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RESEARCH BRIEF

Opioid Prescribing Safety Measures in Medicaid Enrollees With and Without Cancer

Patience Moyo, PhD,[1] Walid F. Gellad, MD, MPH,[2,3,4] Lindsay M. Sabik, PhD,[5] Gerald T. Cochran, PhD, MSW,[2,6,7] Evan S. Cole, PhD,[5] Adam J. Gordon, MD, MPH,[7,8] David K. Kelley, MD, MPA,[9] Julie M. Donohue, PhD[2,5]

Introduction: Opioid prescribing safety among individuals with cancer is poorly understood. This study estimates the prevalence of Pharmacy Quality Alliance opioid measures among individuals with cancer undergoing or not undergoing active treatment versus those without cancer.

Methods: Pennsylvania Medicaid data (2016) were analyzed in 2018 to identify adults aged 18–64 years with and without cancer diagnoses who had 2 or more opioid prescriptions. Active cancer treatment, defined as having chemotherapy, radiotherapy, cancer surgery, or hospitalization with a primary diagnosis of cancer, was evaluated from October 2015 to December 2016 allowing a ≥3-month look-back period for cancer diagnoses observed in the first quarter of 2016. Opioid dosages (>120 morphine milligram equivalents for ≥90 consecutive days), multiple providers (4 or more prescribers and 4 or more pharmacies), and opioid and benzodiazepines overlapping ≥30 days were evaluated.

Results: The sample with opioid prescriptions included 111,491 enrollees without cancer diagnoses and 12,819 with cancer, 58.8% of whom were not in active cancer treatment. Among enrollees undergoing cancer treatment, with cancer but not in active treatment, and without cancer, the prevalence of high morphine milligram equivalents was 7.1%, 6.0%, and 4.7% ($p<0.001$), respectively. The corresponding prevalence of multiple providers was 6.7%, 4.1%, and 3.4% ($p<0.001$). Concurrent opioid and benzodiazepine prescriptions occurred in 28.6%, 30.5%, and 26.8% ($p<0.001$), respectively.

Conclusions: Individuals with cancer, regardless of treatment status, had higher-risk opioid use based on Pharmacy Quality Alliance measures versus those without cancer. Their systematic exclusion from opioid quality surveillance could create missed opportunities to identify patients at high risk of adverse opioid-related outcomes.

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From the [1]Department of Health Services, Policy, and Practice, Brown University School of Public Health, Providence, Rhode Island; [2]Center for Pharmaceutical Policy and Prescribing, University of Pittsburgh Health Policy Institute, Pittsburgh, Pennsylvania; [3]Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania; [4]Division of General Internal Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [5]Department of Health Policy & Management, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania; [6]University of Pittsburgh, School of Social Work, Pittsburgh, Pennsylvania; [7]Program for Addiction, Research, Clinical Care, Knowledge, and Advocacy, Division of Epidemiology, Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, Utah; [8]Informatics, Decision-Enhancement and Analytic Sciences (IDEAS) and Vulnerable Veteran Innovative PACT (VIP) Initiative, Veterans Affairs Salt Lake City Health Care System, Salt Lake City, Utah; and [9]Pennsylvania Department of Human Services, Harrisburg, Pennsylvania

Address correspondence to: Julie M. Donohue, PhD, Department of Health Policy & Management, Graduate School of Public Health, University of Pittsburgh, 130 De Soto St., Pittsburgh PA 15213.
E-mail: jdonohue@pitt.edu.

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INTRODUCTION

In response to increased opioid morbidity, health systems have implemented programs to identify potentially unsafe opioid prescribing. National organizations have introduced quality metrics to guide these surveillance efforts.[1,2] Pharmacy Quality Alliance (PQA) measures (high dose, multiple providers, and concurrent opioids and benzodiazepines) examine prescribing and behavioral risk factors strongly linked to prescription opioid overdose.[3–5] Individuals with cancer diagnoses, however, are systematically excluded from PQA and similar measures,[6] as cancer pain historically has been regarded differently from other chronic pain conditions.[7] Yet, cancer patients are diverse, and pain management needs may differ by cancer stage and site, treatment and prognosis, comorbid conditions, and myriad other factors.[8]

Inconsistencies in guideline recommendations on pain management among cancer survivors highlight the need for studies to inform opioid prescribing.[7] With increasing long-term cancer survivorship,[9] high rates of polypharmacy,[10] and complexities of managing cancer and treatment-related pain,[11] nuanced considerations of opioid prescribing throughout the cancer care continuum are warranted.[12] This study applies PQA opioid measures to Medicaid data to (1) compare the prevalence of opioid safety measures among those with and without cancer and (2) determine whether these measures vary among individuals with a cancer diagnosis based on cancer treatment status. The hypotheses are that PQA measures have greater prevalence among individuals with cancer versus those without cancer, and that those in active treatment would have higher rates.

METHODS

This study used de-identified Pennsylvania Medicaid enrollment, inpatient, outpatient, and professional claims from fee-for-service and managed care enrollees. Calendar year 2016 data were used to measure cancer diagnoses and opioid prescribing. Data for October 1 to December 31, 2015 were added to categorize enrollees regarding cancer treatment status.

Enrollees who were aged <18 or ≥65 years, dually enrolled in Medicare, received long-term care or hospice services, or had a gap >45 days in Medicaid enrollment were excluded from analyses (Appendix Figure 1, available online). Following PQA specifications, to define individuals likely to have chronic opioid use, analyses were limited to enrollees with 2 or more opioid prescriptions on ≥2 separate days and ≥15 days supplied during the calendar year. Injectable forms and treatments for opioid use disorder were not counted as prescription opioids.

Medicaid eligibility, age, sex, race/ethnicity, comorbidities, and cancer treatment were analyzed. To create the cancer cohort, 2016 medical claims were searched for 1 or more ICD-10 codes for current or past diagnosis of cancer, excluding benign neoplasm, carcinoma in situ, or nonmelanoma skin cancer, following PQA methods and prior research.[13] Those with at least 1 pharmacy claim for chemotherapy agents; at least 1 procedure or revenue code for chemotherapy, radiotherapy, or cancer surgery; or 1 or more inpatient claim with a cancer as the primary diagnosis between October 1, 2015 and December 31, 2016 (allowing a 3-month look-back before 2016) were categorized as undergoing cancer treatment (Appendix Table 1, available online).[14–16] Metastatic cancer, at diagnosis or later progression, was measured using ICD-10 codes for secondary cancer.[8,17,18]

Opioid use measures examined during calendar year 2016 were the following:

1. Opioid dosages >120 morphine milligram equivalents (MMEs) for ≥90 consecutive days (hereafter considered high MMEs according to the PQA definition in 2016 [lowered to 90 MMEs in 2018][19]);
2. Multiple providers, defined as 4 or more prescribers and 4 or more pharmacies; and
3. Opioid and benzodiazepine prescriptions overlapping ≥30 days.[2]

This study compared the percentage of enrollees meeting thresholds for the PQA measures among the following 3 groups: (1) those with cancer with active treatment, (2) those with cancer without active treatment, and (3) those without cancer. All analyses were conducted in SAS, version 9.4. The University of Pittsburgh IRB designated this study as exempt.

RESULTS

Among enrollees meeting initial inclusion criteria, 57.1% of those with cancer (n=12,819) and 37.3% of those without cancer (n=111,491) who had opioid use meeting PQA thresholds were analyzed (Table 1). The 5 most common cancer types were bone/soft tissue (15.3%), head/neck (15.3%), breast (13.9%), noncolon gastrointestinal (12.2%), and lung (10.8%) (Appendix Table 2, available online). Overall, 19.4% had an ICD-10 indication of metastatic cancer. Of enrollees diagnosed with cancer, 58.8% were not currently in active cancer treatment.

Among enrollees without cancer, the prevalence of high MMEs, multiple providers, and concurrent opioid and benzodiazepine prescriptions were 4.7%, 3.4%, and 26.8%, respectively, consistently lower than among those with cancer (Figure 1). Among enrollees with cancer, those not in active treatment had a lower prevalence of high MMEs (7.1% vs 6.0%, p=0.01) and multiple providers (6.7% vs 4.1%, p<0.001), but a greater proportion of overlapping opioid and benzodiazepine prescriptions (28.6% vs 30.5%, p=0.02) than those undergoing treatment. For each PQA measure, comparisons across all 3 groups (without cancer and cancer with and without active treatment) had p<0.001.

DISCUSSION

This study found that the prevalence of the PQA opioid measures was consistently higher among enrollees with

Table 1. Characteristics of Pennsylvania Medicaid Enrollees Prescribed Opioids, Categorized by Cancer Status, 2016

Characteristics	Enrollees with cancer			Enrollees without cancer
	All, *n* (%)	Active cancer treatment, *n* (%)	No active cancer treatment, *n* (%)	All, *n* (%)
Total	12,819 (100.0)	5,285 (100.0)	7,534 (100.0)	111,491 (100.0)
Age in years, mean ± SD	50.4 ± 10.3	51.5 ± 10.1	49.6 ± 10.5	44.6 ± 11.4
18–29	682 (5.3)	255 (4.8)	427 (5.7)	14,214 (12.8)
30–39	1,594 (12.4)	517 (9.8)	1,077 (14.3)	26,317 (23.6)
40–49	2,847 (22.2)	1,071 (20.3)	1,776 (23.6)	28,576 (25.6)
50–64	7,696 (60.0)	3,442 (65.1)	4,254 (56.5)	42,384 (38.0)
Female sex	8,140 (63.5)	3,312 (62.7)	4,828 (64.1)	67,622 (60.7)
Race and ethnicity				
White non-Hispanic	8,474 (66.1)	3,324 (62.9)	5,150 (68.4)	71,338 (64.0)
Black non-Hispanic	2,899 (22.6)	1,290 (24.4)	1,609 (21.4)	26,853 (24.1)
Hispanic and other	1,446 (11.3)	671 (12.7)	775 (10.3)	13,300 (11.9)
Medicaid eligibility category[a]				
Expansion	6,206 (48.4)	2,715 (51.4)	3,491 (46.3)	61,243 (54.9)
Disabled	5,387 (42.0)	2,126 (40.2)	3,261 (43.3)	33,322 (29.9)
Other	1,226 (9.6)	444 (8.4)	782 (10.4)	16,926 (15.2)
Modified Elixhauser comorbidity index,[b] mean ± SD	4.8 ± 2.9	5.4 ± 2.9	4.4 ± 2.9	2.7 ± 2.4
0	505 (3.9)	94 (1.8)	411 (5.5)	20,039 (18.0)
1 to 2	2,481 (19.4)	706 (13.4)	1,775 (23.6)	41,281 (37.0)
≥3	9,833 (76.7)	4,485 (84.9)	5,348 (71.0)	50,171 (45.0)
Died during year	723 (5.6)	614 (11.6)	109 (1.5)	1,032 (0.9)

[a]Enrollees were categorized into mutually exclusive groups based on a hierarchy that first identified those covered under the Affordable Care Act Medicaid expansion. The remaining enrollees were grouped as disabled or other eligibility.
[b]Excludes cancer-related comorbidities (lymphoma, solid tumor without metastasis, and metastatic cancer) from total count.

cancer regardless of cancer treatment status than those without cancer. Additionally, among enrollees with cancer, differences in the prevalence of the PQA measures between those currently undergoing cancer treatments versus those not in treatment were modest.

Individuals with cancer may be more prone to unsafe opioid prescribing than those without cancer and therefore may benefit from routine monitoring of opioid use, potential misuse, and diversion risks. Excluding cancer populations from opioid surveillance efforts may have unintended consequences, and could inhibit efforts to appropriately manage opioid use in a population with complex health needs.

Although opioid prescribing varied by active cancer treatment status, the absolute differences (versus without active treatment) were minimal (high MMEs, 1.1%; multiple providers, 2.6%; concurrent opioids and benzodiazepines, −1.9%). Notably, concurrent opioid and benzodiazepine prescriptions were common among all groups and highest among enrollees with cancer but not in active treatment. Although higher prevalence of depression and anxiety in the latter group may explain higher concurrent use of opioids and benzodiazepines, the appropriateness of concurrent use is uncertain.

Similar to a study using 2004–2014 commercial and Medicare data,[8] most of those with cancer diagnoses in Pennsylvania Medicaid were not in active treatment. The large proportion of individuals with cancer diagnoses but not in active treatment may reflect providers' tendency to continue listing cancer-related diagnostic codes on medical records for purposes of monitoring cancer recurrence or cancer-related pain arising from toxicities of treatment, even after treatment concludes. It thus may be appropriate for controlled substance surveillance programs relying on large administrative data sets to acknowledge the substantial heterogeneity in pain needs among individuals with a cancer diagnosis and potentially include patients who have cancer but are not in active treatment.

Limitations

Claims data may not adequately capture disease stage, timing of initial diagnosis, severity, or treatment; however, they provide the ability to assess risk at the population level. Secondary cancer codes may not completely or accurately represent metastasis. It is uncertain whether cancer patients without active treatment were long-term survivors or never received treatment (e.g., owing to absence of

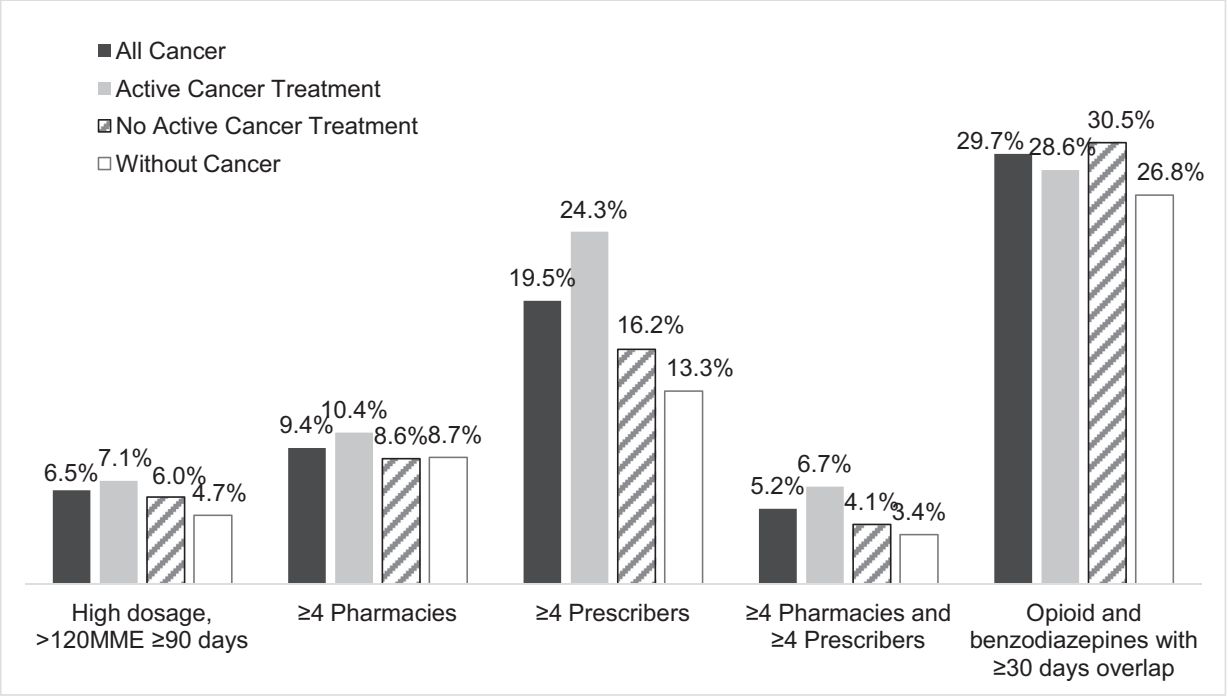

Figure 1. Prevalence of opioid quality measures among Pennsylvania Medicaid enrollees with and without cancer diagnoses in 2016.

Note: between All Cancer and Without Cancer were statistically significant across all measures with maximum p=0.013 (≥4 pharmacies); all other comparisons had p<0.0001. Differences between Active Cancer Treatment and No Active Cancer Treatment were statistically significant across all measures with maximum p=0.021 (opioid and benzodiazepine with ≥30 days overlap). Differences between No Active Cancer Treatment and Without Cancer were statistically significant across all measures with p<0.0001 with exception of ≥4 pharmacies with p=0.141.

[a]Among the total cancer sample, 7 (0.05%) had missing pharmacy data, and 380 (3.0%) had missing prescriber data. In the noncancer sample, 154 (0.14%) and 6,217 (5.6%) enrollees lacked pharmacy and prescriber data, respectively.

MME, morphine milligram equivalent.

treatment need, futility of treatment, or other reasons). Although focused on chronic noncancer pain, the Centers for Disease Control and Prevention guideline published in March 2016 may also have influenced opioid prescribing patterns for those with cancer.[20] PQA specifications for high dosage changed after the study period from 120 MMEs/day to 90 MMEs/day to align with the guideline.[19] What constitutes high MMEs at an individual level may differ from population-level benchmarks, as the threshold above which opioid risk increases could be lower for individuals with mental health or substance use disorders.[21] Finally, the findings from Medicaid may not generalize to older or higher-income populations.

CONCLUSIONS

Medicaid enrollees with cancer consistently had a greater prevalence of PQA measures that are associated with potential opioid-related risks than individuals without cancer. Most individuals with cancer were not undergoing active cancer treatment—an indication that this population may benefit from routine monitoring of opioid use.

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PM had access to all aspects of the research and writing process and takes full responsibility for this manuscript. She conducted and interpreted all analyses and conceptualized the research question and design; WFG, JMD, AJG, GTC, and LMS assisted with the conception and design of the study; JMD and DKK facilitated the acquisition of data; ESC provided critical feedback on analytic file development; all authors were involved in reviewing and editing the final manuscript.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2019.05.019.

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