

Claims Identification of Patients With Severe Cancer-Related Symptoms

Richard W. DeClue, PhD, MPH; Dana Drzayich Antol, MS; Adrienne W. Casebeer, PhD, MS, MPP; Todd Michael, PharmD, RPh; Marina Sehman, PharmD; Andrew Renda, MD, MPH; Sarika Ogale, PhD; Stephen Stemkowski, PhD, MHA; and Bryan Loy, MD

Patients with cancer often experience a myriad of symptoms, which can include pain, depression, fatigue, and sleep disturbance.¹⁻⁶ Epidemiological studies have shown that these conditions and others are common in patients receiving treatment for their cancer, and in spite of advancement in therapeutic options, cancer treatment remains a difficult and often painful experience.^{7,8} As expected, for patients with cancer, untreated symptoms may affect adherence to and persistence with cancer treatments and hence the efficacy of cancer treatments, which can add significantly to the patient's burden of enduring cancer treatment and add to the cost of care.⁹⁻¹²

The symptoms experienced by these patients tend to present in clusters as opposed to in isolation, and these clusters have been defined as 2 or more symptoms that are often related and occur together.¹³⁻¹⁷ Few studies have examined symptom clusters in relation to specific disease states^{16,18}; however, for patients with lung cancer, the cluster of pain, depression, and fatigue is by far the most common symptom cluster that has been identified.¹⁹ This particular cluster has been recognized as significant, with a call for research at the National Institutes of Health State-of-the-Science Conference to help understand how to identify patients with lung cancer at risk for this cluster of symptoms and to identify specific interventions that have been effective.¹⁹

For both men and women, lung cancer dominates in causes of cancer mortality and is the second most common cancer diagnosed in the United States.²⁰ In 2017, it was estimated that 225,000 lung cancer cases were diagnosed, comprising 25% of all cancer cases in the United States.²⁰ The diagnosis of non-small cell lung cancer (NSCLC) accounts for approximately 80% to 85% of all lung cancer cases, with small cell lung cancer making up the remaining 15% to 20%.²¹ The 5-year overall survival rate for patients with this disease, often diagnosed after metastasis, is less than 5%, and more than half of all patients with metastatic NSCLC (mNSCLC) die within a year of receiving their diagnosis.²⁰

mNSCLC can place extreme burdens on patients and their families. In contrast to patients with other types of cancer, patients with lung cancer have been documented as experiencing a greater symptom

ABSTRACT

OBJECTIVES: The goal of this study was to establish a claims-based mechanism for identifying patients with metastatic non-small cell lung cancer (mNSCLC) and high levels of patient-reported cancer-related symptoms who could benefit from engagement with health care programs.

STUDY DESIGN: A cross-sectional survey of patients with mNSCLC was conducted from July 2017 to May 2018. Surveys were mailed to patients who were within 3 months of cancer treatment and enrolled in a Medicare Advantage health plan.

METHODS: Pain, fatigue, and sleep disturbance were measured using the Patient-Reported Outcomes Measurement Information System. Depression was assessed using the Patient Health Questionnaire-2. Medical claims were linked to survey results to identify comorbidities and assess preindex health care resource utilization. Cluster analysis was used to differentiate patients based on patient-reported pain interference, pain intensity, depression, and sleep disturbance. Logistic regression was used to identify claims-based measures associated with more severe symptoms.

RESULTS: For 698 respondents, 2 distinct symptom clusters were identified: a less severe (38.4%) cluster and a more severe (61.6%) cluster. Patients in the more severe cluster were younger, were more frequently dually eligible for Medicare and Medicaid, and more frequently had prescription fills for opioids. Claims-based factors associated with the more severe cluster included 2 or more 30-day fills for opioids in the prior 6 months, age younger than 75 years, depression diagnosis or antidepressants, bone metastases, and pain-related outpatient visits.

CONCLUSIONS: The claims-based factors associated with the severe symptom cluster can enable identification of patients with mNSCLC who could benefit from clinical outreach programs to enhance the care and support provided to these patients.

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TAKEAWAY POINTS

We established a claims-based mechanism for identifying patients with metastatic non–small cell lung cancer with more severe patient-reported cancer-related symptoms who could benefit from engagement with health care programs.

- ▶ Two distinct pain, fatigue, depression, and sleep disturbance clusters were identified.
- ▶ Depression, 2 or more 30-day opioid fills in a 6-month period, age younger than 75 years, bone metastases, and pain-related outpatient visits were associated with the more severe symptom cluster in adjusted analysis.
- ▶ This information could be used to identify patients using administrative claims for programs to improve symptom management or for referral to interventions linking patients to needed resources.

burden, as well as higher levels of psychological distress.^{22,23} A study by Sung and colleagues²⁴ in 2017 demonstrated that the unmet needs of patients with lung cancer have remained unchanged over the last 10 years and include physical and psychological issues, support with daily living, and the need for help in obtaining information about their disease.^{24,25}

The objective of this study was to develop a mechanism for identification of patients with mNSCLC and advanced cancer-related symptoms in administrative claims data who may benefit from cancer-specific outreach programs to ameliorate symptoms and improve health-related quality of life.

METHODS

Study Design

To conduct a cross-sectional survey of patients with mNSCLC, paper surveys were mailed to patients with mNSCLC, aged 50 to 89 years, who had received cancer treatment within 3 months prior to the survey date and were enrolled in a Humana Medicare Advantage health plan with a pharmacy benefit. Cancer treatment was defined as National Comprehensive Cancer Network–recommended systemic biologic or cytotoxic therapy, radiotherapy, or cancer-related surgery for the treatment of mNSCLC. Eligible patients were identified from pretreatment authorization requests for NSCLC biologic or chemotherapy infusions made by the treating physician between January 2017 and May 2018. Receipt of infusion therapy, radiotherapy, or cancer-related surgery within 3 months of survey completion was confirmed using medical and pharmacy claims.

Patient metastatic status was established using either data from provider pretreatment authorization requests or medical claims. Metastatic status in claims was identified as having at least 2 medical claims with codes for a secondary malignant neoplasm (*International Classification of Diseases, Ninth Revision, Clinical Modification*: 196.x, 197.x, 198.x; *International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]*: C77.x, C78.x, C79.x) occurring on separate days within 2 years prior to the anticipated survey date.

Eligibility required enrollment in the health plan at index date (ie, the survey date), as well as continuous enrollment for 6 months prior. Patients who initiated hospice in the preindex period were

excluded from the study. This study was approved by the Advarra Institutional Review Board.

Patient-Reported Measures

Measures of pain, fatigue, depression, and sleep disturbance were captured on the patient survey to establish self-reported symptom clusters.

The Patient-Reported Outcomes Measurement Information System (PROMIS) adult Pain Interference 6-item scale was used to measure the degree to which pain interfered with the patients' daily, social, and family-related activities in the prior 7 days.²⁶ Responses were calibrated to a T score. A score of 50, with an SD

of 10, is equivalent to the general US population. This scale, as well as all other PROMIS scales used in this study, has been previously implemented in studies of patients with NSCLC.²⁷ Pain intensity was measured using a Likert pain rating scale that ranged from 1 to 10, with 1 indicating no pain and 10 indicating the worst possible pain in the prior 7 days. For the purpose of comparing groups, pain intensity was categorized into none/mild pain (scores ≤ 3), moderate pain (4-6), and severe pain (7-10).

The PROMIS adult Fatigue 6-item scale was used to measure the frequency, duration, and intensity of fatigue experienced by patients and the impact of fatigue on physical and mental health in the prior 7 days.²⁷ Similar to the pain interference scale, responses were calibrated to a T score, with 50 equivalent to the general US population.

The Patient Health Questionnaire-2 (PHQ-2) was included on the survey to assess depression.²⁸ The PHQ-2 is a screening tool for major depressive disorders that captures the frequency of depressive mood over the prior 2 weeks. PHQ-2 scores range from 0 to 6, with higher scores associated with greater risk of depression. A cut point of 3 has been identified for depression screening and was used to construct a dichotomous depression variable when comparing groups.

Sleep disturbance was assessed using the PROMIS Sleep Disturbance 4-item scale.²⁷ This scale asks patients to indicate quality of sleep, restoration following sleep, and difficulty sleeping over the prior 7 days. Similar to other PROMIS scales, the sleep disturbance scale was calibrated to a T score, with 50 equal to the US population.

Clinical Characteristics

We wanted to determine if symptom clusters differed by the level of patient comorbidity or for specific comorbid conditions. The level of patient comorbidity during the 6 months preindex was reported using the Deyo-Charlson Comorbidity Index (DCCI) with the Klabunde modification.²⁹⁻³¹ The tool calculates a weighted score from 17 categories of comorbidity from claims data. The DCCI estimates the likelihood of 1-year mortality. Cancer and metastatic cancer were excluded from DCCI calculations. The individual conditions used to calculate the DCCI score were also reported if

the prevalence was 5% or greater for the study cohort. In addition, the presence of depression, anxiety, and bone metastases in medical claims was evaluated during the preindex period.

Symptom-Related Pharmacotherapy

Symptom-related pharmacotherapy was considered to determine its association with patient-reported symptom clusters. Pharmacy claims were used to ascertain prescription fills for the following classifications of pharmaceuticals used in the management of cancer symptoms, including patient-centered pain management, in the preindex period: opioids, antidepressants, antiepileptics/anticonvulsants, muscle relaxants, and glucocorticosteroids. Presence of at least 1 fill for each type of symptom-related pharmacotherapy preindex and the number of 30-day fills were reported.

Utilization

Health care resource utilization (HCRU) related to the management of pain and fatigue was also explored to evaluate an association between utilization and patient-reported symptom cluster. HCRU was assessed using medical claims in the preindex period. Pain-related HCRU was defined as a diagnosis code, in any claims position, for lung cancer–related pain (*ICD-10-CM*: G89.12, G89.18, G89.22, G89.28, G89.3) or unspecified pain (*ICD-10-CM*: R52). Fatigue-related HCRU was defined as a diagnosis code for cancer-related fatigue (*ICD-10-CM*: R53.0) or other fatigue (*ICD-10-CM*: R53.83). Pain- and fatigue-related physician office and outpatient visits were assessed. The presence of at least 1 visit and the mean number of visits were reported.

Statistical Analysis

For all PROMIS measures utilized in this study, higher scores are indicative of greater symptom severity. Significant levels of each symptom measured using the PROMIS scale were defined as a T score of 60 or greater, which is 1 or more SD above the mean.

Cluster analysis is a machine learning procedure that permits the identification of groups or clusters of like cases within a data set.³² This unsupervised machine learning technique was used to identify groups of patients whose variable responses within an identified cluster were more similar to those of patients in that cluster and less similar compared with those of patients in a different cluster. Specifically, hierarchical cluster analysis was employed to differentiate patients with mNSCLC into clusters based on the patient-reported pain interference, pain intensity, depression, and sleep disturbance measures. All scale scores were kept as continuous to improve the robustness of the cluster analysis. Hierarchical clustering using the Ward method, which makes no assumption about the number of clusters, was applied with the distance matrix as the data source.³³ The resulting pseudo-F and t^2 statistics were reviewed to judge the appropriate number of clusters.

We compared the characteristics of patients between the resultant clusters using χ^2 tests for categorical variables and t tests for continuous variables. A multivariable logistic regression model was developed using stepwise selection to assess the association

between demographic and claims-based clinical characteristics and the more severe patient-reported symptom cluster. All demographic and clinical characteristics presented were considered for inclusion in variable selection. All statistical tests were 2-tailed and conducted in SAS Enterprise Guide version 7.1 (SAS Institute).

RESULTS

Surveys were mailed to 3310 eligible patients and returned by 990 (29.9% response rate). To ensure that the analysis included data from eligible patients, post hoc exclusions were applied. Survey data were excluded if the respondent indicated that they were not the patient, there was no claims data evidence of treatment for mNSCLC during the 3 months prior to the survey date, the patient initiated hospice within the 6 months prior to the survey, or the patient was no longer enrolled in a Humana health plan at the time of survey completion. Application of post hoc exclusions reduced the sample size to 744 patients. The final analytic sample size was 698 patients, after 46 patients were dropped from the study due to lack of valid scores for at least 3 of the patient-reported measures used for constructing the symptom clusters: pain interference, pain intensity, fatigue, depression, and sleep disturbance.

The claims-based characteristics of survey responders, after post hoc exclusions ($n = 744$), were compared with those of survey nonresponders to understand the generalizability of our study findings ([eAppendix](#) [available at [ajmc.com](#)]). Survey responders were older than nonresponders and less frequently dually enrolled in Medicare and Medicaid. Survey responders had a lower level of comorbidities, most notably anxiety, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, and diabetes.

The patient-reported outcomes cluster analysis revealed 2 distinct pain, fatigue, depression, and sleep disturbance clusters among the final 698 patients: a less severe symptom cluster and a more severe symptom cluster. The more severe symptom cluster included 430 (61.6%) patients with higher scores, on average, for all measures of interest ([Table 1](#)). Patients in the more severe symptom cluster reported having significant challenges (eg, higher levels of pain, fatigue, depression, and sleep disturbance) more frequently than those in the less severe symptom cluster.

The mean (SD) age of the cohort was 72.8 (6.7) years; 47.6% were female and 87.8% were white ([Table 2](#)). Patients in the more severe symptom cluster were younger, were more frequently dually eligible for Medicare and Medicaid, and had a higher mean adjusted DCCI score. Additionally, more frequent anxiety, peripheral vascular disease, diabetes (with and without chronic complications), and bone metastases were found in patients in the more severe symptom cluster.

More than 70% of patients with mNSCLC had at least 1 pharmacy fill for opioids during the 6 months prior to taking the survey ([Table 3](#)). A greater proportion of patients in the more severe symptom cluster had at least 1 fill for opioids (81.2% vs 53.4%; $P < .001$). For patients with at least 1 fill for opioids, the mean (SD) was 1.5 (2.6) fills; as expected, the mean (SD) number of opioid prescription fills was

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TABLE 1. Patient-Reported Survey Measures Used to Develop the Symptom Clusters^a

Patient-reported pain, fatigue, depression, and sleep disturbance cluster	Total (N = 698)	Less severe symptom cluster (n = 268)	More severe symptom cluster (n = 430)	P
Significant pain interference				
Number of respondents	684	261	423	
Significant pain interference, ^b n (%)	246 (36.0)	<10	240 (56.7)	
Pain intensity				
Number of respondents	666	252	414	
Pain intensity, ^c n (%)				
None/mild pain, ≤3	383 (57.5)	246 (97.6)	137 (33.1)	<.001
Moderate pain, 4-6	167 (25.1)	<10	162 (39.1)	
Severe pain, 7-10	116 (17.4)	<10	115 (27.8)	
Significant fatigue				
Number of respondents	690	267	423	
Significant fatigue, ^b n (%)	328 (47.5)	67 (25.1)	261 (61.7)	<.001
Presence of depression				
Number of respondents	679	264	415	
Presence of depression, ^d n (%)	206 (30.3)	26 (9.9)	180 (43.4)	<.001
Presence of sleep disturbance				
Number of respondents	642	241	401	
Presence of sleep disturbance, ^b n (%)	61 (9.5)	13 (5.4)	48 (12.0)	.006

^aCell sizes less than 10 were suppressed.

^bDefined as a Patient-Reported Outcomes Measurement Information System standardized T score of 60 or higher. The T score rescales the raw score into a standardized score with a mean of 50 and an SD of 10. A score of 60 represents 1 SD higher than the mean.

^cPain intensity was categorized into patient scores of none/mild pain (scores ≤3), moderate pain (4-6), and severe pain (7-10).

^dDefined as a Patient Health Questionnaire-2 score of 3 or higher.

higher for patients in the more severe symptom cluster (2.0 [2.9] vs 0.3 [1.0]; $P < .001$). More than half of the overall cohort had at least 1 pharmacy fill for glucocorticosteroids, and 27.7% and 20.8% of the overall cohort had at least 1 fill for antidepressants and antiepileptic/anticonvulsant medications, respectively. For all these medications, a greater proportion of patients had at least 1 pharmacy fill in the more severe symptom cluster compared with in the less severe symptom cluster; however, there was no statistically significant difference between clusters with regard to the mean number of 30-day fills among those with at least 1 fill.

Pain- and fatigue-related HCRU during the 6 months preindex is presented in **Table 4**. Nearly 25% and 15% of patients in the more severe symptom cluster had at least 1 pain-related outpatient visit and pain-related physician office visit, respectively. Only 7.5% and 4.9% of those in the less severe symptom cluster had at least 1 pain-related outpatient or physician office visit ($P < .001$). There were no mean differences in the number of visits among those with at least 1 visit during the preindex period. Although 27.1% and 15.6% of the overall cohort had at least 1 fatigue-related outpatient visit and physician office visit, respectively, there were no differences between clusters.

Results from the multivariable logistic regression model are shown in **Table 5** and describe the claims-based factors associated

with the odds of being in the more severe patient-reported symptom cluster. Most notably, patients with 2 or more 30-day fills for opioids during the 6 months preindex were more than 6 times more likely to be in the more severe symptom cluster than those with no fill or 1 fill ($P < .001$). In addition, the odds of being in the more severe symptom cluster were 2.58 times higher for patients with at least 1 pain-related outpatient visit ($P < .001$), 1.41 times higher for those younger than 75 years ($P = .045$), and 2.32 times higher for patients who had an adjusted DCCI score of 5 or more ($P = .011$). Patients with a diagnosis of depression or at least 1 pharmacy fill for antidepressants during the 6 months preindex had 66% increased odds of being in the more severe symptom cluster than those without either ($P = .012$). Finally, bone metastases resulted in 65% increased odds of being in the more severe symptom cluster ($P = .006$).

DISCUSSION

This study advances the literature by identifying clusters of patient-reported symptoms and associating these clusters with claims-based correlates. The ability of health care stakeholders to use claims to identify patients with mNSCLC who have more severe symptoms can create opportunities to enhance patient care. The results of the survey and cluster analysis that we conducted indicated that we can apply these data to find patients who could be connected to clinical programs in an effort to ameliorate their symptoms and improve their quality of life.

In this study, we found patients with mNSCLC could be divided into 2 clusters based on their predominant symptoms: more or less intense levels of pain, fatigue, depression, and sleep disturbance. For clustering, all measures were kept continuous, which generated more robust results than if we had used cutoffs for categorical variables. In multivariable logistic regression modeling, age, adjusted DCCI score, depression/antidepressants, bone metastases, number of 30-day opioid pharmacy fills, and pain-related outpatient visits were identified as significant predictors of being in the more severe symptom cluster from forward stepwise selection. All these characteristics identified through modeling could be used for identifying patients for outreach programs.

In addition to the characteristics used for modeling, patient-reported symptoms of pain, fatigue, depression, and sleep disturbance can be used together for clustering groups of patients. Although the cluster of pain, fatigue, and depression has been recognized as a common symptom cluster in patients with lung cancer, sleep disturbance has been gaining attention as a condition that should

be considered in conjunction with these symptoms.^{1,5,6,19,34} In fact, patients with lung cancer have been documented as having greater sleep disturbance relative to patients with other solid tumors, resulting in significantly lower sleep efficiency and lower daily activity.^{35,36} This lack of rest has an impact on patient quality of life and has been associated with poorer functional status and impaired cognitive function.^{6,26}

Identifying patients with mNSCLC who are experiencing more severe symptoms presents an opportunity for clinicians and other health care stakeholders to improve the health-related quality of life for these patients through outreach programs. For instance, those involved in care delivery could identify and engage patients in programs to improve symptom management or refer patients to interventions that could link them to needed resources, such as programs that can help support their physical and psychological needs.^{25,37}

Limitations

This study has several limitations that need to be considered when interpreting these findings. Survey responders were older and had a less severe comorbidity profile than survey nonresponders; hence, the claims-based factors identified as associated with the more severe symptom cluster may not be generalizable to younger patients and those with more comorbidities. The findings of the study can be applied only to patients who have the physical and mental ability to complete a survey. It is possible that administrative claims data may have inaccurate, misclassified, or missing data, which could affect estimates of their association with patient-reported symptom clusters.

CONCLUSIONS

Patients with mNSCLC with more severe cancer-related symptoms who could benefit from targeted outreach programs to enhance their care, outcomes, and quality of life can be identified in data such as electronic health records and treatment authorizations that are available to clinicians and other health care stakeholders. Future studies should validate the approach that was developed in this study and explore its applicability for patients with other types of cancer. ■

TABLE 2. Demographic and Clinical Characteristics by Symptom Cluster^a

Patient-reported pain, fatigue, depression, and sleep disturbance cluster	Total (N = 698)	Less severe symptom cluster (n = 268)	More severe symptom cluster (n = 430)	P
Age in years, mean (SD)	72.8 (6.7)	73.9 (6.3)	72.0 (6.8)	<.001
Sex, n (%)				
Female	332 (47.6)	130 (48.5)	202 (47.0)	.694
Race, n (%)				
White	613 (87.8)	227 (84.7)	386 (89.8)	.141
Geographic region, n (%)				
Northeast	27 (3.9)	10 (3.7)	17 (4.0)	.841
Midwest	176 (25.2)	64 (23.9)	112 (26.0)	
South	461 (66.0)	179 (66.8)	282 (65.6)	
West	34 (4.9)	15 (5.6)	19 (4.4)	
Dual eligible for Medicare/Medicaid, n (%)	96 (13.8)	26 (9.7)	70 (16.3)	.014
Adjusted DCCI score, ^b mean (SD)	1.7 (1.8)	1.4 (1.6)	1.9 (1.9)	.002
Comorbid conditions, n (%)				
Depression	33 (4.7)	<10	27 (6.3)	
Anxiety	130 (18.6)	32 (11.9)	98 (22.8)	<.001
Myocardial infarction	35 (5.0)	13 (4.9)	22 (5.1)	.876
Congestive heart failure	81 (11.6)	33 (12.3)	48 (11.2)	.644
Peripheral vascular disease	113 (16.2)	34 (12.7)	79 (18.4)	.047
Cerebrovascular disease	40 (5.7)	15 (5.6)	25 (5.8)	.905
Chronic pulmonary disease	350 (50.1)	126 (47.0)	224 (52.1)	.192
Mild liver disease	41 (5.9)	11 (4.1)	30 (7.0)	.117
Diabetes without chronic complication	141 (20.2)	42 (15.7)	99 (23.0)	.019
Diabetes with chronic complication	61 (8.7)	15 (5.6)	46 (10.7)	.020
Renal disease	97 (13.9)	35 (13.1)	62 (14.4)	.614
Bone metastases, n (%)	258 (37.0)	77 (28.7)	181 (42.1)	<.001

DCCI, Deyo-Charlson Comorbidity Index.

^aCell sizes less than 10 were suppressed.

^bBoth *metastatic cancer* and *solid tumor without metastasis* comorbidity categories were excluded from the DCCI score calculations.

TABLE 3. Symptom-Related Pharmacotherapy Use During the 6-Month Preindex Period by Symptom Cluster

Patient-reported pain, fatigue, depression, and sleep disturbance cluster	Total (N = 698)	Less severe symptom cluster (n = 268)	More severe symptom cluster (n = 430)	P
Opioids, n (%)	492 (70.5)	143 (53.4)	349 (81.2)	<.001
Mean (SD) 30-day pharmacy fills ^a	1.5 (2.6)	0.3 (1.0)	2.0 (2.9)	<.001
Antidepressants, n (%)	193 (27.7)	51 (19.0)	142 (33.0)	<.001
Mean (SD) 30-day pharmacy fills ^a	3.4 (2.9)	3.3 (2.8)	3.4 (3.0)	.823
Antiepileptics/anticonvulsants, n (%)	145 (20.8)	35 (13.1)	110 (25.6)	<.001
Mean (SD) 30-day pharmacy fills ^a	2.6 (1.8)	3.1 (2.0)	2.5 (1.8)	.122
Muscle relaxants, n (%)	55 (7.9)	12 (4.5)	43 (10.0)	.008
Mean (SD) 30-day pharmacy fills ^a	1.4 (1.9)	1.3 (1.5)	1.4 (2.0)	.950
Glucocorticosteroids, n (%)	379 (54.3)	128 (47.8)	251 (58.4)	.006
Mean (SD) 30-day pharmacy fills ^a	0.6 (1.2)	0.6 (1.0)	0.6 (1.2)	.593

^aCalculations were limited to patients with at least 1 pharmacy fill with any days' supply.

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TABLE 4. Health Care Resource Utilization During the 6-Month Preindex Study Period by Symptom Cluster

Patient-reported pain, fatigue, depression, and sleep disturbance cluster	Total (N = 698)	Less severe symptom cluster (n = 268)	More severe symptom cluster (n = 430)	P
Pain-related physician office visits				
At least 1 visit, n (%)	77 (11.0)	13 (4.9)	64 (14.9)	<.001
Mean (SD) visits*	3.4 (2.7)	2.2 (2.0)	3.7 (2.8)	.081
Pain-related outpatient visits				
At least 1 visit, n (%)	125 (17.9)	20 (7.5)	105 (24.4)	<.001
Mean (SD) visits*	5.1 (7.8)	6.0 (16.4)	4.9 (4.9)	.778
Fatigue-related physician office visits				
At least 1 visit, n (%)	109 (15.6)	44 (16.4)	65 (15.1)	.645
Mean (SD) visits*	2.8 (2.7)	2.8 (2.7)	2.8 (2.8)	.925
Fatigue-related outpatient visits				
At least 1 visit, n (%)	189 (27.1)	67 (25.0)	122 (28.4)	.330
Mean (SD) visits*	3.9 (5.1)	4.3 (6.2)	3.7 (4.5)	.505

*Calculations were limited to patients with at least 1 visit.

TABLE 5. Claims-Based Factors Associated With More Severe Patient-Reported Pain, Fatigue, Depression, and Sleep Disturbance

Claims-based factors	Odds ratio	95% CI	P
Age			
<75 years	1.41	1.01-1.98	.045
≥75 years	Reference	Reference	-
Adjusted DCCI score			
0-4	Reference	Reference	-
≥5	2.32	1.22-4.44	.011
Depression/antidepressants (yes vs no) ^a	1.66	1.12-2.45	.012
Bone metastases (yes vs no)	1.65	1.15-2.36	.006
Number of 30-day opioid pharmacy fills			
0 or 1	Reference	Reference	-
≥2	6.25	3.32-11.77	<.001
Pain-related outpatient visits (yes vs no)	2.58	1.50-4.43	<.001

DCCI, Deyo-Charlson Comorbidity Index.

^aDefined as a diagnosis of depression in medical claims or at least 1 pharmacy fill for an antidepressant medication.

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SO); critical revision of the manuscript for important intellectual content (RWD, DDA, AWC, TM, MS, AR, SO, SS, BL); statistical analysis (RWD); administrative, technical, or logistic support (DDA); and supervision (SS).

Address Correspondence to: Adrienne W. Casebeer, PhD, MS, MPP, Humana Inc, 515 W Market St, 7th Floor, Louisville, KY 40202. Email: acasebeer@humana.com.

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eAppendix. Demographic and Clinical Characteristics of Survey Respondents vs Nonrespondents

Patient-reported pain, fatigue, depression, sleep disturbance cluster	Survey Respondents (n = 744)	Survey Non-respondents (n = 2,320)	P value
Age, mean [SD]	72.9 [6.7]	71.7 [7.2]	< 0.001
Sex, n (%)			
Female	359 (48.3)	1,068 (46.0)	0.291
Race, n (%)			
White	651 (87.5)	1,862 (80.3)	< 0.001
Geographic region, n (%)			
Northeast	29 (3.9)	72 (3.1)	0.153
Midwest	189 (25.4)	513 (22.1)	
South	490 (65.9)	1,627 (70.1)	
West	36 (4.8)	108 (4.7)	
Dual eligible - Medicare/Medicaid, n (%)	103 (13.8)	394 (17.0)	0.043
Adjusted Deyo-CCI, mean [SD] ^a	1.7 [1.8]	2.0 [1.9]	< 0.001
Comorbid conditions, n (%)			
Depression	33 (4.4)	135 (5.8)	0.149
Anxiety	140 (18.8)	560 (24.1)	0.003
Myocardial infarction	37 (5.0)	160 (6.9)	0.063
Congestive heart failure	85 (11.4)	350 (15.1)	0.013
Peripheral vascular disease	122 (16.4)	392 (16.9)	0.751
Cerebrovascular disease	44 (5.9)	250 (10.8)	< 0.001
Chronic pulmonary disease	370 (49.7)	1,382 (59.6)	< 0.001
Mild liver disease	43 (5.8)	155 (6.7)	0.384
Diabetes without chronic complication	145 (19.5)	558 (24.1)	0.010
Diabetes with chronic complication	65 (8.7)	248 (10.7)	0.126
Renal disease	99 (13.3)	326 (14.1)	0.609
Bone metastases, n (%)	271 (36.4)	815 (35.1)	0.520

SD, Standard deviation; CCI, Charlson Comorbidity Index

^a Both *metastatic cancer* and *solid tumor without metastasis* comorbidity categories were excluded from the Deyo-Charlson Comorbidity Index score calculations.