Final Progress Report

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Stemming the Tide of Prescription Opioid-Related Morbidity among Injured Workers

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NIOSH grant: R03OH010943
Project dates: September 1, 2018 - August 31, 2021
Final report date: September 1, 2021

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List of Terms and Abbreviations

ACOEM	American College of Occupational and Environmental Medicine
AE	Adverse effects
AMDG	Agency Medical Directors Group
APS/AAPM	American Pain Society/American Academy of Pain Medicine
ASIPP	American Society of Interventional Pain Physicians
AZ	Arizona
BcA	Bias-corrected and accelerated
BLS	Bureau of Labor Statistics
CI	Confidence interval
CO	Colorado
CPS	Current Population Survey
CSTE	Council of State and Territorial Epidemiologists
DHS	Department of Health Services
DOH	Department of Health
DWC	Division of Workers' Compensation
E-code	ICD-9-CM external cause of injury code
ELF	Employed Labor Force
HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ITSA	Interrupted time series analysis
L&I	Washington State Department of Labor & Industries
Mg	Milligrams
MEDD	Morphine equivalent daily dose
MI	Michigan
NJ	New Jersey
NR	Not reported due to small cell size (≤10)
NY	New York
PMP	Prescription Monitoring Program
Q	Quarter
SC	South Carolina
UT	Utah
PI	Principal Investigator
SID	State Inpatient Databases (HCUP)
U.S.	United States
WA	Washington State
WC	Workers' compensation
WCB	Workers' Compensation Board

Abstract

Project title: Stemming the Tide of Prescription Opioid-Related Morbidity among Injured Workers

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High-risk opioid prescribing practices in workers' compensation settings are associated with excess opioid-related morbidity, longer work disability and higher workers' compensation costs. Accurate surveillance of opioid morbidity rates and demographic patterns is necessary for effective prevention planning, intervention, and evaluation. This study characterized the burden of prescription opioid-related hospitalizations among injured workers. Hospital discharge data for eight states (Arizona, Colorado, Michigan, New Jersey, New York, South Carolina, Utah, Washington) were obtained from the State Inpatient Databases, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. Injured workers were identified using payer (workers' compensation) and external cause of injury codes. There were about six times as many adverse effect hospitalizations as overdose hospitalizations, on average. State-based five-year (2010-2014) average annual rates of prescription opioid overdose/adverse effect hospitalizations among injured workers ranged from 0.3 to 1.2 events per 100,000 employed workers. Among inpatients aged 15 to 64 (age range was restricted to enhance comparability across groups), rates for injured workers ranged from 0.3 to 1.1 events per 100,000 employed workers, while rates for all inpatients ranged from 39.6 to 78.2 events per 100,000 civilian population. Estimated five-year average annual rates for men were higher than those for women. Among those hospitalized with prescription opioid overdose/adverse effects, injured workers were more likely than other inpatients to have a low back disorder diagnosis, and less likely to have a diagnosis of opioid dependence/abuse or cancer, or a fatal outcome. In the four states with estimated rates for every age category, there was a monotonic rate increase with age. Rates for injured workers aged 65 and older were two to six times the overall injured-worker rates, ranging from 1.9 to 4.4 per 100,000 employed workers. These markedly higher rates among older workers suggest that clinicians prescribing opioids to older workers should carefully assess potential risk related to physiologic changes associated with aging, as well as presence of chronic conditions, social and mental health factors, and other prescription medications. Several important barriers to accurate opioid morbidity surveillance among injured workers were identified, centering around the small number of prescription opioid-related events billed to workers' compensation. Case capture of prescription opioid overdose/adverse effects increased by about 3% when using injured worker E-codes in addition to workers' compensation as payer. First-listed diagnoses/E-codes captured about 60% of the prescription overdose/adverse effect cases that were captured when using all-listed diagnoses/E-codes. The extent to which work-related prescription opioid morbidity is not covered by workers' compensation is unknown. Among injured workers who were identified using only E-codes, workers' compensation was the primary expected payer for 67% of all hospitalizations, versus 59% when restricted to prescription opioid overdose/adverse effect hospitalizations, suggesting that workers' compensation may be somewhat less likely to cover opioid morbidity-related hospitalizations compared to other hospitalizations. In sum, this research bolsters the sparse epidemiological evidence regarding opioid-related morbidity among injured workers. Additional research is needed to further assess the degree to which workers' compensation as payer adequately identifies work-related opioid morbidity for research and surveillance purposes.

Section 1

Significant or Key Findings

Hospital discharge data for eight states (Arizona, Colorado, Michigan, New Jersey, New York, South Carolina, Utah, Washington) were used to quantify the burden of hospitalizations related to prescription opioid poisonings (overdose) and adverse effects (AE) among injured workers. Injured workers were identified using workers' compensation (WC) as payer and external cause codes. These research findings were published in Occupational and Environmental Medicine, a journal targeted to occupational medicine clinicians.

Prescription opioid overdose/AE hospitalization rates were relatively low among injured workers. State-based five-year (2010-2014) average annual crude rates of prescription opioid overdose/AE hospitalizations among injured workers ranged from 0.3 to 1.2 events per 100,000 employed workers. Among inpatients aged 15 to 64 (the age range was restricted to enhance comparability across groups), rates for injured workers ranged from 0.3 to 1.1 events per 100,000 employed workers, while rates for all inpatients ranged from 39.6 to 78.2 events per 100,000 civilian population.

There were about six times as many AE hospitalizations as overdose hospitalizations, on average. Overdose counts were too low to estimate rates for overdose and AE separately.

Rates for injured workers aged 65 and older were two to six times the overall injured-worker rates. Averaged across eight states, 28% of injured workers with prescription opioid overdose/AE hospitalizations were 55-64, and 13% were 65 and older. In the four states with estimated rates for every age category, there was a monotonic rate increase with age. Rates for injured workers aged 65 and older ranged from 1.9 to 4.4 per 100,000 employed workers.

Estimated five-year average annual rates for men were higher than those for women, for each of the six states with adequate data. However, the difference was small in some states.

Among those hospitalized with prescription opioid overdose/AE, injured workers were more likely than other inpatients to have a low back disorder diagnosis, and less likely to have a diagnosis of opioid dependence/abuse or cancer, or to have a fatal outcome. The prevalence of a low back disorder diagnosis among injured workers hospitalized with prescription opioid overdose/AE was 29.34%, compared to 8.97% for other inpatients with prescription opioid overdose/AE (P<.0005). The prevalence of an opioid dependence/abuse diagnosis among injured workers hospitalized with prescription opioid overdose/AE was 6.10%, compared to 19.43% for other inpatients with prescription opioid overdose/AE (P<.0005). The prevalence of a cancer diagnosis among injured workers hospitalized with prescription opioid overdose/AE was <1% (n<11), compared to 9.11% for other inpatients with prescription opioid overdose/AE (P<.0005). The percentage of inpatient deaths among injured workers hospitalized with prescription opioid overdose/AE was <1%, compared to 1.86% for other inpatients with prescription opioid overdose/AE (P=.001).

Several important barriers to accurate opioid morbidity surveillance among injured workers were identified*.* Despite use of a case definition that relied on both work-related external cause of injury codes (E-codes) and WC as payer, small numbers presented particular challenges. These challenges included: (1) inability to age/sex adjust rates; (2) suppression of many counts and estimates to comply with HCUP reporting restrictions; (3) 50% of states did not have enough prescription opioid overdose hospitalizations to enable reporting overdose separately from AE (the appropriateness of combining these two categories is an unresolved

point of discussion in the literature); and (4) due to small numbers, all available diagnosis and E-code fields were used, rather than the recommended practice of restriction to the lowest number of fields common to all included states and years. However, despite these challenges, many metrics were roughly similar across the eight states, demonstrating stability despite the relatively small numbers of events. Prescription opioid overdose/AE case capture increased by about 3% when using injured worker E-codes in addition to WC as payer. First-listed diagnoses/E-codes captured about 60% of the prescription opioid overdose/AE cases that were captured when using all-listed diagnoses/E-codes. The extent to which work-related prescription opioid morbidity is not covered by WC is unknown. Among injured workers 15 and older who were identified using only E-codes, WC was the primary expected payer for 67.43% of hospitalizations for any diagnosis (averaged across all eight states), compared to 59.42% when restricted to prescription opioid overdose/AE hospitalizations. These coverage levels were roughly comparable to previous estimates of WC coverage of industrial injury hospitalizations, and suggested that WC may be somewhat less likely to cover opioid morbidity-related hospitalizations compared to other hospitalizations.

Translation of Findings

Although this study did not result in a product directly transferable to workplaces, the primary translation goal was to quantify rates and trends of opioid-related morbidity among injured workers, filling important gaps in the epidemiological evidence. This information can be used to motivate and support investment in policy changes and prevention opportunities targeted at preventing prescription opioid-related morbidity among injured workers. This study involved ongoing collaboration with the Washington State Department of Labor and Industries (L&I).

Research Outcomes/Impact

There are several important potential outcomes of this research. This research has contributed to an understanding of the strengths and limitations of using hospital discharge data to identify opioid overdose/AE among injured workers, which may be valuable in planning and evaluation of prevention programs, improved case ascertainment, and identification of high-risk populations and emerging opioid morbidity patterns. We identified several barriers to accurate opioid morbidity ascertainment, which will help guide future researchers in feasible and appropriate uses of hospital discharge data. Further, we estimated opioid-related morbidity among injured workers, for whom population-based estimates are almost nonexistent. Accurate surveillance of opioid morbidity rates and demographic patterns is necessary for effective prevention. Additional research is needed to further assess the degree to which WC as payer adequately identifies work-related opioid morbidity for research and surveillance purposes.

This study also documented gender and age-related disparities across multiple states. Specifically, although observed rates of prescription opioid overdose/AE hospitalizations were relatively low for injured workers, rates for injured workers aged 65 and older were two to six times the overall rates. These findings suggest that clinicians prescribing opioids to older workers should carefully assess potential risk related to physiologic changes associated with aging, as well as presence of chronic conditions, social and mental health factors, and other prescription medications. Therefore, these research findings were published in *Occupational and Environmental Medicine*, a journal targeted to occupational medicine clinicians.

In sum, this research bolsters the sparse epidemiological evidence regarding opioid-related morbidity among injured workers and will support implementation of effective policies targeted at stemming the rising tide of prescription opioid-related morbidity that constitutes an unacceptable and preventable iatrogenic burden on injured workers, WC systems, and society at large.

Section 2

Scientific Report

Background

It is well-documented that changes in opioid prescribing practices over the past two decades have resulted in a national epidemic of opioid overdoses and poisoning deaths.[1-4] The national rate of hospitalizations involving opioid overuse increased more than 150% from 1993 to 2012.[5] By 2006, U.S. unintentional poisoning deaths accounted for 20% of years of potential life lost before age 65,[6] and Washington State's drug-related death rate surpassed that from motor vehicle crashes that same year.[7] Injured workers, many of whom experience chronic pain, have been exposed to dramatic temporal changes in opioid prescribing practices.[8,9] Opioid prescriptions, particularly early high-dose prescriptions, are associated with longer work disability.[10-12] Yet few studies have assessed the impact of opioid policies on health and disability outcomes among injured workers.[13]

Both implementation and rigorous evaluation of policies intended to stem the tide of opioid-related morbidity and mortality are in their infancy.[13] Until the latter 1990s, use of long-term opioid therapy for chronic non-cancer pain was essentially prohibited in most states. Opioid policies were later liberalized in many states,[14] followed by dramatic increases in average morphine equivalent daily doses (MEDD), and a rise in prescription medication deaths.[9,15] Concomitantly, state and national opioid prescribing guidelines began to emerge, and were focused on best practices such as use of a single physician and/or single pharmacy, opioid treatment agreements, and comprehensive patient risk evaluation at treatment onset. However, none included specific opioid dosing guidance. There is now increasingly compelling evidence of a relationship between higher opioid doses and morbidity/mortality.[16-20] Per the CDC, the 20% of patients prescribed high-dose opioids (≥100 mg MEDD) account for 80% of opioid overdoses.[2] Patients on long-term opioids may experience a decrease in analgesic efficacy but remain at risk for respiratory depression and sleep apnea.[21] A population-based study in a large health plan in Washington State demonstrated a 9-fold increase in overdose risk at doses ≥100 mg MEDD relative to <20 mg.[17] Population-based research is sparse, but several studies indicate that men are at higher risk than women for escalation to high-dose opioid therapy[22] and opioid-related mortality.[22-25] Middle-aged and older adults have the highest risk of prescription opioid-related mortality.[23-25] The causes of opioid-related morbidity and the impact of opioid policies may differ for injured workers, e.g., injured workers have a relatively low rate of alcohol or illicit drug use in association with prescription opioid-related deaths.[9] A systematic review found that the mean opioid dose prescribed in WC settings was higher than other settings,[26] potentially due to WC's first-dollar prescription coverage, prevalence of chronic musculoskeletal disorders, and/or chronic work disability.[12,26] A recent Manitoba study found that, compared with the general population, average opioid doses were rising faster for WC recipients, who were also twice as likely to be prescribed doses >120mg MEDD.[27] These key points suggest that specific high-dose prescribing guidelines could potentially reverse the epidemic proportions of unintentional poisoning deaths and severe morbidity associated with opioid therapy.

In 2007, Washington was the first state to implement an opioid guideline with a high-dose threshold.[28] Several other states, including Colorado and Utah, have since followed suit.[28] We hypothesized that opioid guidelines have a beneficial effect on opioid-related morbidity via a direct effect on provider prescribing practices.[29] In turn, this should have a positive impact on other downstream worker outcomes, including time off work, work functioning, re-injury, and new work injuries.[10-12] A Michigan study found that long-acting opioids were an independent risk factor for the development of catastrophic WC claims (≥$100,000), with opioid use rather than

opioid cost as the major driver.[30] It has been estimated that WC covers <25% of the cost of occupational injuries and illnesses,[31] so society shares this burden, including costs associated with potential development of opioid dependence and addiction. Reducing opioid-related morbidity should mitigate the overall burden of work disability and associated costs on injured workers, their families, WC systems, broader health care systems (via cost-shifting mechanisms), and society as a whole.

Prescription opioids have been studied as both a risk factor for and a consequence of work-related injuries.[32] In the National Employer Survey, 8% of employers reported experiencing a prescription opioid-related workplace overdose incident;[33] however, overdose related to treatment of work injuries may occur at work or elsewhere. Though overdose and AE from opioid pain medications prescribed for occupational injuries may be covered by WC, courts have variably ruled in cases involving an independent intervening act breaking the chain of causation from injury to overdose (e.g., opioids inappropriately prescribed or not taken as prescribed).[34] Potential work-related scenarios include prescription opioid overdose/AE: (1) from opioids prescribed for a work injury or ensuing surgery; (2) from non-medical use of prescription opioids, subsequent to opioid prescribing for a work injury; (3) during WC-covered opioid use disorder treatment; (4) causing or concurrent with a work injury incident; or (5) during inpatient treatment/surgery for a work injury. Regardless of the specific scenario, prescription opioid-related morbidity among injured workers constitutes an unacceptable, preventable, and largely iatrogenic burden on WC, workers, and society overall.

There are significant knowledge gaps regarding prevalence of opioid-related morbidity among injured workers, in part due to the difficulty of identifying work-related events in many population-based data sets. Most states do not have a population-based WC system, inhibiting the use of state WC data to assess the burden of opioid-related morbidity on workers, or to compare findings across states. In 2005, Franklin et al.[9] first identified the emerging opioid epidemic using WC data from Washington—one of only four states with an exclusive State Fund and no private WC insurers.

Few population-based estimates of opioid-related morbidity/mortality rates among workers exist. Washington State researchers used WC data to calculate annual rates (2004-2010) of prescription opioid poisonings among workers with opioid prescriptions paid for by WC (roughly 3-5 per 10,000) and AE (roughly 9-15 per 10,000).[35] We were unable to identify other rate estimates specific to overdose resulting from prescription opioids taken consequent to work injury/illness. However, one study estimated the annual fatal drug overdose rate (not limited to opioids) in U.S. workplaces as 0.09 per 100,000 full-time equivalents (FTE) between 2011 and 2016.[36] In another study, the five-year average annual fatal opioid overdose rate among Massachusetts workers was estimated at 25.1 deaths per 100,000 workers (not restricted to employed workers or to workplace fatalities), based on death certificates.[37] Long-term accidental poisoning mortality for West Virginia injured workers with low back pain was significantly higher than for the general population (standardized mortality ratio: 1.62); 92% of these deaths involved opioid overdose.[38] Long-term drug-related mortality hazard was two to three times higher for New Mexico injured workers compensated for over seven days of lost work, compared to workers receiving only medical benefits.[39] The latter two studies assessed the general risk of work injury and associated disability on long-term opioid-related mortality (up to 17 and 19.5 years after injury, respectively), but did not assess risk related to opioids prescribed for the work injury.

Specific Aims

Aim 1: **Quantify the burden of inpatient hospitalizations due to opioid poisoning and opioid adverse effects among workers covered by WC, and describe demographics.** Calculate population-based crude and age/sex-adjusted rates of opioid morbidity for 8 states. Model temporal trends in these rates from 2003-2014.

Aim 2: **Determine whether trends in the rates of opioid-related morbidity among workers covered by WC changed after implementation of opioid prescribing guidelines with a high-dose component.** States with later—or no—implementation of similar guidelines will be used as comparators. Our *working hypothesis* is that opioid prescribing guidelines implemented in Colorado, Utah, and Washington State had measurable beneficial effects on trends in opioid-related morbidity among workers covered by WC, compared with within-state trends prior to guideline implementation, and compared with concurrent trends in comparator states without such guidelines.

The **Methodology** and **Results and Discussion** sections are organized by specific aim.

Specific Aim 1

Aim 1: **Quantify the burden of inpatient hospitalizations due to opioid poisoning and opioid adverse effects among workers covered by WC, and describe demographics.** Calculate population-based crude and age/sex-adjusted rates of opioid morbidity for 8 states. Model temporal trends in these rates from 2003-2014.

Methodology

Data source and study population. Eight distinct population-based state hospital discharge databases were used for this study. Hospital discharge data for Arizona, Colorado, Michigan, New Jersey, New York, South Carolina, Utah, and Washington State, for calendar years from 2003 through 2014, were obtained from the State Inpatient Databases (SID), Healthcare Cost and Utilization Project (HCUP).[40] These states represented diverse geographic areas and satisfied selection criteria including presence of a payer category specific to WC, and consistent and highly prevalent usage of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) external cause of injury codes (E-codes), which were required to identify adverse effects.[41] All available states with state guidelines implemented during this timeframe that addressed high-dose opioids were included (Colorado, Utah, Washington). Hospital discharges for state residents aged 15 years and over were included. Hospital discharges for persons aged 65 and older were excluded from primary payer percentage calculations and from comparisons between injured workers and the general inpatient population. In previous work with the SID, those aged 65 and older comprised under 10% of occupational injury hospitalizations but roughly half of the non-occupational injury hospitalizations.[42,43] This study did not involve identifiable human subjects, and thus did not require Institutional Review Board approval.

Data definitions. Most prior studies have focused on opioid fatalities or non-fatal overdoses, which represent a fraction of opioid-related morbidity. In this study, we included both opioid poisonings and opioid adverse effects. We used ICD-9-CM diagnoses and E-codes to define four categories of opioid morbidity (see **Table 1** for codes): (1) prescription opioid overdose, (2)

prescription opioid AE, (3) heroin overdose, and (4) heroin AE. Prescription opioids were defined as all opioids other than heroin, including methadone. The ICD-9-CM lexicon does not differentiate synthetic opioids, nor does it identify whether the opioids were obtained via prescription.

Injured workers were defined in two ways. First, persons whose hospital discharges had WC listed as primary expected payer were presumed to be injured workers. The Council of State and Territorial Epidemiologists (CSTE) uses WC as primary payer as a proxy for work-relatedness of hospitalized injuries,[44] which has been estimated to be 89% sensitive and 98% specific.[45] Second, we expanded that definition by including hospitalizations with all-listed E-codes that specifically identified work as the external cause of the hospitalization (see **Table 1** for codes).[45] Several other data definitions were based on ICD-9-CM diagnosis and/or E-codes (see **Table 1** for specific codes).

The definition of opioid dependence or abuse included all-listed diagnoses for opioid dependence (alone or in combination with other drugs), or nondependent opioid abuse. The definition of cancer—of interest because taking opioids for cancer-related pain might escalate opioid-related morbidity—included all-listed cancer diagnoses, excluding non-melanoma skin cancer. Injury hospitalizations were defined as any first-listed diagnosis contained in the injury section within the Injury and Poisoning chapter of the ICD-9-CM lexicon. Low back disorder was based on all-listed diagnoses and defined as specified for the CSTE Occupational Heath Indicator #20 (per the Guide's Table 1 on page 123; the Guide's Table 3 exclusions were not applied).[44]

Race/ethnicity was based on the HCUP uniform data element, which contains mutually exclusive race and ethnicity categories within one data element (RACE). When constructing the uniform data element from separate race and ethnicity data fields in state source data, HCUP gave ethnicity precedence over race. For this study, several race/ethnicity categories were collapsed because counts were too low to meet HCUP reporting requirements.

Table 1. Data definitions

Definitions	ICD-9-CM Codes
Opioid overdose and adverse effects (all-listed diagnoses)	
Prescription opioid overdose	
Poisoning: Opium/alkaloids unspecified	965.00
Poisoning: Methadone	965.02
Poisoning: Other opioids	965.09
Accidental poisoning: Methadone	E850.1
Accidental poisoning: Other opioids	E850.2
Prescription opioid adverse effects	
Adverse effects: Methadone	E935.1
Adverse effects: Other opioids	E935.2
Heroin overdose	
Poisoning: Heroin	965.01
Accidental poisoning: Heroin	E850.0
Heroin adverse effects	E935.0
Injured workers (all-listed E-codes; first-listed payer)	
Civilian activity done for income or pay	E000.0
Railway employee injured in railway accident	E800.0-E807.0 (only if fifth digit=0)
Watercraft crew injured in water transport accident	E830.2-E838.2 (only if fifth digit=2)
Dockers/stevedores injured in water transport accident	E830.6-E838.6 (only if fifth digit=6)
Aircraft crew injured in air transport accident	E840.2-E845.2 (only if fifth digit=2)
Ground crew injured in air transport accidents	E840.8-E845.8 (only if fifth digit=8)
Accidents involving powered vehicles used solely within buildings and premises of industrial or commercial establishments	E846
Expected payer=WC (first-listed payer only)	(payer codes for WC vary by state and year)
Opioid dependence or abuse (all-listed diagnoses)	304.0x, 304.7x, 305.5x
Cancer, excluding non-melanoma skin cancer (all-listed diagnoses)	140.x-172.x, 174.x-209.x, 230.x-234.x
Injury hospitalization (first-listed diagnosis only)	800.x-959.x
Low back disorder (all-listed diagnoses)	721.3, 721.42, 722.10, 722.32, 722.52, 722.73, 722.83, 722.93, 724.02, 724.2, 724.3, 724.6, 738.4, 739.3, 739.4, 756.11, 756.12

E-codes, ICD-9-CM external cause of injury codes; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; WC, workers' compensation.

Rates and denominators. For each of the eight included states—for injured workers and for all inpatients—we calculated five-year average annual rates of prescription opioid overdose/AE hospitalizations, along with Poisson exact 95% confidence intervals. We also calculated age and gender-specific rates where there were adequate counts. Counts were generally too low to support direct standardization. However, in previous occupational injury studies based on the SID, we found only slight and unremarkable differences between crude and age-adjusted estimates.[42,43] Employed worker denominators used to calculate rates for injured workers were based on the Bureau of Labor Statistics' Current Population Survey (CPS), using the Employed Labor Force (ELF) query system.[46] Civilian population denominators used to calculate rates for all inpatients were based on U.S. Census Bureau annual estimates.[47]

Data analysis. The percentage of hospital discharges with WC listed as primary expected payer was calculated for the prescription opioid overdose/AE hospitalization subset, and—for comparison purposes—for several other diagnostic subsets. Among persons aged 15 to 64 who were hospitalized with prescription opioid overdose/AE, we compared injured workers to other inpatients regarding prevalence of several diagnostic categories—averaging across the eight states due to small numbers. Among workers hospitalized with prescription opioid overdose/AE, we used descriptive statistics to summarize demographic characteristics, associated discharge diagnoses, and inpatient deaths. In accordance with HCUP data use requirements, data were

not reported for table cells containing fewer than 11 hospital discharges, or when reporting would enable calculation of adjacent small cell sizes. Statistical tests were two-tailed, with statistical significance defined as p≤0.05. Analyses were conducted using Stata/MP 15.1 for Windows.[48]

Research obstacles. Four data analysis elements were included in Aim 1:

1. Quantify the burden of inpatient hospitalizations due to opioid poisoning and opioid adverse effects among workers covered by WC.
2. Describe demographics for opioid poisoning and opioid adverse effects among workers covered by WC.
3. Calculate population-based crude and age/sex-adjusted rates of opioid morbidity for 8 states.
4. Model temporal trends in these rates from 2003-2014.

We encountered unanticipated obstacles to completing some of these elements, centering around the unexpectedly low number of prescription opioid-related events billed to WC (despite prior evidence of workers having elevated exposure to high-risk opioid prescribing practices in the WC system). We successfully completed Elements 1 and 2. We partially completed Element 3—we were able to calculate crude rates, but prescription opioid overdose/AE counts were too low to calculate age/sex adjusted rates as originally planned; there were numerous age/sex cells with zero or very low counts. Although we completed Element 4, this analysis was not deemed worthy of publication, due to very low annual prescription opioid overdose/AE counts, and very high variance. There was also a specific concern about the accuracy of Arizona data prior to 2008, which is described below. We begin by describing obstacles and attempts at mitigation related to the incomplete elements of this aim, and then present methodology and findings for the completed elements.

The primary obstacle involved the unexpectedly low number of prescription opioid-related events billed to WC. WC covered <1% of opioid overdose/AE events vs. 6% to 8% of traumatic injuries. The number of opioid poisonings billed to WC were too low to report for most states and years, and too low to provide a reliable numerator for rate and trend calculation. HCUP does not allow reporting of cells based on ≤10 hospital discharges. In addition, numerous sources recommend rate calculation and age/sex standardization only when there are a minimum of 20 events in the numerator, to ensure reasonable reliability.[49-52]

A second obstacle concerned the accuracy of Arizona data prior to 2008. The concern is clearly displayed in **Figure 1**, showing the very large jump in rates from 2007 to 2008, only for Arizona. We took a closer look at these data (see **Table 2**), and found that this jump was due to a large increase in use of certain E-codes beginning in 2008, particularly E935.2 (Other opioid AE) and E850.2 (Other opioid poisoning). It is not clear what accounted for this change. In 2007, 8% of all Arizona hospital discharges had any E-codes, compared to 19% in 2008. There may have been a push to add E-codes beyond emergency department cases at that time, or possibly a push to code opioid events with E-codes, but this is speculation. In years 2003 through 2007, 88.6% (2007=88.0%) of Arizona hospital discharges identified as opioid overdose/AE had any E-codes, compared to >99.9% from 2008 through 2014 (2008=99.2%).

Figure 1. Annual rates of opioid overdose/AE for all hospital discharges (not restricted to WC); denominators for rate calculations were based on U.S. Census Bureau annual estimates of the civilian population.[47]

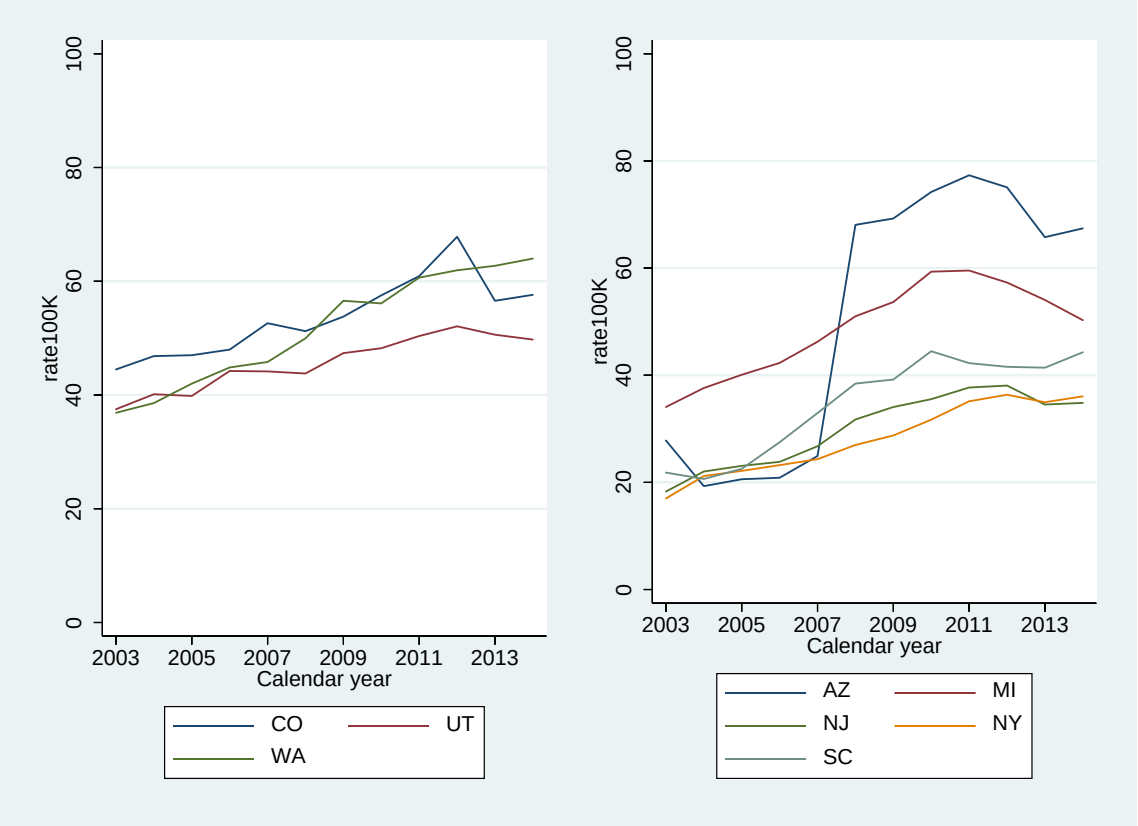


Table 2. Counts of first-listed diagnosis code or E-code (Arizona; not restricted to WC)

Code	Description	2007	2008
E850.0	Heroin poisoning	64	70
E850.1	Methadone poisoning	77	93
E850.2	Other opioid poisoning	370	616
E935.0	Heroin AE	0	0
E935.1	Methadone AE	<11	45
E935.2	Other opioid AE	201	2364
965.0x	Opioid poisonings	878	1049

Given these obstacles, we made several methodological decisions in order to address as much of Aim 1 as possible:

1. The case definition of injured workers was expanded beyond WC as payer by including hospitalizations with all-listed E-codes that specifically identified work as the external cause of the hospitalization (see **Table 1**).[45,53] This increased prescription opioid overdose/AE case capture by about 3%. Place of injury E-codes were not used, in order to maintain high specificity.
2. Due to the small numbers of events, 5-year average annual rates were calculated (as opposed to annual rates), for calendar years 2010 through 2014. This timeframe was selected for several reasons: (1) it was the most recent timeframe available to us (we

had data for 2003 through 2014); (2) it excluded the years prior to 2008, which were the years that Arizona had concerning data issues (markedly lower use of certain E-codes); and (3) new ICD-9-CM E-codes indicating work-relatedness were first introduced as of October 1, 2009 (E000.x).[54] (Note: The ICD-10-CM lexicon took effect on October 1, 2015.)

3. We used all listed diagnoses and E-codes to identify opioid overdose/AE—a more sensitive approach than using just first-listed codes.[55] First-listed diagnoses/E-codes captured about 60% of the prescription opioid overdose/AE cases that were captured when using all-listed diagnoses/E-codes. Further, because we decided to estimate 5-year annual average rates, rather than trends in annual rates, we used all available data fields (ranging 9 to 30 for diagnoses, see **Table 3**; and ranging 6 to 16 for E-codes, see **Table 4**), rather than restricting to the lowest number of each type of data field common to all included states and years.

Table 3. Actual number of diagnosis fields provided by each state data source

State	2010	2011	2012	2013	2014
Arizona	25	25	26	25	25
Colorado	30	30	30	30	30
Michigan	30	30	30	30	30
New Jersey	24	24	24	24	24
New York	15	25	25	25	25
South Carolina	15	15	15	15	15
Utah	9	9	9	9	18
Washington	25	25	25	25	25

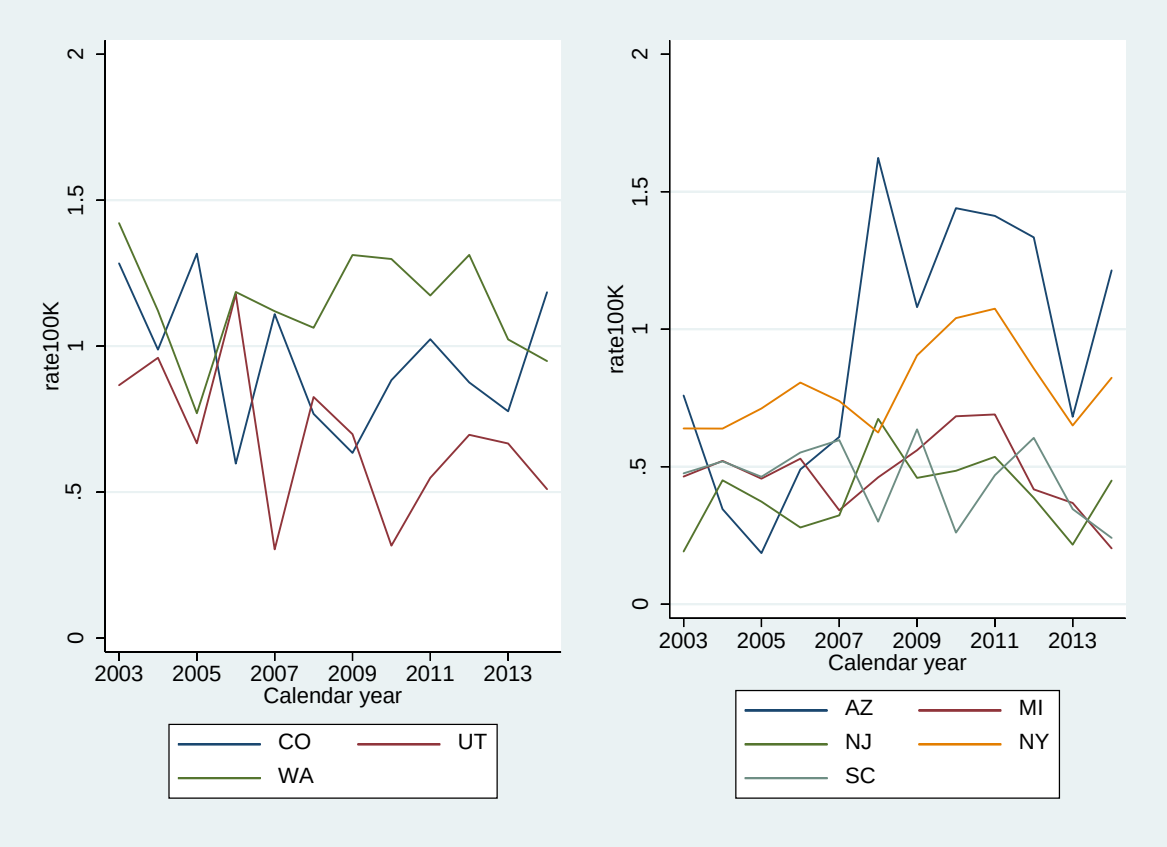
Table 4. Actual number of E-code fields provided by each state data source

State	2010	2011	2012	2013	2014
Arizona	6	6	6	6	6
Colorado	11	16	16	13	11
Michigan	10	10	9	9	9
New Jersey	9	8	10	10	10
New York	7	8	10	8	9
South Carolina	9	11	8	10	8
Utah	7	8	8	9	8
Washington	8	10	8	8	10

4. Even after applying #1, #2, and #3 above, most states still did not have enough events (N≥20) to calculate reliable prescription opioid overdose rates (see **Table 6** in the next section). Therefore, we combined opioid overdose (poisoning) and AE events into a single metric. The appropriateness of combining these two categories is an unresolved point of discussion in the literature.[35,56,57] ICD-9-CM coding guidance defines drug poisoning as resulting from errors made in drug prescribing or administration, including the wrong substance or dose, and defines AE as resulting from correct prescribing and proper administration of the correct drug.[54] An overdose resulting from a correctly prescribed/administered dose might be classified as either overdose or AE, which lends some support to combining these two categories for this study.[35]

5. Counts were generally too low to support age/sex adjustment or direct standardization, and we therefore reported only crude rates (Element 3 of Aim 1). However, in previous occupational injury studies based on the SID, we found only slight and unremarkable differences between crude and age-adjusted estimates.[42,43]
6. We calculated and graphed annual rates to assess trends (Element 4 of Aim 1), but did not publish them, due to unreliably low counts and high variance (see **Figure 2**). Methodological details differed for these annual rate calculations (vs. 5-year annual average rates), because assessing trends required stable methods over time. First, the E-code E000.0 was excluded from the injured worker definition, because it did not exist prior to October 1, 2009. Second, the number of diagnosis and E-code data fields used for ascertainment were restricted to the minimum number available across all states and all years from 2003 through 2014 (i.e., 9 diagnosis fields and 5 E-code fields).

Figure 2. Annual rates of opioid overdose/AE-related hospital discharges among injured workers; denominators for rate calculations were based on the Bureau of Labor Statistics' Current Population Survey (CPS), using the Employed Labor Force (ELF) query system.[46]



Results and Discussion

Among inpatients aged 15 to 64 (not restricted to injured workers), WC was the primary expected payer for less than 1% of prescription opioid overdose/AE hospitalizations, averaged across eight states (0.22% of overdose hospitalizations and 1.27% of AE hospitalizations). In contrast, WC was listed as the primary expected payer for roughly 6% of injury hospitalizations and roughly 5% of hospitalizations with a low back disorder diagnosis (**Table 5**). Among injured workers 15 and older who were identified using only E-codes, WC was the primary expected payer for about two-thirds (67.43%) of hospitalizations for any diagnosis, and for 59.42% when restricted to prescription opioid overdose/AE hospitalizations, averaged across all eight states.

Table 5. Percentage of hospitalizations with workers' compensation listed as primary expected payer, by diagnosis subset and state (among inpatients aged 15-64, not restricted to injured workers)

Diagnosis subset	AZ	CO	MI	NJ	NY	SC	UT	WA	8 states[a]
Prescription opioid overdose/adverse effect	0.58	0.86	0.37	0.62	1.10	0.40	0.47	1.13	0.75
Opioid dependence/abuse diagnosis	0.55	0.60	0.43	0.74	0.55	NR	NR	1.48	0.66
Cancer diagnosis	NR	NR	0.50	0.95	1.03	NR	NR	0.58	0.71
Low back disorder diagnosis	3.37	4.14	3.11	5.72	6.83	2.77	4.31	5.04	4.67
Injury hospitalization	4.98	6.15	4.90	6.64	6.67	4.54	7.33	8.45	6.16

AZ, Arizona; CO, Colorado; MI, Michigan; NJ, New Jersey; NR, not reported due to small cell size (≤10), in accordance with HCUP guidance; NY, New York; SC, South Carolina; UT, Utah; WA, Washington State.
[a] Percentages in the 8-states column were averaged across all eight states, including cells not separately reported.

The prevalence of an opioid dependence/abuse diagnosis among injured workers hospitalized with prescription opioid overdose/AE was 6.10%, compared to 19.43% for other inpatients with prescription opioid overdose/AE (P<.0005). The prevalence of a low back disorder diagnosis among injured workers hospitalized with prescription opioid overdose/AE was 29.34%, compared to 8.97% for other inpatients with prescription opioid overdose/AE (P<.0005). The prevalence of a cancer diagnosis among injured workers hospitalized with prescription opioid overdose/AE was <1% (n<11), compared to 9.11% for other inpatients with prescription opioid overdose/AE (P<.0005). The percentage of inpatient deaths among injured workers hospitalized with prescription opioid overdose/AE was <1%, compared to 1.86% for other inpatients with prescription opioid overdose/AE (P=.001).

Counts of prescription overdose/AE hospitalizations among injured workers are presented in **Table 6**. On average, there were about six times as many AE hospitalizations as overdose hospitalizations. Prescription opioid overdose/AE case capture increased by about 3% when using injured worker E-codes in addition to WC as payer. First-listed diagnoses/E-codes captured about 60% of the prescription overdose/AE cases captured when using all-listed diagnoses/E-codes. Small numbers posed a challenge; 50% of states did not have enough prescription opioid overdose hospitalizations to enable reporting overdose separately from AE. There were fewer than 11 heroin overdose hospitalizations and no heroin AE hospitalizations identified among injured workers across all eight states and all five years.

Averaged across eight states, 5.65% of injured workers with prescription opioid overdose/AE were Black/African-American, 1.17% were Asian/Pacific Islander, and <1% were Native American (due to small numbers, these categories were included within Other/multiple in **Table 7**). Averaged across states, 2.70% were aged 15-24, 8.80% were 25-34, 28.40% were 55-64, and 13.10% were 65 and older. Place of injury was largely unspecified; four categories (farm, recreation/sport, street/highway, public building)—each averaging under 2.5%—were included

within other/unspecified. Descriptive characteristics were broken out by state where counts sufficed, with some age and race/ethnicity categories collapsed (**Table 7**).

Table 6. Counts of prescription opioid overdose and adverse effect hospitalizations among injured workers, by event type, injured worker definition,[a] and state (2010-2014)

Prescription opioid event and worker definition	AZ	CO	MI	NJ	NY	SC	UT	WA	8 states[b]
Overdose, all-listed									
Injured worker definition: Payer only	14	NR	11	NR	49	NR	NR	36	138
Injured worker definition: Payer + E-codes	16	NR	11	NR	49	NR	NR	37	142
Adverse effect, all-listed									
Injured worker definition: Payer only	110	NR	73	NR	290	NR	NR	144	835
Injured worker definition: Payer + E-codes	117	NR	73	NR	291	NR	NR	149	859
Overdose or adverse effect, all-listed[c]									
Injured worker definition: Payer only	124	104	83	81	339	31	30	180	972
Injured worker definition: Payer + E-codes	133	110	83	85	340	31	32	186	1,000
Overdose or adverse effect, first-listed									
Injured worker definition: Payer only	54	61	51	64	192	27	15	130	594
Injured worker definition: Payer + E-codes	56	64	51	64	192	27	15	131	600

AZ, Arizona; CO, Colorado; E-codes, ICD-9-CM external cause of injury codes; MI, Michigan; NJ, New Jersey; NR, not reported due to small cell size (≤10), in accordance with HCUP guidance; NY, New York; SC, South Carolina; UT, Utah; WA, Washington State; WC, workers' compensation.

[a] Two injured worker definitions are used in this table: (1) payer only, and (2) payer along with ICD-9-CM E-codes. Details are presented in Table 1.

[b] Totals in the 8-states column were summed across all eight states, including cells not separately reported.

[c] In some cases, all-listed overdose and all-listed adverse effects sum to less than all-listed overdose or adverse effects, because a few hospital discharge records were counted in both categories.

Table 7. Worker and event characteristics (percentages) among injured workers with prescription opioid overdose or adverse effect hospitalizations, by state (2010-2014)

Characteristic	AZ (N=133)	CO (N=110)	MI (N=83)	NJ (N=85)	NY (N=340)	SC (N=31)	UT (N=32)	WA (N=186)	8 states[a] (N=1000)
Gender									
Men	61.65	66.36	55.42	63.53	53.24	NR	NR	63.98	60.10
Women	38.35	33.64	44.58	36.47	46.76	NR	NR	36.02	39.90
Age									
15-34	13.53	16.36	21.69	NR	10.00	NR	NR	6.45	11.50
35-44	13.53	12.73	20.48	NR	21.47	NR	NR	20.43	18.90
45-54	21.05	31.82	25.30	40.00	30.00	NR	NR	22.04	28.10
55+	51.88	39.09	32.53	27.06	38.53	35.48	50.00	51.08	41.50
Race/ethnicity									
Non-Latino White	76.69	66.67	92.31	65.06	78.82	87.10	79.17	90.18	79.21
Latino/Hispanic	NR	18.18	NR	16.87	7.94	NR	NR	NR	9.91
Other/multiple	NR	15.15	NR	18.07	13.24	NR	NR	NR	10.87
Place of injury									
Home	9.77	14.55	NR	NR	8.24	NR	NR	NR	8.80
Industrial/mine/quarry	22.56	10.00	NR	NR	5.29	NR	NR	NR	7.80
Residential institution[b]	17.29	24.55	19.28	NR	6.47	NR	NR	11.29	13.00
Other/unspecified	50.38	50.91	62.65	80.00	80.00	74.19	53.13	80.11	70.40
Low back disorder	18.80	29.09	25.30	37.65	35.59	NR	NR	25.81	28.60

AZ, Arizona; CO, Colorado; HCUP, Healthcare Cost and Utilization Project; MI, Michigan; NJ, New Jersey; NR, not reported due to small cell size (≤10), in accordance with HCUP guidance; NY, New York; SC, South Carolina; UT, Utah; WA, Washington State.

[a] Percentages in the 8-states column were averaged across all eight states, and include cells not separately reported.

[b] Residential institution category includes hospitals, nursing homes, assisted living, jail, prison, etc. Event could have occurred while a resident, at work, or visiting.

State-based five-year average annual crude rates of prescription opioid overdose/AE hospitalizations among injured workers ranged from 0.3 to 1.2 events per 100,000 employed workers (**Table 8**). Among inpatients ages 15 to 64 (age range restricted to enhance comparability across groups), rates for injured workers ranged from 0.3 to 1.1 events per 100,000 employed workers, while rates for all inpatients ranged from 39.6 to 78.2 events per 100,000 civilian population.

Table 8. Five-year average annual crude rates[a] of prescription opioid overdose or adverse effect hospitalizations among injured workers (per 100,000 employed workers) and among all inpatients (per 100,000 civilian population), by state (2010-2014)

Population	AZ Rate (N) (CI[b])	CO Rate (N) (CI[b])	MI Rate (N) (CI[b])	NJ Rate (N) (CI[b])	NY Rate (N) (CI[b])	SC Rate (N) (CI[b])	UT Rate (N) (CI[b])	WA Rate (N) (CI[b])
Injured workers Ages 15+	0.94 (133) (0.79, 1.12)	0.86 (110) (0.71, 1.03)	0.39 (83) (0.31, 0.48)	0.41 (85) (0.33, 0.51)	0.77 (340) (0.69, 0.86)	0.31 (31) (0.21, 0.44)	0.49 (32) (0.33, 0.69)	1.16 (186) (1.00, 1.34)
Injured workers Ages 15-64	0.77 (104) (0.63, 0.94)	0.81 (99) (0.66, 0.98)	0.38 (77) (0.30, 0.47)	0.39 (76) (0.31, 0.49)	0.71 (296) (0.63, 0.79)	0.31 (29) (0.21, 0.44)	0.44 (28) (0.29, 0.64)	1.05 (160) (0.89, 1.22)
All inpatients Ages 15-64	78.2 (16,505) (77.0, 79.4)	61.8 (10,851) (60.6, 62.9)	63.6 (20,960) (62.8, 64.5)	39.6 (11,689) (38.8, 40.3)	40.5 (26,820) (40.0, 41.0)	47.3 (7294) (46.2, 48.4)	60.6 (5523) (59.0, 62.2)	60.4 (13,945) (59.4, 61.4)

AZ, Arizona; CO, Colorado; MI, Michigan; NJ, New Jersey; NY, New York; SC, South Carolina; UT, Utah; WA, Washington State.

[a] Employed worker denominators were used to calculate injured worker rates, and were based on the Bureau of Labor Statistics' Current Population Survey (CPS). Civilian population denominators were used to calculate rates for all inpatients, and were based on U.S. Census Bureau annual estimates.

[b] Poisson exact 95% confidence intervals.

Five-year average annual age and gender-specific rates of prescription opioid overdose/AE hospitalizations among injured workers were reported for six states (**Table 9**). In each state, the estimated rate for men was higher than that for women. In the four states with estimated rates for every age category, there was a monotonic increase with age. Rates for injured workers ages 65 and older ranged from 1.9 to 4.4 per 100,000 employed workers.

Table 9. Five-year average annual gender-specific and age-specific rates[a] of prescription opioid overdose or adverse effect hospitalizations among injured workers (per 100,000 employed workers), by state[b] (2010-2014)

Population	AZ Rate (N) (CI[c])	CO Rate (N) (CI[c])	MI Rate (N) (CI[c])	NJ Rate (N) (CI[c])	NY Rate (N) (CI[c])	WA Rate (N) (CI[c])
Gender-specific						
Men	1.07 (82) (0.85, 1.33)	1.06 (73) (0.83, 1.33)	0.41 (46) (0.30, 0.55)	0.49 (54) (0.37, 0.64)	0.79 (181) (0.68, 0.91)	1.40 (119) (1.16, 1.68)
Women	0.79 (51) (0.59, 1.04)	0.63 (37) (0.44, 0.86)	0.36 (37) (0.25, 0.50)	0.32 (31) (0.22, 0.45)	0.75 (159) (0.64, 0.88)	0.89 (67) (0.69, 1.13)
Age-specific						
15-34	0.37 (18) (0.22, 0.58)	0.40 (18) (0.24, 0.64)	0.25 (18) (0.15, 0.40)	NR	0.22 (34) (0.16, 0.31)	0.22 (12) (0.12, 0.39)
35-44	0.57 (18) (0.33, 0.90)	0.48 (14) (0.26, 0.81)	0.37 (17) (0.21, 0.59)	0.46 (20) (0.28, 0.71)	0.80 (73) (0.63, 1.01)	1.06 (38) (0.75, 1.46)
45-54	0.88 (28) (0.59, 1.27)	1.22 (35) (0.85, 1.69)	0.40 (21) (0.25, 0.62)	0.66 (34) (0.46, 0.93)	1.00 (102) (0.81, 1.21)	1.14 (41) (0.82, 1.55)
55-64	1.79 (40) (1.28, 2.43)	1.59 (32) (1.09, 2.24)	0.60 (21) (0.37, 0.91)	0.39 (14) (0.21, 0.66)	1.17 (87) (0.94, 1.44)	2.52 (69) (1.96, 3.19)
65 and older	4.36 (29) (2.92, 6.26)	1.97 (11) (0.98, 3.53)	NR	NR	1.92 (44) (1.40, 2.58)	3.55 (26) (2.32, 5.20)

AZ, Arizona; CO, Colorado; MI, Michigan; NJ, New Jersey; NR, not reported due to small cell size (≤10), in accordance with HCUP guidance; NY, New York; WA, Washington State.

[a] Employed worker denominators were used to calculate injured worker rates, and were based on the Bureau of Labor Statistics' Current Population Survey (CPS).

[b] South Carolina and Utah were excluded from table 5 due to small numbers.

[c] Poisson exact 95% confidence intervals.

Five-year average annual crude rates of prescription opioid overdose/AE hospitalizations among injured workers varied by state, but were in the general neighborhood of 1 event per 100,000 employed workers. Among those hospitalized with prescription opioid overdose/AE, injured workers were more likely than other inpatients to have a low back disorder diagnosis, and less likely to have a diagnosis of opioid dependence/abuse or cancer, or to have a fatal outcome. In each state, the estimated rate for men was higher than that for women, though the difference was quite small in some states. Several studies indicate that men are at higher risk than women for escalation to high-dose opioid therapy and opioid-related mortality.[22,58,59]

Findings by age were particularly notable. Averaged across eight states, 28% of injured workers with prescription opioid overdose/AE hospitalizations were ages 55-64, and 13% were 65 and older. In the four states with estimated rates for every age category, there was a monotonic increase with age, and rates for injured workers ages 65 and older ranged from two to six times the overall rates. Middle-aged adults have the highest prescription opioid-related mortality rates,[58,59] but adults aged 65 and older have recently had the largest increases in both opioid-related overdose hospitalizations[60] and mortality.[58,59] Prescription opioid-related morbidity may be exacerbated for older workers due to physiologic changes associated with aging, as well as higher prevalence of chronic conditions, complex social needs, mental health issues, and multiple prescription medications (with potential adverse drug interactions).[60]

Five-year average annual crude rates of prescription opioid overdose/AE hospitalizations rates for all inpatients (ages 15 to 64) ranged from about 40 to 78 events per 100,000 civilian population—many times higher than for injured workers. Among all inpatients aged 15 to 64 (not restricted to injured workers), WC was the primary expected payer for less than 1% of prescription opioid overdose/AE hospitalizations, averaged across all eight states. In contrast, WC was listed as the primary expected payer for roughly 6% of injury hospitalizations and 5% of hospitalizations with a low back disorder diagnosis, averaged across all eight states. It could be that WC is not paying for some WC-related overdose/AE events. Alternatively, these events could truly be much rarer among injured workers; however, previous research showing higher opioid doses in WC settings raises the possibility of higher but largely undetected morbidity/mortality rates.[26] Among injured workers 15 and older who were identified using only E-codes, WC was the primary expected payer for 67% of hospitalizations for any diagnosis, and for 59% when restricted to prescription opioid overdose/AE hospitalizations, averaged across all eight states. These coverage levels are roughly comparable to previous estimates of WC coverage of industrial injury hospitalizations,[61] and suggest that WC may be somewhat less likely to cover opioid morbidity-related hospitalizations compared to injury hospitalizations.

Identification and surveillance of work-related injury/illness in clinical databases often rely on using WC as payer—including the analyses conducted for this study. However, for work-related injury/illness not covered by WC, consequent prescription opioid overdose/AE would also not be covered—and thus obscured from surveillance. Alternative research approaches are needed to assess the degree to which WC as payer identifies work-related opioid morbidity. These could include linking WC claims to other databases containing opioid-related outcomes (e.g., emergency medical services, emergency department visits, hospital discharges).

The extent to which work-related prescription opioid morbidity is not covered by WC is unknown. However, an estimated 75% of the economic burden of work-related injury/illness (including direct health care costs and indirect work productivity, lost wages, and home production costs) is transferred as an externality from the responsible employers to society more generally (e.g., workers and their families, non-WC insurers, health care systems, the social safety net, taxpayers).[31,62] Health care providers employing high-risk opioid prescribing practices further contribute to this burden.

Many state agencies and WC systems are actively engaged in prevention efforts focused on curbing high-risk opioid prescribing practices. Successful opioid morbidity reduction will also depend on appropriate WC coverage for treatment of opioid use disorders stemming from opioids prescribed after a work injury. Improved surveillance is possible through real-time tracking of opioid overdose/AE, with reports to the prescribing and/or primary care provider—important because most patients surviving these events continue to be prescribed opioids and are at high risk for repeat overdose.[20]

Although our case definition ensured that hospital discharges were limited to injured workers (i.e., WC as primary expected payer or work-related E-code), the prescription opioid morbidity we identified could involve several different work-related scenarios, as described earlier. Caution is needed when comparing rates across states, or across years within states, due to variation in factors such as: penetration of WC coverage, coverage rules, counts of E-code and diagnosis fields, usage of specific E-codes, the proportion of overdose/AE events that are treated on an inpatient basis. The states included in this study were selected in part due to E-code usage criteria, and findings may not generalize to all states. Further, this study has limited generalizability beyond the U.S. As Ho (2019)[63] comprehensively described, many factors have

contributed to the U.S. being an international outlier in drug overdose mortality since the early 2000s, including: (1) wider and more permissively regulated use of opioids for non-cancer pain; (2) reimbursement practices favoring prescription drugs over alternative pain therapies; (3) wider use of benzodiazepines; (4) fragmented health care system; and (5) scarcity of substance use treatment. Whether the U.S. is unique, provides a cautionary example, or is leading an emerging international trend is not yet known. However, similar trends are emerging in several other developed countries. Despite more limited access to opioids, developing countries have impending risk, due to aggressive pharmaceutical marketing along with weaker regulatory, health care, and surveillance systems. These factors undoubtedly also affect opioid morbidity/mortality risk for injured workers, but we identified no pertinent international research—indicating an important research gap.

Small numbers presented particular challenges, despite our use of a case definition that relied on both work-related E-codes and WC as payer, as well as use of all-listed diagnosis/E-code fields. We were unable to age/sex adjust rates, and needed to suppress many counts and estimates to comply with HCUP reporting restrictions. Overdose counts were too low to present rates for overdose and AE separately. The appropriateness of combining these two categories is an unresolved point of discussion in the literature.[35,56,57] Due to small numbers, we also included all available diagnosis and E-code fields, rather than restricting to the lowest number common to all included states and years. As a counterpoint, many of our metrics were roughly similar across the eight states, showing stability despite the relatively small numbers of events.

This study did not attempt to quantify all opioid-related morbidity. However, hospital discharge data do capture a large share of opioid morbidity. Based on Washington State WC billing data, over 40% of opioid poisonings and AE were treated on an inpatient basis,[35] and a nationally representative study documented that over half of prescription opioid poisonings presenting to an emergency department were admitted to the hospital.[64]

Specific Aim 2

Aim 2: **Determine whether trends in the rates of opioid-related morbidity among workers covered by WC changed after implementation of opioid prescribing guidelines with a high-dose component.** States with later—or no—implementation of similar guidelines will be used as comparators. Our ***working hypothesis*** is that opioid prescribing guidelines implemented in Colorado, Utah, and Washington State had measurable beneficial effects on trends in opioid-related morbidity among workers covered by WC, compared with within-state trends prior to guideline implementation, and compared with concurrent trends in comparator states without such guidelines.

Methodology

The objective of this aim was to determine whether opioid guidelines with a component addressing high-dose prescribing practices have had a positive impact on opioid-related morbidity among injured workers. Methods followed those described for Aim 1, except where otherwise specified.

Opioid prescribing guidelines. Opioid-related prescribing guidelines for each candidate state were obtained and parsed, and state health department and/or WC staff were directly queried

where there was any policy ambiguity. Colorado, Utah, and Washington were identified as eligible SID states that had implemented opioid prescribing guidelines with a high-dose component during the 2003-2014 timeframe (see **Table 10**). Of these, only Washington State had a specific recommendation to document functional improvement or seek expert consultation at doses >120 mg MEDD. Other high-dose guidelines recommend closer monitoring and/or expert consultation at a stated threshold, but did not have specific directives.[65] As such, the Washington guideline may have had a stronger effect on reducing opioid morbidity related to high doses. Several relevant opioid guidelines were promulgated by national organizations that could also affect trends across states (see **Table 11**). Though focused more on curbing patient misuse and multiple prescribers than on prescribing practices, PMPs were also increasingly prevalent (**Table 10**), with preliminary evidence for their effectiveness.[66] These varied policy efforts highlight the importance of incorporating concurrent comparator states and impacts of competing policy events into the study design.

Table 10. Characteristics of hospital discharge data sources and relevant state opioid guidelines/policies

State	WC system: State Fund	PMP start date	Guideline date(s)*	Relevant high-dose opioid prescribing guidelines*
AZ	Non-exclusive	1/2008	Comparator	DHS 11/14*: >50-100 mg MEDD, re-evaluate therapy[67]
CO	Non-exclusive	4/2008	1: 2012 Q1 2: 2014 Q2	DWC 2/12: >120 mg MEDD, vigilance/consult, avoid >200 mg MEDD[28,68]; Department of Regulatory Agencies 7/14: ≥120 mg MEDD, vigilance/consult[69]
MI	No state fund	2/2003	Comparator	Boards of Medicine and Osteopathic Medicine 2003: no dose threshold[70]
NJ	No state fund	1/2012	Comparator	None identified
NY	Non-exclusive	4/1973	Comparator	DOH 4/08: no dose threshold[71]; WCB 12/14*: >100 mg MEDD, vigilance/consult[72]
SC	No state fund	6/2008	Comparator	Board of Medical Examiners 7/09: no dose threshold[73]; Joint Boards 11/14*: reassess when ≥80 mg MEDD for >3 continuous months[74]
UT	Non-exclusive	1/1997	1: 2009 Q1	DOH 3/09: >120-200 mg MEDD, consider pain consult[65]
WA	Exclusive	4/2012	1: 2007 Q1 2: 2010 Q2 3: 2012 Q1 4: 2013 Q3	AMDG: >120 mg MEDD, document functional improvement or seek expert consult; 3/07: educational pilot; 6/10: legislative guideline[75]; 7/11: pain management rules adopted pursuant to 6/2010 guideline for dentistry, podiatry, nursing, osteopathy; 1/12: pain management rules adopted pursuant to 6/2010 guideline for medicine; L&I 7/13: updated guidelines, same dose threshold[76]

AMDG, Agency Medical Directors Group; DHS, Department of Health Services; DOH, Department of Health; DWC, Division of WC; L&I, Department of Labor & Industries; mg, milligrams; MEDD, morphine equivalent daily dose; PMP, Prescription Monitoring Program; Q, quarter; WCB, Workers' Compensation Board.
*Guidelines adopted by several comparator states in 11/2014 were disregarded for guideline/comparator classification purposes. Detail censored after 2014 (several states have since developed new guidelines).

Table 11. National opioid dosing guidelines/policies

Entity	Guideline date(s)	Relevant high-dose opioid prescribing guidelines/policies[a]
ACOEM	1: 2012 Q4 2: 2014 Q4	12/18/12: ↑ vigilance at ≥120 mg MEDD[77] (no dose thresholds earlier[78]) Recommended maximum limit of 50 mg MEDD for acute or chronic pain
APS/AAPM	1: 2009 Q1	Increased monitoring at doses >200 mg MEDD[79]
ASIPP	1: 2012 Q3	Consider pain management consult at doses >90 mg MEDD[80]

ACOEM, American College of Occupational and Environmental Medicine; APS/AAPM, American Pain Society/American Academy of Pain Medicine; ASIPP, American Society of Interventional Pain Physicians; mg, milligrams; MEDD, morphine equivalent daily dose; Q, quarter.

Study design and research obstacles. Staggered implementation of opioid guidelines across multiple states set the stage for a natural experiment.[81-83] A multiple baseline interrupted time series analysis (ITSA) design with multiple concurrent comparator states was originally proposed to assess the effect of qualifying opioid guidelines on trends in opioid morbidity.[84-87] Each guideline state was to be compared in turn to all comparator states, using ITSA models.[86,87] The use of a multiple baseline approach improves internal validity and generalizability.[84,85] Because implementation dates differed, guideline states could not be pooled; the ability to model calendar-based temporal prescribing trends and national guidelines was deemed more important than being able to align and pool the 3 guideline states via recoding calendar time as sometimes done.[88] Identifying suitable comparators can pose a major challenge to policy evaluations.[89] In the absence of randomization, comparative ITSA designs are among the strongest study designs available.[13,84,85,87] The original plan was to calculate quarterly rates, to provide adequate observations for ITSA analysis. However, the low unreliable rates and high variables made the ITSA study design infeasible (**Figure 2**). ITSA models require a minimum of 8 observations before and after guideline implementation,[87] in order to correctly model autocorrelation and baseline trends.[86] Instead, after considering all available options for the Aim 2 analysis, we used a difference-in-differences study design[90] that compared year-over-year trends pre- and post-guideline adoption, using multiple concurrent comparator states. Unfortunately, because a time series design was not feasible, it was also not feasible to assess and/or control for the impact of national guidelines and competing state guidelines.

Data analysis. Hospital discharge data sets from the separate states were appended into a single analytic data set after alignment of key variables across states and calculation of state-specific annual counts of prescription opioid overdose/AE. Eligible cases for these counts differed slightly from Aim 1, because assessing trends required stable case ascertainment over time. First, the E000.0 E-code was excluded from the injured worker definition, because it did not exist prior to October 1, 2009. Second, the number of diagnosis and E-code data fields used for ascertainment were restricted to the minimum number available across all states and all years from 2003 through 2014 (i.e., 9 diagnosis fields and 5 E-code fields). In an alternative attempt to identify enough cases to address this aim, we added place of injury codes for farm (E849.1), mine/quarry (E849.2), and industrial place of injury (E849.3) to the injured worker definition. The few cases with a diagnosis of cancer in any field (aside from non-melanoma skin cancer) were excluded from Aim 2 analyses, because opioid prescribing guidelines do not generally apply to cancer-related pain. Negative binomial panel regression models were used to model trends in annual opioid overdose/AE hospitalizations, adjusting for state-specific employed population denominators, and controlling for state-level baseline rates and for trends before the guideline adoption year.[91-93] Bias-corrected and accelerated (BcA) 95% confidence intervals, which correct for bias and skewness in the distribution of bootstrap estimates,[94] were bootstrapped using 1000 replications (random sampling with replacement), while accounting for state-level panel structure. Analyses were conducted using Stata/SE 15.0 for Windows.[48] Each model included one guideline state panel and five comparator state panels; trends for all six states in each model were interrupted at the relevant guideline adoption year. Thus, trends for the five comparator states were interrupted at different times in separate models, enabling the multiple baseline design. Each model included variables representing guideline vs. comparator state (binary), calendar year (continuous), pre-post guideline adoption year (binary), and saturated (all possible combinations of) interaction terms. The three-way interaction term (guideline state x year x pre-post) represented the post-guideline trend for the guideline state relative to the five comparator states; in other words, it represented the divergence in prescription opioid overdose/AE trend associated with dosing guideline implementation.

Results and Discussion

Table 12 presents the annual counts of prescription opioid/AE hospitalizations used in Aim 2 analyses, by state and year. Counts that were 20 or higher, thus meeting our reliability standard, are presented in bold font. Counts were very low in most states, and many were <11, requiring suppression per HCUP guidelines. **Table 13** presents the results of the negative binomial regression panel models. Very few findings were statistically significant. Further, due to the low unreliable counts and high variance by year (per **Table 12** and **Figure 2**), we lacked confidence in these findings regardless of statistical significance. Therefore, we have chosen not to report or publish these findings outside the confines of this final report.

Table 12. Counts of prescription opioid overdose and adverse effect hospitalizations among injured workers, by state and year (2003-2014)

Year	State							
	AZ	**CO**	**MI**	**NJ**	**NY**	**SC**	**UT**	**WA**
2003	19	**30**	**22**	NR	**57**	NR	NR	**41**
2004	NR	**24**	**25**	19	**57**	NR	11	**34**
2005	NR	**32**	**22**	16	**64**	NR	NR	**24**
2006	14	15	**25**	12	**73**	11	15	**38**
2007	18	**29**	16	14	**67**	12	NR	**37**
2008	**48**	**20**	**21**	**29**	**57**	NR	11	**35**
2009	**31**	16	**24**	19	**81**	12	NR	**42**
2010	**41**	**22**	**29**	**20**	**92**	NR	NR	**41**
2011	**40**	**26**	**29**	**22**	**94**	NR	NR	**37**
2012	**37**	**22**	18	16	**75**	12	NR	**42**
2013	19	**20**	16	NR	**58**	NR	NR	**33**
2014	**35**	**32**	NR	19	**74**	NR	NR	**31**

AZ, Arizona; CO, Colorado; MI, Michigan; NJ, New Jersey; NR, not reported due to small cell size (≤10), in accordance with HCUP guidance; NY, New York; SC, South Carolina; UT, Utah; WA, Washington State.

Table 13. Results of negative binomial regression panel models

State	Guideline adoption year	Mean annual trend divergence (vs comparator states)	95% CI (conventional)	95% CI (bootstrapped, BcA)
CO	2012	1.45	0.95, 2.22	1.30, 1.73
UT	2009	1.23	0.91, 1.68	1.15, 1.34
WA	2007	1.13	0.87, 1.47	0.96, 1.17
WA	2010	1.12	0.93, 1.33	1.06, 1.21
WA	2012	0.99	0.69, 1.41	0.90, 1.18
WA	2013	0.79	0.38, 1.62	0.63, 1.52

BcA, bias-corrected and accelerated; CO, Colorado; UT, Utah; WA, Washington State.

Conclusions

Accurate surveillance of opioid morbidity rates and demographic patterns is necessary for effective prevention. In this study, we estimated opioid-related morbidity among injured workers, for whom population-based estimates are almost nonexistent. Estimated prescription opioid overdose/AE hospitalization rates were quite low, roughly 1 per 100,000 workers. Rates were highest among male workers and older workers. Strikingly, rates for workers aged 65 and older were two to six times higher than the overall average rates.

We identified several important barriers to accurate opioid morbidity surveillance among injured workers using hospital discharge data, which will help guide future researchers in feasible and appropriate uses of hospital discharge data for related purposes. Small numbers presented particular challenges, despite our use of a case definition that relied on both work-related E-codes and WC as payer, as well as use of all-listed diagnosis/E-code fields. We were unable to age/sex adjust rates, and needed to suppress many counts and estimates to comply with HCUP reporting restrictions. Overdose counts were too low to present rates for overdose and AE separately, or to evaluate the effectiveness of high-dose opioid prescribing guidelines.

The extent to which work-related prescription opioid morbidity is not covered by WC is unknown. Among injured workers 15 and older who were identified using only E-codes, WC was the primary expected payer for 67% of hospitalizations for any diagnosis (averaged across eight states), compared to 59% when restricted to prescription opioid overdose/AE hospitalizations. These coverage levels were roughly comparable to previous estimates of WC coverage of industrial injury hospitalizations, and suggested that WC may be somewhat less likely to cover opioid morbidity-related hospitalizations compared to other hospitalizations. Identification and surveillance of work-related injury/illness in clinical databases often rely on using WC as payer—including the analyses conducted for this study. However, for work-related injury/illness not covered by WC, consequent prescription opioid overdose/AE would also not be covered—and thus obscured from surveillance. Alternative research approaches are needed to assess the degree to which WC as payer identifies work-related opioid morbidity. These could include linking WC claims to other databases containing opioid-related outcomes (e.g., emergency medical services, emergency department visits, hospital discharges).

Additional research is needed to: (1) further characterize the burden of opioid-related morbidity and mortality among injured workers, including the downstream impact of high-risk opioid prescribing practices pursuant to work injury/illness, (2) evaluate the effectiveness of guidelines and policies designed to improve opioid prescribing practices, and (3) assess the degree to which WC as payer adequately identifies work-related opioid morbidity for research and surveillance purposes.

Publications

Sears JM, Hogg-Johnson S, Sterling RA, Fulton-Kehoe D, Franklin GM: [2020] Prescription Opioid Overdose and Adverse Effect Hospitalisations among Injured Workers in Eight States (2010-2014). Occupational and Environmental Medicine 77:439-445. PubMed Central PMCID: PMC7745640.

Inclusion Enrollment Report

Not applicable. This project did not involve human subjects research.

Inclusion of Gender and Minority Study Subjects

Not applicable. This project did not involve human subjects research.

Inclusion of Children

Not applicable. This project did not involve human subjects research.

Materials Available for Other Investigators

Not applicable. This project relied on existing state hospital discharge data that are publicly available (for purchase) from the Healthcare Cost & Utilization Project (HCUP), Agency for Healthcare Research and Quality (AHRQ).

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