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Gender differences in prescription opioid use

Mirsada Serdarevic¹, Catherine W Striley¹, and Linda B Cottler¹

¹University of Florida, Florida, US, Department of Epidemiology, College of Public Health and Health Professions, College of Medicine, 2004 Mowry Road, PO Box 100231, Gainesville, FL 32610

Abstract

Purpose of review—Recent literature focused on prescription opioids has neglected gender differences in use. Here we evaluated the recent literature (since 2015) examining gender differences in prescription opioid use.

Recent findings—Between 2015 and 2016, our review found only eight articles addressing gender differences in prescription opioid use mostly opioid misuse in North America among individuals with chronic pain. Risk factors included depression, pain, and poly-drug use. In addition to that review, we had the opportunity to further address gender differences in, and risk factors for, prescription opioid use through a community engagement program, HealthStreet. Among the sample ($n=8,525$, $M_{age} = 43.7$ years, 58.6% female), approximately half reported use of prescription opioids. Women were significantly more likely to report lifetime use (54.9% vs 42.2%; $p < .0001$) and report cancer compared to men, yet, women with cancer had a significantly reduced risk of using opioids compared to men with cancer (OR: 0.46; 95% CI, 0.36–0.59).

Summary—Only a few recently published studies analyzed gender differences related to prescription opioid use. Findings from the literature and our data suggest women are more likely to use prescription opioids compared to men. There is limited information on gender differences in opioid use risk factors and outcomes and more research in this area is warranted.

Keywords

gender differences; prescription opioids; opioid use

INTRODUCTION

The prevalence of opioid use globally among adults is 0.7%, representing approximately 33 million users (1). Prescription opioid use has become a public health concern due to an increase in morbidity and mortality (2), especially in the United States where opioid related deaths have quadrupled since 1999 (3). Every day, approximately 91 people die from opioid overdose (4) and over 1,000 people are treated for prescription opioid misuse in the emergency department (ED). This is an example of how certain forms of drug use may change in their prevalence and health impacts. While men are more likely to die from

Corresponding author: Mirsada Serdarevic, mserdarevic@ufl.edu, Telephone: 352-294-5953, Fax: 352-273-5365.

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prescription overdose than women (5), overdoses related to opioids have greatly increased in women compared to men (6); further, women are approximately twice as likely to be prescribed prescription opioids compared to men (7). Additionally, pain sensitivity varies between men and women, with women reporting more chronic conditions that cause pain (8); these conditions may be associated with higher prescription rates of opioids. Understanding gender differences related to prescription opioid use is important because differences in use by gender can result in differential consequences that matter such as serious morbidity and mortality. Despite the importance of these gender differences, there has been little attention to how such gender differences impact both risk factors for and outcomes of opioid use.

Between early 2015 and late 2016 we identified only eight articles (Table 1) published in English which address gender and prescription opioid use, though there may be additional published manuscripts written in other languages. The current publications identified included two scoping reviews, two clinic based studies, and four population based studies which examined prescription opioid use specifically and other opioid use (mix of prescribed opioids and illicit opioids).

Scoping reviews

The scoping review by Hemsing et al., identified 57 articles published between 1990 and 2014 which examined risk factors for pain and misuse of prescription opioids among women. A majority of the studies identified in this review were descriptive with only a few interventional studies targeting pain, trauma and misuse of prescription opioids. Those who had experienced violence and trauma, aboriginal women, pregnant women, women who are sexual minorities (i.e., lesbian, bisexual), and transgender women were all at heightened risk for pain and misuse of prescription opioids according to this review (9). A second review authored by Graziani and Nistico summarized literature published between 1995 and 2015 to analyze gender differences in the pharmacokinetic and pharmacodynamic effects of oxycodone and hydrocodone. This review suggested that there has been an increase in oxycodone and hydrocodone abuse among women but found no differences in pharmacokinetic or pharmacodynamic effects by gender (10). This indicates that there is some factor other than biological differences in the processing of opioids that accounts for the difference in prescription opioid abuse between men and women.

Clinic based studies

The two clinic based studies examined gender differences among individuals misusing opioids. Bawor and colleagues used data from a multicenter cohort study (n=503). Participants receiving methadone treatment who met Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) (11) criteria for opioid dependence disorder were used in their regression models and descriptive statistical analyses to examine past 30 day opioid use (this could include illicit or prescription opioids). The authors found women compared with men were more likely to have a family history of mental illness and to initiate opioid use through a physician. Alternatively, men were found to have higher rates of cigarette smoking and cannabis use compared to women (12). The other clinic based study used a cross-sectional method to interview 162 participants as part of a 7-week inpatient and 12-week

outpatient study. Participants who met DSM-IV criteria for opioid dependence in the past 6 months (prescription opioids with or without heroin) were included in the descriptive statistics, t-tests, and chi-square analyses. The authors found 60% of the participants had back pain, women had greater psychiatric co-morbidity and endorsed greater pain compared to men, while men reported more antisocial behaviors such as police arrests compared to women (13).

Population based studies

Of the four population-based studies which considered gender effects, Fink and colleagues examined cross-sectional data from the National Survey on Drug Use and Health (NSDUH) which is conducted annually in the United States. In the 2011–2012 cohort, (n= 113,665) analyzed using multinomial logistic regression for past year misuse of prescription opioids, misuse of prescription opioids and major depressive episodes (MDE) were prevalent among women but not for men (14). Additionally, poly-drug use was found to be more prevalent among those with comorbid misuse of prescription opioids and MDE than persons with prescription opioid misuse alone or MDE alone. Evans and colleagues used a retrospective cohort design conducted in California (n=20,758) to examine risks for mortality by gender by linking vital statistics data to individuals who were admitted to a publicly funded opioid treatment program (any type of opioid) in California between 2006 and 2010. Using standardized mortality ratios and Cox proportional hazards authors determined effects of gender on hazard of all-cause mortality. They reported an increased risk of mortality from opioid use among those being treated for opioid dependence. Further, full-time employment decreased mortality risk and medical problems increased mortality risk among men. For women, concurrent opioid and methamphetamine/cocaine use increased mortality risk (15). The third population based study was conducted in British Columbia (BC), Canada by Gladstone and colleagues using an ecological method (16). Data from BC PharmaNet an information system on prescription drug dispensations and cause of death from vital statistics records were used to identify patterns and geographic areas in prescription opioid dispensations to individuals who suffered a prescription opioid-related death between 2004 and 2013. The authors found that relationship between prescription opioid dispensing and rates of unintentional death was significant for both genders, with the exception that opioid related deaths for men were more likely due to their using diverted pills (16). The remaining population based cross-sectional study by LeResche et al., examined sex and age differences in pain status among chronic opioid therapy users (17). Participants (n= 2,163) who were enrolled in chronic opioid therapy for at least one year and filled an opioid prescription within the last 30 days completed a telephone survey relating to their pain level and functioning status; findings included women reporting higher pain levels compared to men. Specifically, the authors found young and middle aged women were at highest risk for pain among those receiving chronic opioid therapy (17).

The recent literature reviewed here has examined gender differences in prescription opioid use; however, significant challenges to the field remain. One challenge includes the geographic homogeneity of most studies. Research on opioid use and gender has primarily been conducted among populations in North America though other parts of the globe such as Afghanistan (18), Australia (19) and other countries are also affected by opioid use. In the

future there may be more information available from these countries with regards to gender differences due to new studies that are currently being conducted (20).

In addition, research in this area typically examines only the “tip of the iceberg”; or those cases that are clinical cases or cases brought to the attention of clinicians or the ED. Finally, there are challenges in the interpretation of the findings of opioid use research when we have inconsistent nomenclature resulting from a broad range of terminology that describes “use”, misuse, abuse and dependence.

Population based studies can be useful for addressing the gap between gender differences and prescription opioid use; they can provide information from broad population groups to help identify factors that can influence effectiveness of interventions. We add to this review through analysis of original data from North Central Florida that addresses gender differences in prescription opioid use. We examine risk factors for prescription opioid use including differences by gender in rates of pain, depression and cancer among a community based sample addressing common risk factors in the literature.

METHODS FOR COMMUNITY BASED STUDY

Participants were part of a community outreach program, HealthStreet, based out of the University of Florida Clinical and Translational Science Institute. Through HealthStreet, Community Health Workers (CHWs) directly engage with community members in locations such as grocery stores, parks, and libraries. With a University of Florida Institutional Review Board (IRB) approved Health Intake, CHWs assess demographics and social determinants of health, research perceptions, medical conditions, and drug use. Based on these data, community members are linked to medical and social services and opportunities to participate in health research. The variables we are using in our analyses are shown in Table 2.

Statistical analyses

SAS version 9.4 (21) was used for analysis with chi-square tests of independence. An independent t-test compared mean ages. Multinomial and multivariate logistic regression were used to calculate adjusted odds ratios (ORs) and 95% confidence intervals.

RESULTS

Among the sample of 8,470, 58.6% were female, 61.3% black, 60.0% had at least a high school education, 27.5% reported depression, 43.6% reported back pain, 8.0% were cancer survivors, 32.6% had visited an ED in the last 6 months, 66.5% had visited a doctor in the last 6 months, and 23.5% reported binge drinking in the past 30 days. Approximately half (49.7%) reported prescription opioid use in their lifetime; 13.7% reported past 30 day use (Table 3).

When stratified by gender, we found statistically significant associations for all variables with the exception of age. Women compared to men were significantly more likely to be white, educated, depressed, report back pain and cancer, and report visiting the ED and

doctor in the past 6 months. Men were more likely to report current binge drinking than women. Regarding opioid use, women were more likely than men to report recent (past 30 day) and non-recent (lifetime but not past 30 days) prescription opioid use (54.9% women vs 42.2% men).

Table 4 provides results of the adjusted multinomial logistic regression model predicting lifetime use of prescription opioids and past 30 day prescription opioid use with never use as the reference group for the regression. After adjustment for covariates, women were significantly more likely to report both lifetime and past 30 day use of prescription opioids compared to men. Additionally, risk factors for lifetime use of prescription opioids included older age, being white, more educated, history of depression, past 6 month doctor and ED visits, and past 30 day binge drinking. The strongest risk factor for lifetime use of prescription opioids was history of back pain with those who reported such a history being 1.66 times as likely to report lifetime use of prescription opioids (95% CI, 1.50–1.85) compared to those with no history of back pain. Following history of back pain, cancer was the second strongest risk factor for lifetime use of prescription opioids (adjusted OR: 3.66; 95% CI, 2.97–4.51).

Risk factors for past 30 day use of prescription opioids yielded similar results to lifetime use of prescription opioids including older age, being white, and having a history of depression. Those with back pain were 2.85 times more likely to report past 30 day use of opioids compared to those without history of back pain (95% CI, 2.45–3.32). History of cancer, visiting the ED in the past 6 months, and binge drinking were also risk factors for past 30 day prescription opioid use. Seeing a doctor in the past 6 months was the strongest risk factor for past 30 day use of prescription opioid use, with a visit increasing the odds nearly 4 times over those who did not visit a doctor (adjusted OR: 3.66; 95% CI, 2.97–4.51). We ran a separate logistic regression stratified by gender (results not shown) and found that the majority of the risk factors remained the same for men and women with the exception of cancer among women which had a lower association with opioids compared to that for men (adjusted OR: 0.46; 95% CI, 0.36–0.59).

DISCUSSION

The use of prescription opioids continues to be a significant public health problem contributing to a number of poor health outcomes. Upon examining the recent literature we were only able to identify eight publications regarding gender differences in prescription opioid use. The challenges identified within this field of research include geographic homogeneity, primary focus on opioid dependent populations, discrepancy in terminology for reporting use, and the limited amount of epidemiologic data available for addressing gender and prescription opioid use. We had the opportunity to address some of these challenges by using a community based study to further examine gender differences in prescription opioid use.

HealthStreet is an ongoing community engagement program that recruits community members and conducts real time assessment on their health conditions and concerns. Using HealthStreet and this community based sample we were able to assess gender-based patterns

of prescription opioid use. This current analysis shows that approximately half of the community sample had used prescription opioids in their lifetime. The prevalence of past 30 day prescription opioid use (13.7%) was higher than what previous national surveys have reported (6.9%) (22). However, consistent with the findings of the recent literature examined, we found that women were more likely to report use of prescription opioids compared to men. In accordance with findings from LeResche et al., and Fink et al., we also found that women were more likely to report chronic health conditions including pain (17) and depression (14).

Further, this analysis demonstrates that there are differences in prescription opioid use and patterns of use between genders. Women not only had higher rates of prescription opioid use currently but also before the past 30 days compared to men, consistent with the national trends which puts them at risk for being prescribed these medications. Additionally, the literature reports pain sensitivity differed by gender with women reporting lower pain sensitivity than men (23,24) and more chronic conditions that cause pain (8) which are associated with pain pill use. Previous studies have also found men to be less likely to seek help from health professionals (25) which may be the reason women are also more likely to be prescribed and to use prescription opioids (26). In contrast to previous findings, our results also showed more women in the sample reported cancer compared to men (27); however, we found women with cancer had a significantly reduced risk of using opioids compared to men. This suggests that women using prescription opioids are using them for indications other than cancer or could reflect differential mortality from cancer. Further research is needed to investigate opioid use by cancer status.

There are a few limitations to these findings. The cross-sectional nature of the data limits the ability to establish temporality between prescription opioid use and several variables described above. Self-report of prescription opioid use only was assessed; without information regarding misuse or dependence. However, strengths of this analysis include use of a community based sample in examining gender differences and prescription opioid use. We contribute to the literature by providing data from a large sample that addressed risks for both lifetime and 30 day use.

CONCLUSION

Only 8 recent studies have been published that cover gender differences related to prescription opioid use. Findings from the literature and our data suggest women are more likely to use prescription opioids compared to men. There is limited information on gender differences in opioid use risk factors and outcomes and more studies focused on this aspect are warranted.

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Key points

- There is limited research focusing on gender differences and opioid use; current research has primarily been conducted in North America.
- This research confirmed the importance of depression among women, cancer among men.
- Similar to the recent literature, stratification by gender identified woman to be more likely to report prescription opioid use compared to men (54.9% vs 42.2%) in a community sample.
- Prevalence of back pain and cancer were higher among women, further significant risk factors for non-current opioid use includes history of back pain and cancer whereas risk factors of current prescription use include doctor visits.

Table 1

Recently published literature on gender differences in prescription opioid use

Citation	Title	Aim	Method	Sample	Source	Findings
Scoping reviews						
Graziani and Nisticò June 2016	Gender difference in prescription opioid abuse: a focus on oxycodone and hydrocodone	Focus on literature that analyzed gender differences in pharmacokinetic and pharmacodynamic effects of oxycodone and hydrocodone	Review (1995–2015)	N/A	PubMed	Oxycodone and hydrocodone pharmacokinetic and pharmacodynamic effects did not differ by gender.
Hensing et al., April 2016	Misuse of prescription opioid medication among women: a scoping review	Examine risks for prescription opioid misuse among women with pain and trauma	Review (1990–2014)	N/A	MEDLINE, PsychINFO, etc.,	Identifies 57 articles that identified subgroups of women including victims of violence and trauma who are at risk for prescription opioid misuse.
Clinic based study						
Bawor et al., Nov. 2015	Sex differences in substance use, health, and social functioning among opioid users receiving methadone treatment: a multicenter cohort study	Evaluate sex differences in substance use, health, social functioning and health among those receiving methadone treatment	Cohort	N=503	Genetics of Opioid Addiction research program	Women had physical and psychological problems, family history of psychiatric illness, and obtained opioids through a physician more often than men while men had higher rates of smoking and cannabis use.
Manubay et al., Jan. 2016	Sex differences among opioid-abusing chronic pain patients in a clinical trial	Examine sex differences in demographic and behavioral attributes of patients with chronic pain and opioid abuse	Cross-sectional	N= 162	Outpatient study at New York State Psychiatric Institute	Women reported more psychiatric comorbidities and pain than men while men reported more deviant behaviors.
Population based study						
Evans et al., Oct. 2015	Gender differences in mortality among treated opioid dependent patients	Assess gender differences in characteristics, mortality, and risk factors of death among individuals who are opioid depended	Retrospective cohort	N=20,758	California Outcomes Monitoring System	Women had an increased risk of mortality compared to men. Concurrent meth/cocaine use was a risk factor for women while employment was a protective factor for men.
Fink et al., Aug. 2015	Patterns of major depression and nonmedical use of prescription opioids in the united states	Examine how demographics and substance use differs among individuals with major depressive episodes or opioid misuse	Cross-sectional	N=113,665	National Survey on Drug Use and Health (NSDUH)	Women reported more major depressive episodes and comorbid misuse of opioids compared to men who reported misuse alone
Gladstone et al., Nov. 2015	Geographic variations in prescription opioid dispensations and deaths among women and men in British Columbia, Canada	Examine the association between opioid dispensation and prescription opioid related deaths in British Columbia, Canada	Ecological	N= 1,172	British Columbia PharmaNet	Men compared to women were more likely to die from pills not prescribed to them (71% vs 46 %)
LeResche et al., July 2015	Sex and age differences in global pain status among patients using opioids	Characterize pain status among chronic opioid therapy users stratifying by sex and age	Cross-sectional	N=2,163	Consortium to Study Opioid Risk Trends	Women had worse pain status compared to men among those receiving chronic opioid therapy.

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Citation	Title	Aim	Method	Sample	Source	Findings
	long term for chronic non-cancer pain					Young and middle aged women were at highest risk for poor pain levels than older women.

Table 2

Variables used and how variables were coded in the current community based analyses

Demographics	Health conditions	Access to healthcare	Substance use
Age (continuous) Gender (male/female)	Have you ever been told you had, or have you ever had a problem with <i>depression</i> ? (yes/no)	Have you seen a doctor for any reason in the last 6 months? (yes/no)	Alcohol within the last 30 days: Have you had more than (4 for men, 3 for women) drinks like beer, wine, or liquor in a single day? (yes/no)
Race (black/white/other) Educational attainment (12 years />12 years)	Have you ever been told you had, or have you ever had a problem with <i>back pain</i> ? (yes/no) Have you ever been told you had, or have you ever had a problem with <i>cancer</i> ? (yes/no)	How many times have you been to the ED in the last 6 months for your own injury, illness, or condition? (yes/no)	Prescription opioid use: Have you ever used prescription pain medication like Vicodin®, Oxycodone, codeine, Demerol®, morphine, Percocet®, Darvon® ? If yes, they were asked if they used prescription pain medications in the last 30 days?" (never user/lifetime not in past 30 days/past 30 day use)

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Table 3

Characteristics of HealthStreet members stratified by gender (N=8,470)

Characteristics	Total (n=8,470) n (%)	Men (n=3,510) n (%)	Women (n=4,960) n (%)	p value
Mean Age (±SD) :	43.6 (16.2)	43.6 (16.1)	43.6 (16.3)	.9874
Race:				
Caucasian	2689 (31.8)	1044 (29.8)	1645 (33.2)	
Black	5198 (61.5)	2210 (63.1)	2988 (60.3)	.0031
Other	571 (6.8)	251 (7.2)	320 (6.5)	
Education :				
12 years	5078 (60.0)	2275 (64.8)	2803 (56.5)	<.0001
>12 years	3392 (40.1)	1235 (35.2)	2157 (43.5)	
Hx of depression:	2217 (27.5)	757 (21.6)	1560 (31.6)	<.0001
Hx back pain:	3689 (43.6)	1380 (39.4)	2309 (46.6)	<.0001
Hx of cancer:	672(8.0)	192 (5.5)	480 (9.7)	<.0001
ED visit (past 6 months):	2631 (32.6)	956 (28.9)	1675 (35.2)	<.0001
Doctor visit (past 6 months):	5636 (66.5)	2052 (58.5)	3584 (72.3)	<.0001
Binge drinking (past 30 days):	1990 (23.5)	1038 (29.6)	952 (19.2)	<.0001
Prescription opioid use:				
Never	4267 (50.4)	2030 (57.8)	2237 (45.1)	<.0001
Lifetime, not past 30 days	3042 (35.9)	1076 (30.7)	1966 (39.6)	
Past 30 days	1161 (13.7)	404 (11.5)	759 (15.3)	

Note: P value= P value of chi-square or t-test

Adjusted odds ratios for the association between reported Rx opioid use and risk factors among HealthStreet members (n=8,470)

Table 4

Characteristic	Adjusted odds ratio for lifetime use of Rx use (n=3,042)	Adjusted odds ratio for past 30 day use of Rx opioids (n=1,161)		
	AOR	95% CI	AOR	95% CI
Age :	1.01	1.01, 1.02**	1.02	1.01, 1.02**
Gender:				
Men	-	-	-	-
Women	1.46	1.31, 1.62**	1.34	1.15, 1.56*
Race:				
Other	-	-	-	-
Black	0.72	0.59, 0.88*	1.27	0.92, 1.76
White	1.48	1.20, 1.82*	1.51	1.08, 2.12*
Education:				
12 years	-	-	-	-
>12 years	1.42	1.28, 1.58**	1.13	0.97, 1.31
Hx of depression:				
No depression	-	-	-	-
Depression	1.52	1.34, 1.71**	1.91	1.63, 2.23**
Hx of back pain:				
No pain	-	-	-	-
Pain	1.66	1.49, 1.84**	2.85	2.45, 3.32**
Hx of Cancer:				
No cancer	-	-	-	-
Cancer	1.62	1.32, 2.00**	2.10	1.60, 2.66**
ED visit (past 6 months):				
No visit	-	-	-	-

Characteristic	Adjusted odds ratio for lifetime use of Rx use (n=3,042)		Adjusted odds ratio for past 30 day use of Rx opioids (n=1,161)	
	AOR	95% CI	AOR	95% CI
Visit	1.27	1.13, 1.43**	2.31	1.98, 2.69**
Doctor visit (past 6 months):				
No visit	-	-	-	-
Visit	1.51	1.35, 1.70**	3.66	2.97, 4.51**
Binge drinking (past 30 days):				
No alcohol use	-	-	-	-
Alcohol use	1.38	1.22, 1.56**	1.58	1.34, 1.88**

** $p < .0001$

* $p < .05$