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Article

Predictors of Chronic Opioid Use: A Population-Level Analysis of North Carolina Cancer Survivors Using Multi-Payer Claims

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Abstract

Background: No population-based studies have examined chronic opioid use among cancer survivors who are diverse with respect to diagnosis, age group, and insurance status. **Methods:** We conducted a retrospective cohort study using North Carolina cancer registry data linked with claims from public and private insurance (2006-2016). We included adults with nonmetastatic cancer who had no prior chronic opioid use (n = 38 366). We used modified Poisson regression to assess the adjusted relative risk of chronic opioid use in survivorship (>90-day continuous supply of opioids in the 13-24 months following diagnosis) associated with patient characteristics. **Results:** Only 3.0% of cancer survivors in our cohort used opioids chronically in survivorship. Predictors included younger age (adjusted risk ratio [aRR] 50-59 vs 60-69 = 1.23, 95% confidence interval [CI] = 1.05 to 1.43), baseline depression (aRR = 1.22, 95% CI = 1.06 to 1.41) or substance use (aRR = 1.43, 95% CI = 1.15 to 1.78) and Medicaid (aRR vs private = 1.93, 95% CI = 1.56 to 2.40). Survivors who used opioids intermittently (vs not at all) before diagnosis were twice as likely to use opioids chronically in survivorship (aRR = 2.62, 95% CI = 2.28 to 3.02). Those who used opioids chronically (vs intermittently or not at all) during active treatment had a nearly 17-fold increased likelihood of chronic use in survivorship (aRR = 16.65, 95% CI = 14.30 to 19.40). **Conclusions:** Younger and low-income survivors, those with baseline depression or substance use, and those who require chronic opioid therapy during treatment are at increased risk for chronic opioid use in survivorship. Our findings point to opportunities to improve assessment of psychosocial histories and to engage patients in shared decision-making around long-term pain management, when chronic opioid therapy is required during treatment.

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Chronic opioid use is associated with an increased risk for serious harms, including cardiovascular events, fractures, opioid use disorder, and overdose (1). In the context of the US opioid crisis, routine interactions with the health-care system are increasingly examined for their potential to inadvertently lead to chronic opioid use. For example, recently published studies have shown that emergency department visits, common surgical procedures, and hospitalizations can lead to chronic opioid use among patients who were previously opioid naïve (2-4).

Despite having high rates of opioid exposure during treatment and a high burden of chronic pain that persists after treatment (5-7), cancer survivors—defined here as individuals treated for cancer with curative intent—are critically underrepresented in the chronic opioid use literature. To our knowledge, only a handful of prior studies have examined chronic opioid use (ie, continuous opioid use for 3 months or longer) among cancer survivors at a population level. Two of these studies used Surveillance, Epidemiology, and End Results–Medicare data and, as a result, were limited to Medicare beneficiaries aged 65 years and older (8,9). One study included younger as well as older adult cancer survivors; however, this study was largely limited to male cancer survivors and was conducted within the Veterans Affairs (VA) system, where risk factors for opioid abuse and dependence are much more prevalent than in the general population. Thus, the field still lacks essential information about the prevalence and predictors of chronic opioid use within the general population of cancer survivors.

To address these gaps, we leveraged unique data from the North Carolina Central Cancer Registry (NCCCR) linked with Medicare, Medicaid, and private insurance claims. We

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examined the prevalence of and factors associated with chronic opioid use among adult cancer survivors including all ages and those with public and private insurance. Our goals were to: 1) provide objective estimates of chronic opioid use among real-world cancer survivors and help patients and providers make informed decisions regarding opioid use during active cancer treatment, and 2) elucidate priorities for intervention research by identifying subgroups of cancer survivors with an increased likelihood of developing chronic opioid use; these subgroups may be most likely to benefit from strategies to achieve effective chronic pain management while reducing the risk of opioid-related harms.

Methods

Data Source and Population Studied

We conducted a retrospective cohort study using the University of North Carolina's Cancer Information and Population Health Resource (CIPHR) (10). CIPHR consists of data from the NCCCR linked with insurance claims from Medicare, North Carolina Medicaid, and private insurance. We used the NCCCR data to select the study cohort, including cancer survivors diagnosed at age 19 years or older, with a first primary diagnosis of a nonmetastatic solid tumor (breast, cervical, colorectal, endometrial, esophageal, head and neck, lung, melanoma, ovarian, prostate, testicular) from January 1, 2007, to December 31, 2014. We used insurance claims from January 1, 2006, through December 31, 2016, to provide 1 year of claims prior to cancer diagnosis (to ascertain comorbidities and prior opioid use) and 2 years of claims following diagnosis to ascertain cancer treatment and chronic opioid use. Patients were required to have continuous medical and prescription drug insurance coverage from 12 months prior to cancer diagnosis through 24 months following cancer diagnosis; we included those who switched insurance types (eg, private to Medicare). We excluded cancer survivors with chronic opioid use in the 12 months prediagnosis.

Measures

Our outcome was a binary indicator of chronic opioid use in the 13- to 24-month period following cancer diagnosis (ie, the early survivorship period) as the time period during which most patients complete primary and adjuvant cancer therapy and recover from acute toxicity (11). Consistent with prior studies (1,8,9), we defined chronic opioid use as having a continuous supply of opioids for 90 or more days ascertained using prescription drug claims. For pain management regimens with concomitant prescription of long-acting and immediate-release opioids, we used the cabinet supply approach (9,12) for adjusting total days' supply for overlapping opioid prescriptions sharing the same active ingredient, route, and formulation.

Factors evaluated for their associations with chronic opioid use in early survivorship included: 1) demographic characteristics, including age at diagnosis, gender, race and ethnicity, urban or rural residence, area-level measures of income and education, and insurance provider (Medicaid, Medicare, or private); 2) cancer- and treatment-related factors, including cancer type and stage (local or regional), receipt of surgery, radiation, and/or chemotherapy (identified using claims data; see the Supplementary Methods, available online), and cancer treatment setting (academic or community); 3) other health-related characteristics, including baseline comorbidity burden (13), prior mental health and substance use disorder diagnoses and prior chronic pain diagnoses (14); and 4) previous opioid use, including opioid use prior to cancer diagnosis and opioid use during the 12-month period following cancer diagnosis (ie, active treatment period). Because we excluded individuals with chronic opioid use prior to diagnosis, opioid use prior to diagnosis was characterized as none or intermittent (any opioid use in the 12-month period prior to cancer diagnosis that did not meet criteria for chronic opioid use) (11).

Statistical Analysis

We used descriptive statistics to characterize the analytic cohort, overall and by chronic use of opioids in the early survivorship period. Unadjusted differences between cancer survivors who did and did not use opioids chronically in early survivorship were assessed using χ^2 tests for categorical variables and t tests for continuous variables. Multivariable analysis used modified Poisson regression (15) to assess the adjusted relative risk of chronic opioid use associated with patient demographic and clinical characteristics. In secondary analysis, we stratified the analysis by cancer type. Because of small sample sizes, we could not run stratified models for testicular, ovarian, cervical, or esophageal cancer.

We conducted 2 sensitivity analyses. First, we excluded patients who received any cancer treatment (cancer-related surgery, radiation, or chemotherapy) in the 13- to 24-month period following diagnosis, in an attempt to exclude those who were delayed in initiating treatment or experienced disease recurrence. Second, we excluded patients who died in the 25- to 27-month period following cancer diagnosis, in an attempt to exclude chronic opioid use associated with end-of-life care. Because results were unchanged, estimates from the sensitivity analyses are not presented.

Results

Characteristics of the Analytic Cohort

A total of 38 366 cancer survivors met study criteria (Figure 1), 52.1% of whom were female and 19.0% of whom were non-White (Table 1). Mean age at diagnosis was 68 (Standard Deviation: 11) years, and most (71.1%) cancer survivors were insured by Medicare; 21.9% and 7.0% were insured by Medicaid and private plans, respectively. The most common cancer diagnoses were prostate (32.3%) and breast (31.5%). Approximately 8% of cancer survivors had a prior diagnosis of depression, anxiety, or chronic pain and 1.7% had a prior substance use disorder diagnosis.

Opioid Use Before Diagnosis, During Active Treatment, and in Early Survivorship

The majority (82.5%) of cancer survivors were opioid naïve at diagnosis (Table 1). In the active cancer treatment period, 51.5% of cancer survivors used no opioids, 46.0% used opioids intermittently, and 2% used opioids chronically. In the early survivorship period (13 to 24 months postdiagnosis), 3.0% of cancer survivors used opioids chronically.

In Figure 2, we depict opioid use among cancer survivors—including those who exhibited chronic opioid use prior to diagnosis and thus were excluded from our final analytic cohort—across the cancer care continuum, from the prediagnosis to

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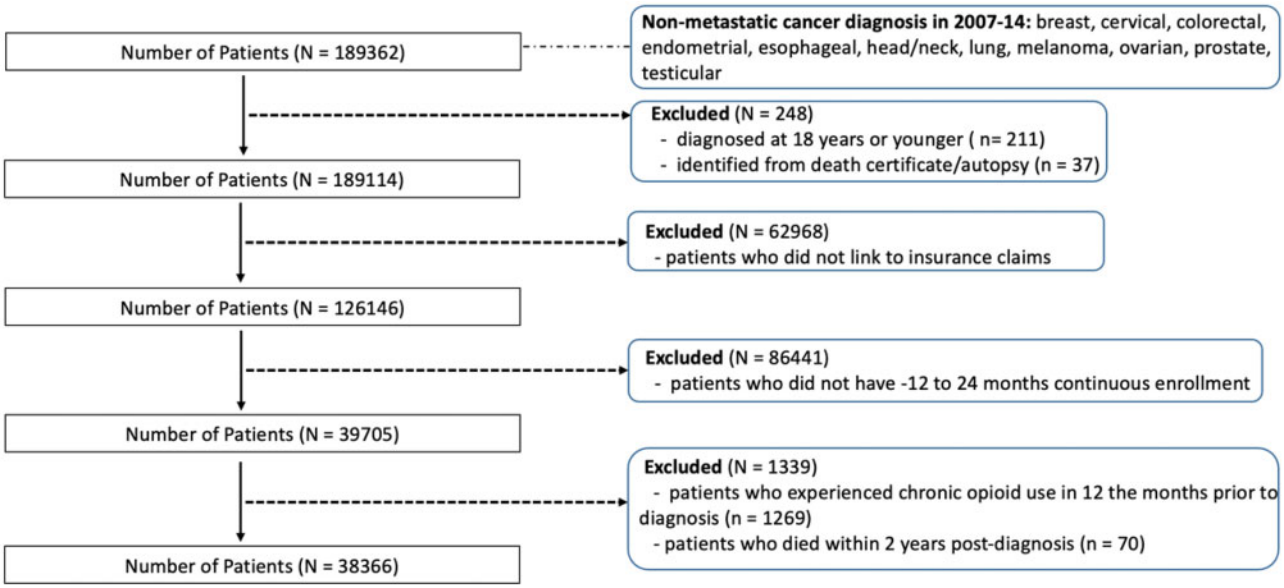

Figure 1. CONSORT diagram. Our analytic cohort included diagnosed with nonmetastatic cancer at age 19 years or older who had continuous insurance enrollment for 12 months before and 24 months after cancer diagnosis and who did not have chronic opioid use in the 12 months before diagnosis.

early survivorship period. Patients who were opioid naïve prior to cancer diagnosis and who used opioids intermittently during treatment largely returned to non-use in early survivorship (64.0%); 33.9% continued to use opioids intermittently in early survivorship, and only 2.1% progressed to chronic use. Those who were intermittent opioid users prior to cancer and during active cancer treatment largely remained intermittent users in early survivorship (54.9%); 5.9% progressed to chronic use in early survivorship. Regardless of opioid use status in the pre-diagnosis period (none, intermittent, chronic), the majority (58.0% to 83.6%) of cancer survivors who used opioids chronically during the active treatment period went on to use opioids chronically in early survivorship.

Factors Associated With Chronic Opioid Use in Early Survivorship

In unadjusted analyses, demographic factors associated with an increased likelihood of chronic opioid use in early survivorship included age and insurance provider (Table 1). We also observed unadjusted differences by cancer type and receipt of adjuvant chemotherapy. With respect to other health characteristics, comorbidity burden, prior depression, anxiety, chronic pain, and substance use disorder diagnoses were statistically significantly associated with chronic opioid use in early survivorship ($P < .001$). In addition, previous opioid use patterns—both prior to cancer diagnosis and during the active cancer treatment period—were statistically significantly associated with chronic opioid use in early survivorship ($P < .001$).

Multivariable Analysis of Factors Associated With Chronic Opioid Use in Early Survivorship

After adjustment, age differences persisted (adjusted risk ratio [aRR] 50-59 years vs 60-69 years = 1.23, 95% confidence interval [CI] = 1.05 to 1.43). Differences by insurance provider also persisted. Specifically, compared with those with private insurance, Medicare beneficiaries were 74% more likely (aRR = 1.74, 95% CI = 1.43 to 2.12) and Medicaid beneficiaries were nearly twice as likely to exhibit chronic opioid use (aRR = 1.93, 95% CI = 1.56 to 2.40).

The only cancer diagnosis independently and statistically significantly associated with chronic opioid use was lung cancer (aRR lung vs melanoma = 1.26, 95% CI = 1.03 to 1.53). Prior substance use disorder (aRR = 1.43, 95% CI = 1.15 to 1.78), depression (aRR = 1.22, 95% CI = 1.06 to 1.41), and chronic pain (aRR= 1.48, 95% CI= 1.30 to 1.69) diagnoses were also positively and statistically significantly associated with the likelihood of chronic opioid use in early survivorship, as was overall comorbidity burden (aRR Charlson comorbidity index 2+ vs 0 = 1.37, 95% CI = 1.21 to 1.56; Table 2).

Compared with cancer survivors who were opioid naïve prior to diagnosis, those who used opioids intermittently prior to diagnosis were more than twice as likely to use opioids chronically in early survivorship (aRR = 2.62, 95% CI = 2.28 to 3.02). Finally, compared with cancer survivors who used no opioids or who used opioids intermittently during the active treatment period, cancer survivors who used opioids chronically during the active treatment period had a nearly 17-fold increased likelihood of chronic use in early survivorship (aRR = 16.65, 95% CI = 14.29 to 19.37).

Results from the stratified models were consistent overall, with insurance status, previous opioid use, and mental health comorbidities remaining strong predictors of chronic opioid use across most cancer types (see Supplementary Tables 1-7, available online).

Discussion

We conducted a retrospective cohort study to characterize chronic opioid use among cancer survivors using North Carolina cancer registry–linked public and private insurance claims data from 2006-2016. Overall, a small proportion (3.0%) of cancer survivors in our cohort exhibited chronic opioid use in early survivorship. This estimate is consistent with Medicare-based estimates (8,9) and lower than VA-based estimates (11).

Table 1. Cohort characteristics, overall and by long-term use in year 2 (months 13-24) postdiagnosis

Variable	All patients (N = 38 366) No. (%)	Long-term opioid use (n = 1158), No. (%)	No long-term opioid use (n = 37 208), No. (%)	P[a]
Sociodemographic characteristics				
Mean age (SD), y	68.2 (11.1)	65.0 (11.6)	68.3 (11.0)	<.001
Age, categorized, y				<.001
Category 1 (19-49)	2534 (6.6)	109 (9.4)	2425 (9.5)	
Category 2 (50-59)	4801 (12.5)	251 (21.7)	4550 (21.2)	
Category 3 (60-69)	12 396 (32.3)	389 (33.6)	12 007 (32.3)	
Category 4 (70-79)	13 552 (35.3)	294 (25.4)	13 258 (35.6)	
Category 5 (≥80)	5083 (13.3)	115 (9.9)	4968 (13.4)	
Gender				<.001
Male	18 374 (47.9)	483 (41.7)	17 891 (48.1)	
Female	19 992 (52.1)	675 (58.3)	19 317 (51.9)	
Race/Ethnicity				<.001
Non-Hispanic White	31 080 (81.0)	853 (73.7)	30 227 (81.2)	
Non-Hispanic Black	6004 (15.7)	260 (22.5)	5744 (15.4)	
Hispanic or other	1282 (3.3)	45 (3.9)	1237 (3.3)	
Rural/Urban residence				<.001
Rural	10 190 (27.0)	363 (32.1)	9827 (26.9)	
Urban	27 505 (73.0)	769 (67.9)	26 736 (73.1)	
Percentage of residents with high school education in census track of residence				<.001
Quartile 1	9232 (24.6)	413 (36.5)	8819 (24.3)	
Quartile 2	9366 (25.0)	324 (28.7)	9042 (24.9)	
Quartile 3	9489 (25.3)	240 (21.2)	9249 (25.4)	
Quartile 4 (highest)	9418 (25.1)	154 (13.6)	9264 (25.5)	
Median household income in census track of residence				<.001
Quartile 1 (highest)	9547 (25.4)	170 (15.0)	9377 (25.7)	
Quartile 2	9454 (25.1)	259 (22.9)	9195 (25.2)	
Quartile 3	9372 (24.9)	310 (27.4)	9062 (24.8)	
Quartile 4	9293 (24.7)	392 (34.7)	8901 (24.4)	
Insurance provider				<.001
Any Medicaid	2698 (7.0)	253 (21.9)	2445 (6.6)	
Any private	8386 (21.9)	140 (12.1)	8246 (22.2)	
Medicare only	27 282 (71.1)	765 (66.1)	26 517 (71.3)	
Clinical characteristics				
Cancer type				<.001
Breast	12 065 (31.5)	353 (30.5)	11 712 (31.5)	
Prostate	12 390 (32.3)	259 (22.4)	12 131 (32.6)	
Colorectal	4972 (13.0)	182 (15.7)	4790 (12.9)	
Lung	2308 (6.0)	150 (13.0)	2158 (5.8)	
Endometrial/Uterine	2052 (5.4)	59 (5.1)	1993 (5.4)	
Melanoma	2708 (7.1)	61 (5.3)	2647 (7.1)	
Head/neck	996 (2.6)	58 (5.0)	938 (2.5)	
Other	875 (2.2)	36 (3.1)	839 (2.2)	
Cancer stage				<.001
Local	29 048 (75.7)	783 (67.6)	28 265 (76.0)	
Regional	9318 (24.3)	375 (32.4)	8943 (24.0)	
Charlson comorbidity index				<.001
0	18 029 (47.0)	313 (27.0)	17 716 (47.6)	
1	3230 (8.4)	56 (4.8)	3174 (8.5)	
2+	17 107 (44.6)	789 (68.1)	16 318 (43.9)	
Prior diagnosis of depression and/or anxiety				
Anxiety	2981 (7.8)	215 (18.6)	2766 (7.4)	<.001
Depression	3350 (8.7)	243 (21.0)	3107 (8.4)	<.001
Substance use disorder	654 (1.7)	97 (8.4)	557 (1.5)	<.001
Prior diagnosis of fibromyalgia or chronic pain	2841 (7.4)	281 (24.3)	2560 (6.9)	<.001
Prior opioid use (12 to 2 months before diagnosis)				
None	31 669 (82.5)	462 (39.9)	31 207 (83.9)	
Intermittent	6697 (17.5)	696 (60.1)	6001 (16.1)	
				<.001

(continued)

Table 1. (continued)

Variable	All patients (N = 38 366) No. (%)	Long-term opioid use (n = 1158), No. (%)	No long-term opioid use (n = 37 208), No. (%)	P[a]
Opioid use during active treatment/acute toxicity period (-1 to 12 months after diagnosis)				
None	19 757 (51.5)	0 (0.0)	19 757 (53.1)	
Intermittent	17 658 (46.0)	572 (49.4)	17 086 (45.9)	
Long-term	951 (2.5)	586 (50.6)	365 (1.0)	
Opioid use during active treatment/acute toxicity period (-1 to 12 months after diagnosis)				<.001
Non long-term	37 415 (97.5)	572 (49.4)	36 843 (99.0)	
Long-term	951 (2.5)	586 (50.6)	365 (1.0)	
Cancer treatment				
Adjuvant chemotherapy				
Yes	10 294 (26.8)	394 (34.0)	9900 (26.6)	<.001
No	28 072 (73.2)	764 (66.0)	27 308 (73.4)	
Surgery and radiation				
Surgery	27 075 (70.6)	822 (71.0)	26 253 (70.6)	.75
Radiation	16 576 (43.2)	517 (44.7)	16 059 (43.2)	.31
Treatment setting				.48
Major medical center	6895 (18.0)	199 (17.2)	6696 (18.0)	
Community-based cancer center	31 471 (82.0)	959 (82.8)	30 512 (82.0)	

[a] χ^2 tests were used for categorial variables and t tests for continuous variables; tests were 2-sided.

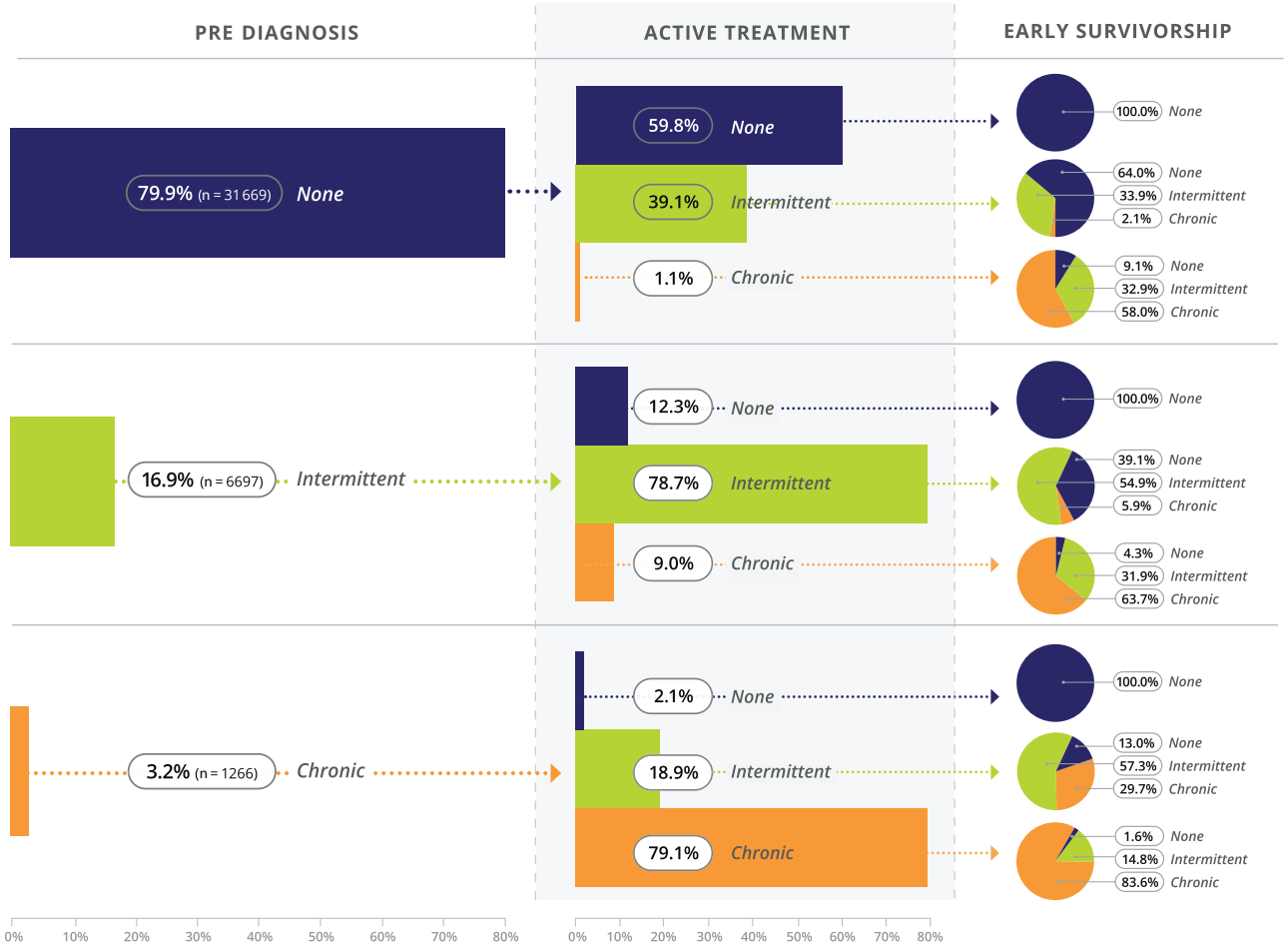

Figure 2. Opioid use across the cancer care trajectory. Intermittent and chronic opioid use before cancer diagnosis, during the active treatment period (12 months from diagnosis), and during the early survivorship period (13-24 months from diagnosis).

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Table 2. Modified Poisson model–estimated risk ratios of chronic opioid use in the early survivorship period

Variable	Risk ratios (95% confidence interval)
Sociodemographic characteristics	
Age, categorized, y	
Category 1 (19-49)	1.15 (0.93 to 1.43)
Category 2 (50-59)	1.23 (1.05 to 1.43)
Category 4 (70-79)	0.78 (0.68 to 0.89)
Category 5 (≥80)	0.86 (0.71 to 1.04)
Category 3 (60-69)	Referent
Gender	
Female	1.07 (0.91 to 1.27)
Male	Referent
Race/Ethnicity	
Non-Hispanic Black	0.52 (0.24 to 1.14)
Hispanic	1.00 (0.88 to 1.15)
Other	1.01 (0.78 to 1.32)
Non-Hispanic White	Referent
Rural/Urban residence	
Rural	1.03 (0.92 to 1.16)
Urban	Referent
Percentage of residents with high school education in census track of residence	
Quartile 1	1.15 (0.94 to 1.40)
Quartile 2	1.07 (0.89 to 1.30)
Quartile 3	1.30 (1.05 to 1.61)
Quartile 4 (highest education)	Referent
Median household income in census track of residence	
Quartile 2	1.19 (0.99 to 1.43)
Quartile 3	1.11 (0.91 to 1.35)
Quartile 4	1.14 (0.92 to 1.41)
Quartile 1 (highest income)	Referent
Insurance provider	
Any Medicaid	1.93 (1.56 to 2.40)
Medicare only	1.74 (1.43 to 2.12)
Any private	Referent
Clinical characteristics	
Cancer type	
Breast	0.91 (0.76 to 1.10)
Cervical	0.83 (0.44 to 1.58)
Endometrial/Uterine	0.97 (0.73 to 1.29)
Esophageal	0.93 (0.51 to 1.68)
Head/neck	0.97 (0.73 to 1.28)
Lung (non-small cell)	1.26 (1.03 to 1.53)
Melanoma	0.78 (0.60 to 1.01)
Ovarian	1.09 (0.60 to 2.00)
Prostate	0.88 (0.72 to 1.09)
Testicular	1.65 (0.84 to 3.25)
Colorectal	Referent
Cancer stage	
Regional	1.08 (0.95 to 1.22)
Local	Referent
Charlson comorbidity index	
1	1.07 (0.82 to 1.39)
≥2	1.37 (1.21 to 1.56)
0	Referent
Prior diagnoses	
Anxiety	
Yes	1.03 (0.88 to 1.19)
No	Referent
Depression	
Yes	1.22 (1.06 to 1.41)
No	Referent
Substance use disorder	
Yes	1.43 (1.15 to 1.78)
No	Referent

(continued)

Table 2. (continued)

Variable	Risk ratios (95% confidence interval)
Prior diagnosis of fibromyalgia or chronic pain	
Yes	1.48 (1.30 to 1.69)
No	Referent
Prior opioid use	
Intermittent	2.62 (2.28 to 3.02)
None	Referent
Opioid use during active treatment/acute toxicity period (-1 to 12 months after diagnosis)	
Long-term use	16.65 (14.30 to 19.40)
Non long-term use	Referent
Cancer treatment	
Adjuvant chemotherapy	
Yes	1.04 (0.92 to 1.18)
No	Referent
Surgery	
Yes	1.05 (0.90 to 1.22)
No	Referent
Radiation	
Yes	0.99 (0.88 to 1.12)
No	Referent
Treatment setting	
Major medical center	1.01 (0.88 to 1.17)
Community-based cancer center	Referent

Although chronic opioid use in early survivorship was relatively uncommon overall, prevalence varied across age groups, insurance providers, and to a lesser extent, cancer type. Prevalence also varied based on cancer survivors' medical and mental health histories and, most markedly, based on their previous experiences using opioids, both prior to cancer diagnosis and during active cancer treatment.

Our study provides new information about chronic opioid use among cancer survivors who are diverse with respect to age group and insurance provider. Using the unique North Carolina CIPHR database, we observed statistically significant differences in the likelihood of developing chronic opioid use across age groups and insurance providers. Specifically, younger cancer survivors were more likely to exhibit chronic opioid use than older cancer survivors. This finding may reflect more cautious opioid prescribing among older adults (16-18). Although older age was independently associated with a decreased likelihood of chronic opioid use in early survivorship, insurance through Medicare (vs private insurance) was independently associated with an increased likelihood of developing chronic opioid use. These findings are somewhat contradictory and suggest that Medicare status may serve as an indicator for medical complexity and associated propensity for chronic pain (eg, from arthritis or other chronic conditions) (19). Although our multivariable model adjusted for chronic pain using an established claims-based algorithm, chronic pain is often underdiagnosed among older adults (20) and therefore may be undercaptured in claims data. Underdiagnosis of chronic pain may also explain the observed association of overall comorbidity burden with chronic opioid use. Alternatively or in addition, patients who see multiple providers for various conditions could plausibly receive overlapping opioid prescriptions from more than 1 of their providers (21), resulting in chronic opioid use per our claims-based definition.

Medicaid beneficiaries in our cohort were nearly twice as likely as privately insured cancer survivors to use opioids chronically. This finding is consistent with those of a recently published integrative review that synthesized research on factors associated with long-term opioid therapy among cancer survivors, defined as any opioid use after completion of curative-intent treatment, regardless of duration or continuity of opioid use (22). Our findings are also consistent with opioid use patterns observed in the general US population. Specifically, low-income individuals in the United States are prescribed opioids at twice the rate of higher-income individuals (23). There are 2 potential explanations for these patterns. First, low-income individuals may experience an increased burden of chronic pain (24,25). Prior research suggests that the relationship between low socioeconomic status and pain may be mediated by psychological factors including lower perceived control (26-28). Second, low-income individuals may be more likely to use opioids chronically due to lack of access to nonpharmacological pain management interventions (29,30). Based on the results of our study and others, a multidisciplinary approach to pain management—particularly one that addresses psychological factors that contribute to pain—may be particularly important for low-income cancer survivors. Efforts to enhance access by the integrating nonpharmacological pain management approaches into routine cancer care are critically needed.

We also observed that a prior substance use disorder diagnosis was associated with an increased risk of chronic opioid use. This finding is consistent with the results of the VA-based study of chronic opioid use among cancer survivors conducted by Vitzhum and colleagues (11). Whether these patterns reflect drug-seeking behavior is not clear. However, prior substance use disorder is a known risk factor for opioid misuse and overdose (31,32). The American Society of Clinical Oncology recommends that clinicians screen all patients for substance use disorder history to inform a risk-stratified approach to monitoring opioid adherence (33). Yet, available data indicate that clinicians frequently do not ask their patients about substance use disorder history (34). Further, patients may be reluctant to inform clinicians of prior experiences with addiction. In this context, our observation that patients with a prior substance use

disorder diagnosis were more likely to use opioids chronically indicates that oncology clinicians may lack knowledge about patients' substance use history and associated risks. Our findings point to an important opportunity to improve implementation of guideline-recommended screening for prior substance use disorder in ways that are acceptable from both the clinician and patient perspectives.

Finally, our study provides highly clinically relevant information about how patients' experiences with opioid use both prior to cancer diagnosis and while undergoing cancer treatment impact their likelihood of using opioids chronically after treatment and into survivorship. Of cancer survivors in our cohort, 85% were opioid naïve at diagnosis, and about half of them began using opioids intermittently while undergoing active treatment. The majority of cancer survivors in this group successfully discontinued opioid therapy by early survivorship. Although about one-third continued to use opioids intermittently in early survivorship, very few used opioids chronically during treatment or in early survivorship. In the context of concerns about opioid dependence, these findings may be reassuring for both patients and providers.

On the other hand, cancer survivors who used opioids chronically during cancer treatment—irrespective of their experience with opioids prior to cancer diagnosis—were more likely than not to continue chronic opioid use into survivorship. This finding raises the question of whether limiting opioid use to fewer than 90 continuous days during active cancer treatment may help mitigate chronic use after treatment. In addition, it highlights a potential opportunity for shared decision-making with patients who require intensive and continuous opioid therapy to manage acute toxicity during and immediately following treatment. It may be important for oncology clinicians to assess and revisit patients' functional goals and pain management preferences.

It is worth noting that a few of our findings diverged from those of other studies examining opioid use patterns among cancer survivors. In particular, in other studies, race and ethnicity and rural residence have been found to be associated with long-term opioid therapy (ie, any opioid use after treatment completion) as have cancer type and treatment received (22). We examined a different outcome—chronic use, defined as at least 90 days of continuous use in the 13-24 months following diagnosis—which may explain the divergent findings, particularly with respect to cancer type and treatment. With respect to race and ethnicity and rurality specifically, it is possible that associations of these variables with the outcome did not persist after adjustment because of our inclusion of Medicaid status and area-level socioeconomic indicators as covariates.

This study has several limitations. First, we were unable to distinguish between chronic opioid use that may represent potentially avoidable prescribing and chronic opioid use that is indicative of appropriate pain management. Second, using claims data, we could only assess filled opioid prescriptions; we could not assess cancer survivors' opioid-use behaviors. Third, our study design required that we exclude individuals who died within 24 months of cancer diagnosis. This includes individuals who may have experienced disease regression and died from their cancer and those who died of an opioid overdose [a rare event (35)]. Fourth, it is unclear whether our results generalize to other states. Notably, compared with a national cohort, members of our North Carolina–based cohort were slightly older on average and less racially and ethnically diverse; we had relatively small numbers of Latinx, Asian, and American Indian individuals.

Based on our findings, relatively few cancer survivors use opioids chronically in early survivorship. Providers and patients may be reassured that intermittent opioid use appears to be associated with infrequent progression to chronic use in early survivorship. Nonetheless, we identified several subgroups of cancer survivors who may be substantially more likely to use opioids chronically. These include low-income individuals, those with a history of a substance use disorder, those with a history of intermittent opioid use, and those who use opioids chronically while undergoing treatment. Our results suggest that there may be value in improving assessments of substance use disorder histories at diagnosis, addressing psychosocial factors that contribute to pain, and engaging patients in shared decision-making about long-term pain management plans, when intensive opioid therapy is needed to manage pain during treatment.

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Notes

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Data Availability

The data underlying this analysis were provided by the Cancer Information and Population Health Resource (CIPHR) under license and data use agreement. Researchers interested in the CIPHR data may submit an inquiry online: https://ciphr.unc.edu/ciphr-data-inquiry.php.

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