Trends in Opioid Use Among Older Survivors of Colorectal, Lung, and Breast Cancers

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abstract

PURPOSE Cancer survivors may be at increased risk for opioid-related harms. Trends in opioid use over time since diagnosis are unknown.

METHODS Using data from SEER and Medicare, we conducted multilevel logistic regression analyses to compare chronic opioid use (≥ 90 consecutive days) among opioid-naïve survivors of colorectal, lung, and breast cancers diagnosed from 2008 to 2013 and matched with noncancer controls. Among cases and controls with chronic use, we compared rates of high-dose opioid use (average ≥ 90 morphine milligram equivalents daily).

RESULTS We included 46,789 survivors and 138,136 noncancer controls. In the first year after the index date (survivor's diagnosis date), chronic use among colorectal and lung cancer survivors exceeded chronic use among controls (colorectal cancer: odds ratio, 1.34; 95% CI, 1.22 to 1.47; lung cancer: odds ratio, 2.55; 95% CI, 2.34 to 2.77). Differences in chronic use between survivors and controls declined each year after the index date. Chronic use among breast cancer survivors was less than that of controls each year after the index date. Survivors with chronic use were more likely to have a high daily dose than controls with chronic use in the first 3 to 5 years.

CONCLUSION Among three large populations of older cancer survivors, chronic opioid use varied by cancer. However, by 6 years after diagnosis, survivors were no longer more likely to be chronic users than controls. Strategies for appropriate pain management during and after cancer treatment should take into account the risks associated with chronic high-dose opioid use.

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INTRODUCTION

Opioids are an established pain management strategy for cancer pain, leaving cancer survivors vulnerable to opioid dependence and other opioid-related harms.^{1,2} There is strong evidence from the general population that even brief exposure to opioids contributes to the risk of long-term opioid dependence.^{3,4} The potential for opioid exposure continues after the completion of cancer treatment, because up to 40% of cancer survivors experience pain and may receive opioids for pain management.⁵⁻¹¹ Few studies have characterized long-term opioid use among cancer survivors.^{12,13}

Aside from opioid exposure, risk factors for opioid dependence are prevalent in cancer survivors, including a history of substance abuse disorder (especially relevant for smoking- or alcohol-related cancers), anxiety, and post-traumatic stress.^{11,14-16} In addition, adverse effects of opioids in the general population (eg, constipation, sedation, endocrinopathies, immune dysfunction, and osteoporosis) may be exacerbated in patients with cancer, in part due to late effects of cancer treatment.^{17,18} This risk is particularly salient for older

cancer survivors, with polypharmacy causing harmful drug interactions.^{19,20} Furthermore, patients with cancer tend to be older, and opioid use among older adults in the general population is associated with falls, fractures, and increased mortality.²¹⁻²³

Cancer survivors may have greater pain management needs, experience greater health risks, and have less coordinated care than patients without cancer. Our study focused on chronic opioid use, which has unclear benefits and is associated with long-term harms, including dependence, overdose, and fractures.²⁴ We investigated whether older cancer survivors of three common cancers were at increased risk for chronic opioid use and high-dose opioid use in the years after cancer treatment, accounting for trends in the general population.

METHODS

Data Source

The SEER registry linked to Medicare claims was used to identify cases of primary colorectal, lung, and breast cancers. These cancers were selected for their high

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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incidence among older populations and to represent clinical and demographic diversity. The SEER registry covers approximately 28% of the US population and includes information regarding the site and extent of disease, patient demographics, and survival for incident cancer cases.²⁵⁻²⁷

SEER also provides information regarding a 5% sample of Medicare beneficiaries who live in a SEER region and do not have a documented history of cancer. Demographic information is linked to Medicare claims. This study was deemed exempt by the Institutional Review Board of Memorial Sloan Kettering Cancer Center and was performed under a data use agreement with the National Cancer Institute.

Identification of Opioids and Definition of Chronic and High-Dose Opioid Use

Opioids were identified from a list of generic names obtained from the Centers for Medicare & Medicaid Services and from clinician review of all pharmacy dispensings²⁸ (Appendix Table A1, online only). Consistent with prior studies, chronic opioid use was defined as 90 consecutive days of opioid use, allowing for up to a 7-day gap between consecutive refills.^{24,29} Days covered by overlapping dispensings were counted once. Average daily dose was defined as the total morphine milligram equivalents (MME) divided by the number of days covered by an opioid dispensing. High-dose use was defined as an average daily dose of 90 or more MME.³⁰

Cohort

Patients with colorectal, lung, or female breast cancer diagnosed between 2008 and 2013 as their first and only cancer (survivors) were identified. Survivors 66 years of age and older at diagnosis were included to ensure a 1-year look-back period for comorbidities and opioid use. We restricted analyses to survivors who were opioid naïve at diagnosis, which was defined as the absence of chronic opioid use in the year before diagnosis. Patients with opioid use who did not meet the threshold for chronic opioid use were included to avoid the exclusion of patients using opioids for acute episodes of pain or diagnostic work-up related to their cancer. Survivors were required to have complete coverage in Medicare parts A, B, and D from diagnosis through the end of 2014 or death, whichever occurred first. We excluded survivors diagnosed with stage 0 or IV disease or at death. Patients in the 5% noncancer sample were eligible to be considered as noncancer controls if they met the same coverage criteria as survivors.

Matching

Survivors were matched at the date of diagnosis (index date) without replacement to three controls on sex, race (white, black, other), Charlson comorbidity score (excluding malignancies; 0, 1, $\geq$ 2) in the year before the index date, region, and year of birth. Controls were required

to be opioid naïve in the year before the index date. Exact matching of each survivor to three controls was required for all characteristics except for year of birth ($\pm$ 2 years).

Analyses

Analyses were restricted to pairs with 90 days or more of follow-up. Chronic opioid use was described (1) by calendar year (2008 through 2014) and (2) in each of the 6 years after the index date. Pairs were censored if either member died or entered hospice. If chronic use spanned 2 analysis years, the episode was attributed to the second year.

The primary analysis first described chronic opioid use among controls to identify patterns of chronic opioid use from 2008 through 2014 (secular trends in each group of matched controls) and patterns of chronic opioid use as controls aged throughout the follow-up period (aging trends in each group of matched controls), with the caveat that these trends did not generalize to the entire population of cancer-free individuals in the Medicare population. We then compared these secular and aging trends with trends in opioid use among survivors to illustrate the independent effects of each cancer on chronic opioid use. We computed the odds ratios (ORs) and 95% CIs for chronic opioid use for survivors compared with matched controls in each year after the index date, using a hierarchic logistic regression model accounting for matching and repeated measurements across years.

To investigate the intensity of chronic opioid use, we compared high-dose opioid use between the subsets of cases and controls who had chronic opioid use. For this analysis, we defined chronic use more conservatively as 90 or more days of continuous dispensing within each specific year of interest, excluding formulations for which daily dose was unavailable¹⁷ (Appendix Table A1). Among those with chronic use in each year after the index date, we compared the likelihood of high-dose use between survivors and controls using hierarchic logistic regression. By restricting analyses to patients with chronic opioid use, we did not use matched pairs; updated censoring dates reflected the death or hospice entry date of the individual (rather than the pair, as in the primary analysis).

Sensitivity Analyses

To account for potential increases in opioid use before death from cancer, the analyses were repeated with censoring 3 or 9 months before deaths attributed to cancer. Analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC), using the GLIMMIX procedure for hierarchic modeling.

RESULTS

Cohort

After all survivors were successfully matched and after excluding pairs without 90 or more days of follow-up,

13,101 colorectal, 11,859 lung, and 21,829 breast cancer survivors were included in the analyses (Table 1).

Secular Trends in Chronic Opioid Use Within Each Group of Matched Controls

Rates of chronic opioid use among each group of matched controls seemed to be stable or declined minimally over the calendar years in the analysis period (Tables 2-4). For example, in the first year after the index date, for controls matched to colorectal cancer survivors diagnosed in 2008, 2.2% of controls had chronic opioid use, whereas 1.5% of controls matched to colorectal cancer survivors diagnosed in 2013 had chronic opioid use (Table 2). Similar patterns were apparent among controls matched to lung and breast cancer survivors.

Aging Trends in Chronic Opioid Use Within Each Group of Matched Controls

In contrast to relatively stable or declining chronic opioid use over calendar years, chronic opioid use among matched controls increased from the first to the last year after the index date, observed in each calendar diagnosis year for each group of matched controls (Tables 2-4). This increase as controls aged was most dramatic among controls matched to patients with breast cancer, from 2.9% chronic opioid use in the first year after the index date to 7.3% in the sixth year after the index date, combining across calendar diagnosis years (Table 4).

Trends in Chronic Opioid Use Over Time Since Diagnosis Among Cancer Survivors

Colorectal cancer. Across all diagnosis years, the percentage of colorectal cancer survivors with chronic opioid use ranged from 2.7% in the first year after the index date to 4.0% 6 years after the index date (Table 2). Survivors were more likely to have chronic opioid use for the first 2 years after the index date compared with controls (OR, 1.34; 95% CI, 1.22 to 1.47; and OR, 1.17; 95% CI, 1.07 to 1.29 in the first and second years, respectively). By 3 years, the difference between survivors and controls was no longer statistically significant (Fig 1A). Among colorectal cancer survivors and controls with chronic opioid use, cancer survivors were more likely than controls to have high-dose use in the first 3 years after the index date (ORs ranged from 1.79 to 2.61 across the first 3 years of follow-up; all P values $< .05$; Fig 2A).

Lung cancer. Lung cancer survivors had the highest unadjusted rates of chronic opioid use compared with the other survivor populations when comparing within years after diagnosis and within each calendar year (Tables 2-4). Lung cancer survivors were more likely to have chronic opioid use compared with controls for the first 5 years after the index date (Fig 1B). The extent to which lung cancer survivors were more likely than controls to have chronic opioid use decreased over time after the index date (OR, 2.55; 95% CI, 2.34 to 2.77 in year 1; to OR, 1.34; 95% CI, 1.08 to 1.66 in year 5; Fig 1B). Among lung cancer

survivors and controls with chronic opioid use, cancer survivors were more likely than controls to have high-dose use of opioids for the first 4 years after the index date (ORs ranged from 3.65 to 5.54 across the first 4 years of follow-up; all P values $< .05$; Fig 2B).

Breast cancer. Across all diagnosis years, the rate of chronic opioid use among breast cancer survivors ranged from 1.9% to 3.7% from the first to sixth year after the index date (Table 4). Breast cancer survivors were less likely to have chronic opioid use compared with controls during each year after the index date (Fig 1C). However, among breast cancer survivors and controls with chronic opioid use, survivors were more likely than controls to have high-dose use in the first 3 years after the index date (ORs for first 3 years after the index date ranged from 1.32 to 1.85; P values $< .05$; Fig 2C).

Sensitivity Analyses

After censoring follow-up 3 and 9 months before cancer-attributed deaths, results for chronic opioid use and for high-dose use were similar in magnitude and significance, although attenuated (Appendix Table A2, online only).

DISCUSSION

Our study identified trends in chronic opioid use among older survivors of three common cancers. We found evidence that both cancer survivors and matched controls were more likely to have chronic opioid use as they aged. Increases in chronic opioid use likely attributable to cancer were apparent among opioid-naïve lung and colorectal cancer survivors. Opioid-naïve breast cancer survivors were less likely to have chronic opioid use compared with matched controls. For all three cancers, survivors had more intense chronic opioid use, characterized by a higher likelihood of high average daily opioid dose (≥ 90 MME) for the initial years after diagnosis.

Differences in opioid use by disease site were also found in a retrospective cohort study by Sutradhar et al¹² of cancer survivors 18 to 64 years of age. Survivors of lung, gastrointestinal, and gynecologic cancers had higher rates of opioid use than controls, whereas breast and colorectal cancer survivors did not. In our study, 5.3% of opioid-naïve lung cancer survivors used opioids for at least 90 days in the year after diagnosis, and chronic use remained higher than in controls, even among longer-term lung cancer survivors. Prevalence of pain in the early stages of lung cancer has been reported to be as high as 56%.³¹ Pain in lung cancer survivors, including prolonged surgical pain and neuropathic pain, may prompt new chronic opioid use. In the context of history of substance abuse or comorbid illness, lung cancer survivors' risk of new chronic opioid use is thus considerable. It is not surprising that in colorectal cancer, with lower prevalence of pain (39% in early stages and 46% in late stages), we found lower rates of chronic opioid use, with shorter duration of increased risk for chronic opioid use.³¹

TABLE 1. Cohort Characteristics of Patients With Cancer and Matched Patients Without Cancer (controls)

Characteristic	Colorectal	Lung	Breast
No. of cases	13,101	11,859	21,829
No. of matched pairs*	38,608	34,945	64,583
Year of diagnosis			
2008	16.8	16.8	14.1
2009	16.2	17.1	15.5
2010	16.0	15.4	15.7
2011	16.5	15.7	16.7
2012	17.1	16.6	17.8
2013	17.5	18.3	20.3
Age at diagnosis (years)†			
65-69	15.7	21.8	23.2
70-74	23.2	27.6	26.3
75-79	21.1	24.1	21.0
80-84	20.5	16.9	16.1
≥ 85	19.6	9.6	13.4
Stage			
I	31.2	50.1	56.2
II	36.2	9.2	33.7
III	32.5	40.7	10.0
Sex†			
Female	59.3	55.7	100.0
Male	40.7	44.3	—
Race†			
White	81.5	83.9	85.4
Black	7.5	8.0	7.3
Other	11.0	8.1	7.3
Charlson comorbidity index (year prior to diagnosis)†			
0	47.0	33.9	55.8
1	25.4	31.0	24.1
≥ 2	27.6	35.1	20.1
Geographic region†			
West	38.6	35.5	41.3
Northeast	21.6	21.9	20.5
Midwest	14.4	11.8	13.5
South	25.5	30.8	24.7

NOTE. Data are presented as % unless otherwise indicated.

*After restricting analysis to matched pairs with ≥ 90 days of follow-up, > 95% of survivors were matched with three controls. The remaining survivors were matched with one or two controls.

†Matching variables.

Fewer breast cancer survivors had chronic opioid use than survivors of lung and colorectal cancers, and rates of chronic opioid use among breast cancer survivors were lower than among matched controls. This result, which

runs counter to the hypothesis that survivors are at higher risk of chronic use than the general population, may have several explanations. Most breast cancer survivors in our sample had early-stage disease, which may be associated with low prevalence of treatment-related pain. Furthermore, early-stage disease is commonly screen-detected, which may reflect a population with greater access to appropriate care and who may have few risk factors for progressing to chronic use.³²⁻³⁴ Nonetheless, high-dose chronic use was more common among breast cancer survivors than matched controls for the first 3 years, suggesting that cancer-related differences in opioid use exist in this population.

Cancer-associated chronic opioid use among colorectal and lung cancer survivors declines after diagnosis. By 3 to 6 years after diagnosis, depending on disease, rates of chronic opioid use did not differ statistically between survivors and matched controls. Similarly, for three cancers in this study, rates of high-dose use among survivors with chronic use exceeded rates among matched controls for 3 to 4 years after diagnosis. The first year after diagnosis may be characterized by cancer treatment, when opioids are commonly prescribed to address treatment-related pain, which may lessen over time. Also, fewer survivors are alive each year after diagnosis, and those who live many years past diagnosis may be healthier and less likely to experience pain.

The low overall rate of chronic opioid use in older cancer survivors contrasts with trends observed in younger cancer survivors. Sutradhar et al¹² studied survivors 18 to 64 years of age and found a 22% higher rate of opioid prescriptions compared with age- and sex-matched noncancer controls, with the increase apparent among survivors diagnosed more than 5 years prior.¹² The discrepancy between these findings and our findings of diminishing use may be due in part to the Canadian study's cancer survivors having more comorbid conditions than controls (8.0% of cancer survivors had a Charlson score ≥ 1, compared with 6.1% among matched controls), the aggregation of cancer sites in the analysis, younger age (with likely commensurate higher opioid use), and disparate opioid use metrics.

The extent to which chronic or high-dose opioid use represents appropriate pain management is unclear. Pain during cancer therapy is often undertreated, although undertreatment may be declining.³⁵ The appropriate treatment of pain after completion of therapy has not been established, and little is known about pain management in long-term survivors. As toxicities persist, worsen, or appear in the years after treatment, or as nonopioid approaches are exhausted, pain management with opioids may be warranted. Recent American Society for Clinical Oncology guidelines regarding pain management recommend opioids in some cases, prescribed in conjunction with other pain management approaches.¹¹ As cancer survivors receive improved curative treatments and live longer, the

TABLE 2. Chronic (90-day) Opioid Use: Colorectal Cancer

Year of Diagnosis	Year					
	1	2	3	4	5	6
Overall						
No. matched pairs	38,608	26,820	17,649	10,969	6,283	2,703
Chronic use: cancer	1,027 (2.7)	1,014 (3.8)	721 (4.1)	468 (4.3)	282 (4.5)	108 (4.0)
Chronic use: noncancer	772 (2.0)	870 (3.2)	703 (4.0)	505 (4.6)	307 (4.9)	115 (4.3)
2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
No. matched pairs	6,480	5,283	4,359	3,596	3,132	2,703
Chronic use: cancer	171 (2.6)	187 (3.5)	199 (4.6)	163 (4.5)	155 (4.9)	108 (4.0)
Chronic use: noncancer	144 (2.2)	169 (3.2)	163 (3.7)	163 (4.5)	145 (4.6)	115 (4.3)
2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	
No. matched pairs	6,255	5,216	4,337	3,687	3,151	
Chronic use: cancer	147 (2.4)	222 (4.3)	179 (4.1)	138 (3.7)	127 (4.0)	
Chronic use: noncancer	136 (2.2)	189 (3.6)	189 (4.4)	176 (4.8)	162 (5.1)	
2010	2010-2011	2011-2012	2012-2013	2013-2014		
No. matched pairs	6,172	5,184	4,328	3,686		
Chronic use: cancer	164 (2.7)	186 (3.6)	171 (4.0)	167 (4.5)		
Chronic use: noncancer	128 (2.1)	179 (3.5)	189 (4.4)	166 (4.5)		
2011	2011-2012	2012-2013	2013-2014			
No. matched pairs	6,365	5,420	4,625			
Chronic use: cancer	168 (2.6)	221 (4.1)	172 (3.7)			
Chronic use: noncancer	140 (2.2)	180 (3.3)	162 (3.5)			
2012	2012-2013	2013-2014				
No. matched pairs	6,594	5,717				
Chronic use: cancer	170 (2.6)	198 (3.5)				
Chronic use: noncancer	120 (1.8)	153 (2.7)				
2013	2013-2014					
No. matched pairs	6,742					
Chronic use: cancer	207 (3.1)					
Chronic use: noncancer	104 (1.5)					

NOTE. Data are presented as No. or No. (%) unless otherwise indicated. The No. of matched pairs equals the No. of controls. The bold type along the diagonals highlights the comparable outcome period for assessing Chronic opioid use. Secular trends can be observed among noncancer controls within each column. Aging trends can be observed among noncancer controls within each row.

risks of long-term opioid use are important to consider when managing pain. Our study highlights the excess chronic use compared with the general population for survivors of certain cancers. However, the increased rates of chronic use (and high-dose chronic use) among these survivors diminishes over time since cancer diagnosis, suggesting less concern for opioid-related harms when prescribing to patients who are opioid naïve during treatment.

The trend of diminishing chronic opioid use over time since cancer diagnosis is reassuring, especially considering the risks older survivors face. With some survivors experiencing cancer-related pain extending beyond treatment and a

general rise in opioid use in the population, the prevalence of chronic opioid use among cancer survivors is perhaps surprisingly low. A recent study found that 10% of patients who were opioid naïve received opioids 90 to 180 days after curative-intent surgery, suggesting an alarming potential for patients with cancer receiving opioids to be at risk for harms associated with long-term opioid therapy.¹³ Our findings suggest that a longer follow-up may reveal less long-term risk for chronic opioid use, at least among older cancer survivors. However, future analyses may reveal more risk for chronic opioid use among subpopulations receiving different treatments. Although we observed little difference in chronic opioid use by calendar year, guidelines on opioid

FIG 1. Chronic opioid use by year postdiagnosis: (A) Colorectal cancer, (B) lung cancer, and (C) breast cancer.

FIG 2. High-dose daily opioid use among cases and controls with chronic opioid use: (A) Colorectal cancer, (B) lung cancer, and (C) breast cancer. The number of patients with high-dose chronic opioid use was too small to report in the fifth year for lung cancer and in the sixth year for colorectal, lung, and breast cancers. NA, not available.

TABLE 3. Chronic (90-day) Opioid Use: Lung Cancer

Year of Diagnosis	Year					
	1	2	3	4	5	6
Overall						
No. matched pairs	34,945	18,785	9,899	5,478	2,737	1,018
Chronic use: cancer	1,850 (5.3)	1,298 (6.9)	685 (6.9)	377 (6.9)	210 (7.7)	75 (7.4)
Chronic use: noncancer	751 (2.1)	633 (3.4)	419 (4.2)	273 (5.0)	160 (5.8)	68 (6.7)
2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
No. matched pairs	5,884	3,577	2,252	1,659	1,297	1,018
Chronic use: cancer	328 (5.6)	265 (7.4)	181 (8.0)	121 (7.3)	108 (8.3)	75 (7.4)
Chronic use: noncancer	116 (2.0)	126 (3.5)	89 (4.0)	85 (5.1)	75 (5.8)	68 (6.7)
2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	
No. matched pairs	5,983	3,811	2,406	1,811	1,440	
Chronic use: cancer	338 (5.6)	280 (7.3)	180 (7.5)	127 (7.0)	102 (7.1)	
Chronic use: noncancer	138 (2.3)	143 (3.8)	129 (5.4)	104 (5.7)	85 (5.9)	
2010	2010-2011	2011-2012	2012-2013	2013-2014		
No. matched pairs	5,386	3,675	2,592	2,008		
Chronic use: cancer	273 (5.1)	236 (6.4)	147 (5.7)	129 (6.4)		
Chronic use: noncancer	127 (2.4)	133 (3.6)	95 (3.7)	84 (4.2)		
2011	2011-2012	2012-2013	2013-2014			
No. matched pairs	5,496	3,712	2,649			
Chronic use: cancer	295 (5.4)	257 (6.9)	177 (6.7)			
Chronic use: noncancer	130 (2.4)	121 (3.3)	106 (4.0)			
2012	2012-2013	2013-2014				
No. matched pairs	5,818	4,010				
Chronic use: cancer	311 (5.3)	260 (6.5)				
Chronic use: noncancer	113 (1.9)	110 (2.7)				
2013	2013-2014					
No. matched pairs	6,378					
Chronic use: cancer	305 (4.8)					
Chronic use: noncancer	127 (2.0)					

NOTE. Data are presented as No. (%) unless otherwise indicated. The No. of matched pairs equals the No. of controls. The bold type along the diagonals highlights the comparable outcome period for assessing chronic opioid use. Secular trends can be observed among noncancer controls within each column. Aging trends can be observed among noncancer controls within each row.

prescribing for noncancer pain were being developed and implemented during this period.^{36,37} Some of these guidelines and policies may have influenced prescribing to cancer survivors, especially in the later years after cancer diagnosis. Centers for Disease Control and Prevention reports indicate that opioid prescribing for noncancer pain peaked in 2010 and then declined slowly.³⁸

Our study has limitations. We cannot determine whether chronic opioid use in our population was indicative of appropriate pain management. We could not exclude patients with progressive or recurrent disease. However, we attempted to exclude patients at the end of life, when opioids can provide necessary palliation, by requiring those

in the analytic sample not be enrolled in hospice, and our sensitivity analyses excluding patients 3 or 9 months before a death from cancer demonstrated only slightly attenuated trends of opioid use. We also did not distinguish between patients who continued to have chronic opioid use over time and those who started chronic opioid use anew; this is a topic of future research. Last, rates of chronic opioid use among controls cannot be extrapolated to the general cancer-free Medicare population because of the matched nature of the analysis.

Our study characterizes chronic use among older survivors. Although more in-depth analyses of treatment-related effects and other cancer groups are warranted, these findings

TABLE 4. Chronic (90-day) Opioid Use: Breast Cancer

Year of Diagnosis	Year					
	1	2	3	4	5	6
Overall						
No. matched pairs	64,583	47,341	33,004	21,453	12,430	5,347
Chronic use: cancer	1,235 (1.9)	1,529 (3.2)	1,242 (3.8)	826 (3.9)	418 (3.4)	196 (3.7)
Chronic use: noncancer	1,885 (2.9)	2,216 (4.7)	1,877 (5.7)	1,384 (6.5)	878 (7.1)	392 (7.3)
2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
No. matched pairs	9,076	8,158	7,248	6,448	5,839	5,347
Chronic use: cancer	129 (1.4)	198 (2.4)	222 (3.1)	239 (3.7)	179 (3.1)	196 (3.7)
Chronic use: noncancer	264 (2.9)	378 (4.6)	446 (6.2)	448 (6.9)	419 (7.2)	392 (7.3)
2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	
No. matched pairs	9,979	9,119	8,191	7,347	6,591	
Chronic use: cancer	164 (1.6)	264 (2.9)	334 (4.1)	266 (3.6)	239 (3.6)	
Chronic use: noncancer	306 (3.1)	455 (5.0)	487 (5.9)	503 (6.8)	459 (7.0)	
2010	2010-2011	2011-2012	2012-2013	2013-2014		
No. matched pairs	10,150	9,334	8,439	7,658		
Chronic use: cancer	229 (2.3)	345 (3.7)	367 (4.3)	321 (4.2)		
Chronic use: noncancer	307 (3.0)	443 (4.7)	473 (5.6)	433 (5.7)		
2011	2011-2012	2012-2013	2013-2014			
No. matched pairs	10,779	9,981	9,126			
Chronic use: cancer	202 (1.9)	311 (3.1)	319 (3.5)			
Chronic use: noncancer	368 (3.4)	525 (5.3)	471 (5.2)			
2012	2012-2013	2013-2014				
No. matched pairs	11,509	10,749				
Chronic use: cancer	262 (2.3)	411 (3.8)				
Chronic use: noncancer	311 (2.7)	415 (3.9)				
2013	2013-2014					
No. matched pairs	13,090					
Chronic use: cancer	249 (1.9)					
Chronic use: noncancer	329 (2.5)					

NOTE. Data are presented as No. (%) unless otherwise indicated. The No. of matched pairs equals the No. of controls. The bold type along diagonals highlights the comparable outcome period for assessing chronic opioid use. Secular trends can be observed among noncancer controls within each column. Aging trends can be observed among noncancer controls within each row.

point to the low long-term risk of chronic opioid use in older cancer survivors. Attention should focus on older survivors

with chronic opioid use, who consistently receive higher doses than their noncancer counterparts.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Trends in Opioid Use Among Older Survivors of Colorectal, Lung, and Breast Cancers**

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APPENDIX

TABLE A1. Generic Names of Opioids

Generic Name
Acetaminophen with codeine
ASA/codeine phosphate*
Buprenorphine (patch/transdermal only)
Butalbital/acetaminophen/caffeine/codeine
Butorphanol tartrate
Codeine/butalbital/acetaminophen/caffeine
Codeine/butalbital/ASA/caffeine
Codeine/carisoprodol/ASA
Codeine phosphate/carisoprodol/ASA*
Codeine phosphate/pyrilamine maleate†
Codeine/promethazine HCL *† ^b
Codeine sulfate*
Codeine sulfate
Dihydrocodeine/ASA/caffeine
Dihydrocodeine bt/acetaminophen/caffeine
Fentanyl
Fentanyl citrate
Guaifenesin/codeine phosphate*†
Guaifenesin/hydrocodone bitartrate*†
Hydrocodone/acetaminophen
Hydrocodone bitartrate
Hydrocodone bitartrate/acetaminophen*
Hydrocodone bitartrate/homatropine*
Hydrocodone bitartrate/homatropine me-br
Hydrocodone/chlorpheniramine polis*†
Hydrocodone/chlorpheniramine p-stirex†
Hydrocodone/ibuprofen
Hydromorphone HCL
Hydromorphone HCL/pf
Ibuprofen/oxycodone HCL
Levorphanol tartrate
Meperidine HCL
Meperidine HCL/pf
Methadone HCL
Morphine sulfate
Morphine sulfate/naltrexone*
Morphine sulfate/pf
Nalbuphine HCL
Opium*†
(continued in next column)

TABLE A1. Generic Names of Opioids (continued)

Generic Name
Opium/belladonna alkaloids†
Opium tincture*†
Oxycodone HCL
Oxycodone HCL/acetaminophen
Oxycodone HCL/ASA
Oxycodone HCL/oxycodone terephthalate/ASA
Oxymorphone HCL
Pentazocine HCL/acetaminophen
Pentazocine HCL/naloxone HCL
Pentazocine lactate
P-ephed HCL/codeine/chlorpheniramine*†
P-ephed HCL/codeine/guaifenesin*†
P-ephed HCL/dihydrocodeine bt/cp*†
P-ephed HCL/hydrocodone*†
P-ephed HCL/hydrocodone bitartrate*
P-ephed HCL/hydrocodone/bpm*†
P-ephed HCL/hydrocodone/cp*†
P-ephed/hydrocodone/chlorpheniramine*†
P-ephed/hydrocodone/dexbrompheniramine
Potassium guaiacolsulfonate/hydrocodone bitartrate*
Tapentadol HCL
Tramadol HCL
Tramadol HCL/acetaminophen

Abbreviations: ASA, acetylsalicylic acid; bpm, brompheniramine maleate; bt, bitartrate; cp, chlorphen-phenyleph; HCL, hydrochloride; me-br, methylbromide; p-ephed, pseudoephedrine; pf, preservative-free; polis, polistirex.

*Drug was identified via physician review of all generic names of drugs to patients in our final study cohort. All others were identified via the list from Center for Medicaid & Medicare Services.

TABLE A2. Sensitivity Analyses by Post-Diagnosis Year Censoring at 3 and 9 Months Before Cancer-Attributed Death

Cancer Type	Year After Index Date	Chronic Use Analysis (months) Odds Ratio (95% CI)		Dose Analysis (months) Odds Ratio (95% CI)	
		3	9	3	9
Colorectal	1	1.31 (1.19 to 1.44)	1.27 (1.15 to 1.40)	2.36 (1.61 to 3.45)	2.14 (1.45 to 3.16)
	2	1.14 (1.04 to 1.25)	1.10 (1.00, 1.21)	1.62 (1.14 to 2.30)	1.50 (1.05 to 2.15)
	3	1.00 (0.89 to 1.11)	0.96 (0.86, 1.07)	2.27 (1.54 to 3.34)	1.91 (1.28 to 2.86)
	4	0.91 (0.80 to 1.04)	0.91 (0.80, 1.03)	1.17 (0.72 to 1.89)	1.18 (0.73 to 1.92)
	5	0.87 (0.73 to 1.03)	0.83 (0.70, 0.98)	0.98 (0.57 to 1.71)	0.92 (0.52 to 1.61)
	6	0.91 (0.69 to 1.19)	0.92 (0.70, 1.20)	Not available	Not available
Lung	1	2.21 (2.02 to 2.42)	1.95 (1.77, 2.15)	3.98 (2.99 to 5.29)	3.48 (2.59 to 4.67)
	2	1.97 (1.78 to 2.18)	1.68 (1.51, 1.87)	4.45 (3.23 to 6.14)	3.34 (2.39 to 4.66)
	3	1.64 (1.45 to 1.87)	1.53 (1.35, 1.75)	3.39 (2.24 to 5.14)	3.23 (2.12 to 4.94)
	4	1.37 (1.17 to 1.62)	1.31 (1.11, 1.55)	4.23 (2.69 to 6.65)	3.47 (2.17 to 5.54)
	5	1.29 (1.04 to 1.60)	1.24 (1.00, 1.55)	Not available	Not available
	6	1.13 (0.80 to 1.59)	1.13 (0.80, 1.59)	Not available	Not available
Breast	1	0.63 (0.59 to 0.68)	0.61 (0.57, 0.66)	1.40 (1.07 to 1.83)	1.28 (0.97 to 1.69)
	2	0.67 (0.63 to 0.72)	0.66 (0.62, 0.70)	1.72 (1.33 to 2.22)	1.65 (1.27 to 2.13)
	3	0.65 (0.60 to 0.69)	0.64 (0.59, 0.69)	1.29 (0.99 to 1.69)	1.33 (1.01 to 1.74)
	4	0.58 (0.53 to 0.64)	0.57 (0.52, 0.62)	0.87 (0.63 to 1.21)	0.81 (0.58 to 1.14)
	5	0.45 (0.40 to 0.51)	0.45 (0.40, 0.51)	0.90 (0.58 to 1.40)	0.90 (0.58 to 1.40)
	6	0.47 (0.40 to 0.56)	0.47 (0.39, 0.56)	Not available	Not available

NOTE. Bold type indicates $P < 0.05$.