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# Pain management practices for outpatients with breast cancer



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ABSTRACT

Objectives: Pain is a significant problem in patients with breast cancer. Limited data exist regarding the nature and extent of pain management in women with breast cancer visiting outpatient settings. This study examined the pain management practices and the factors associated with prescribing pain medications among breast cancer patients. Methods: This cross-sectional study used the National Ambulatory Medical Care Survey (NAMCS) 2011-2016, nationally representative outpatient survey data. Women (age  $\geq$ 18 years) with breast cancer as the primary diagnosis were included. Weighted descriptive analyses examined national-level pain management practices, while multivariable logistic regression evaluated the factors associated with the prescribing of pain medications and opioids. Results: There were 23.95 million (95% confidence interval [CI], 19.29-28.60) outpatient visits for breast cancer during the study period. Pain medications were prescribed in 27.12% of these visits, with non-opioids prescribed in 17.13% and opioids in 15.16% of visits. Logistic regression analyses revealed that patients on Medicaid/other statebased insurance (odds ratio [OR] = 2.38, 95% CI:1.15-4.93), those visiting general/family practice physicians (OR = 3.18, 95% CI:1.22-8.29) and patients receiving adjuvant pain medications (OR = 4.74, 95% CI: 3.10-7.24) were associated with a greater odds of receiving pain medications; while patients who were white (OR = 0.50, 95% CI:0.3–0.85), those residing in the northeast region (OR = 0.31, 95% CI: 0.10–0.99), and non-primary care provider visits (OR = 0.37, 95% CI:0.15–0.94) were associated with lower odds of receiving pain medications. Regional variations were observed among those receiving pain medications: women in the Northeast (OR = 0.06, 95%CI:0.01–0.29), Midwest (OR = 0.15, 95% CI:0.04–0.62), and South (OR = 0.24, 95% CI:0.06–0.92) regions were less likely to receive opioids. However, patients visiting general and family practice specialties (OR = 6.76, 95% CI:1.71-26.70) were more likely to prescribe opioids than non-opioids. Conclusions: The national survey data revealed one in four women visits and one in seven office visits for breast cancer

received pain medication prescriptions and opioid medications, respectively. Both patient and provider characteristics contribute to variations in pain management in breast cancer patients. Further research is needed to evaluate the long-term consequences of these variations in breast cancer.

### 1. Introduction

Breast cancer is the most frequently reported female malignancy in the United States, with an estimated 281,550 new diagnoses in a year.<sup>1</sup> It is prevalent majorly among middle-aged to older women.<sup>2</sup> During the disease trajectory, 25–89% of breast cancer patients experience at least some level of pain, from mild to severe, short episodes to longer-lasting pain.<sup>3,4</sup> This could be due to cancer itself and/or due to treatments such as surgery, chemotherapy, radiation therapy, hormonal therapy, and other anti-cancer medications.<sup>3,5–8</sup> Pain or discomfort caused by treatments for breast cancer is observed regardless of the stage of the disease.<sup>3</sup> Thus, patients fear most breast cancer's pain and incapacitating symptoms.<sup>5,8,9</sup>

Despite growing knowledge about the pathophysiological mechanisms of pain and the increased availability of pain management therapies, about 40% of cancer patients in the United States have undertreated pain.<sup>10</sup> A recent systematic review conducted by Greco et al. found that although there was a decrease in untreated pain, about one-third of cancer patients do not receive pain medication proportional to their pain intensity.<sup>11</sup> One of the goals of the American Cancer Society (ACS) was the elimination of inequalities based on income, race/ethnicity, gender, where they live, or age, collectively termed as healthcare disparities observed in the burden of cancer.<sup>12</sup> In general, research has found pain management insufficient among African American and Hispanic patients relative to Caucasian and non-Hispanic patients.<sup>13–17</sup> Clinical and demographic factors can also partially explain the higher rates of pain and its undertreatment among minority patients with breast cancer.<sup>18–22</sup> However, no study has evaluated pain management among outpatients with breast cancer. It has been known that healthcare disparities can negatively

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influence patient health outcomes; therefore, understanding the factors leading to disparities could improve the quality of life of the patients and aid in reducing overall healthcare costs.

The World Health Organization (WHO) has guidelines for the treatment of cancer pain and for prescribing opioids to patients with cancer in advanced stages.<sup>4,23–25</sup> Initial treatment involves acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID). If not sufficient, guidelines suggest a weak opioid and then escalate to a strong opioid and combinations later. However, as the disease progresses, the pain experienced by the patient also increases, thus, necessitating the administration of opioids and adjuvant analgesics to breast cancer patients experiencing severe pain. Even though opioids have a potent pain-relieving effect, they are associated with side effects like constipation, nausea, and vomiting, but majorly the fear of dependence and tolerance.<sup>26</sup> Its progression from appropriate use to dependence and abuse poses a serious risk with overall poor outcomes.<sup>26</sup> Little is known about analgesic usage among outpatients with breast cancer in the US. Recently, there has been growing interest in understanding opioid use among breast cancer patients.<sup>27-29</sup> However, these studies included active cases of breast cancer patients or survivors and have evalutaed opioid medications only using claims data until 2015.<sup>30</sup> None of the previous studies have examined the prescribing patterns of analgesics: non-opioids and opioids to understand the overall prescribing practices in ambulatory settings in the US, covering both-insured and uninsured patients. With pain being one of the most common reasons for physician office visits, understanding the use of pain medications and their predictors may help identify ways to optimize pain medication use in outpatient settings. Most importantly, it would be of paramount interest to understand the prescribing pattern of opioids which are often prescribed in the outpatient setting, irrespective of the stage of cancer (actives /survivors), and as prior studies have shown that from 1992 to 2010, opioid prescriptions in this type of setting have increased.<sup>31</sup> Therefore, the objective of this study was to examine the pain management practices and the factors associated with the prescription of pain medications, especially opioids, in women with breast cancer using the multi-year National Ambulatory Medical Care Survey (NAMCS).

#### 2. Materials and methods

### 2.1. Data source

This study analyzed six years of nationwide office visit data -the NAMCS from 2011 to 2016.<sup>32–37</sup> The NAMCS, a national probability sample survey, has been administered annually since 1989 by the National Center for Health Statistics of the Center for Disease Control and Prevention, with the most recently available data being from 2016 at the time of the study. This cross-sectional survey provides data about the use of office-based medical care services, which helps in understanding the patterns of office-based patients in the US. The data are based on a sample of visits to non-federally employed office-based physicians who provide direct patient care. The NAMCS survey involves a multi-stage probability sampling design of primary sampling units, physician practices within these units, and patient visits within practices. The survey obtains information about the outpatient visits from their health care providers or staff regarding patient characteristics and the services rendered, including diagnostic tests and medication. Data about physician and their practice characteristics are collected during a survey induction interview. Additional information on the NAMCS data can be found on the National Center for Health Statistics website.<sup>38</sup> The record of medications prescribed during the visit is captured and coded based on the Multum Lexicon drug classification system. This study was approved under the exempt category by the Institutional Review Board for the protection of human subjects at the University of Houston.

## 2.2. Study population and measures

This study involved adult women (age  $\geq 18$  years) with breast cancer as the primary diagnosis identified using the International Classification of Diseases, Ninth and Tenth Revision Clinical Modification codes: ICD-9CM code (174.9)<sup>39</sup> and ICD-10-CM code (C50.919).<sup>40</sup> The primary measure of interest was the prescription of pain medications, with a further focus on opioid medications in breast cancer patients. Pain medications for cancer-related pain were operationally defined using the WHO ladder<sup>26</sup> and identified using Multum Lexicon®.

All the drug classes and drugs were operationally defined using the American Hospital Formulary Service classification (AHFS).<sup>41</sup> Pharmacologic analgesics included non-opioids, opioids, and a combination of both.<sup>4</sup> The non-opioid analgesics included NSAIDs, salicylates, and acetaminophen, while the opioids included codeine, fentanyl, hydrocodone, hydromorphone, meperidine, morphine, methadone, oxycodone, oxymorphone, tapentadol, tramadol, and combinations of these drugs.<sup>42</sup> Clinically adjuvant analgesics consisted of a diverse range of drug classes, including anticonvulsants such as barbiturates, antidepressants, such as selective serotonin reuptake inhibitors (SSRI) serotonin-norepinephrine reuptake inhibitors (SNRI), tricyclic antidepressants (TCA), and corticosteroids.<sup>4</sup> Pain medications prescribed during the visit were identified using the Multum Lexicon codes. Opioid medications were identified using the Multum drug classification category "060" for narcotic analgesics or "191" for narcotic analgesic combinations.

#### 2.3. Statistical analyses

Descriptive weighted analyses such as the chi-square test were conducted to examine the pain management practices in outpatient visits by women with breast cancer. Two multivariable logistic regression analyses were performed to achieve the study's aims. First, a multivariable model was used to identify the factors associated with the prescription of pain medications, and the second model identified the factors associated with the prescription of opioids among those taking pain medications. For the first analysis, the dependent variable was pain medication therapy versus no pain medication therapy in breast cancer patients. In the second analysis, the dependent variable was opioid therapy (opioid medication or combination of opioids) versus non-opioid therapy (NSAIDs, acetaminophen, salicylates) as the reference group.

The conceptual framework of the Andersen Behavioral Model (ABM) was used to identify independent variables for both multivariable analyses.<sup>43</sup> According to the ABM, health service utilization is a function of three factors: predisposing, enabling, and need. Predisposing factors describe the tendency of an individual to use healthcare services, including age, sex, race, and ethnicity. Enabling factors define the ability of an individual to secure healthcare services, including region, year of visit, health insurance, physician characteristics, and metropolitan statistical area. Need factors represent an individual's perceived and actual health status and include adjutant therapies<sup>4</sup> and comorbid conditions identified using the Charlson comorbidities.<sup>44</sup> All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, North Carolina) at a statistical significance level of 0.05. The analyses accounted for the complex sample design and adjusted for the weighted data using the SAS survey procedures.

#### 3. Results

According to the national surveys, 23.95 million (95% CI: 19.29–28.60) office visits were made by women with breast cancer as the primary diagnosis from 2011 to 2016. Table 1 describes the characteristics of women with breast cancer visiting the outpatient setting. Most of the visits by women with breast cancer patients involved whites 20,041,991 (83.7%), non-Hispanics 21,880,370 (91.37%), 40–64 year olds 12,167,867 (50.81%), from the Northeast region of US 7,857,334 (32.81%), and from the the metropolitan statistical area 22,904,861 (95.65%). Most of the visits were made to general and family practice settings 20,340,034 (84.93%), while most of the patients were seen before or were established, 21,130,365 (88.24%). Among the women with breast cancer, depression (n = 2,057,021 [8.59%]) and diabetes (n = 417,702 [1.74%]) were the most commonly observed comorbidities. Smaller sample sizes (<30, unweighted) of other comorbidities resulted in their exclusion from analysis.

#### Table 1

Demographic characteristics of office visits by women with breast cancer.

Patient Characteristics	Unweighted Frequency	Weighted Frequency	Percentage
Sex			
Female	1653	30,640,632	100
Age, years			
18–39	73	1,283,536	5.36
40-64	873	12,167,867	50.81
65 and above	707	10,495,903	43.83
Race		- , ,	
White	1423	20,041,991	83.7
Black/African American	170	2,855,792	11.93
Other <sup>a</sup>	60	1,049,524	4.38
Ethnicity			
Hispanic or Latino	129	2,066,937	8.63
Not Hispanic or Latino	1524	21,880,370	91.37
Region			
Northeast	438	7,857,334	32.81
Midwest	392	4,950,378	20.67
South	516	7,509,467	31.36
West	307	3,630,128	15.16
Metropolitan Statistical Area (MSA)		-,,	
MSA	1531	22,904,861	95.65
Non-MSA	122	1,042,446	4.35
Payment Source	100	1,0 12,110	1100
Private Insurance	778	10,186,040	42.54
Medicare	627	9,206,696	38.45
Medicaid/other state-based program	110	1,782,864	7.44
Other <sup>b</sup>	138	2,771,706	/
Type of Provider	100	2,771,700	
Physician	879	11,950,151	49.90
Physician Assistant or Nurse	0/9	11,900,101	19.90
Practitioner	95	1,545,325	6.45
Other <sup>c</sup>	679	10,451,831	43.65
Patient seen before	075	10,451,051	43.03
Yes, established	1455	21,130,365	88.24
No, new patient	198	2,816,942	11.76
Primary Physician	170	2,010,742	11.70
Yes	72	1,451,423	6.06
No	1476	21,680,199	90.53
Other <sup>d</sup>	105	815,684	90.55 3.41
Solo Practice	105	615,064	3.41
Solo	295	51,86,445	21.66
Other <sup>e</sup>		, ,	
	1358	18,760,861	78.34
Specialty	1010	20.240.024	84.02
General and family practice	1012	20,340,034	84.93
General surgery	117	565,040	2.36
Others <sup>f</sup>	524	3,042,233	12.70
Comorbidities	1.41	0.057.001	0.50
Depression	141	2,057,021	8.59
Diabetes	29	417,702	1.74
Adjuvant therapy	360	5,435,628	22.70

<sup>a</sup> Includes the categories Asian, Native Hawaiian/other Pacific Islander, American Indian/ Alaska Native, and those individuals indicating more than one race.

<sup>b</sup> Includes Worker's compensation, self-pay, no charge/charity, other, and unknown.

<sup>c</sup> Includes Mental health provider, RN/LPN and other providers.

<sup>d</sup> Includes Blank and Unknown.

<sup>e</sup> Includes Non-solo and unknown.

<sup>f</sup> Includes Dermatology, Urology, Pediatrics, Psychiatry, Neurology, Obstetrics and Gynecology, Ophthalmology, Orthopedic surgery, Otolaryngology, Cardiovascular diseases, All other specialties.

Table 2 provides pain management practices during office-based visits by women with breast cancer. In the study, an estimated 6.5 million (27.12%) patients received pain medications, of which 15.16% (95% CI: 8.75–21.57) involved prescribing opioids and 17.13% (95% CI: 12.46–21.80) involved non-opioid analgesics. Tramadol (3.75%) was the most prescribed opioid, followed by oxycodone (1.57%). Combination opioids were prescribed in 10.27% of the visits. Among the non-opioid drugs, salicylates (8.92%) and NSAIDs (5.82%) were the most frequently prescribed pain medications. Ibuprofen (3.73%) was the most prescribed drug among NSAIDs, followed by naproxen (1.27%).

#### Table 2

Prescribing of pain medications among women with breast cancer as primary diag-	
nosis, NAMCS visits 2011–2016).	

Drug class and	Unweighted	Weighted	95% CI
names	frequency	frequency	5670 61
	. 1	(%)	
Opioids	214	3,629,661 (15.16)	2,095,085 to
			5,164,237
Oxycodone	32	376,574 (1.57)	
Tramadol	32	898,011 (3.75)	
Combinations	132	2,459,466(10.27)	
Other opioids <sup>a</sup>	54	572,917(2.39)	
Non-opioids	271	4,101,750 (17.13)	2,983,838 to
			5,219,663
1. NSAIDS	98	1,394,156 (5.82)	
Ibuprofen	56	892,645 (3.73)	
Naproxen	24	303,933 (1.27)	
Other non-opioids <sup>b</sup>	41	445,788(1.86)	
2. Salicylates	143	2,136,522 (8.92)	
3. Acetaminophen	49	786,195(3.28)	
Adjuvant Therapies	360	5,435,628(22.7)	3,755,987 to
			7,115,269
1.Antidepressants			
SSRI	104	1,206,954 (5.04)	
SSNRI	64	952,027 (3.98)	
Other	59	1,124,168(4.69)	
Antidepressants <sup>c</sup>			
2.Anticonvulsants			
Benzodiazepine	110	1,821,994(7.61)	
Gamma	60	787,943(3.29)	
Other	10	227,807(0.95)	
anticonvulsants <sup>d</sup>			
3.Corticosteroids			
Glucocorticoids	76	1,672,374(6.98)	

<sup>a</sup> Includes morphine, fentanyl, hydromorphone, oxymorphone, propoxyphene, methadone, and hydrocodone.

<sup>b</sup> Includes Cox-2 inhibitors, diclofenac, meloxicam, sulindac, nabumetone, etodolac, and ketorolac.

<sup>c</sup> Includes tricyclic, tetracyclic, phenylpiperazine, monoamine oxidase inhibitors
<sup>d</sup> Includes hydantoin, succinimide, barbiturate, misc., oxazolidinedione,

dibenzoazepine, fatty acid derivatives, triazaine, gamma reuptake inhibitors, carbamate, pyrrolidine, carbonic anyhydrase

Table 3 shows the results of multivariable logistic regression evaluating the factors associated with prescribing pain medications among women with breast cancer. Women in the Northeast (OR = 0.31, 95% CI: 0.10-0.99) region were less likely to receive pain medication prescriptions than those in the west region. White patients [Odd Ratio (OR) = 0.50, 95% CI:0.3-0.85] had lower odds of receiving pain medications than black women. Women with Medicaid or other state-based programs as the payment source (OR = 2.38, 95% CI: 1.15-4.93) were more likely to receive pain medications than those with private insurance. The odds of prescribing pain medications were significantly higher for women prescribed adjuvant therapy (OR = 4.74, 95% CI: 3.10-7.24) compared to patients who were not prescribed any such medications. General and family practice specialties (OR = 3.18, 95% CI: 1.22-8.29) were associated with a higher odds of prescribing pain medications than other specialties. Non-primary care physicians (OR = 0.37, 95% CI: 0.15–0.94) were less likely to prescribe pain medications than visits involving primary care physicians.

Table 4 reports the results of the multivariable logistic regression analysis examining the factors influencing opioid prescriptions among women with breast cancer who were receiving pain medications. Women residing in the Northeast (OR = 0.06, 95% CI: 0.01–0.29), Midwest (OR = 0.15, 95% CI: 0.04–0.62), and South (OR = 0.24, 95% CI: 0.06–0.92) regions were less likely to receive opioid prescriptions than those residing in the west region. General and family practice clinicians (OR = 6.76, 95% CI:1.71–26.70) were more likely to prescribe opioids than their counterparts. None of the other characteristics were significantly associated with opioid prescribing.

#### Table 3

Factors associated with prescribing of pain medications (non-opioids, opioids or combinations) as compared to no pain medications prescribed among women visiting office based- setting due to breast cancer.

Patient Characteristics	Pain Medication	P-value
	Adjusted OR (95% CI)	
Age, years		
18–39	0.634 (0.31-1.28)	0.21
40–64	0.71 (0.44-1.14)	0.16
65 and above	REF	
Race		
Black/African American	REF	
White	0.50 (0.3–0.85)	$0.02^{i}$
Other <sup>a</sup>	0.27 (0.027-2.62)	0.26
Ethnicity		
Hispanic or Latino	0.85 (0.46-1.58)	0.61
Not Hispanic or Latino	REF	
Region		
Northeast	0.31 (0.10-0.99)	0.04 <sup>i</sup>
Midwest	0.94 (0.32-2.73)	0.91
South	0.37 (0.13-1.02)	0.05
West	REF	
Metropolitan Statistical Area (MSA)		
MSA	0.90 (0.40-2.06)	0.81
Non-MSA	REF	
Year of visit		
2011-2012	1.49 (0.56-3.98)	0.43
2013-2014	0.77 (0.40-1.49)	0.44
2015–2016	REF	
Payment Source		
Private Insurance	REF	
Medicare	1.46 (0.89-2.41)	0.13
Medicaid/other state-based program	2.38 (1.15-4.93)	$0.02^{i}$
Other <sup>b</sup>	0.53 (0.18-1.56)	0.25
Type of Provider		
Physician	1.13 (0.57-2.24)	0.73
Physician Assistant or Nurse Practitioner	REF	
Other <sup>c</sup>	0.90 (0.42-1.94)	0.79
Patient seen before		
Yes, established	1.60 (0.76-3.40)	0.22
No, new patient	REF	
Primary Physician		
Yes	REF	
No	0.37 (0.15-0.94)	0.04 <sup>i</sup>
Other <sup>d</sup>	0.65 (0.14-3.06)	0.59
Solo Practice		
Solo	1.68 (0.92-3.06)	0.09
Other <sup>e</sup>	REF	
Specialty		
General and family practice	3.18 (1.22-8.29)	$0.02^{i}$
General surgery	1.59 (0.75–3.39)	0.23
Others <sup>f</sup>	REF	
Depression		
Yes	0.80 (0.33-1.94)	0.63
No	REF	
Diabetes		
Yes	2.65 (0.84-8.37)	0.1
No	REF	
Adjuvant therapy		
Yes	4.74 (3.10-7.24)	< 0.001 <sup>i</sup>
No	REF	

<sup>a</sup> Includes the categories Asian, Native Hawaiian/other Pacific Islander,

American Indian/ Alaska Native, and those individuals indicating more than one race.

<sup>b</sup> Includes Worker's compensation, self-pay, no charge/charity, other, and unknown.

<sup>c</sup> Includes Mental health provider, RN/LPN and other providers.

<sup>d</sup> Includes Blank and Unknown.

<sup>e</sup> Includes Non-solo and unknown.

<sup>f</sup> Includes Dermatology, Urology, Pediatrics, Psychiatry, Neurology, Obstetrics and Gynecology, Ophthalmology, Orthopedic surgery, Otolaryngology, Cardiovascular diseases, All other specialties.

<sup>i</sup> Statistically significant at  $\alpha \leq 0.05$ .

## Table 4

Factors associated with prescribing of opioid medications as compared to non-opioids among women visiting office based-setting due to breast cancer.

Patient Characteristics	Opioid Therapy Adjusted OR (95% CI)	P-value	
Age, years			
18–39	REF		
40–64	0.37 (0.09-1.43)	0.15	
65 and above	0.26 (0.06-1.06)	0.06	
Race			
White	REF		
Black/African American	1.30 (0.40-4.22)	0.66	
Other <sup>a</sup>	10.67 (0.78-146.4)	0.08	
Ethnicity			
Hispanic or Latino	1.02 (0.30-3.56)	0.98	
Not Hispanic or Latino	REF		
Region			
Northeast	0.06 (0.01-0.29)	< 0.01 <sup>i</sup>	
Midwest	0.15 (0.04–0.62)	<0.01 <sup>i</sup>	
South	0.24 (0.06–0.92)	0.04 <sup>i</sup>	
West	0.24 (0.00–0.92) REF	0.04	
Metropolitan Statistical Area (MSA)	ILLI'		
MSA	1.43 (0.43-4.77)	0.56	
Non-MSA	1.43 (0.43–4.77) REF	0.50	
	IVEL		
Year of visit	416 (0.00.17 (0)	0.05	
2011-2012	4.16 (0.98–17.68)	0.05	
2013-2014	0.55 (0.20–1.50)	0.24	
2015-2016	REF		
Payment Source			
Private Insurance	REF		
Medicare	0.81 (0.33-2.01)	0.65	
Medicaid/other state-based program	1.61 (0.38–6.74)	0.52	
Other <sup>b</sup>	1.63 (0.44–6.09)	0.46	
Type of Provider			
Physician	0.75 (0.25–2.26)	0.61	
Physician Assistant or Nurse Practitioner	REF		
Other <sup>c</sup>	1.46 (0.44–4.87)	0.53	
Patient seen before			
Yes, established	0.70 (0.20-2.39)	0.57	
No, new patient	REF		
Primary Physician			
Yes	REF		
No	0.84 (0.24-3.03)	0.79	
Other <sup>d</sup>	1.12 (0.23-5.49)	0.89	
Solo Practice	·····		
Solo	0.86 (0.34-2.17)	0.74	
Other <sup>e</sup>	REF		
Specialty			
General and family practice	6.76 (1.71-26.70)	< 0.01 <sup>i</sup>	
General surgery	0.70 (0.08–6.08)	0.74	
Others <sup>f</sup>	REF	0.7 4	
Depression	1111		
Yes	1 00 (0 41 2 00)	0.87	
	1.09 (0.41–2.90)	0.87	
No	REF		
Diabetes	0 (0 (0 11 4 00)	0.00	
Yes	0.69 (0.11-4.22)	0.69	
No	REF		
Adjuvant therapy			
Yes	1.82 (0.97–3.43)	0.06	
No	REF		

<sup>a</sup> Includes the categories Asian, Native Hawaiian/other Pacific Islander,

American Indian/ Alaska Native, and those individuals indicating more than one race. <sup>b</sup> Includes Worker's compensation, self-pay, no charge/charity, other, and un-

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e Includes Non-solo and unknown.

<sup>f</sup> Includes Dermatology, Urology, Pediatrics, Psychiatry, Neurology, Obstetrics and Gynecology, Ophthalmology, Orthopedic surgery, Otolaryngology, Cardiovascular diseases, All other specialties.

Statistically significant at  $\alpha \leq 0.05$ .

#### 4. Discussion

The current study revealed that about one in four visits by women with breast cancer received pain medication prescriptions, non-opioids, and/or opioids. Previous literature focusing on breast cancer pain following surgical intervention found that pain is a significant problem in 25–50% of patients with breast cancer, among which 13% had severe pain.<sup>45</sup> Another study focusing on opioid use in older adult women following breast cancer treatment found that nearly a quarter had received opioid therapy for 10% of their active cancer period.<sup>46</sup> Our findings are at the lower end of this range as our study evaluated office visits involving all stages of breast cancer patients, including surgical and non-surgical patients, active cancer patients, or survivors.

The study found that non-opioids and opioid analgesics were prescribed for pain management in breast cancer. Among the non-opioid drugs, salicylates and NSAIDs were the most frequently prescribed pain medications. This study's most commonly prescribed opioid was tramadol, which is considered a weaker opioid. This result was consistent with prior findings highlighting an increased use of tramadol among breast cancer patients.<sup>47</sup> Tramadol prescriptions have doubled between 2007 and 2015, becoming the second most prescribed opioid in the US.<sup>48</sup> Prior literature suggests that patients receiving tramadol alone after surgery have shown that it is at least as likely as other opioids to be continued long-term,<sup>49</sup> which is a surrogate measure for abuse and overdose.<sup>48,50</sup> Thus, it is vital to monitor its use to address abuse and overdose potential.

The NAMCS data can effectively identify disparities in outpatient care in the US.<sup>51</sup> The multivariable analyses found that white women were less likely to receive pain medications as compared to black women, though there were no differences observed in terms of receiving opioid medication prescriptions. This is consistent with prior studies investigating postsurgery pain management in breast cancer patients undergoing oncological treatments.<sup>15,16,52–54</sup> The literature suggests that racial disparities exist due to a number of complex reasons for racial/ethnic disparities in pain management, including limited access to care and treatments, differences in attitudes, beliefs, knowledge, and behaviors among practitioners and patients.<sup>55,56</sup> Breuer and colleagues found that Caucasians had experienced pain for a significantly longer period of time than the other groups, but had a lower average pain severity.<sup>25,56</sup> The racial and ethnic variations have been observed for non-cancerous pain such as abdominal pain or back pain in prior studies.<sup>13,14,17</sup> Therefore, more research is needed to address pain management to reduce disparities.

Women with Medicaid or other state-based programs as the payment source were more likely to receive pain medications than those with private insurance. This finding is consistent with a previous study assessing the use of opioids for non-malignant pain.<sup>57</sup> This finding could be attributed to the socioeconomic status of patients under Medicaid or other state-based programs and the coverage of pain medications under these programs. However, this finding has an important public health implication in terms of ambulatory healthcare costs by breast cancer patients contributing to national expenditures with Medicaid bearing the costs of pain management. Hence, there is a need for judicious use of pain management among outpatients suffering from breast cancer.

Women in the Northeast, Midwest, and South regions were less likely to receive opioid prescriptions than those in the West region. These findings suggest that there exists regional variation in opioid prescribing. These observed regional variations could be attributed to differences in prescribing practices, patient preference, or formulary structure across geographic regions. A prior study involving breast cancer patients found that there exist geographic variations in the use of opioids.<sup>42</sup> Another NAMCS study also reported differences in opioid prescribing based on the region.<sup>57</sup> Thus, further assessment of regional variations in prescribing factors that may impact the use of opioids is needed.

This study found that pain medications and, more specifically, opioids were more likely to be prescribed in patients visiting general and family practice settings and for patients seeing their primary care physician than those who were visiting any other specialty providers or their non-primary care physicians. This result is consistent with literature that found that patients seeing primary care physicians (PCPs) were about two times more likely to report the use of opioids than those visits recorded from specialty physicians.<sup>57</sup> The findings reflect differences in prescribing of analgesics according to physician type. These findings suggest that primary care providers often address and treat patients with pain in their practice.<sup>58</sup> Therfore, pain management educational efforts could be directed at primary care providers to change opioid prescribing practices.

This study also found that patients were four times more likely to receive pain medication prescriptions if patients were receiving adjuvant therapy medications as compared to those not receiving any adjuvant therapy. These findings suggest that adjuvant therapy medications are often coprescribed to manage other pain conditions such as neuropathic pain, which is common in post-mastectomy patients.<sup>45</sup> However, no significant differences in prescribing opioid or non-opioid medications among patients receiving adjuvant medications were observed.

Overall, this study found a variation in the use of pain medications in women with breast cancer. Salicylates and NSAIDs were the most frequently prescribed pain medications in women with breast cancer. Tramadol was the most prescribed opioid, followed by oxycodone in women with breast cancer visiting outpatient settings. The study found that patient and provider characteristics are significantly associated with prescribing pain medications and opioids in women with breast cancer. The findings from this research can help to understand national-level patterns and drivers of pain medications in general and opioids in specific. The results have important implications for policymakers, clinicians, and payers in understanding the opioid and non-opioid prescribing practices among breast cancer patients. Concerted efforts by all stakeholders are needed to optimize opioid and non-opioid prescribing in this patient population.

#### 4.1. Strengths and limitations

The nationally representative survey data used in this study provides reliable information about physician office-based visits and ambulatory services provided to the US population, covering both insured and uninsured populations. Using patient weights and adjusting for the survey design complexities aids in estimating high generalizabile national estimates. Even though this study presented some important findings, there are limitations to this study. First, the data collected is based on visits to the office-based settings; hence, and cannot address the population prevalence or actual percentage of patients taking opioids and non-opioids. Second, due to data source limitations, utilization of pain medication prescriptions according to the pain severity or breast cancer stages could not be evaluated. In addition, no information was available to describe the initiation or duration of pain medications. Due to the nature of the data, we could not address the indication or long-term management for pain, but we considered only patients with the primary reason of visit as breast cancer to understand pain management patterns. Also, the demographic and clinical characteristics evaluated were limited to only those captured in the NAMCS. Although the study was conducted over six years, this was a cross-sectional study due to the survey design of the NAMCS. Our data includes all prescription and OTC medications ordered by the providers; however, the NAMCS does not capture the OTC products bought by patients.

#### 5. Conclusion

The national survey data revealed that about one in four women visits with breast cancer received pain medication prescriptions: non-opioids and/or opioids. One in seven office visits by women with breast cancer involved opioids. Both patient and provider characteristics contribute to the variation in pain medication prescription in breast cancer patients. The study also found differences exist between those prescribed pain medications and opioids.

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#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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