, and symptom characteristics, as well as QOL outcomes among the four pain groups.

PATIENTS AND METHODS

Patients and Settings

This study is part of an ongoing, longitudinal study of the symptom experience of oncology outpatients receiving CTX.⁶⁴ Eligible patients were 18 years of age; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received CTX within the preceding four weeks; were scheduled to receive at least two additional cycles of CTX; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 1528 patients were approached and 926 consented to participate (60.6% response rate). The major reason for refusal was being overwhelmed with their cancer treatment.

Instruments

A demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. Alcohol use was evaluated using the Alcohol Use Disorders Identification Test (AUDIT).⁸³

The Karnofsky Performance Status (KPS) scale is widely used to evaluate functional status in patients with cancer and has well-established validity and reliability. Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms).⁴⁸

The Self-Administered Comorbidity Questionnaire (SCQ) is a short and easily understood instrument that was developed to measure comorbidity in clinical and health service research settings.⁸² The questionnaire consists of 13 common medical conditions that were simplified into language that could be understood without any prior medical knowledge. Patients were asked to indicate if they had the condition; if they received treatment for it; and did it limit their activities. For each condition, a patient can receive a maximum of 3 points. Total scores can range from 0 to 39. The SCQ has well-established validity and reliability and has been used in studies of patients with a variety of chronic conditions.^{16,82}

Occurrence of pain was evaluated using the Brief Pain Inventory.²⁸ Patients who responded yes to the question about having pain were asked to indicate if their pain was or was not related to their cancer and/or its treatment. Based on these responses, patients were categorized into one of four groups (i.e., no pain, only NCP, only CP, both CP and NCP). Patients rated the intensity of the pain (i.e., now, average, worst) using 0 (none) to 10 (excruciating) numeric rating scales (NRS).

The Center for Epidemiological Studies-Depression scale (CES-D) consists of 20 items selected to represent the major symptoms in the clinical syndrome of depression. A total score can range from 0 to 60, with scores of 16 indicating the need for individuals to seek clinical evaluation for major depression. The CES-D has well-established validity and reliability.^{78,85} In this study, the Cronbach's alpha for the CES-D total score was 0.89.

The Spielberger State-Trait Anxiety Inventories (STAI-T and STAI-S) each consist of 20 items that are rated from 1 to 4. The scores for each scale are summed and can range from 20 to 80. Cutoff scores of 31.8 and 32.2 indicate high levels of trait and state anxiety, respectively. The STAI-S and STAI-T inventories have well-established validity and reliability.^{49,86} In this study, the Cronbach's alphas for the STAI-T and STAI-S were 0.92 and 0.96, respectively.

The General Sleep Disturbance Scale (GSDS) consists of 21 items designed to assess the quality of sleep in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of the seven subscale scores that can range from 0 (no disturbance) to 147 (extreme sleep disturbance). A higher score indicates higher levels of sleep disturbance. A GSDS total score of 43 indicates a significant level of sleep disturbance.⁵² The GSDS has well-established validity and reliability.^{52,67} In this study, the Cronbach's alpha for the GSDS total score was 0.83.

The Pittsburgh Sleep Quality Index (PSQI) consists of 19 items designed to assess the quality of sleep in the past month. The global PSQI score is the sum of the seven component scores. The global PSQI score ranges from 0 to 21 with higher scores indicating a higher level of sleep disturbance. A global PSQI score of >5 indicates a significant level of sleep disturbance.¹⁹ The PSQI has well-established validity and reliability.^{7,19,21} In this study, the Cronbach's alpha for the global PSQI score was 0.72.

The Lee Fatigue Scale (LFS) consists of 18 items designed to assess physical fatigue and energy.⁵³ Each item was rated on a 0 to 10 NRS. Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items, with higher scores indicating greater fatigue severity and higher levels of energy. Patients were asked to rate each item based on how they felt "right now," within 30 minutes of awakening (i.e., morning fatigue, morning energy) and prior to going to bed (i.e., evening fatigue, evening energy). Cutoff scores of 3.2 and 5.6 indicated high levels of morning and evening fatigue, respectively.³⁸ Cutoff scores of 6.0 and 3.5 indicate low levels of morning and evening energy, respectively. The LFS was chosen for this study because it is relatively short, easy to administer, and has well established validity and reliability.^{53,65} In this study, Cronbach's alphas for the evening and morning fatigue scales were 0.95 and 0.96, respectively. Cronbach's alphas for the evening and morning energy scales were 0.93 and 0.95, respectively.

The Attentional Function Index (AFI) consists of 16 items designed to measure attentional function.²⁴ A higher total mean score on a 0 to 10 scale indicates greater capacity to direct attention. Scores are grouped into categories of attentional function (i.e., <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function). The AFI has well-established reliability and validity.²⁴ In this study, the Cronbach's alpha for the total AFI score was 0.93.

Quality of life was evaluated using generic (i.e., Medical Outcomes Study-Short Form-12 (SF-12))⁹⁰ and disease-specific (i.e., Quality of Life Scale-Patient Version (QOL-PV))^{36,37} measures. The SF-12 consists of 12 questions about physical and mental health as well as overall health status. The individual items on the SF-12 are evaluated and the instrument is

scored into two components that measure a physical component summary (PCS) and a mental component summary (MCS). These scores can range from 0 to 100. Higher PCS and MCS scores indicate a better QOL. The SF-12 has well-established validity and reliability.⁹⁰

The QOL-PV is a 41-item instrument that measures four dimensions of QOL (i.e., physical, psychological, social, and spiritual well-being) in cancer patients, as well as a total QOL score. Each item is rated on a 0 to 10 NRS with higher scores indicating a better QOL. The QOL-PV has well-established validity and reliability.^{36,37} In this study, the Cronbach's alpha for the QOL-PV total score was 0.92.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the CTX infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Depending on the length of their CTX cycles, patients completed questionnaires in their homes, a total of six times over two cycles of CTX (i.e., prior to CTX administration (i.e., recovery from previous CTX cycle), approximately 1 week after CTX administration (i.e., acute symptoms), approximately 2 weeks after CTX administration (i.e., potential nadir)). For this analysis, data from the enrollment assessment, that asked patients to report on their pain experience for the week prior to the administration of the next cycle of CTX, were analyzed. Medical records were reviewed for information on cancer and its treatments.

Data Analysis

Data were analyzed using SPSS version 22 (IBM, Armonk, NY). Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics. Differences in demographic, clinical, and symptoms characteristics, as well as QOL outcomes, were evaluated using analysis of variance (ANOVA), Chi Square tests, and Kruskal-Wallis tests with Bonferroni corrected post hoc contrasts. A p-value of <.05 was considered statistically significant. All calculations used actual values. Adjustments were not made for missing data. Therefore, the cohort for each of these analyses was dependent on the largest set of complete data among the pain groups.

RESULTS

Occurrence rates for pain group membership

Of the 926 patients in this study, 72.5% reported pain. Of the 671 patients who reported pain, 21.5% (n=144) reported only NCP, 37.0% (n=248) reported only CP, and 41.5% (n=279) reported both CP and NCP.

Differences in demographic and characteristics among the pain groups

As shown in Table 1, differences were found among the pain groups in age, gender, education, marital status, living situation, child care responsibilities, employment status, and income. Patients with only NCP were significantly older than the other three groups. Patients with no pain were significantly older than patients with only CP. Compared to the no pain

group, a significantly higher percentage of females reported both CP and NCP. Compared to patients with no pain, patients with both CP and NCP were less likely to be married or partnered, more likely to live alone, less likely to be employed, and more likely to have an annual household income of <\$30,000. Additional between group post hoc comparisons are provided in Table 1.

Differences in clinical characteristics among the pain groups

A number of clinical characteristics differed among the pain groups (Table 1). Compared to the no pain and only NCP groups, patients in the only CP and both CP and NCP groups had lower KPS scores. In terms of number of comorbidities, all of the pain groups had a higher number of comorbidities than the no pain group. In terms of SCQ scores, the differences among the groups were as follows: no pain < only CP < only NCP < both CP and NCP.

The occurrence of a number of comorbidities differed among the pain groups. Compared to the no pain group, a higher percentage of patients in the non-cancer pain and both CP and NCP groups had high blood pressure. Compared to the no pain group, a higher percentage of patients in the NCP group had lung disease. Compared to the other three pain groups, a higher percentage of patients in the CP and NCP groups reported ulcer or stomach disease. Compared to both the no pain and only NCP groups, a higher percentage of patients with both CP and NCP reported anemia and depression. A higher percentage of patients with NCP and both CP and NCP reported osteoarthritis compared to the other two pain groups. The patterns of occurrence for back pain were as follows: no pain < the other three pain groups and only CP < NCP and both CP and NCP groups.

Differences in pain severity ratings among the three pain groups

For pain now and worst pain, patients with both CP and NCP reported significantly higher scores than the only NCP and only CP groups (Table 2). For average pain, patients with both CP and NCP reported higher scores than patients with only CP.

Differences in symptom severity scores among the pain groups

Table 2 summarizes the differences in severity ratings for depression, anxiety, sleep disturbance, fatigue, energy, and attentional function among the four pain groups. In terms of CES-D scores, compared to the no pain group, patients with only CP and both CP and NCP reported significantly higher scores. In addition, patients with both CP and NCP had higher CES-D scores than patients with only NCP or only CP.

In terms of STAI-T scores, compared to the no pain group, patients in the other three pain groups had significantly higher scores. In addition, patients with both CP and NCP had higher STAI-T scores than patients with only NCP or only CP. In terms of STAI-S scores, the post hoc comparisons were identical to those found for the CES-D scores.

In terms of the sleep disturbance measures, the post hoc contrasts for the GSDS scores were identical to those found for the CES-D and the STAI-S scores. In terms of PSQI scores, patients in the only CP and both the CP and NCP groups had significantly higher scores, than patients in the other two pain groups.

The patterns for the post hoc contrasts for morning and evening fatigue differed among the pain groups. For morning fatigue, patients with only CP or both CP and NCP had significantly higher scores than the other two pain groups. In addition, patients with both CP and NCP had higher morning fatigue scores than patients with only CP. In terms of evening fatigue, compared to patients with no pain, patients with only CP or both CP and NCP reported higher scores.

The patterns for the post hoc contrast for morning and evening energy were identical. Compared to the no pain group, patients with only CP and both CP and NCP reported significantly lower morning and evening energy scores.

In terms of the AFI scores, the post hoc contrasts were identical to those found for the STAI-T scores.

Differences in QOL scores among the pain groups

The subscale and summary scores for the SF-12 are listed in Table 3. For the physical functioning, general health, social functioning, role emotional, and mental health scores, the post hoc contrasts revealed an identical pattern (i.e., only CP and both CP and NCP < no pain, as well as both CP and NCP < only NCP and only CP). For the role physical scale, compared to patients with no pain or only NCP, patients in the other two pain groups had lower scores. For bodily pain and the PCS scores, the post hoc contrasts revealed an identical pattern (i.e., both CP and NCP < only CP < only NCP < no pain). For the vitality score, patients in the only CP or both CP and NCP groups had lower scores than the no pain group. In terms of MCS scores, compared to the other three pain groups, patients with both CP and NCP had lower scores.

The subscale and total scores for the QOL-PV are summarized in Table 3. For the physical and social well-being subscales, post hoc contrasts revealed an identical pattern (i.e., only CP and both CP and NCP < no pain and only NCP). For psychological well-being, compared to patients with no pain, patients with only CP or both CP and NCP reported lower scores. In addition, compared to patients with only NCP and only CP, patients with both CP and NCP reported lower scores. In terms of total QOL scores, compared to patients with no pain or only NCP, patients with only CP and both CP and NCP reported lower scores. In addition, compared to patients with only CP, patients with both CP and NCP reported lower total QOL scores.

DISCUSSION

This study is the first to provide detailed, self-reported occurrence rates for various types of pain among oncology outpatients receiving CTX. Over 70% of our patients reported pain which is higher than the 59% reported in a systematic review⁸⁸ and may be partially explained by the inclusion of NCP in our analysis. Of note, over 60% of the patients in our study had NCP. As expected, patients with both CP and NCP reported the highest pain severity scores. Of note, for all three pain groups, worst pain scores were in the moderate to severe range.^{75,84,91} In fact, 29.9% of the patients with only NCP, 27.0% with only CP, and 46.5% with both CP and NCP reported worst pain scores of >7. Despite the publication of

numerous clinical practice guidelines,^{43,62,70} these findings suggest that both CP and NCP continue to be undertreated. Our findings support our initial hypothesis that an evaluation of both CP and NCP is extremely important given the increased number of older adults with^{6,22,46} and the increased number of comorbid conditions^{77,79} in patients with cancer.

Demographic characteristics

Patients with only NCP were significantly older than the other three pain groups. This association may be partially explained by the relatively high occurrence rates for osteoarthritis, back pain, and rheumatoid arthritis reported by these patients.

Compared to the no pain group, a higher percentage of females reported both CP and NCP. While several chronic pain conditions have higher prevalence rates in females (e.g., migraine headache,^{18,58} osteoarthritis⁷⁶), findings regarding gender differences in CP are inconsistent with some studies reporting no differences^{33,50} and others reporting higher rates in females.^{25,57,74}

In terms of social characteristics, compared to patients with no pain or only CP, a higher percentage of patients with both CP and NCP were single and lived alone. Consistent with prior research,^{5,15,41} lack of social support may amplify patients' pain experiences.

While over 50% of our sample was not employed, compared to the no pain and only CP groups, significantly fewer patients with both CP and NCP were employed and these patients reported lower household incomes overall. These findings may be partially explained by the significant disability associated with persistent pain in this pain group.

Clinical characteristics

Consistent with previous reports,⁵⁴ a higher level of comorbidity was identified in the only NCP and the both CP and NCP groups. Osteoarthritis, back pain, and rheumatoid arthritis were the most common painful conditions reported by these two pain groups. In addition, ~30% of the patients with both CP and NCP reported the occurrence of depression. Of note, ~40% of the patients with only NCP and both CP and NCP reported hypertension, which is known to increase pain severity in a variety of persistent pain conditions. (for review see 81) Taken together, these findings suggest that clinicians who care for oncology patients need to collaborate with patients' primary care practitioners to manage their patients' chronic NCP.

Patients with only CP and both CP and NCP had significantly lower KPS scores than patients in the other two pain groups. Of note, these differences in KPS scores for the two pain groups compared to the no pain ($d=0.63$ to 0.79) and only NCP groups ($d=0.57$) represent clinically meaningful differences in KPS scores.^{71,72}

Compared to patients with no pain, patients with both CP and NCP had received more cancer treatments. These treatments may contribute to the development of persistent pain (e.g., post-surgical pain syndromes,^{2,8,63,68} radiation-,^{35,56} and CTX-induced^{20,26} neuropathies). Additional research is warranted to determine the specific etiologies for the pain.

Common symptoms

Consistent with previous reports of patients with CP^{32,39} and NCP,^{1,34,47} the occurrence of moderate to severe pain was associated with a higher symptom burden. The severity of depression and anxiety differed among the pain groups. Patients with both CP and NCP had CES-D scores above the clinically meaningful cutoff score, as well as the highest occurrence rate for depression (i.e., 29.4%) on the SCQ. In addition, this pain group had the highest trait and state anxiety scores, as well as the lowest SF-12 MCS scores. Potential reasons for the higher scores in this group include that these patients were younger, had a higher level of comorbidities, and were living alone.

While CTX is associated with sleep disturbance,^{11,12} patients with pain had higher scores than the no pain group. Of note, sleep disturbance scores of patients with only CP and both CP and NCP were comparable to those reported by shift workers.⁵²

Patients receiving CTX report high levels of fatigue.^{9,10} However, only a few studies have reported on diurnal variations in fatigue severity^{30,31} and none have evaluated the relationships between pain and diurnal variations in fatigue. In a study of patients at the initiation of RT, the LFS morning fatigue score was 2.38⁶⁶ which is comparable to patients in the no pain group. However, patients with only CP and both CP and NCP reported morning fatigue scores that were above the clinically meaningful cutoff. Since these patients were evaluated prior to receiving their next dose of CTX, these between group differences suggest that CP is associated with increases in morning fatigue. Since pain is known to disrupt sleep,¹⁷ these relatively high levels of morning fatigue may be related to the higher levels of both pain and sleep disturbance reported by these patients.

In terms of evening fatigue, patients at the initiation of RT reported a mean score of 4.23.⁶⁶ While all four groups in this study reported higher evening fatigue scores, only patients in the both CP and NCP group reported scores that were above the clinically meaningful cutoff. Taken together, findings for both morning and evening fatigue suggest that pain, as well as sleep disturbance, contribute to higher levels of morning and evening fatigue in patients undergoing CTX.

Evidence from oncology³ and HIV⁵⁵ patients suggests that decrements in energy levels are a distinct symptom from fatigue. For all four groups of patients in this study, morning and evening energy scores were lower than those reported by patients undergoing RT.⁶⁶ While patients in the only CP and both CP and NCP groups, compared to the no pain group, reported significantly lower levels of morning energy, none of their scores were below the clinically meaningful cutoff. In contrast, all of the groups' evening energy scores were below the clinically meaningful cutoff. Similar to morning energy, patients with only CP and both CP and NCP reported the lowest evening energy scores. Given the limited amount of information on diurnal variations in energy levels, these findings warrant confirmation.

While CTX is associated with decreases in cognitive function,^{44,61,69} the relationship between pain and cognitive function has not been evaluated in patients on CTX. AFI scores for patients in our study were slightly lower than scores of patients at the initiation of RT⁶⁰ or prior to breast cancer surgery.⁵⁹ All four pain groups had AFI scores that were in the

moderate range which suggests decrements in cognitive function.²⁴ Compared to the no pain group, the other three groups had significantly lower AFI scores. These decreases in attentional function could be due to the CTX itself,^{44,61,69} the amount of sleep disturbance these patients were experiencing,^{23,45} and/or the pain itself or the use of analgesic medications.⁸⁹

QOL outcomes

While all of the SF-12 subscale scores were lower than in healthy individuals,⁹⁰ compared to the no pain group, patients in the other three groups had poorer outcomes. In general, the differences in SF-12 subscale scores between the no pain group and the other three groups represent clinically meaningful differences in QOL (see effect size calculations on Table 3).^{71,72} An evaluation of the PCS and MCS scores, with 50 being the normative score for the general United States population,⁹⁰ suggests that while both scores are below the normative value, the occurrence of pain has a greater impact on patients' physical functioning than on their mental functioning.

In terms of the disease-specific measure of QOL, all of the QOLS-PV scores in this study were similar to previous reports.^{14,73,87} Similar to the SF-12 scores, most of the differences between the no pain and the other three pain groups represent clinically meaningful differences in QOL. Patients with both CP and NCP had the worst outcomes using both measures of QOL.

Limitations and Implications

First, detailed information on the exact causes of both CP and NCP were not evaluated. In addition, while the sample size was large, the percentages of males and members of ethnic minority groups were relatively small. Therefore, our findings may not generalize to all oncology patients receiving CTX. Finally, data on symptom management interventions are not available.

Despite the publication of numerous clinical practice guidelines^{43,62,70} and the incorporation of pain as the 5th vital sign in clinical practice, our findings demonstrate that unrelieved CP and NCP remain significant problems for oncology patients receiving CTX. Of note, for all three groups of patients who reported pain, depression, anxiety, sleep disturbance, fatigue, and decreases in energy and attentional function are worse than for patients without pain. The high prevalence rates for CP and NCP, as well as the high severity scores for other common symptoms, identified in this study suggest that little progress has been made in the management of pain in oncology patients since Bonica published his work on the worldwide prevalence of pain over 30 years ago.¹³

Because patients provided self-reports of the causes of their pain, future studies need to evaluate the exact etiologies of the pain. In addition, longitudinal studies are needed that evaluate for changes in the occurrence and severity of CP and NCP during and following cancer treatment. In addition, these longitudinal studies need to evaluate how changes in CP and NCP influence the severity of other symptoms and impact patients' functional status and QOL. Intervention studies are warranted that evaluate the impact of single or multimodal interventions on pain and other co-occurring symptoms. Until these intervention studies are

completed, clinicians who care for oncology patients need to perform ongoing assessments of both CP and NCP and develop appropriate pain management plans. In addition, future guidelines on the management of pain in oncology patients need to incorporate recommendations on the assessment and treatment of both CP and NCP. Finally, strategies need to be developed to insure that oncology patients receive more effective treatments for their unrelieved pain.

Acknowledgments

This study was funded by the National Cancer Institute (NCI, CA134900). Dr. Miaskowski is supported by a K05 award from the NCI (CA168960).

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Table 1
Differences in Demographic and Clinical Characteristics Among the Pain Groups (n = 926)

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	58.57 (11.79)	62.16 (11.56)	54.75 (11.15)	56.16 (12.24)	F=13.99; p<.0001 1 > 3 2 > 1, 3, and 4
Education (years)	16.38 (3.05)	16.18 (3.10)	16.61 (2.92)	15.75 (2.96)	F=3.85; p=.009 3 > 4
Body mass index (kg/m ²)	25.77 (5.60)	26.39 (6.44)	26.01 (5.26)	26.39 (5.93)	F=0.65; p=.584
Karnofsky Performance Status score	85.65 (10.39)	82.98 (11.62)	78.03 (11.31)	76.07 (12.44)	F=34.02; p<.0001 1 and 2 > 3 and 4
Number of comorbidities	1.76 (0.92)	2.81 (1.48)	2.08 (1.21)	3.05 (1.54)	F=53.20; p<.0001 1 < 2, 3, and 4 2 and 4 > 3
SCQ score	4.03 (1.94)	6.01 (3.16)	4.89 (2.54)	7.03 (3.64)	F=53.63; p<.0001 1 < 3 < 2 < 4
AUDIT score	2.97 (2.14)	2.46 (1.86)	3.10 (2.86)	2.75 (2.23)	F=1.78; p=.150
Time since cancer diagnosis (years)	1.74 (3.16)	2.57 (3.97)	2.30 (4.10)	2.40 (4.92)	KW; p=.089
Time since cancer diagnosis (median)	0.40	0.69	0.44	0.47	
Number of prior cancer treatments	1.50 (1.41)	1.94 (1.62)	1.76 (1.53)	1.80 (1.58)	F=2.99; p=.030 1 < 2
Number of metastatic sites including lymph node involvement	1.12 (1.62)	1.33 (1.24)	1.27 (1.28)	1.38 (1.32)	F=2.05; p=.106
Number of metastatic sites excluding lymph node involvement	0.69 (1.00)	0.87 (1.07)	0.82 (1.09)	0.92 (1.16)	F=2.10; p=.099

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
	% (N)	% (N)	% (N)	% (N)	
Gender					$\chi^2=13.61$; p =.003 4>1
Female ⁺	72.5 (185)	82.6 (119)	77.4 (192)	84.6 (236)	
Male	27.5 (70)	16.7 (24)	22.6 (56)	15.4 (43)	
Transgender*	0.0 (0)	0.07 (1)	0.0 (0)	0.0 (0)	
Ethnicity					
White	74.1 (186)	78.6 (110)	69.4 (170)	66.3 (179)	
Black	6.8 (17)	5.7 (8)	8.6 (21)	7.0 (19)	
Asian or Pacific Islander	11.2 (28)	10.0 (14)	13.1 (32)	12.2 (33)	$\chi^2=13.71$; p=.133
Hispanic Mixed or Other	8.0 (20)	5.7 (8)	9.0 (22)	14.4 (39)	
Married or partnered (% yes)	74.6 (188)	65.0 (93)	71.5 (176)	56.0 (154)	$\chi^2=24.04$; p<.0001 1 and 3 > 4
Lives alone (% yes)	16.7 (42)	21.0 (30)	16.3 (40)	27.3 (76)	$\chi^2=12.90$; p=.005 4 > 1 and 3
Child care responsibilities (% yes)	22.9 (58)	11.4 (16)	25.2 (61)	26.5 (72)	$\chi^2=13.16$; p=.004 1, 3 and 4 > 2
Care of adult responsibilities (% yes)	7.5 (18)	8.6 (11)	5.3 (12)	11.8 (30)	$\chi^2=7.07$; p=.070
Currently employed (% yes)	43.7 (111)	31.7 (45)	39.0 (96)	25.3 (70)	$\chi^2=22.40$; p<.0001 1 and 3 > 4
Income					KW; p<.0001
< \$30,000 ⁺	10.5 (24)	17.9 (22)	10.2 (23)	29.4 (74)	
\$30,000 to <\$70,000	18.4 (42)	26.8 (33)	20.4 (46)	23.4 (59)	4 > 1 and 3
\$70,000 to < \$100,000	17.1 (39)	13.8 (17)	19.6 (44)	14.7 (37)	2 > 1

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
\$100,000	53.9 (123)	41.5 (51)	49.8 (112)	32.5 (82)	
Specific comorbidities (% yes)					
Heart disease	3.9 (10)	6.2 (9)	4.4 (11)	7.2 (20)	$\chi^2=3.46$; $p=.327$
High blood pressure	24.3 (62)	38.2 (55)	25.4 (63)	36.9 (103)	$\chi^2=17.07$; $p<.001$ 2 and 4 > 1 and 4 > 3
Lung disease	7.8 (20)	18.1 (26)	9.7 (24)	14.3 (40)	$\chi^2=11.97$; $p=.007$ 2 > 1
Diabetes	5.9 (15)	11.8 (17)	7.3 (18)	9.7 (27)	$\chi^2=5.32$; $p=.150$
Ulcer or stomach disease	2.0 (5)	1.4 (2)	2.0 (5)	9.7 (27)	$\chi^2=29.67$; $p<.0001$ 4 > 1, 2, and 3
Kidney disease	0.8 (2)	1.4 (2)	0.4 (1)	1.1 (3)	$\chi^2=1.24$; $p=.743$
Liver disease	4.3 (11)	4.9 (7)	7.7 (19)	6.1 (17)	$\chi^2=2.86$; $p=.413$
Anemia or blood disease	7.8 (20)	9.7 (14)	9.7 (24)	19.0 (53)	$\chi^2=19.10$; $p<.0001$ 4 > 1 and 3
Depression	11.4 (29)	19.4 (28)	17.7 (44)	29.4 (82)	$\chi^2=28.28$; $p<.0001$ 4 > 1 and 3
Osteoarthritis	3.9 (10)	22.9 (33)	5.2 (13)	20.4 (57)	$\chi^2=60.60$; $p<.0001$ 2 and 4 > 1 and 3
Back pain	4.3 (11)	38.2 (55)	16.5 (41)	47.0 (131)	$\chi^2=149.60$; $p<.0001$ 2, 3, and 4 > 1 2 and 4 > 3
Rheumatoid arthritis	0.8 (20)	8.3 (12)	2.0 (5)	5.4 (15)	$\chi^2=19.07$; $p<.0001$ 2 and 4 > 1 2 > 3

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Exercise on a regular basis (% yes)	76.8 (195)	66.7 (96)	67.2 (166)	65.7 (180)	$\chi^2=9.32$; $p=.025$ $1 > 4$
Smoking, current or history of (% yes)	36.8 (93)	35.5 (50)	31.4 (76)	38.4 (106)	$\chi^2=2.95$; $p=.399$
Cancer diagnosis					
Breast	40.4 (103)	40.3 (58)	41.9 (104)	39.4 (110)	
Gastrointestinal	30.2 (77)	27.1 (39)	28.2 (70)	25.1 (70)	
Gynecological	15.3 (39)	14.6 (21)	21.8 (54)	22.6 (63)	$\chi^2=15.51$; $p=.078$
Lung	14.1 (36)	18.1 (26)	8.1 (20)	12.9 (36)	
Type of prior cancer treatment					
No prior treatment	23.7 (59)	20.6 (29)	18.9 (46)	20.2 (56)	
Only surgery, CTX, or RT	43.8 (109)	32.6 (46)	46.7 (114)	42.2 (117)	$\chi^2=13.48$; $p=.142$
Surgery & CTX, or Surgery & RT, or CTX & RT	19.7 (49)	31.2 (44)	20.1 (49)	21.3 (59)	
Surgery & CTX & RT	12.9 (32)	15.6 (22)	14.3 (35)	16.2 (45)	

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, CTX = chemotherapy, kg = kilograms, KW = Kruskal Wallis; m^2 = meter squared, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation

* Chi Square analysis and post hoc contrasts done without the transgender patient include in the analyses

† Reference group for the post hoc comparisons

Table 2

Differences in Symptom Severity Scores Among the Pain Groups (n = 926)

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Symptom Scores					
Center for Epidemiological Studies – Depression Scale score	9.28 (7.66)	11.28 (9.03) [0.21]	13.20 (9.00) [0.41]	16.64 (10.71) [0.76]	F=29.31; p<.0001 1 < 3 and 4 2 and 3 < 4
Trait Anxiety Inventory score	31.07 (9.03)	34.50 (10.67)[0.32]	35.06 (9.95) [0.37]	39.53 (11.17) [0.79]	F=30.13; p<.0001 1 < 2, 3, and 4 2 and 3 < 4
State Anxiety Inventory score	29.75 (10.60)	32.38 (12.30) [0.21]	33.59 (11.41) [0.31]	37.89 (13.71) [0.65]	F=20.34; p<.0001 1 < 3 and 4 2 and 3 < 4
General Sleep Disturbance score	45.55 (18.51)	49.84 (19.87) [0.21]	53.75 (19.87) [0.41]	59.44 (19.55) [0.69]	F=23.40; p<.0001 1 < 3 and 4 2 and 3 < 4
Pittsburgh Sleep Quality Index score	6.76 (3.50)	7.09 (3.78) [0.09]	8.13 (3.61) [0.36]	9.22 (4.00) [0.64]	F=22.04; p<.0001 1 and 2 < 3 and 4
Morning fatigue score	2.25 (1.89)	2.67 (2.01) [0.20]	3.31 (2.09) [0.49]	3.87 (2.31) [0.75]	F=29.49; p<.0001 1 and 2 < 3 and 4 3 < 4
Evening fatigue score	4.88 (2.17)	5.11 (2.01) [0.11]	5.52 (2.03) [0.30]	5.67 (2.08) [0.38]	F=7.43; p<.0001 1 < 3 and 4
Morning energy score	4.99 (2.33)	4.40 (2.28) [-0.26]	4.42 (2.11) [-0.26]	3.97 (2.10) [-0.46]	F=9.33; p<.0001 1 > 3 and 4
Evening energy score	3.89 (2.09)	3.56 (1.92) [-0.16]	3.35 (1.93) [-0.27]	3.39 (2.06) [-0.25]	F=3.64; p=.013 1 > 3 and 4
Attentional Function Index score	7.06 (1.70)	6.54 (1.60) [-0.29]	6.33 (1.75) [-0.41]	5.74 (1.76) [-0.75]	F=25.84; p<.0001 1 > 2, 3, and 4 2 and 3 > 4
Pain Scores					
Pain now	n/a	1.45 (1.88)	1.47 (1.88)	2.22 (2.17)	F=10.19; p<.0001 2 and 3 < 4
Average pain score	n/a	2.90 (1.94)	2.67 (1.84)	3.41 (2.02)	F=8.38; p<.0001 3 < 4

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Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Worst pain score	n/a	5.41 (2.67)	5.54 (2.56)	6.75 (2.33)	F=17.54; p<.0001 2 and 3 < 4

Abbreviations: n/a = not applicable, SD = standard deviation

Numbers in the brackets below the mean scores are the effect size calculations that compare the no pain group to each of the other three pain groups.

Table 3

Differences in Quality of Life Scores Among the Pain Groups (n = 926)

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
MOS-SF-12 (SF-12) Subscale and Summary Scores					
Physical functioning	63.28 (32.19)	55.08 (33.96) [0.24]	48.61 (33.74) [0.43]	40.64 (33.25) [0.66]	F=20.72; p<0001 1 > 3 and 4 2 and 3 >4
Role physical	63.40 (29.24)	57.76 (27.58) [0.19]	49.74 (28.70) [0.47]	43.75 (27.34) [0.67]	F=23.30; p<0001 1 and 2 > 3 and 4
Bodily pain	95.60 (12.90)	81.57 (21.50) [0.51]	73.13 (26.99) 0.82]	60.37 (28.74) [1.29]	F=99.65; p<0001 1 > 2 > 3 >4
General health	73.51 (23.87)	67.45 (24.89) [.022]	60.46 (28.66) [0.47]	53.58 (28.20) [0.72]	F=26.11; p<0001 1 > 3 and 4 2 and 3 > 4
Vitality	59.59 (25.44)	46.51 (27.58) [0.26]	42.36 (27.11) [0.42]	39.74 (25.28) [0.52]	F=13.60; p<0001 1 > 3 and 4
Social functioning	76.99 (24.62)	73.72 (29.29) [0.11]	65.73 (30.43) [0.37]	57.46 (33.10) [0.64]	F=21.16; p<0001 1 > 3 and 4 2 and 3 > 4
Role emotional	83.37 (24.28)	79.32 (24.83) [0.15]	75.42 (27.30) [0.29]	67.17 (28.96) [0.59]	F=17.08; p<0001 1 > 3 and 4 2 and 3 > 4
Mental health	78.24 (18.03)	73.18 (20.87) [0.24]	71.33 (20.88) [0.38]	65.11 (22.16) [0.62]	F=18.11; p<0001 1 > 3 and 4 2 and 3 > 4
SF-12 – Physical component summary score	46.50 (8.57)	43.09 (9.25) [0.33]	39.65 (10.36) [0.66]	36.98 (10.20) [0.92]	F=43.61; p<0001 1 > 2 > 3 > 4
SF-12 – Mental component summary score	51.44 (9.36)	49.97 (10.81) [0.14]	48.94 (10.29) [0.24]	46.36 (11.12) [0.48]	F=10.27; p<0001 1, 2, and 3 > 4
Multidimensional QOL-Cancer Subscale and Total Scores					
Physical well-being	7.50 (1.57)	7.20 (1.52) [0.17]	6.14 (1.74) [0.76]	5.93 (1.71) [0.88]	F=52.05; p<0001 1 and 2 > 3 and 4
Psychological well-being	6.23 (1.72)	5.85 (1.86) [0.20]	5.36 (1.76) [0.47]	4.77 (1.81) [0.78]	F=31.44; p<0001 1 > 3 and 4 2 and 3 > 4

Characteristic	No Pain (1) n = 255 27.5%	Only Non-Cancer Pain (2) n = 144 15.6%	Only Cancer Pain (3) n = 248 26.8%	Both Cancer & Non-Cancer Pain (4) n = 279 30.1%	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Social well-being	6.63 (1.79) [0.19]	6.25 (1.91) [0.19]	5.28 (1.82) [0.67]	4.93 (2.02) [0.84]	F=42.46; p<.001 1 and 2 > 3 and 4
Spiritual well-being	5.37 (2.11)	5.23 (2.02)	5.32 (2.03)	5.04 (2.09)	F=0.64; p=.59
Total QOL score	6.41 (1.32)	6.07 (1.38) [0.23]	5.49 (1.36) [0.63]	5.15 (1.42) [0.86]	F=41.41; p<.001 1 and 2 > 3 and 4 3 > 4

Numbers in brackets below the mean scores are effect size calculations that compare the no pain group to each of the other three pain groups.

Abbreviations: MOS-SF-12 = Medical Outcomes Study – Short Form 12 (SF-12), n/a = not applicable, QOL = quality of life, SD = standard deviation