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## Prevalence and characteristics of hospitalized adults on chronic opioid therapy

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### Abstract

**Background**—As chronic opioid therapy (COT) becomes more common, complexity of pain management in the inpatient setting increases; little is known about medical inpatients on COT.

**Objective**—To determine the prevalence of COT among hospitalized patients and to compare outcomes among these patients relative to those not receiving COT.

**Design**—Observational study of inpatient and outpatient administrative data

**Participants**—All Veterans with acute medical admissions to 129 Veterans Administration (VA) hospitals during fiscal years 2009-2011, residing in the community, and with outpatient pharmacy use.

**Measurements**—We defined COT as 90 or more days of opioids prescribed in the 6 months prior to hospitalization. Patient characteristics included demographic variables and major comorbidities; outcomes included 30-day readmission and death during hospitalization or within 30 days, with associations ascertained using multivariable logistic regression.

**Results**—Of 122,794 hospitalized Veterans, 31,802 (25.9%) received COT. These patients differed from comparators in age, sex, race, residence, and presence of chronic non-cancer pain, COPD, complicated diabetes, cancer, and mental health diagnoses including PTSD. After adjustment for demographic factors, comorbidities, and admission diagnosis, COT was associated

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with hospital readmission (odds ratio [OR]: 1.15, 95% confidence interval [95% CI]: 1.10-1.20) and death (OR: 1.19, 95% CI 1.10-1.29).

**Conclusions**—COT is common among medical inpatients; patients on COT differ from patients without COT beyond dissimilarities in pain and cancer diagnoses. Occasional and chronic opioid use are associated with increased risk of hospital readmission, and COT is associated with increased risk of death. Additional research relating COT to hospitalization outcomes is warranted.

### Keywords

hospital medicine; prescription drug abuse; chronic pain; outcomes; veterans

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## INTRODUCTION

Recent trends show a marked increase in outpatient use of chronic opioid therapy (COT) for chronic non-cancer pain (CNCP)<sup>1,2</sup> without decreases in reported CNCP,<sup>3</sup> raising concerns about the efficacy and risk to benefit ratio of opioids in this population.<sup>4-8</sup> Increasing rates of outpatient use likely are accompanied by increasing rates of opioid-exposure among patients admitted to the hospital. To our knowledge there are no published data regarding the prevalence of COT during the months preceding hospitalization.

Opioid use has been linked to increased ER utilization<sup>9,10</sup> and emergency hospitalization,<sup>11</sup> but associations between opioid use and inpatient metrics (e.g. mortality, readmission) have not been explored. Further, lack of knowledge about the prevalence of opioid use prior to hospitalization may impede efforts to improve inpatient pain management and satisfaction with care. While there is reason to expect that strategies to safely and effectively treat acute pain during the inpatient stay differ between opioid-naïve patients and opioid-exposed patients, evidence regarding treatment strategies is limited.<sup>12-14</sup> Opioid pain medications are associated with hospital adverse events, with both prior opioid exposure and lack of opioid use as proposed risk factors.<sup>15</sup> A better understanding of the prevalence and characteristics of hospitalized COT patients is fundamental to future work to achieve safer and more effective inpatient pain management.

The primary purpose of this study is to determine the prevalence of prior COT among hospitalized medical patients. Additionally, we aim to characterize inpatients with occasional and chronic opioid therapy prior to admission in comparison to opioid-naïve inpatients, as differences between these groups may suggest directions for further investigation into the distinct needs or challenges of hospitalized opioid-exposed patients.

## METHODS

We used inpatient and outpatient administrative data from the Department of Veterans Affairs (VA) Healthcare System. The primary data source to identify acute medical admissions was the VA Patient Treatment File, a national administrative database of all inpatient admissions, including patient demographic characteristics, primary and secondary diagnoses (using International Classification of Diseases, Ninth Revision, Clinical

Modification [ICD-9-CM], codes), and hospitalization characteristics. Outpatient pharmacy data were from VHA Pharmacy Prescription Data files. VA Vital Status File provided dates of death.

We identified all first acute medical admissions to 129 VA hospitals during fiscal years (FYs) 2009-2011 (October 2009 to September 2011). We defined first admissions as the initial medical hospitalization occurring following a minimum 365-day hospitalization-free period. Patients were required to demonstrate pharmacy use by receipt of any outpatient medication from VA on two separate occasions within 270 days preceding the first admission, to avoid misclassification of patients who routinely obtained medications from a non-VA provider. Patients admitted from extended care facilities were excluded.

We grouped patients by opioid-use status based on outpatient prescription records: 1) no opioid use, defined as no opioid prescriptions in the 6 months prior to hospitalization; 2) occasional opioid use, defined as patients who received any opioid prescription during the 6 months prior, but did not meet definition of chronic use; and 3) chronic opioid therapy, defined as 90 or more days' supply of opioids received within 6 months preceding hospitalization. We did not specify continuous prescribing. Opioids included in the definition were codeine, dihydrocodeine, fentanyl (mucosal and topical), hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, oxymorphone, pentazocine, propoxyphene, tapentadol, and tramadol.<sup>16,17</sup>

We compared groups by demographic variables including age, sex, race, income, rural vs. urban residence (determined from Rural-Urban Commuting Area [RUCA] codes), region based on hospital location; overall comorbidity using the Charlson Comorbidity Index (CCI),<sup>18</sup> and ten selected conditions to characterize comorbidity (Appendix A). These ten conditions were chosen based on probable associations with chronic opioid use or high prevalence among hospitalized Veterans.<sup>9,19,20</sup>

We used a chronic non-cancer pain definition based on ICD-9 codes.<sup>9</sup> This definition did not include episodic conditions such as migraine<sup>2</sup> or a measure of pain intensity.<sup>21</sup> All conditions were determined from diagnoses coded during any encounter in the year prior to hospitalization, exclusive of the first (i.e. index) admission. We also determined the frequency of palliative care use, defined as presence of ICD-9 code V667 during index hospitalization or within the past year. Patients with palliative care use (N=3070) were excluded from further analyses.

We compared opioid use groups by baseline characteristics using the Chi-square statistic to determine if the distribution was non-random. We used ANOVA to compare hospital length of stay between groups. We used the Chi-square statistic to compare rates of four outcomes of interest: intensive care unit (ICU) admission during the index hospitalization, discharge disposition other than home, 30-day readmission rate, and in-hospital or 30-day mortality.

To assess the association between opioid-use status and the four outcomes of interest, we constructed two multivariable regression models; the first was adjusted only for admission diagnosis using the Clinical Classification Software (CCS)<sup>22</sup> and the second adjusted for demographics, CCI, and the ten selected comorbidities in addition to admission diagnosis.

The authors had full access to and take full responsibility for the integrity of the data. All analyses were conducted using SAS® statistical software version 9.2 (Cary, NC). The study was approved by the University of Iowa Institutional Review Board and the Iowa City VA Health Care System Research and Development Committee.

## RESULTS

### Patient demographics

Demographic characteristics of patients differed by opioid-use group (Table 1). Hospitalized patients who received COT in the six months prior to admission tended to be younger than their comparators, more often female, white, have a rural residence, and live in the South or West.

### Prevalence of opioid use

Among the cohort (N=122,794) of hospitalized Veterans, 66,899 (54.5%) received no opioids from the VA during the 6 month period prior to hospitalization; 31,802 (25.9%) received COT in the 6 months prior to admission. An additional 24,093 (19.6%) had occasional opioid therapy (Table 1). A total of 257,623 opioid prescriptions were provided to patients in the six-month period prior to their index hospitalization. Of these, 100,379 (39.0%) were for hydrocodone, 48,584 (18.9%) for oxycodone, 36,658 (14.2%) for tramadol, and 35,471 (13.8%) for morphine. These four medications accounted for 85.8% of total opioid prescriptions. (Appendix B)

Among the COT group 3,610 (11.4%) received 90 days, 10,110 (31.8%) received between 91 and 179 days, and 18,082 (56.9%) patients received equal to or greater than 180 days supplied in the prior 6 months (Appendix C).

Among the subset of patients with cancer (metastatic and non-metastatic, N=26,944), 29.6% were prescribed COT, and 23.3% had occasional opioid use. Among the subset of patients with CNCP (N=64,453), 37.1% were prescribed COT, and 23.0% had occasional opioid use.

### Comorbid conditions

Compared to patients not receiving opioids, a larger proportion of patients receiving both occasional and chronic opioids had diagnoses of cancer and of CNCP. Diagnoses more common in COT patients included COPD, complicated diabetes, PTSD, and other mental health disorders. In contrast, COT patients were less likely than no-opioid and occasional opioid patients to have heart failure (HF), renal disease, and dementia. Palliative care was used by 2.1% of patients in the no-opioid group, and 3.2% of patients in the COT group (Table 1). Renal disease was most common among the occasional use group.

### Unadjusted hospitalization outcomes

Unadjusted hospitalization outcomes differed between opioid-exposure groups (Table 2). Patients receiving occasional or chronic opioids had shorter length of stay and lower rates of non-home discharge than did patients without any opioid use. The rate of death during

hospitalization or within 30 days did not differ between groups. The occasional use and COT groups had higher 30-day readmission rates than did the no-use group.

### Multivariable models

In the fully adjusted multivariable models, opioid exposure (in the form of either chronic or occasional use) had no significant association with ICU stay during index admission or non-home discharge (Table 3). Both the occasional opioid use and COT groups were more likely to experience 30-day hospital readmission, a relationship that remained consistent across the partially and fully adjusted models. The occasional opioid use group saw no increased mortality risk. In the model adjusted only for admission diagnosis, COT was not associated with increased mortality risk. When additionally adjusted for demographic variables, CCI, and selected comorbidities, however, COT was associated with increased risk of death during hospitalization or within 30 days (OR 1.19, 90% CI 1.10-1.29).

## DISCUSSION

This observational study is, to our knowledge, the first to report prevalence of and characteristics associated with prior opioid use among hospitalized medical patients. The prevalence of any opioid use and of COT was substantially higher in this hospitalized cohort than reported in outpatient settings. The prevalence of any opioid use during one year (FY 2009) among all Veterans with VA primary care use was 26.1%.<sup>23</sup> A study of incident prescribing rates among Veterans with new diagnoses of non-cancer related pain demonstrated 11% received an opioid prescription within one year.<sup>24</sup> Using a definition of 90 consecutive prescription days to define COT, Dobscha *et al*<sup>25</sup> found that 5% of Veterans with persistent elevated pain intensity and no previous opioid prescriptions subsequently received COT within 12 months. The high prevalence we found likely reflects cumulative effects of incident use as well as an increased symptom burden in a population defined by need for medical hospitalization.

While a Veteran population may not be generalizable to a non-Veteran setting, we do note prior studies reporting prevalence of any opioid use in outpatient cohorts (in 2000 and 2005) between 18-30%, with higher rates among women and patients over 65 years of age.<sup>1,2</sup>

Our work was purposefully inclusive of cancer patients, in order that we might assess the degree to which cancer diagnoses accounted for prior opioid use in hospitalized patients. Surprisingly, the rate of COT for patients with cancer was lower than that for patients with CNCP, perhaps reflecting that a cancer condition defined in administrative data may not constitute a pain-causing disease.

Recognition of the prevalence of opioid therapy is important as we work to understand and improve safety, satisfaction, utilization, and long-term health outcomes associated with hospitalization. Our finding that over half of medical inpatients have pre-existing CNCP diagnoses and a not entirely overlapping proportion has prior opioid exposure implies a need for future work to refine expectations and strategies for inpatient management, potentially tailored to prior opioid use and presence of CNCP.

A recent Joint Commission sentinel event alert<sup>26</sup> highlights opioid adverse events in hospital and identifies both lack of previous opioid therapy and prior opioid therapy as factors increasing risk. ICU admission during the hospital stay may reflect adverse events such as opioid-induced respiratory depression; in our study, patients with no opioid use prior to admission were more likely to have an ICU stay, although the effect was small. One might speculate that clinicians, accustomed to treating pain in opioid-exposed patients, are using inappropriately large starting dosages of narcotics for inpatients without first assessing prior opioid exposure. Another possible explanation is that patients on COT are admitted to the hospital with less severe illness, potentially reflecting functional, social, or access limitations that compromise ability to manage illness in the outpatient setting. More detailed comparison of illness severity is beyond the scope of the present work.

Patient satisfaction with pain management is reflected in two of the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) questions, and is publically reported.<sup>27</sup> HCAHPS results also figure in the formula for the Centers for Medicare and Medicaid Services (CMS) value-based purchasing.<sup>28</sup> Preadmission pain is predictive of postoperative pain<sup>29,30</sup> and may shape patient expectations; how preadmission opioid use modulates non-surgical pain and satisfaction with management in the medical inpatient remains to be studied. The high prevalence of prior COT underscores the importance of understanding characteristics of patients on COT, and potential differences and disparities in pain management, when designing interventions to augment patient satisfaction with pain management.

While the age distribution and patterns of comorbidities differed between the opioid use groups, opioid therapy remained a small but significant predictor of hospital readmission; this association was independent of CNCP diagnosis. Functional outcomes are recognized as important measures of efficacy of outpatient pain management strategies<sup>31</sup> with some evidence that opioids are associated with worse functioning.<sup>32,33</sup> Functional limitations, as well as inadequately or inappropriately treated pain, may drive both admissions and readmissions. Alternately, COT may be a marker for unmeasured factors which increase a patient's risk of returning to the hospital. Further work is needed to elucidate the relationship between COT and health care utilization associated with the inpatient stay.

Our finding that patients on COT have an increased mortality risk is concerning, given the rapid expansion in use of these medications. While pain is increasingly prevalent towards end of life,<sup>34</sup> we did not observe an association between either CNCP (data not shown) or occasional opioid use and mortality. COT may complicate chronic disease through adverse drug effects including respiratory depression, apnea, or endocrine or immune alteration; complex chronically ill patients with conditions such as COPD, heart failure (HF), or diabetes may be particularly susceptible to these effects. Incident use of morphine is associated with increased mortality in acute coronary syndrome and HF,<sup>35,36</sup> we are not aware of any work describing the relationship between prior opioid use and incident use during hospitalization in medical patients.

## Limitations

Our work focuses on hospitalized Veterans, a population that remains predominately male, limiting generalizability of the findings. Rates of mental health diagnoses and PTSD, associated with CNCP and COT,<sup>24,37</sup> are higher in this population than would be expected in a general hospitalized population. Because our outcomes included readmission and our definition of opioid exposure was designed to reflect outpatient prescribing, we included only patients without recent hospitalization. Therefore, our results may not be generalizable to patients with frequent and recurring hospitalization.

Our definition of opioid exposure depended on pharmacy dispensing records; we are not able to confirm if Veterans were taking the medications as prescribed. Further, we were not able to capture data on opioids prescribed by non-VA providers, which may have led to underestimation of prevalence.

Our definitions of COT and CNCP are imperfect, and should be noted when comparing to other studies. Because we did not specify continuous 90-days prescribing, we may have misclassified occasional opioid therapy as COT in comparison to other authors. That continuous prescribing is equivalent to continuous use assumes that patients take medications exactly as prescribed. We used occasional opioid therapy as a comparison group, and detailed the distribution of days prescribed among the COT group (Appendix C), to augment interpretability of these results. Our CNCP diagnosis was less inclusive than others,<sup>2</sup> as we omitted episodic pain (e.g. migraine and sprains) and HIV-related pain. As COT for CNCP conditions lacks a robust evidence base,<sup>38</sup> defining pain diagnoses using administrative data to reflect conditions for which COT is used in a guideline concordant way remains difficult.

Lastly, differences observed between opioid use groups may be due to an unmeasured confounder not captured by the variables we included. Specifically, we did not include other long-term outpatient medications in our models; it is possible that COT is part of a larger context of inappropriate prescribing, rather than a single-medication effect on outcomes studied.

## Conclusion

Nearly 1 in 4 hospitalized Veterans has current or recent COT at time of hospital admission for non-surgical conditions; nearly half had been prescribed any opioids. Practitioners designing interventions to improve pain management in the inpatient setting should account for prior opioid use. Patients who are on COT prior to hospitalization differ in age and comorbidities from their counterparts who are not on COT. Further elucidation of differences between opioid use groups may help providers address care needs during the transition to post-hospitalization care. CNCP diagnoses and chronic opioid exposure are different entities and cannot serve as proxies in administrative data. Additional work on utilization and outcomes in specific patient populations may improve our understanding of the long term health effects of chronic opioid therapy.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

Baseline characteristics of hospitalized Veterans by opioid exposure status during 6 months preceding hospitalization (N=122,794)

	<b>No opioids N=66,899 (54.5%)</b>	<b>Occasional opioids N=24,093 (19.6%)</b>	<b>Chronic opioids N=31,802 (25.9%)</b>
<b>Variables</b>			
Age mean (SD)	68.7 (12.8)	66.5 (12.7)	64.5 (11.5)
Age N(%)			
<=59 (reference)	15,170 (22.7)	6,703 (27.8)	10,334 (32.5)
60-65	15,076 (22.5)	5,973 (24.8)	8,983 (28.3)
66-77	17,226 (25.8)	5,871 (24.4)	7,453 (23.4)
>=78	19,427 (29.0)	5,546 (23.0)	5,032 (15.8)
Male N (%)	64,673 (96.7)	22,964 (95.3)	30,200 (95.0)
Race N (%)			
White	48,888 (73.1)	17,358 (72.1)	25,087 (78.9)
Black	14,480 (21.6)	5,553 (23.1)	5,089 (16.0)
Other	1,172 (1.8)	450 (1.9)	645 (2.0)
Unknown	2,359 (3.5)	732 (3.0)	981 (3.1)
Income <=\$20,000 N (%)	40,414 (60.4)	14,105 (58.5)	18,945 (59.6)
Rural residence N (%)	16,697 (25.0)	6,277 (26.1)	9,356 (29.4)
Region N (%)			
Northeast	15,053 (22.5)	4,437(18.4)	5,231(16.5)
South	24,083(36.0)	9,390(39.0)	12,720(40.0)
Midwest	16,000(23.9)	5,714(23.7)	7,762(24.4)
West	11,763(17.6)	4,552(18.9)	6,089(19.2)
Charlson Comorbidity Index mean (SD)	2.3(2.0)	2.6(2.3)	2.7(2.3)
Comorbidities N (%)			
Cancer (not metastatic)	11,818(17.7)	5,549(23.0)	6,874(21.6)
Metastatic cancer	866(1.3)	733(3.0)	1,104(3.5)
Chronic pain	25,748 (38.5)	14,811 (61.5)	23,894 (75.1)
COPD	20,750(31.0)	7,876(32.7)	12,117(38.1)
Diabetes, complicated	10,917(16.3)	4,620(19.2)	6,304(19.8)
Heart failure	14,267(21.3)	5,035(20.9)	6,501(20.4)
Renal disease	11,311(16.9)	4,586(19.0)	4,981(15.7)
Dementia	2,180(3.3)	459(1.9)	453(1.4)
Mental health other than PTSD	33,390(49.9)	13,657(56.7)	20,726(65.2)
PTSD	7,216(10.8)	3,607(15.0)	5,938(18.7)
Palliative care use N(%)	1,407(2.1)	639(2.7)	1,024(3.2)

All comparisons were significant at  $p < .0001$  except for Heart Failure ( $p = .0055$ ).

COPD: Chronic Obstructive Pulmonary Disease; PTSD: Post Traumatic Stress Disorder.

**Table 2**

Unadjusted comparison of hospitalization characteristics and outcomes

	<b>No opioids N=65,492</b>	<b>Occasional opioids N=23,454</b>	<b>Chronic opioids N=30,778</b>	
Hospital length of stay, days, mean (SD)	4.7 (5.1)	4.5 (4.8)	4.5 (4.8)	.0003
ICU stay N(%)	10,281 (15.7)	3,299 (14.1)	4,570 (14.9)	<.0001
Non-home discharge N(%)	2,944 (4.5)	997 (4.3)	1,233 (4.0)	0.0020
30-day readmission N(%)	9,023 (13.8)	3,629 (15.5)	4,773 (15.5)	<.0001
Death during hospitalization or within 30 days N(%)	2,532 (3.9)	863 (3.7)	1,191 (3.9)	0.4057

Patients with palliative care use during hospitalization or 1 year prior to hospitalization were excluded from analysis for all outcomes.

ICU: Intensive Care Unit

**Table 3**

Association of prior opioid use with hospitalization outcomes

	Occasional opioid use		Chronic opioid therapy	
	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
ICU stay	0.94 (0.90, 0.99)	0.95 (0.91, 1.00)	1.00 (0.96, 1.04)	1.01 (0.97, 1.05)
Non-home discharge	0.92 (0.85, 0.99)	0.97 (0.90, 1.05)	0.85 (0.80, 0.92)	0.95 (0.88, 1.03)
30-day readmission	1.14 (1.09, 1.19)	1.14 (1.09, 1.19)	1.14 (1.10, 1.19)	1.15 (1.10, 1.20)
Death during hospitalization or within 30 days	0.96 (0.88, 1.04)	1.04 (0.95, 1.13)	0.96 (0.90, 1.04)	1.19 (1.10, 1.29)

Patients with palliative care use were excluded from analysis of ICU stay, non-home discharge, and death during hospitalization or within 30 days. In addition to patients with palliative care use, patients who died or were transferred to another hospital were excluded from analysis of 30-day readmission.

Model 1 is adjusted for admission diagnosis based on CCS categories.

Model 2 is adjusted for admission diagnosis based on CCS categories, adjustment for age, sex race, income, rural residence, region, CCI, and comorbid conditions: cancer, metastatic cancer, chronic pain, COPD, complicated diabetes, heart failure, renal disease, dementia, mental health diagnosis other than PTSD, and PTSD.

COPD: Chronic Obstructive Pulmonary Disease; PTSD: Post Traumatic Stress Disorder.