Title: The Association of Prescription Opioid use with Incident Cancer: A SEER-Medicare population-based case-control study

Short Running Title: The effect of prescription opioids on incident cancer in the Medicare Population

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- Developed conceptual framework
- Conceived and Designed the Analysis
- Responsible for data acquisition from SEER-Medicare
- Contributed to data analysis
- Wrote the Paper (primary author)
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Precis: We examined the association between prescription opioids and incident cancer in the SEER-Medicare population. Our results suggest a complex relationship exists and that cancer site is an important determinant.

Lay Summary: The role of opioids in cancer development, recurrence, and metastasis is controversial. Using Medicare-SEER database, we examined the association between prescription opioids and ten cancer sites. In both the crude and adjusted models, patients exposed to prescription opioids had a lower odds ratio associated with incident breast and colon cancer, but higher odds ratio for incident lung, leukemia, lymphomas, renal and liver cancer. We did not find any association between prescription opioids and incident brain, esophageal, or bladder cancer. This suggests that opioids may affect cancer development and the type of cancer is a consideration.

Keywords: opioids , cancer , SEER-Medicare , Prescription Opioids , Medicare

ABSTRACT

Background: Cancer is the second leading cause of death globally, and researchers seek to identify modifiable risk factors Over the past several decades, there has been ongoing debate whether opioids are associated with cancer development, metastasis, or recurrence. Basic science, clinical and observational studies have produced conflicting results. We examined the association between prescription opioids and incident cancers using the SEER-Medicare database. We found a complex relationship exists between prescription opioids and incident cancer and cancer site may be an important determinant.

Methods: Using linked SEER cancer registry and Medicare claims from 2008 to 2013, we conducted a case-control study examining the relationship between cancer onset and prior opioid exposure. We used logistic regression to account for differences between cases and controls for ten cancer types.

Results: Of the study population (n = 348,319), 34.0% were prescribed opioids, 79.5% were white, 36.9% were dually eligible, 13.0% lived in a rural area, 52.7% had ≥ 1 comorbidity and 16.0% had a smoking-related diagnosis. Patients exposed to opioids had a lower odds ratio associated with breast cancer (adjusted OR = 0.96; 95% CI: 0.92 to 0.99) and colon cancer (adjusted OR = 0.90; 95% CI: 0.86 to 0.93) compared to controls. Higher odds ratio of kidney, leukemia, liver, lung and lymphoma cancers, ranging from lung (OR = 1.04; 95% CI: 1.01 to 1.07) to liver (OR = 1.19; 95% CI: 1.08 to 1.31) were present in the exposed population.

Conclusions: Our results suggest an association exists between prescription opioids and incident cancer and that cancer site may play an important role. These findings can direct future research on specific patient populations that may benefit or be harmed by prescription opioid exposure.

INTRODUCTION

One in six deaths is attributed to cancer, making it the second most common cause of death worldwide (https://www.who.int/news-room/fact-sheets/detail/cancer, accessed June 2019)(1) . Over 18 million new cancer cases and approximately 9.6 deaths and were reported in 2018 (http://gco.iarc.fr/today/data/factsheets/cancers/39-All-cancers-fact-sheet.pdf, accessed June 2019) (2). Understanding modifiable processes that affect cancer development is fundamental for prevention. Several known, lifestyle-related modifiable risk factors for cancer development account for about 40% of incident cancer cases and include smoking, alcohol, obesity, ultraviolet radiation due to sun exposure, and a sedentary lifestyle (3).

Opioid use is a potentially modifiable risk factor that may impact cancer development .Over the past several decades, animal, in vitro, clinical and observational studies, have demonstrated both protective and harmful effects of opioid administration on cancer development, metastasis, and recurrence. There are limited data from prospective clinical trials to address this issue due in part to the complexity, cost, and ethical considerations. To understand the potential role opioids play in the development of cancer, we analyzed

Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data to examine whether a clinically significant modifiable risk factor, the use of prescription opioids, are associated with incident cancer.

METHODS

Data Sources

Data from the National Cancer Institute's SEER program (https://seer.cancer.gov/data/; accessed February 2019) and data from the 5% random sample Medicare Surveillance Summarized Denominator file were obtained for the years 2007-2013. The SEER program is a population-based tumor registry that identifies incident cancers and patient survival in the United States (4). The SEER cancer registry collects clinical, demographic, and cause of death information. The SEER data are linked to Medicare files based on name, age, date of birth, social security number, and sex (http://healthservices.cancer.gov/seermedicare/ accessed April 2019). Approximately 94% of patients in SEER registries are matched to Medicare enrollment records. The percentage of Medicare Part D beneficiaries has increased since inception on January 1, 2006, including 56% of Medicare beneficiaries enrolled in Medicare Part D in 2007 to 68% in 2013 (https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/CMSProgramStatistics/2013/Enrollment.html#Medicare%20Part%20D%20Enrollment; accessed March 2019).

Study population

The study included patients diagnosed with (cases) or without (controls) one of ten incident cancers between January 2008 and December 2013. Incident cancer cases included in the SEER database were collected from 17 cancer registries (Atlanta, Connecticut, Detroit,

Greater California, Greater Georgia, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Jersey, New Mexico, Rural Georgia, San Francisco, San Jose, Seattle, and Utah). Cancer sites were selected based on those with the highest incidence in the United States, peer-reviewed publications suggesting cancer development from opioid use, and theoretical risk suggested in the basic science literature. The ten selected cancer sites included bladder, brain, breast, colorectal, esophageal, kidney, leukemia, liver, lung, and lymphoma.

Cases and Controls

Cases were defined as patients whose incident cancer was diagnosed between 2008 - 2013 and identified from one of the ten cancer site-specific SEER-Medicare Patient Entitlement and Diagnosis Summary Files. A case was included in the study if continuously enrolled in Parts A, B, and D for one year prior to their diagnosis year (2007-2012), were at least 65 years or older, with non-missing sex data and no previous cancer diagnosis. Since the first possible year of enrollment would be 2007, cases diagnosed 2008-2013 were 66 years or older (Figure 1).

Controls were eligible for the study if a patient was at least 65 years old, continuously enrolled in Parts A, B, and D for at least one year and with non-missing sex data between 2007 and 2012. The controls were selected from the pool of non-cancer cases identified from the random 5% sample of Medicare beneficiaries in the Medicare Surveillance Summarized Denominator file (Figure 1).

Patient Characteristics

Characteristics included age at calendar year and categorized into 5-year age groups of 66-70, 71-75, 76-80, 81-85 and 86+, sex (male/female), calendar year (2008-2013), race (categorized as white, black and other race; other race included Asian, Hispanic, North American Native, other and unknown), SEER registries (listed above), geographic region (urban/rural), dual eligibility (no/yes), comorbidity index (grouped as 0-none, 1, 2+) based on the NCI Comorbidity Index, and a smoking-related variable (smoking no/yes). Patients jointly enrolled in Medicare and Medicaid and eligible to receive benefits from both programs were defined as dual-eligible. Indicators for smoking were based on the International Statistical Classification of Disease and Health-Related Problems 9th edition (ICD - 9) codes of tobacco use disorder including those related to chronic obstructive pulmonary disease and allied conditions (490.x –

492.x; 494.x-496.x), except asthma, personal history of tobacco abuse (V15.82) and non-dependent tobacco use disorder (305.1)(5). The comorbidity index was derived from claims during the exposure year using the NCI Comorbidity Index Klabunde adaptation to the Charlson comorbidity score (6).

Length of Exposure Time

The time period preceding cancer onset during which the exposure (prescription opioid use) could alter the risk was defined as the exposure window. By design, opioid use was only measured during the exposure year. The length of time for the exposure window of 12 months was determined by the minimum period of time during which the presence of the exposure (prescription opioid use) could alter the risk of a cancer case whose diagnosis date was January 1, 2008. Exposure year was defined as 12 months of continuous enrollment in Medicare Parts A, B and D for the years 2007-2012. For cases, the exposure year was the year preceding the cancer diagnosis year. Calendar year was defined as the year following the exposure year.

Exposure

Opioid use was defined as the presence or absence of any prescription opioids in the Medicare Part D prescription drug event files. The exposure year was used to search for any prescription opioid use from one of the 13,661 prescription opioids listed as national drug codes in the Centers for Disease Control resource files (https://www.cdc.gov/drugoverdose/data-files/cdc_mme_table_sept2017.sas7bdat; accessed October, 2018).

Statistical Analysis

Cancer cases were frequency matched to the controls by age group, sex, and calendar year. By matching on calendar year, the controls reflected the underlying population distribution of the cases. Frequency distributions (N, %) for the cancer cases and controls by prescription opioid use and patient characteristics are reported. Additionally, prescription opioid distributions by patient characteristics were determined. Stratification was used to reveal the possible effect modification between exposure (opioid use), outcome (cancer) and a smoking related diagnosis (smoking). Smoking was a confounder and we adjusted by including this factor in the multivariate models. To determine if there is an association between prescription opioids on the development of cancer, multivariable logistic regression models adjusting for patient

characteristics was conducted. Model results are reported as odds ratios (OR) and 95% confidence intervals (CI). Cancer site specific models examined the impact of prescription opioid use on each of the ten cancers. Analyses were conducted in SAS (SAS 9.4 System Options: Reference, 2nd ed; 2011. SAS Institute Inc., Cary, North Carolina).

RESULTS

Of the 348,319 patients who met the eligibility criteria, 143,921 (41.3%) were cancer patients and 204,398 (58.7%) were controls. The majority (79.5%) of the overall study population race was white, 13.0% lived in a rural area, 36.9% were dually eligible for Medicare and Medicaid, 52.7% had at least one comorbidity, and 16.0% had smoking-related diagnoses. (Table 1). Compared to controls, cases were more likely to be white (81.8% vs. 77.8%), living in a rural area (13.7% vs. 12.4%), have more than one comorbidity (30.3% vs. 26.6%) and have a smoking related diagnosis (20.7% vs. 12.6%).

Overall, 34.0% of the study's Medicare population had a claim for prescription opioids, 35.2% for cases, and 33.2% among the controls. An increase in prescription opioid use was found among females, whose race was black, those with a rural residential status, were dually eligible, with more comorbid conditions and had a smoking related diagnosis compared to those with no prescription opioid use (Table 2). Patients with a smoking related diagnosis were found more likely to receive prescription opioids (53% v 31%) and more likely to develop cancer (50% vs. 31%; data not shown).

The use of prescription opioids was associated with a significant increase in incident cancers for patients matched on age, sex, and calendar year (OR 1.10; confidence interval CI: 1.09 to 1.12). The results of the fully adjusted analyses found exposure to prescription opioids did not increase the odds of cancer incidence (OR = 1.01, 95% CI: 0.99 to 1.03). However, analysis of cancer site in relation to opioid use varied from reduced odds to no impact to increased odds depending on cancer site. Distribution of the ten incident cancer sites were as follows: bladder (n=11,623; 8%), brain (n=2,678; 2%), breast (n=34,123; 24%); colon (n=24,540; 17%); esophagus (n=2,311; 2%), kidney (n=6,718; 5%); leukemia (n=6,725; 5%), liver (n=4,457; 3%), lung (n=40,311; 28%) and lymphoma (n=10,435; 7%). Patients who received prescription opioids had lower odds ratio associated with breast cancer (OR = 0.96; 95% CI: 0.92 to 0.99) and colon cancer (OR = 0.90; 95% CI: 0.86 to 0.93) (Figure 2). Patients

exposed to prescription opioids had higher odds ratio associated with kidney, leukemia, liver, lung and lymphoma cancers, ranging from OR = 1.04, 95% CI: 1.01 to 1.07 for lung cancer to an OR = 1.19, 95% CI: 1.08 to 1.21 for liver cancer (Figure 2). Prescription opioid exposure was not associated with bladder, brain, or esophageal cancers.

Adjusted for patient characteristics, a subgroup analysis of the subpopulation of breast and colon cancers cases and matched controls found lower odds for cancer among those prescribed prescription opioids (OR = 0.93; 95% CI: 0.91 to 0.95; Figure 3). Prescription opioid use was associated with a higher incidence of kidney cancer, liver cancer, lung cancer, leukemia, and lymphoma (OR = 1.08; 95% CI: 1.06 to 1.10; Figure 3). The adjustment by a smoking related diagnosis did not significantly impact colon and breast cancer development in patients who received prescription opioids (OR = 1.03; 95% CI: 0.99 to 1.07) but was strongly positively associated with patients who were diagnosed with cancers associated with use of prescription opioids (OR = 2.44; 95% CI: 2.37 to 2.50; Figure 3).

DISCUSSION

Our results suggest an association between prescription opioids and incident cancer that varies by cancer site. We examined ten preselected cancer sites based on evidence published in the medical literature and found a complicated relationship exists between prescription opioid use and incident cancer. In both the crude and adjusted models, patients exposed to prescription opioids had a lower odds ratio associated with breast and colon cancer, but higher odds ratio for incident lung, leukemia, lymphomas, renal and liver cancer. We did not find any association between prescription opioids and esophageal, brain, or bladder cancer in the adjusted models; however, an increased odds ratio was noted in patients diagnosed with bladder cancer in the minimally adjusted model. Among patients with a higher likelihood of incident cancer (lung, leukemia, lymphoma, renal, and liver cancer), an increased odds ratio was noted in patients with a smoking-related diagnosis compared to patients with incident breast or colon cancer.

The controversy surrounding the impact opioids exert on cancer incidence has spanned several decades. Multiple biological mechanisms have been proposed

based on laboratory and clinical research that support and contradict the hypothesis that opioids impact cancer development, metastasis, and recurrence.

One theory suggests opioids exert a direct positive or negative effect on cancer development, metastasis, and recurrence by binding to mu-opioid receptors (MOR) on specific cancer cells. MORs are present in lung, breast, neural tumors, leukemia, gastrointestinal, and bladder cancers (7-15). This theory is supported by research examining the effect of opioid antagonists on cancer. Janku et al. reported an increased median overall survival in patients with advanced cancer who received the opioid antagonist methylnaltrexone to treat opioid-induced constipation (16). Bimonte et al. demonstrated that morphine increases tumor size in mice, and these effects were counteracted by the administration of naloxone (17, 18). Although these investigators reported a negative effect of opioids on cancer, other researchers have suggested opioids may exert a protective effect. Friesen et al. reported that administration of methadone induced cell death in leukemia cells, including apoptosis-resistant and multidrug-resistant leukemia cells (19). In addition, Maneckjee et al. reported that methadone inhibited the growth of lung cancer cells, and this effect was reversed by the administration of naltrexone (20). Our study suggests these contradictory findings may result from varying effects that opioids have on specific cancer sites.

These differences in cancer sites are not entirely apparent; however, other researchers have published similar results, although in different populations. Randall *et al*. reported that in opioid-dependent individuals enrolled in a substitution therapy program in Australia, mortality from liver, lung, and anorectal cancer was higher; however, death from breast cancer was significantly lower than in the general population (21). A population-based study conducted in Denmark examining breast cancer recurrence, Cronin-Fenton et al. found that opioid use was not associated with breast cancer recurrence and that patients who received high dose opioids had lower recurrence rates (22). Several researchers have suggested that the increased number of opioid receptors and opioid requirements are associated with recurrence or decreased overall survival in patients with cancer (23-27). Furthermore, several investigators suggested targeting mu receptors on cancer cells as a possible adjunct for cancer treatment (7, 28).

In addition to the direct effects of opioids on cancer cells, the indirect effects of opioids on cancer development, recurrence, and metastasis have been postulated. Opioids exert immunosuppressive effects, particularly on natural killer cells (NK), which are considered the first line of defense in cancer surveillance (29-33). Investigators have suggested that opioids negatively impact the immune system through several mechanisms, including impaired function of lymphocytes, neutrophils, and dendritic cells (34-41). Another biologically plausible theory suggested is that opioids promote tumor angiogenesis and foster cancer occurrence by modulating the immune system through the sympathetic nervous system and the hypothalamus-pituitary-adrenal axis (18, 42-46).

There are several publications reporting an association between opioids, opium, and esophageal cancer (47, 48). Our study did not demonstrate a significant impact of prescription opioids in patients diagnosed with esophageal cancer in the fully adjusted models. Interestingly, Du et al. reported high dose intraoperative opioids were associated with more prolonged survival in patients with squamous cell carcinoma of the esophagus but demonstrated no difference in patients with esophageal adenocarcinoma. They suggest that opioids may exert different outcomes depending on the type of histological cancer (49). Our study did not differentiate the cancers based on histology. We had a relatively low number of patients diagnosed with esophageal cancer (n = 2,311), and the number of patients may be insufficient to demonstrate any significant finding.

Smoking is a known risk factor for cancer development and is considered a possible confounder in observational studies that should be addressed whenever possible. Stratification is used as an analytic tool used to reveal possible effect modification between exposure (opioid use), outcome (cancer), and a third characteristic (smoking), which may have a different relationship with both the exposure and outcome. We assessed both possible relationships. The smoking-related diagnosis was a confounder; thus, we adjusted by including this factor in the multivariate models. Patients who received one or more opioid prescriptions and had a smoking-related diagnosis demonstrated a significantly increased odds ratio of kidney, leukemia, lymphomas, liver, and lung cancers, which contrasts with patients with incident breast or colon cancer. Although these results are biologically plausible, they should be interpreted with caution since only patients with a smoking-related diagnosis are designated as smokers in our model.

There are several other limitations to our study. The use of Medicare Part D prescription opioid data does not include prescription opioid use from other sources, such as private insurance or the Veteran's Administration. The database does not collect information on the use of non-prescription opioids or monitor opioid consumption. As is typical of observational studies, residual confounding is possible. Our study population is limited to Medicare patients greater than 65 years of age, and these results may not be generalizable to younger populations. It is possible the patient received an opioid prescription for a cancer that has not been diagnosed. There may be a temporal limitation of our research. For this study, we could have obtained different results if we selected a different time of exposure. Finally, this study is subject to limitations of the SEER-Medicare database including the incomplete coding of health conditions in the administrative data. Our findings suggest the need for large, population-based longitudinal studies over many years that can reliably and validly ascertain both opioid use and cancer incidence, along with important covariates, such as smoking.

The clinical impact of opioids on cancer is a complex issue that is not well understood. It has been argued that studies focusing on the association or causal relation between opioids and cancer development have been conducted on animals, in vitro models, or in young, healthy volunteers and may not be clinically applicable to the general or at-risk populations. Our goal was to determine if a clinical association could be determined between prescription opioid use and incident cancer development in the population at risk for cancer development.

There are multiple strengths to our study. The Medicare-SEER database is a large, validated, representative sample of the U.S. population. Approximately 98% of patients over the age of 64 years are enrolled in Medicare, and in 2019, 44.1% of Medicare patients were enrolled in Part D (50). The SEER registries must adhere to strict reporting standards and nearly capture all incident cancers (4). The longitudinal aspect of the database enabled us to verify that patients were not diagnosed with cancer prior to this study and were exposed to prescription opioids prior to a cancer diagnosis. Also, advanced age is a known risk factor for cancer. All patients were matched on age, sex, and calendar year to negate trends in prescribing patterns and control for confounders. The adjusted models controlled for socioeconomic status (SES), diagnoses associated with smoking, and comorbidities index. To our knowledge, we are the first to examine the relationship between prescription opioids and incident cancer.

CONCLUSION

Our study suggests prescription opioids may impact incident cancer rates, and the specific cancer site is likely an important determinant. In both the crude and adjusted models, patients who received one or more opioid prescriptions had a lower odds ratio associated with breast and colon cancer, but higher odds ratio for incident lung, leukemia, lymphomas, renal and liver cancer. Given the fact that cancer is the second leading cause of death worldwide and opioid use by the general public is common, we believe further research in this area is warranted.

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Figure Legends

Figure 1. Case-control eligibility criteria.

Figure 2. Odds ratios (OR) and 95% confidence intervals (95% CI) for the association between cancer status (cases/controls; overall and by cancer site) and prescription opioid use for models minimally and fully adjusted for patient characteristics.

* Minimally adjusted for age, sex, and calendar year. ** Fully adjusted for age, sex and calendar year, race, SEER registry, urban/rural status, dual eligibility, comorbidity index, and smoking status. Abbreviations: SEER - Surveillance, Epidemiology, and End Results.

Figure 3. Odds ratios (OR) and 95% confidence intervals (95% CI) for the association between cancer status (cases/controls) and prescription opioid use and patient characteristics by subpopulations of SEER Medicare population of breast and colon (n = 117,220) and kidney, leukemia, liver, lung, and lymphoma (n = 197,550) cancers.

Abbreviations: SEER - Surveillance, Epidemiology, and End Results

Table 1 Overall and cancer status (cases/controls) distributions by prescription opioid use and patient characteristics among a SEER Medicare population (N = 348,319) diagnosed with and without an incident cancer[1] (2008-2013)

	Total N = 348,319 (100.0%)	**Cases N = 143,921 (41.3%)**	**Controls N = 204,398 (58.7%)**
	n (%)	**n (%)**	**n (%)**
Prescription Opioid Use			
No	229,860 (66.0)	93,274 (64.8)	136,586 (66.8)
Yes	118,459 (34.0)	50,647 (35.2)	67,812 (33.2)
Patient Characteristics ǂ			
Age (years)			
66-70	109,709 (31.5)	35,649 (24.8)	74,060 (36.2)
71-75	76,552 (22.0)	34,776 (24.2)	41,776 (20.4)
76-80	62,924 (18.0)	29,692 (20.6)	33,232 (16.3)
81-85	50,688 (14.6)	23,932 (16.6)	26,756 (13.1)
86+	48,446 (13.9)	19,872 (13.8)	28,574 (14.0)
Gender			
Female	222,716 (63.9)	91,730 (63.7)	130,986 (64.1)
Male	125,603 (36.1)	52,191 (36.3)	73,412 (35.9)
Calendar Year			
2008	56,974 (16.4)	23,233 (16.1)	33,741 (16.5)
2009	57,745 (16.6)	23,355 (16.2)	34,390 (16.8)
2010	57,300 (16.5)	23,233 (16.1)	34,067 (16.7)
2011	57,457 (16.5)	23,390 (16.3)	34,007 (16.7)
2012	58,560 (16.8)	24,494 (17.0)	34,066 (16.7)
2013	60,283 (17.3)	26,216 (18.2)	34,067 (16.7)
Race			
White	276,813 (79.5)	117,793 (81.8)	159,020 (77.8)

Black	29,088 (8.4)	11,804 (8.2)	17,284 (8.5)
Other§	42,418 (12.2)	14,324 (10.0)	28,094 (13.7)
SEER Registry			
Connecticut	21,355 (6.1)	8,352 (5.8)	13,003 (6.4)
Detroit	15,865 (4.6)	6,949 (4.8)	8,916 (4.4)
Iowa	23,225 (6.7)	10,717 (7.5)	12,508 (6.1)
Seattle	16,574 (4.8)	6,827 (4.7)	9,747 (4.8)
Los Angeles	28,852 (8.3)	11,148 (7.8)	17,704 (8.7)
Greater California	62,331 (17.9)	24,760 (17.2)	37,571 (18.4)
Kentucky	28,117 (8.1)	13,046 (9.1)	15,071 (7.4)
New Jersey	49,784 (14.3)	20,695 (14.4)	29,089 (14.2)
Greater Georgia	30,343 (8.7)	12,995 (9.0)	17,348 (8.5)
Other¶	71,873 (20.6)	28,432 (19.8)	43,441 (21.3)
Urban/Rural Status			
Urban	302,903 (87.0)	124,179 (86.3)	178,724 (87.6)
Rural	45,059 (13.0)	19,716 (13.7)	25,343 (12.4)
Dual Eligibility			
No	219,838 (63.1)	91,859 (63.8)	127,979 (62.6)
Yes	128,481 (36.9)	52,062 (36.2)	76,419 (37.4)
Comorbidity Index			
0	164,807 (47.3)	62,940 (43.7)	101,867 (49.8)
1	85,501 (24.6)	37,359 (26.0)	48,142 (23.6)
2+	98,011 (28.1)	43,622 (30.3)	54,389 (26.6)
Smoking			
No	292,620 (84.0)	114,053 (79.3)	178,567 (87.4)
Yes	55,699 (16.0)	29,868 (20.7)	25,831 (12.6)

ǂ Cancers included bladder, brain, breast, colon, esophagus, kidney, leukemia, liver, lung, and lymphoma.

ǂ Missing (n): Urban/Rural Status (357).

§ Other race included unknown race (n = 987).

¶Other registries include San Francisco, Hawaii, New Mexico, Utah, Atlanta, San Jose, Rural Georgia, and Louisiana.

Abbreviations: SEER - Surveillance, Epidemiology, and End Results.

Table 2. Prescription opioid use by patient characteristics among a SEER-Medicare population (N = 348,319)

Patient Characteristics ǂ	No Prescription Opioid Use N = 229,860 (66.0%)	Prescription Opioid Use N = 118,459 (34.0%)
	n (%)	n (%)
Age (years)		
66-70	72,636 (31.6)	37,073 (31.3)
71-75	50,280 (21.9)	26,272 (22.2)
76-80	41,410 (18.0)	21,514 (18.2)
81-85	33,379 (14.5)	17,309 (14.6)
86+	32,155 (13.8)	16,291 (13.8)
Gender		
Female	142,059 (61.8)	80,657 (68.1)
Male	87,801 (38.2)	37,802 (31.9)
Calendar Year		
2008	38,144 (16.6)	18,830 (15.9)
2009	37,661 (16.4)	20,084 (17.0)
2010	37,247 (16.2)	20,053 (16.9)
2011	37,774 (16.4)	19,683 (16.6)
2012	38,664 (16.8)	19,896 (16.8)
2013	40,370 (17.6)	19,913 (16.8)
Race		
White	181,472 (79.0)	95,341 (80.5)
Black	17,403 (7.6)	11,685 (9.9)
Other ǂ	30,985 (13.5)	11,433 (9.7)
SEER Registry		
Connecticut	15,243 (6.7)	5,932 (5.0)
Detroit	10,016 (4.4)	5,849 (4.9)
Iowa	16,061 (7.0)	7,164 (6.1)

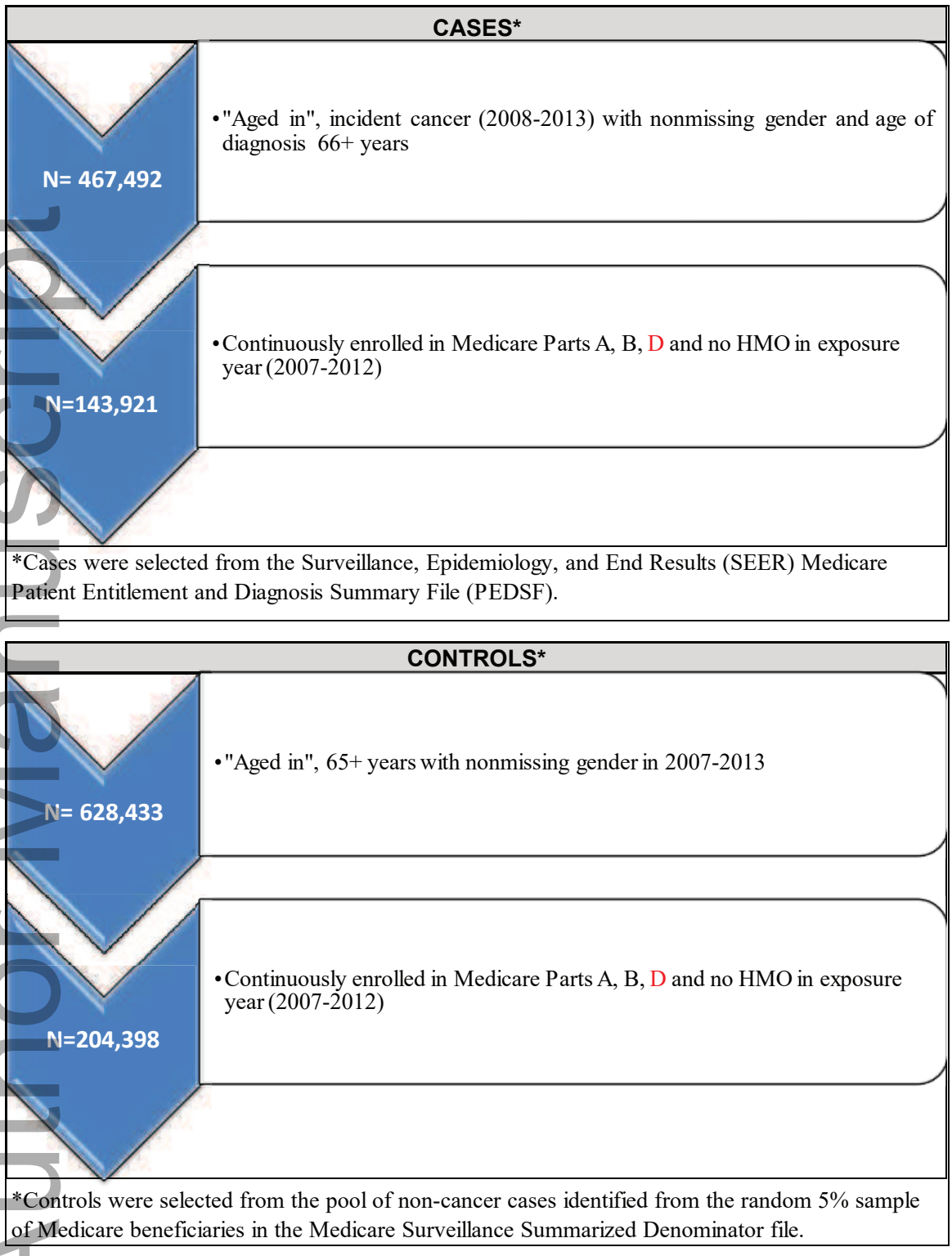
Seattle	10,823 (4.7)	5,751 (4.9)
Los Angeles	19,950 (8.7)	8,902 (7.5)
Greater California	40,315 (17.5)	22,016 (18.6)
Kentucky	16,659 (7.3)	11,458 (9.7)
New Jersey	36,450 (15.9)	13,334 (11.3)
Greater Georgia	17,048 (7.4)	13,295 (11.2)
Other §	47,115 (20.5)	24,758 (20.9)
Urban/Rural Status		
Urban	202,298 (88.1)	100,605 (85.0)
Rural	27,276 (11.9)	17,783 (15.0)
Dual Eligibility		
No	153,138 (66.6)	66,700 (56.3)
Yes	76,722 (33.4)	51,759 (43.7)
Comorbidity Index		
0	123,220 (53.6)	41,587 (35.1)
1	54,421 (23.7)	31,080 (26.2)
2+	52,219 (22.7)	45,792 (23.8)
Smoking		
No	202,291 (88.0)	90,329 (76.3)
Yes	27,569 (12.0)	28,130 (23.8)

ǂ Missing (n): Urban/Rural Status (357).

ǂ Other race included unknown race (n = 987).

§ Other registries include San Francisco, Hawaii, New Mexico, Utah, Atlanta, San Jose, Rural Georgia, and Louisiana.

Abbreviations: SEER - Surveillance, Epidemiology, and End Results.



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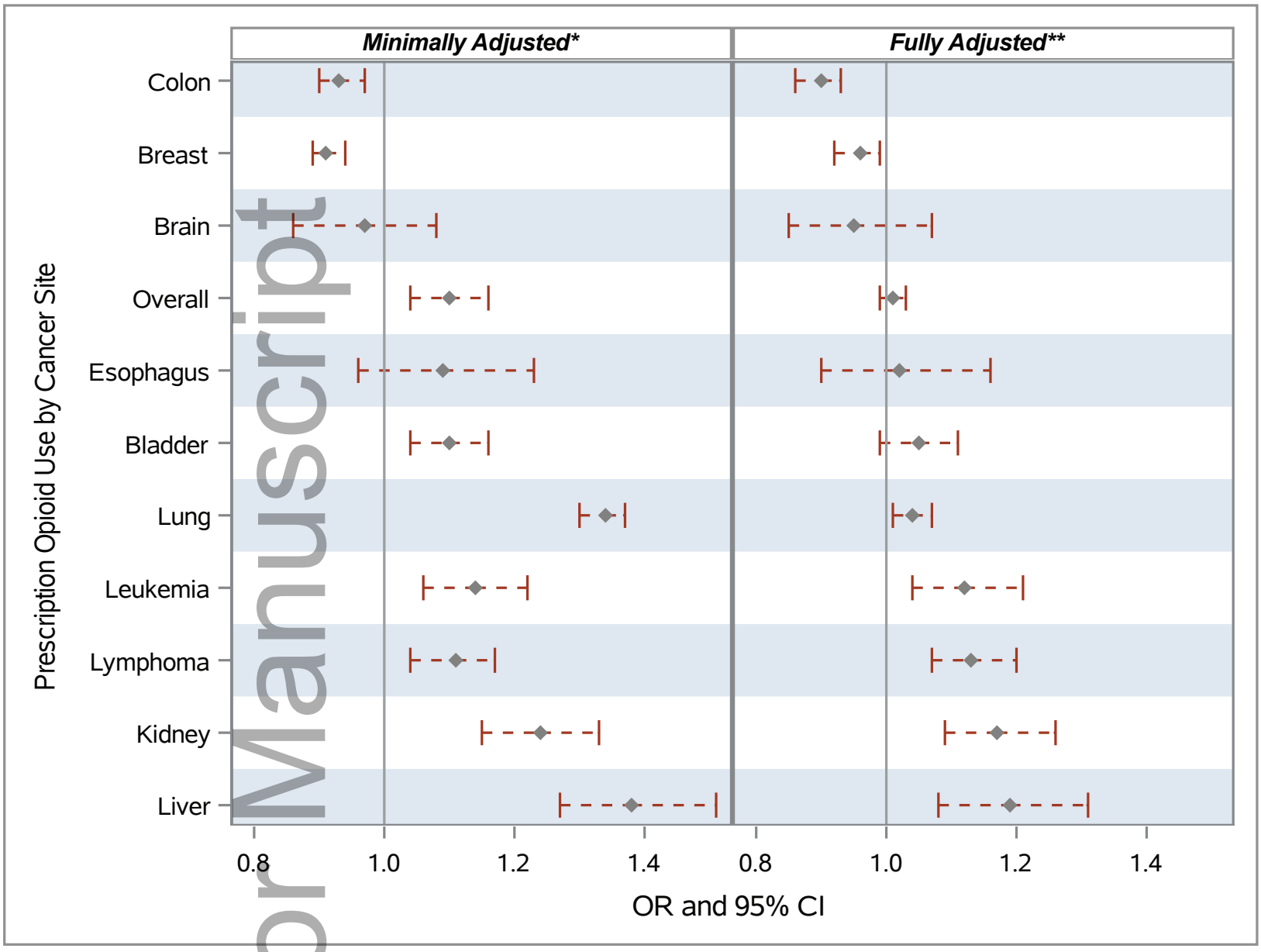

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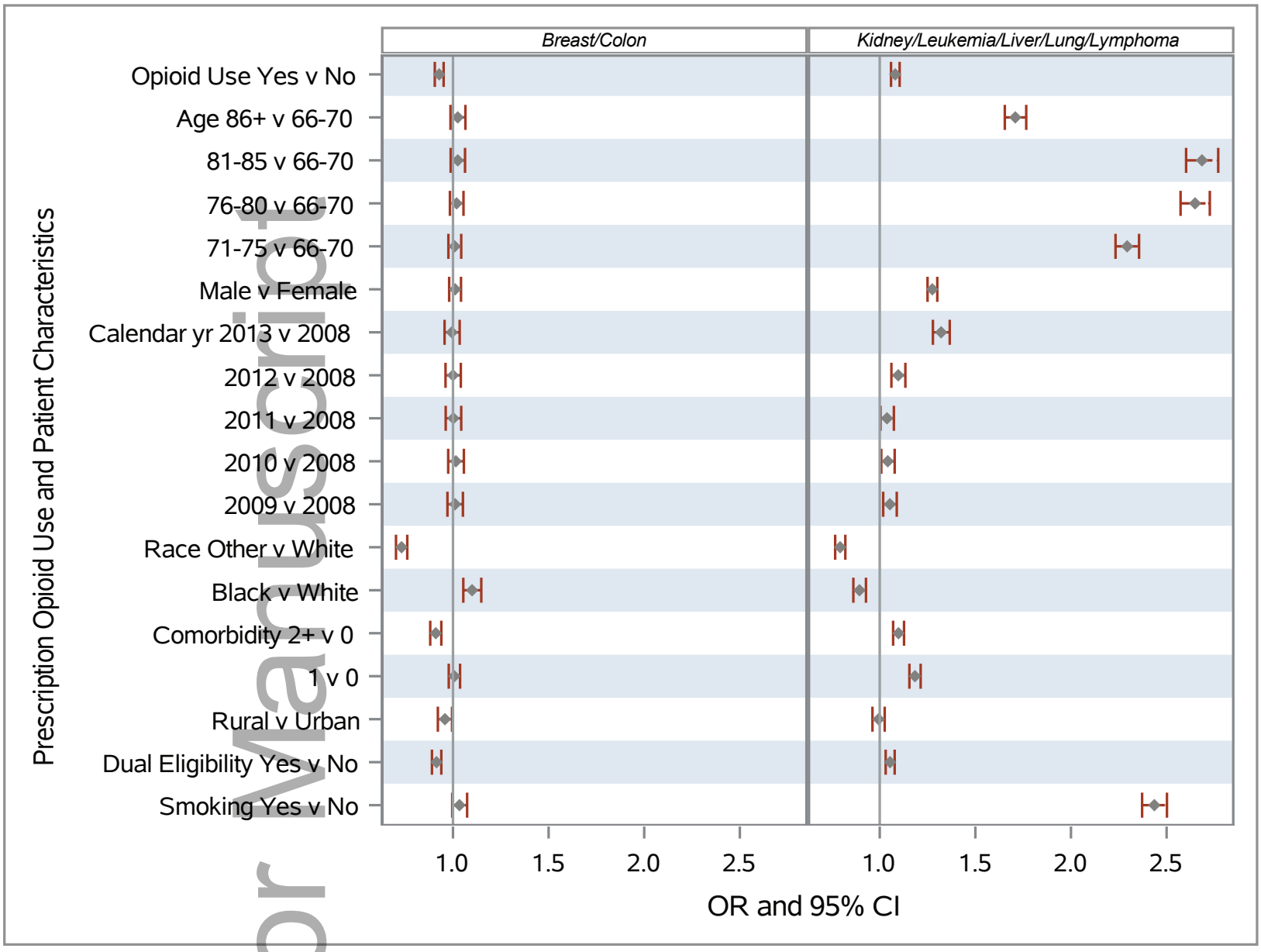

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