

# Psychological Evaluation of Patients With Cancer Presenting to the Emergency Department With Pain: Independent Predictors of Worse Pain Severity, Interference, and Higher Hourly Opioid Administration

Desiree R. Azizoddin, PsyD<sup>1,2,3</sup>; Meghan Beck, BS<sup>4</sup>; K. Mikayla Flowers, MA<sup>4</sup>; Jenna M. Wilson, PhD<sup>4</sup>; Peter Chai, MD<sup>1,3,5,6</sup>; Lily Johnsky, BS<sup>1</sup>; Gabrielle Cremona, MD<sup>7</sup>; Robert Edwards, PhD<sup>4</sup>; Adriana Hasdianda, MD<sup>1</sup>; Edward Boyer, MD, PhD<sup>1</sup>; and Kristin L. Schreiber, MD, PhD<sup>4</sup>

**QUESTION ASKED:** In patients with cancer presenting to the emergency department (ED) with complaints of pain, are there unique characteristics (eg, sociodemographic information, psychological well-being, surgical and medical history, and current opioid use) associated with their self-reported pain severity and interference, the amount of opioids they are given in the ED, and their subsequent hospital admission from the ED? Furthermore, are there differences between individuals who are and those who are not taking opioids before their ED admission?

**SUMMARY ANSWER:** There were unique psychological, socioeconomic, and medication-related patient-specific characteristics that were associated with worse pain severity, pain interference, and higher amounts of opioids given while patients were in the ED. However, there were no individual characteristics associated with whether or not a patient was admitted to the hospital from the ED.

**WHAT WE DID:** Patients with cancer who came to the ED at academic medical center with a complaint of pain were asked to complete self-report questionnaires regarding sociodemographic information, previous surgical and medical history, pain medication use (including opioid use), and psychological well-being (depression, anxiety, sleep disturbance, and pain catastrophizing). Patients also completed the Brief Pain Inventory which asked about their pain severity and how much their pain interfered with their daily activities in the previous week. Additional medical information (previous cancer treatment[s], disease status, opioid administration in the ED, and subsequent hospitalization) was abstracted from the medical record.

**WHAT WE FOUND:** The only characteristic independently related to pain outcomes and higher amounts of opioids given while in the ED was whether or not a patient was

taking opioids before being admitted to the ED. Yet, pain catastrophizing was the only patient-specific variable associated with both pain outcomes, and after controlling for other patient factors, depression, having a history of chronic pain, and income were independently and significantly associated with worse pain, and education level, anxiety, and sleep disturbance were significantly associated with the level of pain interference. There were no significant independent predictors of subsequent hospitalization. Patients who were taking opioids before ED admission were younger, had poorer health literacy, had greater occurrences of metastatic cancer and cancer-related surgery, and also had worse pain catastrophizing, sleep disturbance, depression, and anxiety.

## BIAS, CONFOUNDING FACTORS, REAL-LIFE IMPLICATIONS:

Patients recruited for this study were predominantly White and college educated, both of which affect generalizability to other populations. This study was mostly conducted during the COVID-19 pandemic when patients were likely trying to avoid hospital exposure, so patients in this study may have had particularly severe symptoms. Sociodemographic information, psychological well-being, surgical and medical history, and opioid use should all be considered when developing treatment approaches for patients with cancer presenting to the ED with pain. Importantly, the influence of psychological factors on pain severity and interference, along with outpatient opioid use on ED opioid administration, indicate that patients with cancer may benefit from the addition of psychological therapies for pain in conjunction with pharmaceutical analgesics. Assessment of psychological symptoms may reveal which patients would particularly benefit from psychological interventions to manage pain.

## ASSOCIATED CONTENT

### Appendix

Author affiliations and disclosures are available with the complete article online.

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## CORRESPONDING AUTHOR

Desiree R. Azizoddin, PsyD, University of Oklahoma Health Sciences Center, Stephenson Cancer Center, Health Promotion Research Center, 655 Research Pkwy, Ste 4000, Oklahoma City, OK 73104; Twitter: @DesAzizoddin; e-mail: Desiree-Azizoddin@ouhsc.edu.

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## abstract

**PURPOSE** Pain is a common complaint in patients with cancer presenting to the emergency department (ED). This prospective study evaluated whether biopsychosocial factors could help predict cancer patients with risk of higher pain severity, pain interference, and opioid consumption.

**METHODS** Patients with cancer presenting to the ED with a complaint of moderate-severe pain ( $\geq 4/10$ -numeric rating scale) completed validated self-report measures assessing sociodemographics, cancer-related treatments, pain severity and interference, medication use, and psychological symptoms (depression, anxiety, pain catastrophizing, and sleep disturbance). Opioids administered and subsequent hospitalization were abstracted. Univariable and multivariable regression analyses assessed factors associated with pain-related outcomes.

**RESULTS** Participants ( $n = 175$ ) presented with a variety of cancer types, with 76% having metastatic disease and 42% reporting current outpatient opioid use. Higher pain catastrophizing, lower depressive symptoms, lower income, outpatient opioid use, and historical chronic pain were independently associated with worse pain ( $P \leq .05$ ). Higher pain catastrophizing, anxiety, sleep disturbance, outpatient opioid use, and education were independently associated with worse pain interference ( $P \leq .05$ ). The sole independent predictor of ED opioid administration was outpatient opioid use. Patients taking outpatient opioids were younger, had lower health literacy, worse pain catastrophizing, sleep disturbance, depression/anxiety, and greater rates of metastatic cancer and cancer-related surgery ( $P \leq .05$ ).

**CONCLUSION** Biopsychosocial factors, particularly pain catastrophizing, remained significantly associated with worse pain outcomes for patients with cancer in the ED even after controlling for demographic and clinical variables. Patient outpatient opioid use was independently associated with worse pain, interference, and greater opioid administration, identifying this as a marker for who may benefit most from adjuvant pharmacologic and behavioral interventions.

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## INTRODUCTION

Treating pain in patients with cancer is challenging, whether the pain is caused by local or metastatic cancer, chemotherapeutic agents, or from worsening of other noncancer etiologies.<sup>1,2</sup> Despite a variety of pharmacologic (eg, opioids, nonsteroidal anti-inflammatories, and nerve medications) and behavioral interventions,<sup>3,4</sup> managing pain remains a challenge for patients with cancer.<sup>5</sup> More recently, patients with cancer face increased barriers to opioid access and may fear, and even intentionally avoid, opioid analgesics because of the stigma attached to opioids resulting from the opioid epidemic.<sup>6-8</sup> These limitations, combined with the inherent limitations of opioid-based analgesia (eg,

tolerance, hyperalgesia, and side effects), poor education about proper medication use, and limited access to alternative analgesics, can result in undertreated pain.<sup>6,7,9,10</sup> Although opioids are effective at managing acute pain, the development of tolerance and hyperalgesic states associated with opioids makes the management of pain episodes among patients on chronic opioids particularly challenging.<sup>4,11,12</sup> Pain during cancer also carries increased valence because of the potential negative implications of the pain (eg, fears of pain signifying disease progression), especially during acute pain episodes.<sup>13</sup> The inability to effectively manage pain worsens patients' quality of life and leads to greater

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health care utilization, especially emergency department (ED) visits.<sup>5,14,15</sup>

Almost half of patients with cancer visit the ED at least once within the first year after diagnosis,<sup>16</sup> and patients with cancer account for nearly four million annual ED visits in the United States.<sup>17</sup> Patients often present to the ED with symptoms (eg, pain, nausea/vomiting, and respiratory distress) or complications from cancer treatment (eg, neutropenia) or progression.<sup>18</sup> One of the most prominent primary complaints is pain,<sup>17,19,20</sup> which accounts for 30%-65% of all ED visits among patients with cancer.<sup>14,18,21</sup> Uncontrolled pain may represent a new and serious complication (eg, new fracture), worsening of a previous pain source, or an exhaustion of the resources available to a patient to self-manage ongoing pain.<sup>5,18</sup> Although urgent evaluation is in fact often needed, episodic increases of pain resulting from difficulty with pain self-management, in the absence of urgent cancer-related complications, place a significant burden on patients' quality of life, their caregivers, hospital staff, and health care systems.<sup>14,20,22,23</sup> As EDs experience capacity issues during the COVID-19 pandemic, reducing avoidable and/or unnecessary ED visits would likely benefit patients and payers alike.<sup>23</sup> Of note, a two-fold increase in the incidence of opioid overdose-related ED visits for patients with cancer was observed between 2006 and 2015 in the United States.<sup>24</sup> More comprehensive identification of relevant pain modulatory predictors may inform personalized outpatient cancer pain management, potentially identifying patients who would benefit most from proactive intervention.

The biopsychosocial model of chronic pain (pain lasting  $\geq 3$  months) highlights the importance of not only biological factors on pain but also physiological, cognitive (eg, pain appraisals), behavioral (eg, activity levels), affective, and social/environmental factors.<sup>28</sup> Identifying biopsychosocial predictors of worse pain and higher analgesic requirements at the point of ED admission among patients with cancer can, therefore, inform patient-centered, targeted interventions to improve pain outcomes. Several studies to date have solely evaluated cancer patients' demographics and disease factors, without assessing psychological processes that are highly relevant to pain modulation, in studies of pain during ED admissions.<sup>19,20,22,29</sup> Thus, these previous studies have not comprehensively evaluated all classes of potential predictors of pain together simultaneously to assess whether these biopsychosocial factors have an independent influence on pain outcomes and opioid administration among patients with cancer. Including biopsychosocial factors may help explain individual variability above and beyond demographic or disease variables. As such, this prospective cohort study used simultaneously-administered, validated measures of psychological functioning and pain outcomes to assess the unique relationships between a variety of potential biopsychosocial predictors (sociodemographics, disease status, surgical history, opioid use, and psychological health) and

pain outcomes (pain severity and interference and hourly opioid analgesics administered in the ED). We hypothesized that patients with greater psychological burden (catastrophizing, anxiety, and depression) would report worse pain and require more opioids during their ED stay, even while controlling for other potential drivers of these outcomes (fewer socioeconomic resources, lower health literacy, and greater disease burden).

## METHODS

This prospective observational cohort study recruited patients presenting to the ED at Brigham and Women's Hospital (BWH), an urban, academic, tertiary care center in Boston, MA, between January 2020 and June 2021 (recruitment paused between March 2020 and August 2020 because of COVID-19). The ED evaluates approximately 60,000 individuals annually and serves as the primary ED for the Dana-Farber Cancer Institute. Approximately 30% of ED visits at BWH involve patients with cancer. Study procedures were approved by the Mass General Brigham Institutional Review Board. Research assistants identified eligible patients and approached them to gauge willingness to participate after confirming medical stability with the medical team. Inclusion criteria included age 18 years and older, self-reported cancer treatment (eg, chemotherapy, surgery, immunotherapy, and radiation) within the past 2 years, and a complaint of moderate-severe cancer-related pain ( $\geq 4/10$ ). Exclusion criteria were inability/unwillingness to complete or understand questionnaires, acute medical instability, primary psychiatric complaint, or only a non-life-threatening and/or completely resolved cancer diagnosis (nonmetastatic melanoma, squamous cell, or thyroid carcinoma).

## Measures

Patients completed self-report measures assessing socio-demographics (race, education level, and household income), medication use, and validated psychosocial assessment tools. Patients self-reported recent cancer-related surgical procedures in the past 3 months, history of chronic pain (pain present for  $\geq 3$  months) before their cancer diagnosis, and current outpatient opioid use for pain management. Depression, anxiety, and sleep disturbance were assessed using the NIH Patient Reported Outcome Measurement Information System (PROMIS) short-forms.<sup>30</sup> PROMIS measures use a 5-point Likert scale, with higher scores indicating higher symptom severity. Pain catastrophizing was measured using the 13-item Pain Catastrophizing Scale.<sup>31</sup> Pain Catastrophizing Scale items are rated on a 5-point Likert scale, where higher scores reflect greater pain catastrophizing (range, 0-52). Age, sex, subsequent hospitalization status (patients admitted directly from the ED), length of stay, historical and recent cancer treatment (chemotherapy, radiation, and immunotherapy), and metastatic disease status were abstracted

from the medical record. Outpatient opioid prescriptions were also abstracted from the medical record; however, to have a more accurate measure of medication usage, the patients self-report of opioid consumption was used for analysis.

**Pain severity and interference.** Patients self-reported pain severity and pain interference using the Brief Pain Inventory (BPI).<sup>32</sup> The BPI queries about worst, least, and average pain within the past 7 days, as well as current pain, with the four ratings averaged to calculate pain severity (range, 0-10). The BPI also contains 10 questions asking patients to rate the degree to which pain interferes with their daily activities. Items are then summed to give the pain interference (range, 0-100).

**ED opioid administration.** All opioids administered while in the ED were normalized by converting each opioid administration to morphine milligram equivalents (MMEs). MMEs per hour were calculated by dividing total MMEs by total time (in hours) in the ED.

### Statistical Analysis

To evaluate the relationships between independent (sociodemographics, cancer disease status, recent surgical history, mood, catastrophizing, sleep, current opioid use, and previous history of chronic pain) and dependent variables (pain severity, pain interference, MME per hour, and hospital admission), we conducted univariable and multivariable linear and logistic regression. Selection of independent variables for inclusion in the multivariable models was informed by variables identified as significant on the univariable analysis. Multicollinearity diagnostics indicated no violations (variance inflation factor < 4.0).<sup>33,34</sup> For exploratory group comparisons, Mann-Whitney U, Wilcoxon signed-ranks tests, and  $\chi^2$  tests were used to compare patients taking outpatient opioids to those who were not. All statistical analyses were performed using SPSS-v27.

## RESULTS

In total, 330 patients were screened, 250 were found to be eligible, and 178 signed consent (Appendix Fig A1, online only). Participants with complete data ( $n = 175$ ) were 55% female and 81% White, with a variety of cancer types, frequently with metastatic disease (76%), and most had undergone some treatment for cancer within the past 6 weeks (71%; Table 1). The majority reported pain as the primary reason for the ED visit (69%). Taking outpatient opioids to manage pain was relatively common but not ubiquitous (42%); reported frequency of nonopioid OTC pain medications among the participants was 25%, and cannabis use was 8.5%. Roughly 30% of patients reported chronic pain before cancer diagnosis. Mean scores of depression, anxiety, and sleep disturbance in the 7 days before admission were close to 50th percentile using PROMIS  $t$ -scoring, and participants reported a relatively wide range of pain catastrophizing scores ( $18.1 \pm 12.5$ ).

Patients remained in the ED for an average of  $11 \pm 10$  hours (range, 2-83, median = 7); 59% received opioids during their ED stay, and 65% were admitted as hospital inpatients from the ED. Patients reported variable levels of worst pain (mean  $7.6 \pm 2.7$ ), BPI mean pain severity (mean  $5.9 \pm 3.0$ ), and BPI pain interference (mean  $50.7 \pm 27.0$ ) in the week preceding their ED visit.

### Univariable Linear Regression Analyses

Univariable associations of sociodemographic, disease, opioid use, and psychosocial predictors with pain-related outcomes was assessed using simple linear (pain and opioid consumption) or logistic (hospital admission) regression (Appendix Fig A2, online only). Lower education, higher income, and recent cancer surgery were associated with greater pain severity, but not other outcomes. Older age and female sex were associated with higher hourly MME administration, but not other outcomes. More advanced cancer stage was only associated with subsequent hospital admission, but not other outcomes. Depression, pain catastrophizing, chronic pain before cancer diagnosis, and metastatic cancer were all associated with both greater pain severity and pain interference, but not hourly MME administration in the ED. Greater sleep disturbance was associated with greater pain interference and hospital admission. Higher anxiety and current outpatient opioid use were significantly related to pain severity, pain interference, and hourly MME administration, but not hospital admission.

### Multivariable Linear Regression Models

Recognizing that many sociodemographic, disease, treatment, and psychological variables are themselves inter-related (ie, metastasis related to greater opioid use), we performed multivariable linear regression analyses to identify independent predictors of pain outcomes, including all variables that were significantly associated ( $P \leq .1$ ) with at least one of the predetermined outcomes (pain severity, pain interference, and opioid use) on univariable analysis. Figure 1 summarizes variables that were independently associated with these different outcomes on multivariable analysis.

#### Independent Predictors of Pain Severity

Lower income ( $\beta = -.17$ ,  $P = .015$ ), greater pain catastrophizing ( $\beta = .43$ ,  $P \leq .001$ ), lower depressive symptoms ( $\beta = -.27$ ,  $P = .035$ ), current outpatient opioid use ( $\beta = .33$ ,  $P \leq .001$ ), and previous history of chronic pain before cancer ( $\beta = .17$ ,  $P = .019$ ) were all independently associated with greater pain severity (Table 2, Fig 1).

#### Independent Predictors of Pain Interference

Having a college degree or higher ( $\beta = .17$ ,  $P = .021$ ), greater pain catastrophizing ( $\beta = .26$ ,  $P = .004$ ), anxiety symptoms ( $\beta = .23$ ,  $P = .047$ ), and sleep disturbance ( $\beta = .28$ ,  $P = .001$ ), and current outpatient opioid use

**TABLE 1.** Participant Demographics, Clinical Characteristics, Psychosocial Measures, and Pain

Demographic	No. (%)
Sex (female)	97 (54.5)
Race	
White	144 (80.9)
Black/African American	16 (9.0)
Asian	3 (11.7)
Native Hawaiian/Pacific Islander	1 (0.6)
I do not know	2 (1.1)
Did not respond	12 (6.7)
Ethnicity	
Non-Hispanic/Latino	157 (88.2)
Hispanic/Latino	13 (7.3)
Highest education level	
Some high school	7 (3.9)
High school diploma	32 (18.0)
Some college	54 (30.3)
College degree	39 (21.9)
Higher level degree	42 (21.9)
Marital status	
Married	106 (59.6)
Single	34 (19.1)
Divorced/separated	24 (13.5)
Widowed	11 (6.2)
Income	
0-15K	34 (19.1)
15-25K	69 (38.8)
25-40K	30 (16.9)
40-60K	21 (11.8)
60-75K	15 (8.4)
75-100K	4 (2.2)
> 100K	7 (0.6)
Insurance type	
Private	86 (48.3)
Medicare	54 (30.3)
Medicaid	30 (16.9)
Others	3 (1.7)
Cancer type	
Colorectal	27 (15.2)
Other cancer type	25 (14.0)
Breast	20 (11.2)
Ovarian	20 (11.2)
Lung	19 (10.2)
Pancreatic/liver	15 (9.0)
Prostate	11 (6.2)

(continued in next column)

**TABLE 1.** Participant Demographics, Clinical Characteristics, Psychosocial Measures, and Pain (continued)

Demographic	No. (%)
Urinary	12 (6.7)
Head and neck	7 (3.9)
Leukemia	6 (3.4)
Lymphoma	5 (2.8)
Esophageal/gastric	3 (1.7)
Brain	2 (1.1)
Patients with multiple cancers	27 (15.2)
Cancer stage	
I	20 (11.2)
II	11 (6.2)
III	25 (14.0)
IV	101 (56.7)
Metastatic disease	132 (76.3)
Years since diagnosis	
< 1	81 (47.6)
1-3	40 (22.6)
> 3	49 (28.8)
Spinal metastasis	39 (22.4)
Acute fracture	10 (5.7)
Treatment history	
Chemotherapy	146 (82.0)
Immunotherapy	44 (24.7)
Radiation	79 (44.4)
Surgery	113 (63.5)
Cancer treatment in the past 6 weeks	127 (71.3)
Surgery in the past 6 weeks	25 (14.0)
Outpatient pain medication use (self-report)	
Opioids	75 (42.1)
Short-acting	59 (33.1)
Long-acting	33 (17.4)
OTC	45 (25.3)
Acetaminophen	35 (19.7)
Ibuprofen	19 (10.7)
Other Rx pain meds	16 (9.0)
Cannabis	15 (8.4)
Pain	
Chronic pain before cancer Dx	52 (30.0)
Average pain (BPI), mean (SD)	5.86 (2.99)
Lowest pain (BPI), mean (SD)	2.27 (2.18)
Worst pain (BPI), mean (SD)	7.61 (2.65)
Current pain (BPI), mean (SD)	4.91 (2.63)
Pain interference (BPI), mean (SD)	50.72 (27.04)

(continued on following page)

**TABLE 1.** Participant Demographics, Clinical Characteristics, Psychosocial Measures, and Pain (continued)

Demographic	No. (%)
Psychological symptoms	
Depression PROMIS (T-score), mean (SD)	53.58 (10.21)
Anxiety PROMIS (T-score), mean (SD)	54.30 (11.11)
Pain catastrophizing, mean (SD)	18.16 (12.53)
Sleep PROMIS (T-score), mean (SD)	56.24 (8.62)
Pain as the primary reason for visiting the ED	120 (69.0)
Admitted to the hospital	113 (65.0)

NOTE. (n = 139) Recent cancer surgery was self-reported as surgery within last 3 months. Patient self-reported variables: race, education, income, psychological symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, gender, and metastatic disease.

Abbreviations: BPI, Brief Pain Inventory; Dx, diagnosis; ED, emergency department; OTC, over-the-counter; PROMIS, Patient Reported Outcome Measurement Information System; Rx, treatment; SD, standard deviation.

( $\beta = .32$ ,  $P \leq .001$ ) were independently associated with greater pain interference (Table 3, Fig 1).

#### Independent Predictors of Hourly Opioid Administration

Only current outpatient opioid use ( $\beta = .28$ ,  $P = .002$ ) was independently associated with greater MME/h while in the ED. Anxiety and depressive symptoms were marginally

associated with hourly MME administration ( $P = .063$  and  $.056$ , respectively; Table 4, Fig 1).

#### Hospitalization After ED Evaluation

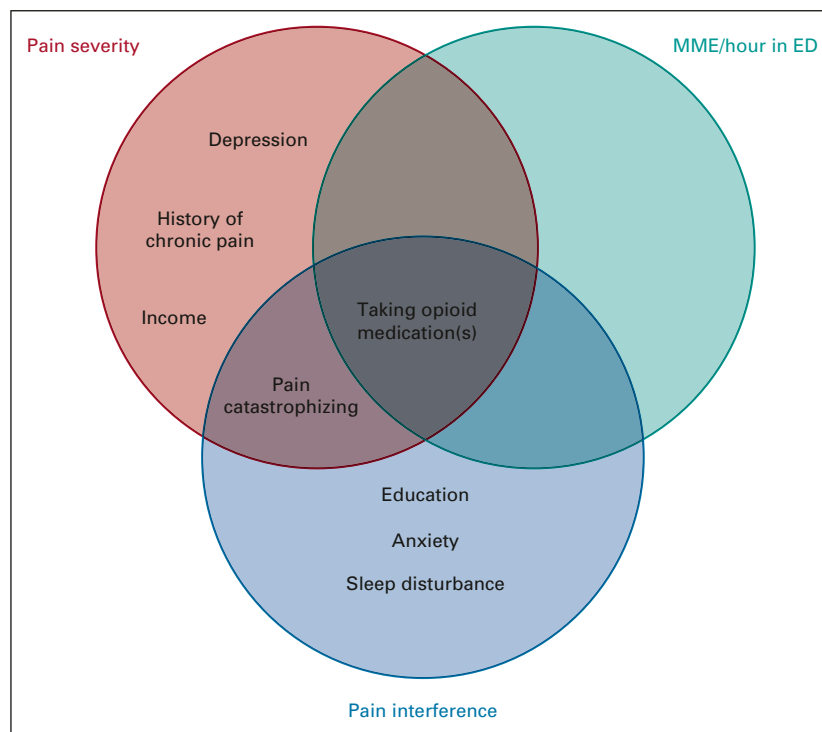
In this multiple logistic regression model, none of the sociodemographic, disease, surgical, psychological, or opioid variables were independently associated with subsequent hospital admission from the ED (Table 5).

#### Comparison of Patients Taking Outpatient Opioids Versus Those Not Taking Opioids

Because current outpatient opioid use was the only significant independent predictor of pain severity, pain interference, and ED opioid administration, we further investigated patient characteristics of this group. Patients who reported current outpatient opioid use were significantly younger, had lower health literacy, and had higher rates of advanced cancer, as well as significantly higher depression, anxiety, sleep disturbance, and pain catastrophizing (Table 6).

#### DISCUSSION

In this prospective cohort study of patients with cancer presenting to the ED with pain, we sought to identify patient-level, biopsychosocial predictors associated with worse pain, greater opioid administration, and subsequent hospitalization. Our hypothesis that greater psychological burden would be independently associated with worse pain



**FIG 1.** Overlap of factors that were independently associated with pain-related outcomes in multivariable regression analyses. ED, emergency department; MME, morphine milligram equivalent.

**TABLE 2.** Multivariable Linear Regression Assessing Independent Associations With Pain Severity

Variable	Unstandardized $\beta$ (95% CI)	$\beta$	P
<b>Demographics</b>			
Age	.01 (-0.01 to 0.03)	.09	.214
Sex	-.24 (-0.81 to 0.33)	-.06	.409
White race	-.29 (-1.13 to 0.56)	-.05	.504
College degree	-.02 (-0.63 to 0.59)	-.01	.938
Average income	-.24 (-0.43 to -0.05)	-.17	<b>.015</b>
<b>Surgical/disease variables</b>			
Recent cancer surgery	.57 (-0.06 to 1.20)	.12	.075
Metastatic disease	.01 (-0.72 to 0.75)	.00	.968
<b>Psychological symptoms</b>			
Depression (4-20)	-.13 (-0.25 to -0.01)	-.27	<b>.035</b>
Anxiety (4-20)	.04 (-0.07 to 0.16)	.09	.444
Sleep disturbance (4-20)	.09 (0.00 to 0.17)	.16	.051
Pain catastrophizing (0-52)	.07 (0.04 to 0.10)	.43	<b>≤ .001</b>
<b>Pain and opioid variables</b>			
Currently taking opioid(s)	1.37 (0.76 to 1.98)	.33	<b>≤ .001</b>
History of chronic pain before cancer	.77 (0.13 to 1.42)	.17	<b>.019</b>

NOTE. (n = 139) Recent cancer surgery was self-reported as surgery within the past 3 months. Patient self-reported variables: race, education, income, psychological symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, sex, and metastatic disease. Bold values indicate significance  $P < \text{or equal to } 0.05$ .

Abbreviations: BPI, Brief Pain Inventory; Dx, diagnosis; ED, emergency department; OTC, over-the-counter; PROMIS, Patient Reported Outcome Measurement Information System; Rx, treatment; SD, standard deviation.

outcomes was generally supported. Several psychological factors, most prominently greater pain catastrophizing, but also anxiety and sleep disturbance, were independently associated with worse pain, even after controlling for the impact of demographic and disease variables. However, psychological factors were not independently associated with greater opioid administration or subsequent hospitalization. Interestingly, but perhaps not surprisingly, current outpatient opioid use was an independent predictor of greater opioid administration in the ED. Outpatient opioid use was also an independent predictor of greater pain severity and interference, indicating a greater difficulty in managing pain, despite higher overall opioid use. Individuals reporting current outpatient opioid use were significantly younger, had higher rates of metastatic disease, and had higher psychological symptoms including greater levels of depression, anxiety, pain catastrophizing, and more disturbed sleep.

Patients in this cohort reported relatively high levels of pain, consistent with previous studies finding pain to be an important driving complaint in ED visits for patients with cancer.<sup>14,18,21</sup> Hospitalization rates in this sample (65%) were similar to other cancer pain ED studies.<sup>18,21</sup> The

**TABLE 3.** Multivariable Linear Regression Assessing Independent Associations With Pain Interference

Variable	Unstandardized $\beta$ (95% CI)	$\beta$	P
<b>Demographics</b>			
Age	.17 (-0.11 to 0.45)	.08	.225
Sex	-4.04 (-11.49 to 3.42)	-.07	.286
White race	-.63 (-11.71 to 10.46)	-.01	.911
College degree	9.38 (1.42 to 17.34)	.17	<b>.021</b>
Average income	.60 (-1.92 to 3.11)	.03	.640
<b>Surgical/disease variables</b>			
Recent cancer surgery	7.16 (-1.01 to 15.32)	.12	.085
Metastatic disease	.70 (-8.75 to 10.15)	.01	.884
<b>Psychological symptoms</b>			
Depression (4-20)	-1.17 (-2.71 to 0.36)	-.19	.133
Anxiety (4-20)	1.48 (0.02 to 2.94)	.23	<b>.047</b>
Sleep disturbance (4-20)	1.97 (0.85 to 3.09)	.28	<b>.001</b>
Pain catastrophizing (0-52)	.57 (0.18 to 0.95)	.26	<b>.004</b>
<b>Pain and opioid variables</b>			
Currently taking opioid(s)	17.81 (9.77 to 25.85)	.32	<b>≤ .001</b>
History of chronic pain before cancer	7.15 (-1.39 to 15.68)	.12	.100

NOTE. (n = 139) Recent cancer surgery was self-reported as surgery within the past 3 months. Patient self-reported variables: race, education, income, psychological symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, sex, and metastatic disease. Bold values indicate significance  $P < \text{or equal to } 0.05$ .

current report corroborated previous findings that up to 60% of patients taking opioids for cancer pain continue to report significant pain.<sup>35</sup> Our subsample of participants (41%) who reported taking outpatient opioids also endorsed mean pain scores in the moderate-severe range ( $5.9 \pm 1.7$  of 10). One striking finding of the multiple regression analyses was the consistency of this factor (taking outpatient opioids) as an independent predictor of both pain outcomes and hourly opioid administration while taking into account many biopsychosocial characteristics. It was in fact the lone independent predictor of opioid administration in the ED. A unique aspect of this study was the simultaneous entry of a wide range of potential biopsychosocial predictors into a multivariable model, after which several factors, including metastatic disease status and race, were not independently predictive of opioid administration.

Although psychological factors were not directly related to hourly ED opioid administration or subsequent hospitalization in the multivariable models, psychological symptoms, including anxiety and pain catastrophizing, were independently associated with worse pain severity and interference. Patients with cancer who presented to the ED with pain and reported taking outpatient opioids also had higher rates of psychological symptoms. Contextually,

**TABLE 4.** Multivariable Linear Regression Assessing Independent Association With Hourly Morphine Milligram Equivalent Administration

Variable	Unstandardized $\beta$ (95% CI)	$\beta$	P
Demographics			
Age	-.02 (-0.08 to 0.03)	-.08	.347
Sex	.43 (-0.95 to 1.81)	.05	.536
White race	.19 (-1.86 to 2.24)	.02	.856
College degree	-1.19 (-2.65 to 0.27)	-.14	.110
Average income	.20 (-0.26 to 0.66)	.07	.387
Surgical/disease variables			
Recent cancer surgery	1.26 (-0.26 to 2.77)	.14	.103
Metastatic disease	.34 (-1.40 to 2.09)	.04	.697
Psychological symptoms			
Depression (4-20)	-.28 (-0.58 to 0.02)	-.29	.063
Anxiety (4-20)	.27 (-0.01 to 0.54)	.28	.056
Sleep disturbance (4-20)	-.03 (-0.24 to 0.18)	-.03	.762
Pain catastrophizing (0-52)	.05 (-0.02 to 0.13)	.17	.129
Pain and opioid variables			
Currently taking opioid(s)	2.39 (0.90 to 3.87)	.28	<b>.002</b>
History of chronic pain before cancer	-.40 (-1.96 to 1.16)	-.04	.614

NOTE. (n = 139) Recent cancer surgery was self-reported as surgery within the past 3 months. Patient self-reported variables: race, education, income, psychological symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, sex, and metastatic disease. Bold values indicate significance  $P <$  or equal to 0.05.

**TABLE 5.** Multivariable Logistic Regression Assessing Independent Association With Subsequent Hospital Admission

Variable	$\beta$	Exp( $\beta$ ) Odds Ratio	P
Demographics			
Age	.01	1.01	.378
Sex	.14	1.15	.696
White race	-.05	0.95	.924
College degree	.33	1.39	.370
Surgical/disease variables			
Metastatic disease	.37	1.45	.392
Psychological symptoms			
Depression	-.06	0.94	.419
Anxiety	.06	1.06	.412
Sleep disturbance score	.08	1.09	.111
Pain catastrophizing	-.01	0.99	.669
Pain and opioid variables			
Taking opioid pain medicine (PR)	.38	1.47	.323
Other chronic pain before cancer Dx (> 3 months)	-.15	0.86	.710

NOTE. (n = 139) Recent cancer surgery was self-reported as surgery within the past 3 months. Patient self-reported variables: race, education, income, psychological symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, sex, and metastatic disease.

Abbreviations: Dx, diagnosis; PR, patient reported.

psychological distress generally increases during cancer treatment, and pain during cancer has been associated with significant suffering and worry about the underlying cause of pain (eg, fears that pain signifies worsening disease or progression).<sup>36,37</sup> Psychological distress and pain also seem to reciprocally augment each other.<sup>38</sup> Pain catastrophizing, which includes rumination about pain, magnification of pain symptoms, and feelings of helplessness in the face of pain, has been consistently associated with worse pain, greater opioid use, and more frequent ED visits in other cohorts with pain.<sup>25,26</sup> As stressors increase (ie, previous chronic pain, pain catastrophizing, worsening disease), any small increase can may push a patient past their pain threshold, where previous opioid doses become insufficient—this process may explain why those taking outpatient opioids experienced significantly greater acute pain leading to an ED admission and the need for further evaluation or increased opioids. We found that pain catastrophizing independently predicted worse pain severity and interference, yet these variables were not related to hourly opioid consumption in the ED, in contrast to previous studies associating psychological variables with higher rates of opioid misuse/overuse and resulting ED visits among patients with noncancer pain.<sup>40</sup> Although recognition of the opioid epidemic may be curbing opioid overprescription, treatment for concurrent psychological symptoms among patients with cancer is certainly an attractive alternative to lessen the overreliance on opioids in patients with cancer.

Future studies should longitudinally evaluate the relationship between biopsychosocial factors and pain among patients with cancer. Although opioids are essential for cancer pain treatment, supplementing pharmacologic treatment with accessible behavioral interventions aimed at pain-related psychological processes (eg, catastrophizing) may improve analgesia and more holistically alleviate cancer pain suffering—as well as potentially reduce ED use for worsening pain.<sup>1,2,36,41</sup> Several investigations have demonstrated that deploying alternative treatments for cancer pain are feasible and may reduce both anxiety and pain.<sup>42-45</sup> Targeted behavioral therapies may be even more effective in improving pain and psychological outcomes for patients with elevated psychological distress, concurrent chronic pain, higher education, lower income, and metastatic disease, although careful attention to patient characterization within future trials is needed to discern differential efficacy. Future studies using remote symptom monitoring systems which track both pain/psychological symptomatology are needed to gauge the efficacy of such a system to help personalize pain management and prevent ED admissions. Although biopsychosocial factors were not found to be related to the likelihood of hospital admission, future studies may explore whether a variety of preventive pain interventions (patient-centered education on analgesic use and



**TABLE 6.** Comparison Between Groups of Patients Who Were Taking Outpatient Opioids and Those Not Taking Opioids at Time of Presentation to the Emergency Department

Variable	n	Taking Opioids	Not Taking Opioids	Z*/Pearson $\chi^2$	P
		No. (group %) or Mean $\pm$ SD	No. (group %) or Mean $\pm$ SD		
Age	172	55.5 $\pm$ 12.0	59.2 $\pm$ 15.0	-2.1	<b>.035</b>
Sex	164			0.2	.660
Female		40 (53.3)	55 (56.7)		
Male		35 (46.7)	42 (43.3)		
Race	164			0.2	.670
Non-White		9 (12.2)	13 (14.4)		
White		65 (87.8)	77 (85.6)		
College graduate	171			2.5	.116
No		45 (60.0)	46 (47.9)		
Yes		30 (40.0)	50 (52.1)		
Average income per person in household	155	2.2 $\pm$ 1.5	2.3 $\pm$ 1.4	-0.9	.391
Health illiteracy	171	1.0 $\pm$ 1.0	0.7 $\pm$ 0.9	-2.0	<b>.044</b>
Insurance type	171			3.7	.294
Private		40 (53.3)	46 (47.9)		
Medicare		18 (24.0)	35 (36.5)		
Medicaid		15 (20.0)	14 (14.6)		
Others		2 (2.7)	1 (1.0)		
Previous cancer surgery	166			3.8	.051
No		26 (36.1)	21 (22.3)		
Yes		46 (63.9)	73 (77.7)		
Cancer stage	155			10.7	<b>.013</b>
I		6 (8.3)	14 (16.9)		
II		4 (5.6)	7 (8.4)		
III		6 (8.3)	18 (21.7)		
IV		56 (77.8)	44 (53.0)		
Metastatic cancer	171			21.2	<b><math>\leq</math> .001</b>
No		5 (6.8)	36 (37.1)		
Yes		69 (93.2)	61 (62.9)		
Depression (range: 4-20)	172	9.4 $\pm$ 4.5	7.3 $\pm$ 3.9	-3.3	<b>.001</b>
Anxiety (range: 4-20)	171	9.2 $\pm$ 4.1	7.9 $\pm$ 4.3	-2.3	<b>.020</b>
Sleep disturbance (range: 4-20)	172	13.8 $\pm$ 3.6	12.4 $\pm$ 4.1	-2.3	<b>.023</b>
Pain catastrophizing (range: 0-52)	171	20.9 $\pm$ 12.8	15.8 $\pm$ 12.0	-2.6	<b>.008</b>
Pain severity (range: 0-10)	168	5.9 $\pm$ 1.7	4.5 $\pm$ 2.1	-4.3	<b><math>\leq</math> .001</b>
Pain interference (range: 0-100)	170	62.3 $\pm$ 22.2	41.2 $\pm$ 27.1	-4.9	<b><math>\leq</math> .001</b>
Previous history of chronic pain before cancer	170			0.7	.399
No		50 (66.7)	69 (72.6)		
Yes		25 (33.3)	26 (27.4)		

NOTE. Patient self-reported variables: race, education, income, health illiteracy, previous cancer surgery, psychological symptoms, pain symptoms, current opioid use, and history of chronic pain before cancer. Abstracted from medical record: age, sex, cancer stage, and metastatic disease. Bold values indicate significance  $P <$  or equal to 0.05.

Abbreviation: SD, standard deviation.

cognitive behavioral therapy directed at patients' pain-related catastrophic thoughts) may help to avoid ED admissions for uncontrolled pain.<sup>27,36,41</sup>

Several limitations are important to consider. The sampling method was relatively inclusive from a diagnostic standpoint, encompassing a variety of cancer types and stages of

progression. Participants had complaints beyond pain and potentially other overlapping sources of pain, ultimately increasing variability in the sample. At the same time, the sample was less racially diverse and more educated than the general population, which may preclude findings from being widely generalizable, although demographics were consistent with patients seen at this tertiary referral level-1 trauma center adjacent to a highly ranked cancer center. Future studies are needed to evaluate these relationships in more diverse, lower income, and community settings. Race and socioeconomic status are known to influence pain management in patients with cancer,<sup>8,46-51</sup> underscoring the importance of understanding whether race moderates the relationship of psychosocial factors to worse pain outcomes.<sup>6,39</sup> Finally, some patients were recruited during the time of the COVID-19 pandemic, although recruitment

was paused during the months of heaviest COVID-related hospitalizations, which may have influenced whether some patients delayed presenting to the ED.

In conclusion, we found that greater psychosocial distress independently predicted worse pain outcomes in this sample of patients with cancer presenting to the ED with acute pain complaints. Taking outpatient opioids served as a consistent risk factor for both worse pain and hourly opioid administration in the ED. Future research which evaluates whether cancer patients with these characteristics may benefit from being identified earlier and targeted for augmentation of pharmacologic analgesia with behavioral interventions is necessary and important for achieving individualized, optimal pain management.

## AFFILIATIONS

<sup>1</sup>Department of Emergency Medicine, Brigham and Women's Hospital, Boston, MA

<sup>2</sup>Health Promotion Research Center, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK

<sup>3</sup>Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, MA

<sup>4</sup>Department of Anesthesiology Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, MA

<sup>5</sup>The Koch Institute for Integrated Cancer Research, Massachusetts Institute of Technology, Cambridge, MA

<sup>6</sup>The Fenway Institute, Boston, MA

<sup>7</sup>Tufts University School of Medicine, Boston, MA

## CORRESPONDING AUTHOR

Desiree R. Azizoddin, PsyD, University of Oklahoma Health Sciences Center, Stephenson Cancer Center, Health Promotion Research Center, 655 Research Pkwy, Ste 4000, Oklahoma City, OK 73104; Twitter: @DesAzizoddin; e-mail: Desiree-Azizoddin@ouhsc.edu.

## PRIOR PRESENTATION

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## AUTHOR CONTRIBUTIONS

**Conception and design:** Desiree R. Azizoddin, K. Mikayla Flowers, Peter Chai, Gabrielle Cremone, Robert Edwards, Edward Boyer, Kristin L. Schreiber

**Financial support:** Desiree R. Azizoddin, Peter Chai, Kristin Schreiber

**Administrative support:** Desiree R. Azizoddin, Kristin Schreiber

**Provision of study materials or patients:** Desiree R. Azizoddin, Edward Boyer, Kristin Schreiber

**Collection and assembly of data:** Desiree R. Azizoddin, Meghan Beck, K. Mikayla Flowers, Lily Johnsky, Gabrielle Cremone, Adriana Hasdianda, **Data analysis and interpretation:** Desiree R. Azizoddin, K. Mikayla Flowers, Jenna M. Wilson, Kristin Schreiber

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

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**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

**Psychological Evaluation of Patients With Cancer Presenting to the Emergency Department With Pain: Independent Predictors of Worse Pain Severity, Interference, and Higher Hourly Opioid Administration**

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**Desiree Azizoddin**

**Research Funding:** National Palliative Care Research Center

**Peter Chai**

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**Research Funding:** E Ink Corporation, NIDA, Hans and Mavis Lopater Foundation, Bill and Melinda Gates Foundation

**Lily Johnsky**

**Employment:** Iterative Scopes

**Travel, Accommodations, Expenses:** Iterative Scopes

**Edward Boyer**

**Research Funding:** NIDA

**Expert Testimony:** Various law firms

**Kristin L. Schreiber**

**Employment:** Pfizer (I)

**Stock and Other Ownership Interests:** Pfizer (I)

**Research Funding:** NIGMS

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