Opioid and Benzodiazepine Use and Risk of Occupational Injury

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Abstract

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BACKGROUND: Opioids and benzodiazepines are central nervous system (CNS) depressants with sedating effects that can adversely impact cognitive as well as motor performance thereby potentially increasing the risk of occupational injury. To date, few studies have assessed the relationships between acute and chronic opioid or benzodiazepine use and occupational injury risk across multiple occupations.

METHODS: The primary objective of this study was to examine the risk of occupational injury associated with acute (60 or fewer prescription days supplied in the 180 days preceding injury) opioid or benzodiazepine use across various occupations and in safety sensitive fields. The secondary aim was to determine whether dose escalation (a dose increase of greater than 10%) among workers who chronically use opioids or benzodiazepines was associated with an increased risk of occupational injury. A case crossover study design, employing injury data from the Washington State Department of Labor and Industries workers' compensation claims database paired with the Washington State Prescription Monitoring Program database, was used to examine the study hypotheses. Each hazard period was matched to four control periods. Statistical analyses were performed for 7-day, 14-day, and 28-day hazard and control periods. Conditional logistic regression was used to calculate odds ratios.

RESULTS: For acute opioid users, there was a statistically significant decreased risk of occupational injury for 7-day, 14-day and 28-day hazard and control period analyses (OR 0.84, 95%CI 0.80 – 0.89; OR 0.87, 95%CI 0.82 – 0.89; and OR 0.83, 95%CI 0.80 – 0.86 respectively). Similar results were obtained when the analyses were restricted to claims among workers in safety sensitive fields. There was no statistically significant association between acute benzodiazepine use and occupational injury risk even among claimants in safety sensitive fields. Among chronic opioid or benzodiazepine users, increase in opioid or benzodiazepine dose was not associated with an increase in occupational injury risk.

CONCLUSION: Acute opioid use was associated with a decreased risk of occupational injury, which was unexpected. This association was similar among claimants in safety sensitive occupations compared to claimants in all occupations. Acute benzodiazepine use was not associated with a statistically significant change in occupational injury risk. Among chronic opioid and benzodiazepine users, increase in medication dose was not associated with a statistically significant change in occupational injury risk. Possible explanations for these findings are explored. These results should be interpreted with caution particularly given potential biases and confounding introduced because of unidirectional control period selection, and opioid prescribing time trends.

INTRODUCTION:

Opioids and benzodiazepines are central nervous system (CNS) depressants with sedating effects that can adversely impact cognitive as well as motor performance thereby contributing to increased injury risk.[1,2] There have been few studies showing an association between opioid or benzodiazepine use and risk of occupational injury. Howard et al demonstrated an increased risk of self-reported accidents in the preceding 3 years among Australian commercial vehicle drivers using opioid analgesics regularly or occasionally compared to drivers who did not (OR 2.40 (95% CI, 1.46 – 3.92)).[3] Among male commercial motor vehicle drivers involved in fatal crashes, though the yearly prevalence of opioid analgesic use between 1993 and 2008 was low (0.1-0.46%), opioid analgesic use as evidenced by postmortem testing was associated with an increased risk of crash responsibility (OR 2.80 (95% CI, 1.64 - 4.81)).[4] In a case control study by Gilmore et al in which the association between prior usage of medication and traumatic occupational injuries was investigated, there was no significant association between narcotic medication purchased during the 30 days prior to injury and acute traumatic occupational injury risk.[5]

Numerous studies have however demonstrated an increased risk of non-occupational injuries among individuals taking opioids and benzodiazepines compared to those who do not. The majority of these studies have examined the impact of opioid analgesic and benzodiazepine use on the risk of motor vehicle accidents among drivers. [6–10] Bachs et al showed that Norwegian drivers using codeine in combination with other impairing drugs were more likely than drivers not using codeine or other impairing drugs to be involved in a motor vehicle accident resulting in personal injury (SIR 1.9 (95% CI, 1.6−2.2)).[6] Among Canadian drivers prescribed opioids, Gomes et al found a significant positive relationship between opioid dose and risk of road trauma.[7] Compared with very low opioid doses, drivers prescribed low doses (20 – 49 MED (morphine equivalent dose)) had a 21% increased odds of road trauma (OR 1.21 (95% CI, 1.02-1.42)); those prescribed moderate doses (50 – 99 MED), a 29% increased odds (1.29 (95% CI, 1.06-1.57)); and those prescribed high doses (100 – 199 MED), a 42% increased odds (1.42 (95% CI, 1.15-1.76)).[7] Furthermore, Norwegian drivers using opium alkaloids, tranquilizing benzodiazepines, and hypnotic benzodiazepines were at 2.0 (SIR 2.0 (95%CI, 1.7−2.4)), 2.9 (SIR 2.9

(95% CI, 2.5−3.5)), and 3.3 (SIR 3.3 (95%CI, 2.1−4.7)) times greater risk respectively of being involved in a road traffic accident with associated personal injury compared to drivers not taking these medications.[11] There have also been studies demonstrating an association between opioid or benzodiazepine use and increased fall risk particularly among elderly individuals. A national Veterans Health Administration cross-sectional study showed that more patients aged 65 and older with fall-related outpatient clinical health encounters used opioid analgesics and narcotics (11.21% vs 9.09%), and benzodiazepines (7.60% vs 5.96%) compared to their age- and sex-matched counterparts.[9] Furthermore, in a matched case control study performed by Kuschel et al, there was an increased risk of falls leading to hospitalization among individuals 65 and older who had used opioids (Men OR 2.30 (95% CI, 2.09–2.53); Women OR 2.00 (95% CI, 1.87–2.12)) or hypnotics/sedatives (Men OR 1.76 (95% CI, 1.61–1.93); Women OR 1.21 (95% CI, 1.14–1.29)) during the 30 days before the fall.[12] Additionally, in a Swedish case crossover study performed to assess the short-term effects of newly prescribed opioids on the risk of fall-related injuries in the general adult population, there was a significant increase in fall risk observed early after treatment initiation particularly among younger adults (Age 18 – 29 years old: OR 7.17 (95% CI, 5.04–10.2)) compared to older adults (Age 70 – 79 years old: OR 2.71 (95% CI, 2.46–2.99).[13]

Alcohol, like opiates and benzodiazepines, is a CNS depressant. There is a greater body of literature supporting the association between alcohol use and risk of work-related injury than for opioids and benzodiazepines.[14–19] Wang et al showed that the risk of agricultural occupational injury among Chinese farmers was greater among current alcohol users, defined as having used alcohol within the preceding 30 days, compared to alcohol non-users (OR 1.77 (95% CI, 1.27 – 2.47)).[14] This study also demonstrated that workers consuming greater than 50ml/day of pure alcohol were 2.07 (OR 2.07 (95% CI, 1.37 – 3.14)) times more likely to sustain a work related injury compared to non-drinkers.[14] Among Chinese construction workers who drank greater than 30ml/day of pure alcohol, the risk of work related injury was 1.73 (OR 1.73, (95 %CI: 1.12–2.69)) times greater than individuals who drank no alcohol.[15] There was also an increased risk of self-reported occupational injury among manual workers in Taiwan who consumed alcoholic energy drinks compared to their counterparts who did not (OR 1.48 (95% CI, 1.14–1.93))[16]; among high school workers in Texas who drank in the preceding 30 days compared to their

counterparts who did not (OR ranging from 1.52 (95% CI, 1.21, 1.91) to 11.77 (05% CI, 5.29, 26.20))[18]; and among farm workers in Colorado who drank 3 or more drinks when they did drink compared to alcohol non-users.[17] In all these studies, there appeared to be a dose-response relationship such that increasing frequency of alcohol use was associated with increased risk of work related injury.[14–19]

Prescription opioid analgesic use among adults in the United States has increased over the past decade.[20,21] In 2006, 47 million prescriptions were dispensed per quarter in the United States for the following opioid analgesics: oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, and tramadol.[21] According to the Medical Expenditure Panel Survey (MEPS), total expenses for outpatient prescription opioids among the U.S. civilian non-institutionalized population more than doubled between 2002 and 2012, increasing from $4.1 billion to $9.0 billion respectively (in 2012 dollars).[22] The National Health and Nutrition and Examination Survey (NHANES) demonstrated that from 1999–2002 to 2011-2012 , the proportion of adults aged 20 and over who had used a prescription opioid analgesic in the preceding 30 days increased from 5.0% to 6.9%.[20] There has also been an increase in use of prescription opioid analgesics with higher potency than morphine.[20] The proportion of adults who used opioids more potent than morphine significantly increased from 17.0% in 1999–2002 to 37.0% in 2011–2012.[20]

Among workers filing workers' compensation claims, there is also a high prevalence of opioid analgesic prescription and use after injury, but not much in the literature about prevalence of opioid prescription and use prior to injury. In the Washington State Workers' Compensation System, prescriptions for schedule II opioids increased from 23,000 annually in 1996 to 57,000 annually in 2002, despite a decrease in workers' compensation claims filed during that period.[23] Among claimants with acute back injuries who filed compensable claims with the Washington State Workers' Compensation System between July 2002 and April 2004 and were therefore out of work for over 3 days, 34.1% were prescribed schedule II opioids in the first 6 weeks following injury.[24] In the Utah Workers' Compensation Fund, 52.2% of claimants with compensable lost-time claims for non-specific lower back pain between January 2002 and Jun 2005 filled at least one schedule II opioid prescription, while 18% filled prescriptions for scheduled II opioids for at least 90 days continuously.[25] In Ohio, the prevalence of opioid use among workers' compensation claimants between fiscal years 2008 and 2009, was 19.2%.[26]

With regards to prescription benzodiazepine use, in 2008, approximately 5.2% of adults in the United States aged 18 to 80 years used benzodiazepines.[27] The percentage of adults using benzodiazepines increased with age from 2.6% (18-35 years) to 5.4% (36-50 years) to 7.4% (51-64 years) to 8.7% (65-80 years).[27] Benzodiazepine use was nearly twice as prevalent in women as men.[27] The proportion of chronic benzodiazepine users increased with age from 14.7% (18-35 years) to 31.4% (65-80 years), while the proportion that received a benzodiazepine prescription from a psychiatrist decreased with age from 15.0% (18-35 years) to 5.7% (65-80 years). In all age groups, roughly one-quarter of individuals receiving benzodiazepines were prescribed long-acting benzodiazepines.[27] Among workers with lost time injury claims between 1999 and 2012 in the Louisiana Worker's Compensation System, the prevalence of benzodiazepine use during the year of injury was 4.9%. [28]

We can postulate, given the data supporting the increased risk of work related injury with alcohol use, non-occupational motor vehicle accidents and falls with opioid or benzodiazepine use, and the high prevalence of opioid or benzodiazepine use among the general US population and the population of workers' compensation claimants, that opioids and benzodiazepines are likely to be associated with an increased risk of occupational injuries. In fact, based on data supporting the association between opioid use and non-occupational motor vehicle crash risk, the American College of Occupational and Environmental Medicine (ACOEM) recently updated their practice guidelines for opioid use and safety sensitive work. ACOEM recommended against the use of acute or chronic opioids for patients performing safety-sensitive jobs.[29] They extended this recommendation beyond operation of motor vehicles to include other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation, work with sharps, work with risk of injury e.g. from heights, and tasks involving high levels of cognitive function.[29]

To date, there have been few studies in which the relationships between opioid or benzodiazepine use and overall occupational injury risk have been assessed. The primary purpose of this study was to determine if acute opioid or benzodiazepine use is associated with an increased risk of occupational injury, particularly in safety sensitive occupations. The secondary aim of this study was to determine

whether there is an increased risk of occupational injury with dose escalation among workers who chronically use opioids or benzodiazepines. This study is one of the first studies to use the case crossover design to assess the relationship between opioid or benzodiazepine use and occupational injury risk.

METHODS:

***Study Aims**:* A case crossover study design, employing data from the Washington State Department of Labor and Industries workers' compensation claims database paired with the Washington State Prescription Monitoring Program database, was used to examine the following study aims:

i. To determine the association between acute opioid or benzodiazepine use and occupational injury risk among workers in all occupations, and in safety-sensitive fields. The working hypothesis was that acute opioid or benzodiazepine use increases the risk of occupational injury among workers in all occupations, but more so among workers in safety-sensitive occupations.

ii. To determine the association between an increase in opioid or benzodiazepine dose and occupational injury risk among workers in all occupations who use opioids or benzodiazepines chronically. The working hypothesis was that an increase in opioid or benzodiazepine dose increases the risk of occupational injury.

Study Design: A case-crossover study design was used. The case crossover study design is useful for assessing the effects of transient or intermittent exposures on acute events.[30,31] In this study design, individuals within a cohort who experience the outcome event (cases) are first identified. Information about each subject's exposure during a time period preceding the outcome event (hazard period) is compared with the same subject's exposure during other times (control or referent periods).[30,31] Given the nature of the case-crossover study design, individuals without any exposure data during the hazard or control periods are dropped out of the study analysis. The self-matching feature of case-crossover studies eliminates confounding from time-invariant individual characteristics. [31] This self-matched design however

prevents examination of exposures that do not change within the individual over the course of the study.[31] Furthermore confounding can still occur if there are characteristics that vary over time within the individual.[31] For the primary aim of this study, the transient exposure was acute opioid or benzodiazepine use and the acute outcome event was occupational injury. For the secondary goal of this study, the transient exposure was a change in opioid or benzodiazepine dose and the acute outcome event was occupational injury.

Case Ascertainment: Data from the Washington State Department of Labor and Industries State Fund Workers' Compensation claims database was used to obtain the cohort of occupational injury cases for this study.[32] Cases comprised the claims of claimants ages 18 through 65 with 'traumatic injuries and disorders' as defined by version 1.01 of the Occupational Injury and Illness Classification system (OIICS)[33], who filed one or more workers' compensation claims during fiscal years 2013, 2014 and 2015. The OIICS version 1.01 categorizes injuries as follows: nature of injury, injured body part, source of injury, and event/exposure (accident type).[33] 'Traumatic injuries and disorders' are classified under 'nature of injury' and defined as the 'acute effects of external agents, and acute poisoning and toxic effects'.[33] A traumatic injury or disorder typically results from a single incident or event, or exposure over the course of a single shift.[33] Examples of traumatic injuries and disorders include spinal cord injuries, fractures, strains/sprains, cuts/lacerations, burns, concussions, and injuries resulting from effects of environmental conditions e.g. hypothermia.[33] Sub-categories under traumatic injuries and disorders include: traumatic injuries to bones, nerves, spinal cord; traumatic injuries to muscles, tendons, ligaments, joints, etc.; open wounds; surface wounds and bruises; burns; intracranial injuries; effects of environmental conditions; multiple traumatic injuries and disorders; and other traumatic injuries and disorders.

Exposure ascertainment: The workers' compensation claims data were paired with data from the Washington State Prescription Monitoring Program (PMP), which has been collected since October 7, 2011.[34,35] The PMP is a prescription review database to which dispensers submit data on Schedules II, III, IV and V controlled substances dispensed to patients throughout the state of Washington. Licensed pharmacies and practitioners that dispense controlled substances in the state of Washington, or to an

address in the state, are required by law to electronically report this prescription data; these data are collected at the point of sale.[34,35] For the purposes of the PMP, 'dispensing' is defined as providing more than a 24-hour supply of a controlled substance for immediate use.[34,35] These data do not include hospital inpatient dispensing data, data from pharmacies operating in the Department of Corrections or pharmacies providing medications to offenders who are in state or county correctional institutions, dispensing for immediate one day use, or data from the administration of controlled substances. [34,35]

Exposure to opioid or benzodiazepine use was ascertained from the paired PMP data. Of note, only claimants with paired PMP data were included in the analysis of measures of excess risk for this study. This was because individuals without any PMP data and therefore without any exposure data would essentially be dropped out of the conditional logistic regression analysis. All opioids were included except narcotic anti-tussive agents and opioid withdrawal agents such as buprenorphine and its associated combination drugs. Sedative non-benzodiazepine agents primarily used as sleep aids such as zolpidem, suvorexant, eszcopicolone, and zaleplon were not included in this study.

Acute Opioid or Benzodiazepine Use:

Acute use of prescription opioids and benzodiazepines can result in CNS depression, characterized by impaired psychomotor abilities and cognitive function, which hypothetically increases the risk of occupational injury. An important part of ascertaining exposure status in the case-crossover design was determining the etiologically relevant time periods for the effects of the exposures of interest. The etiologically relevant time period is the period of time over which opioids and benzodiazepines are most likely to exert their CNS depression effects. For opioids, half-lives and duration of analgesic effects vary between short-acting and long-acting opioids.[36,37] The half-lives of short acting opioids range between 2 – 6 hours, while duration of analgesic effect varies from 3 – 8 hours on average. For long acting opioids, the half-lives range between 4 – 13 hours, while duration of analgesic effect varies from 8 – 72 hours.[36,37] For benzodiazepines, time to mean peak plasma concentration occurs over a few hours with sedative effects often lasting several hours thereafter.[38]

Ideally for this study, the etiologically relevant time period would have been on the scale of hours. However, the opioid and benzodiazepine exposure data available through the WA state PMP were not sufficiently granular to allow determination on an hourly basis of how and when claimants are using these medications prior to injury occurrence. The PMP data only provides information about when prescriptions are dispensed. As such, determining an etiologically relevant time period of risk was challenging. Nonetheless, based on prior case crossover studies,[13,39–41] the pharmacokinetics and pharmacodynamics of opioids and benzodiazepines,[36–38] and the proposed pathophysiologic mechanism of injury, etiologically relevant time periods of 1 week, 2 weeks and 4 weeks preceding injury were chosen for this study. Each individual claim therefore had three separate risk measure assessments based on varying lengths of the hazard and control periods. For each risk measure assessment, there were 4 control periods matched to 1 hazard period, as depicted visually in Figure 1.

The following prescription information was obtained for opioid or benzodiazepine exposure during the hazard and control periods: date prescription was dispensed, last date of service (completion date), drug name, dose per tablet, number of tablets, number of days supplied, drug therapeutic class code (First Data Bank Hierarchical Ingredient Code (HIC3)).[42] For this study, definitions of acute and chronic opioid use were based on the 2017 Bree Collaborative Opioid prescribing metrics, with minor modifications.[43] The Bree Collaborative metrics define chronic opioid use as greater than 60 days of opioid prescription in the a calendar quarter, with days supplied calculated from the total of all opioid prescriptions during the quarter including overlapping prescriptions.[43] For this study, claims with opioid or benzodiazepine prescriptions filled for a cumulative period of 60 or fewer days within the 180 days preceding the injury date were characterized as acute opioid or benzodiazepine users. Claims with opioid or benzodiazepine prescriptions filled for a cumulative period of greater than 60 days within the 180 days preceding the injury date were characterized as chronic opioid or benzodiazepine users. The rationale for defining acute and chronic use within 2 quarters as opposed to 1 quarter was primarily because the combined length of the consecutive 28-day control and hazard periods was greater than 90 days.

Risk of occupational injury was calculated for claims with acute opioid or benzodiazepine use. It was assumed that the opioids and benzodiazepines were taken exactly as prescribed and dispensed. The dispensation dates and completion dates were determined for opioid or benzodiazepine prescriptions dispensed over the hazard and control periods. These dates were overlaid over the hazard and control periods to accurately determine acute opioid or benzodiazepine exposure status during these periods. Exposure to acute opioids or benzodiazepines during the hazard periods 1 week, 2 weeks and 4 weeks immediately preceding injury were compared to their respective control periods. Matched odds ratios were then calculated, and the analysis repeated for safety sensitive occupations.

Dose Escalation Among Chronic Opioid/Benzodiazepine Users:

Claims with opioid or benzodiazepine prescriptions filled for a cumulative period of greater than 60 days within the 180 days preceding the injury date were characterized as chronic opioid or benzodiazepine users. For chronic opioid users, the average daily morphine equivalent doses (MEDs) for hazard and control periods were calculated by dividing the total MED prescribed by the total number of days supplied. The morphine equivalent dose (MED) was calculated using the Agency Medical Director's Group Opioid Dose Calculator.[44] For chronic benzodiazepine users, the average daily diazepam equivalent doses (DEDs) for hazard and control periods was calculated by dividing the total DED prescribed by the total number of days supplied. The diazepam equivalent dose was calculated using the Equivalent Benzodiazepine Calculator.[45]

Among claims with chronic opioid or benzodiazepine use, the MED or DED over the hazard period and control periods was calculated. The difference in MED or DED between consecutive control periods was compared to the difference in MED or DED between the hazard period and the first control period. If the MED or DED in the hazard period was 10% greater than the MED or DED in the first control period, then the claim was categorized as having been exposed. If the MED or DED in the hazard period was less than 10% greater than the MED or DED in the first control period, then the claim was categorized as being unexposed. This same metric was used to categorize exposure status between the preceding consecutive control periods. The change in dose status between control periods 4 and 3, 3 and 2, and 2

and 1 were then compared to the change in dose status between control period 1 and the hazard period. Matched odds ratios were calculated based on these exposure status comparisons.

Safety Sensitive Occupations: A safety sensitive occupation can broadly be defined as one in which the worker is responsible not only for his or her own health and safety but also for the health and safety of others. From the perspective of the federal drug-free workplace executive order, all federal employees involved in 'law enforcement, national security, the protection of life and property, public health or safety, or other functions requiring a high degree of public trust' work in safety and security sensitive industries and are thus subject to mandatory drug testing.[46] In this study, safety sensitive occupations were chosen based on the 2014 Bureau of Labor Statistics non-fatal occupational injury and illness incidence rates.[47] The occupations with incidence rates greater than 100 injuries/illness per 10,000 full-time workers were characterized as safety-sensitive occupations. The Standard Occupational Classification (SOC) system is used by federal statistical agencies to classify workers into occupational categories for the purpose of data collection, analysis and dissemination.[48] There are 2000 (SOC2K) and 2010 versions of the SOC; SOC2K is used by the Washington State Department of Labor and Industries for occupation classification. There are 23 major occupation classification groups, 97 minor groups and 461 broad occupations.[49] For this study, safety sensitive occupations were limited to the following SOC2K major occupation classification groups: healthcare practitioner and technical occupations; healthcare support occupations; protective service occupations; farming, fishing, and forestry occupations; construction and extraction occupations; installation, maintenance and repair occupations; production occupations; transportation and material moving occupations; building and grounds cleaning and maintenance occupations; personal care and service occupations.

Study Subjects: Each claim meeting the inclusion and exclusion criteria was considered a case for the purposes of this study. There were therefore claimants with multiple claims included in the study. Given the case-crossover study design, each claim in the workers' compensation claims database served as their own case and control.

Inclusion criteria:

i. Each claimant was between the ages of 18 and 65 on the date of injury indicated on the claim. This is to capture individuals most likely to be working consistently.
ii. Each claimant had paired PMP data. Of note, claimants who had never filled prescriptions for any Schedule II, III, IV or V controlled substances did not have paired PMP data.
iii. Each claimant had a date of injury occurring in fiscal years 2013, 2014 or 2015.
iv. Claimants with injuries that were categorized in the 'Traumatic injuries and disorders' division under the 'Injury Nature' category of the OIICS version 1.01 code tree were included.

Exclusion criteria:

i. Claimants with injuries that were sub-categorized as follows in the OIICS version 1.01 code tree, were excluded as they did not occur as a consequence of acute effects of external agents, or are poorly defined:
    a. Nature of Injury: diseases and disorders of body systems; infectious and parasitic disease; neoplasms, tumor and cancers; symptoms, signs and ill-defined conditions; other disease, conditions and disorders; exposure to disease – no illness incurred; multiple diseases, conditions, and disorders; non-classifiable.

Data Analysis: All statistical analyses were performed using STATA (version 14.1, StataCorp, College Station TX, USA).

Descriptive Analyses:

Characteristics of the study population:

Claims with paired PMP data were compared to claims without paired PMP data to determine if there were any significant differences between the distribution of demographic, and injury-related variables. Among claims with paired PMP data, the distribution of frequency and daily dose of opioid or

benzodiazepine use during hazard and control periods was also characterized. Descriptive analyses were performed for the following variables:

i. Demographic variables: sex, age at time of injury
ii. Injury-related variables: SOC2K occupational class, year of injury nature of injury, source of injury, body part affected, accident/event type, claim status.
iii. Exposure-related variables: distribution of acute prescription use, distribution of chronic prescription use; opioid use during hazard and control periods; MED/day distribution during hazard and control periods; benzodiazepine use during hazard and control periods; DED/day distribution during hazard and control periods; proportion with opioid or benzodiazepine use within 56 days, 84 days and 168 days prior to injury.

Inferential Analyses:

Primary Study Objective: To determine the association between newly acute opioid or benzodiazepine use and occupational injury risk among workers in all occupations, and in workers in safety-sensitive fields.

The outcome variable was occupational injury. The exposure variables were acute opioid or benzodiazepine use. The exposure variables were coded as binary, either 0 (unexposed) or 1 (exposed) for the presence of exposure in the hazard and control periods. Potential confounding variables could have included seasonal variation in occupational injuries as well as variation over time in opioid or benzodiazepine prescribing practices. These confounding variables were not controlled for in this study, given significant statistical challenges associated with ascertaining and controlling for such trends over time. Effect modification by quarters of the year was however assessed. Effect modification by sex and age was also assessed. The working hypothesis was that acute opioid or benzodiazepine use increases the risk of occupational injury among workers in all occupations, but more so among workers in safety-sensitive occupations. Since this was a case-crossover study, each case served as its own control, therefore all individual time-invariant characteristics were matched and as such controlled for.

As part of this analysis, claimants with opioid or benzodiazepine prescriptions filled for a cumulative period of 60 days or greater within the 180 days preceding the injury date were characterized as chronic opioid or benzodiazepine users. Risk of occupational injury was calculated for acute opioid or benzodiazepine users in all occupations, then repeated for acute opioid and benzodiazepine users in safety sensitive fields combined.

Model 1 (Primary Goal):

$$Logit\ P(X) = \alpha + \beta E + \sum_{i=1}^{n-1} \gamma_i V_i,$$

$$where\ Logit\ P(X) is\ the \log odds\ ratio, E\ is\ the\ exposure\ to\ opioid\ or\ benzodiazepine,$$

$$V_i\ are\ matched\ dummy\ variables, and\ n\ is\ the\ number\ of\ matched\ pairs$$

Null Hypothesis: $\beta = 0$, or $e^{\beta} = 1, where\ OR = e^{\beta}$

Alternate Hypothesis: $\beta \neq 0$, or $e^{\beta} \neq 1, where\ OR = e^{\beta}$

Secondary Study Objective: To determine the association between an increase in opioid or benzodiazepine dose and occupational injury risk among workers in all occupations who use opioids or benzodiazepines chronically.

The outcome variable was occupational injury. The exposure variable was change in opioid or benzodiazepine dose between hazard period and control period 1, and between consecutive preceding control periods. A dose increase between control period 1 and the hazard period, and between preceding consecutive controls periods of greater than 10% categorized as exposed and coded as '1'. Any change in dose less than this was categorized as unexposed, and coded as '0'. The working hypothesis was that an increase in opioid or benzodiazepine dose among chronic opioid or benzodiazepine users increases the risk of occupational injury.

Model 2 (Secondary Goal):

$$Logit\ P(X_1) = \alpha + \beta_1 E_1 + \sum_{i=1}^{n-1} \gamma_{1i} V_{1i},$$

$where\ Logit\ P(X) is\ the \log odds\ ratio, E_1\ is\ the\ change\ in\ \ opioid\ or\ benzodiazepine\ dose\ between\ hazard\ and\ control\ periods, V_{1i}\ are\ matched\ dummy\ variables\ and\ n\ is\ the\ number\ of\ matched\ pairs$

Null Hypothesis: $\beta_1 = 0$, or $e^{\beta_1} = 1, where\ OR = e^{\beta_1}$

Alternate Hypothesis: $\beta_1 \neq 0$, or $e^{\beta_1} \neq 1, where\ OR = \ e^{\beta_1}$

Standard conditional logistic regression methods for matched case-control studies was used to estimate odds ratios. Mcnemar's test was used to further corroborate results obtained from the standard conditional logistic regression analyses. The results are presented as odds ratios with 95% confidence intervals (95% CI).

i. *Injury risk associated with acute opioid or benzodiazepine exposure*: analyses were performed with all opioids or all benzodiazepines combined. For all opioids or benzodiazepines combined, odds ratios for injury risk after exposure to acute opioids in the 4 weeks, 2 weeks and 1 week immediately preceding injury were determined. Additional analyses were conducted for the following safety sensitive SOC2K major occupation classification groups combined: healthcare practitioner and technical occupations; healthcare support occupations; protective service occupations; farming, fishing, and forestry occupations; construction and extraction occupations; installation, maintenance and repair occupations; production occupations; transportation and material moving occupations; building and grounds cleaning and maintenance occupations; personal care and service occupations.

ii. *Injury risk associated with increase in opioid or benzodiazepine dose among chronic opioid or benzodiazepine users*: among identified chronic opioid or benzodiazepine users, analyses were performed with all opioids or benzodiazepines combined to determine the odds ratio of injury risk after

an increase in opioid or benzodiazepine dose in the 4 weeks, 2 weeks and 1 week immediately preceding injury compared to control periods.

Study Power and Sample Size Calculations

An unpublished review and analysis of combined workers' compensation claims data and PMP data suggests that at least 3% of all claimants were on opioids prior to filing a claim, and 1.5% of claimants were on opioids chronically (i.e. for a period of greater than 12 weeks) prior to filing a claim. From L&I claims data for fiscal years 2013, 2014, 2015 combined, there were 237,606 claims filed under injury nature 'Traumatic Injuries and Disorders'.[32] As such, the potential number of workers exposed to opioid analgesics acutely during this period of time was 3564, while the potential number exposed chronically was also 3564 (assuming 1.5% of claimants were on opioids acutely, and 1.5% on opioids chronically prior to filing a claim). Using the STATA 'Test of association in 1:M matched case control study' power and sample size analysis, the needed sample size for both primary and secondary study goals and analyses is at least 3153. This calculation is based on a 1:4 matched case control study with a power of 0.80, alpha (significance) level of 0.05, odds ratio of opioid exposure during the hazard period relative to the control period of 1.5 (estimated based on background literature review), and probability of acute or chronic opioid exposure during the control period of 1.5%. The L&I workers' compensation claims data paired with the PMP data should therefore provide enough cases to detect a statistically significant difference in injury risk between hazard and control periods for opioid exposure.

Assuming, based on general population prevalence of benzodiazepine use, that approximately 5.2% of workers were taking benzodiazepines prior to filing a claim, and that a quarter of them were on benzodiazepines chronically: the potential number of workers exposed to benzodiazepines acutely prior to injury from fiscal year 2013 through 2015 is 9267, while those potentially exposed chronically is approximately 3089.[32] Using the STATA 'Test of association in 1:M matched case control study' power and sample size analysis, the needed sample sizes for primary and secondary study goals and analyses respectively is approximately 2189 and 3768. This calculation is based on a 1:4 matched case control study with a power of 0.80, alpha (significance) level of 0.05, odds ratio of opioid exposure during the

hazard period related to the control period of 1.5, and probability of acute benzodiazepine exposure during control period of 3.75%, and chronic benzodiazepine exposure during the control period of 1.25%. The L&I workers' compensation claims data paired with the PMP data should therefore provide enough cases to detect a statistically significant difference in injury risk between hazard and control periods for acute benzodiazepine exposure, but possibly not for injury risk with chronic benzodiazepine dose escalation.

RESULTS:

Characteristics of All Claimants, Claims and Prescriptions:

Of a total of 238,172 claims, 45.1 % did not have PMP data, 99,291 (41.7%) had prescriptions for controlled substances before injury, while 31,540 (13.2%) had prescriptions for controlled substances after injury only (Figure 2). Of note, 72,569 (30.4%) had prescriptions before injury alone, while 26,722 (11.2%) had prescriptions both before and after injury. The prevalence of opioid and benzodiazepine use did not differ significantly between all workers and workers in safety sensitive occupations (Figure 3). Among claimants with prescriptions before injury, 71.8% had 1 claim, 20.6% had 2 claims and the remainder had 3 or more claims (Figure 4). Claims with prescriptions before injury had a larger proportion of women (37.5%) compared to claims with prescriptions after injury alone (25.4%), and claims without any prescriptions (30.0%) (Table 1, Table S1a). The average age of claimants with prescriptions before injury was 40.1 ± (0.04) years. Claims without paired PMP data had the lowest proportion of compensable claims (11.9%) compared to those with prescriptions before injury (23.7%) or after injury alone (34.7%) (Table1, Table S1a). Among claims with prescriptions before injury, the most prevalent injury nature category was 'traumatic injuries to muscles, tendons, ligaments, joints, etc' (43.3%); injury source was 'persons, plants, animals and minerals' (25.1%); accident type was 'bodily reaction and exertion' (54.1%); and affected body part were the 'upper extremities' (36.6%). The occupational classification group with the highest proportion of claims was the 'transportation and materials moving' (13.3%) category (Table 1, Table S1a).

Characteristics of Opioid Prescriptions & Claims with Opioid Prescriptions:

Of the 1,202,007 opioid prescriptions dispensed to claimants between 2011 and 2017, 44.5% were prescribed before injury and 55.5% prescribed after injury (Table S2). 99.8% of the 535,020 opioid prescriptions dispensed before injury met study criteria for acute use any time before injury, while 0.2% met the criteria for chronic use any time before injury (Table S2). Of the 114,492 opioid prescriptions dispensed within the 180 days preceding injury, 99.7% of them met study criteria for acute use, while 0.3% of them met criteria for chronic use (Table S2). The most commonly prescribed opioid before injury was hydrocodone-acetaminophen, which accounted for 58.3% of all opioids dispensed before injury (Table S4). The mean daily morphine equivalent dose (MED) per claim was 43.4 (± 39.5) mg (Table S6b).

Among claims with prescriptions for controlled substances before injury, 92.2 % had opioid prescriptions (Table 2b, Figure 3). Of the 121,667 claims with opioid prescriptions, 75.3% had prescriptions before injury while 24.7% had prescriptions after injury alone. Of the 91,587 claims with opioid prescriptions before injury, 28% met study criteria for acute opioid use while 5.5% met study criteria for chronic opioid use in the 180 days preceding injury (Table 2a); 66.5% of these claims had opioids dispensed prior to 180 days before injury and therefore did not meet study criteria for acute or chronic opioid use. Claims with any opioid use before injury had a higher proportion of women (37.5%) compared to claims with opioid prescriptions after injury alone (25.4%) (Table S1b). Claims with any opioid prescriptions before injury were less likely be compensable (24.8%) compared to claims with opioid prescriptions after injury alone (35.2%) (Table S1b). Claims with chronic opioid use before injury, and claims with opioid prescriptions after injury only had the highest proportion of compensable claims (35.0% and 35.2% respectively) (Table S1b). Within the 28 days preceding injury: 8.9% of all claims with opioid prescriptions before injury used an opioid, 5.3% used an opioid acutely, and 0.7% used an opioid chronically. Within the 56 days preceding injury: 15.3% of all claims with opioid prescriptions before injury used an opioid, 9.8% used an opioid acutely and 1.2% used an opioid chronically. Within the 86 days preceding injury: 28.4% of all claims with opioid prescriptions before injury used an opioid, 15.9% used an opioid acutely and 5.4% used an opioid chronically.

Characteristics of Benzodiazepine Prescriptions & Claims with Benzodiazepine Prescriptions:

Of the 239,178 benzodiazepine prescriptions dispensed to claimants between 2011 and 2017, 54.7% were prescribed before injury and 45.3% prescribed after injury (Table S3). Of the 130,893 benzodiazepine prescriptions dispensed before injury, 95.1% met the criteria for acute use any time before injury while 4.9% met the criteria for chronic use any time before injury (Table S3). Of the 29,993 benzodiazepine prescriptions dispensed in the 180 days preceding injury, 98.1% met criteria or acute use while 1.9% met criteria for chronic use (Table S3). The most commonly prescribed benzodiazepines before injury were alprazolam, clonazepam and lorazepam, which accounted for 33.3%, 25.6% and 24.7% of all benzodiazepines dispensed before injury respectively (Table S5). The mean daily DED per claim was 11.1 (± 9.5) mg (Table S6b).

Among claims with prescriptions before injury, 25.9 % had benzodiazepine prescriptions (Table 2b, Figure 3). Of the 28,777 claims with benzodiazepine prescriptions, 89.5% had prescriptions before injury while 10.5% had prescriptions after injury alone (Table S3). Of the 25,755 claims with benzodiazepine prescriptions before injury, 20.8% met study criteria for acute opioid use while 10.9% met study criteria for chronic benzodiazepine use (Table 2a); 68.3% of these claims had benzodiazepines dispensed prior to 180 days before injury and therefore did not meet study criteria for acute or chronic benzodiazepine use. Claims with any benzodiazepine use before injury had a higher proportion of women (50%) compared to claims with benzodiazepine prescriptions after injury alone (36.7%) (Table S3). Claims with any benzodiazepine prescriptions before injury were less likely be compensable (30.7%) compared to claims with benzodiazepine prescriptions after injury alone (44.9%) (Table S3). Claims with chronic benzodiazepine use before injury, and claims with benzodiazepines prescriptions after injury only had the highest proportion of compensable claims (33.7 and 44.9% respectively) (Table S3). Within the 28 days preceding injury: 13.3% of all claims with benzodiazepine prescriptions before injury used a benzodiazepine, 5.0% used a benzodiazepine acutely, and 2.1% used a benzodiazepine chronically. Within the 56 days preceding injury: 22.2% of all claims with benzodiazepine prescriptions before injury used a benzodiazepine, 8.2% used a benzodiazepine acutely, and 3.2% used a benzodiazepine chronically. Within the 84 days preceding injury: 45.7% of all claims with benzodiazepine prescriptions

before injury used a benzodiazepine, 14.5% used a benzodiazepine acutely, and 10.9% used a benzodiazepine chronically.

Relationship between Acute Opioid Use and Risk of Occupational Injury:

Among acute opioid users with 60 or fewer days of opioid prescriptions supplied in the 180 days preceding injury there was a statistically significant decreased risk of occupational injury reproduced across analyses with the 7-day, 14-day and 28-day hazard and control periods; the odds ratios obtained using conditional logistic regression were 0.84 (95%CI, 0.8 – 0.89), 0.82 (95%CI, 0.8 - 0.89), and 0.83 (95%CI, 0.80 – 0.86) respectively (Table 3a). This statistically significant decreased risk of occupational injury among acute opioid users persisted when the conditional logistic regression analysis was repeated for all safety sensitive fields combined (Table 3a). Similar odds ratios, also reaching statistical significance were obtained for each hazard period-control period pair using Mcnemar's test (Table S8a).

In terms of effect modification, there was no significant difference in odds ratios between males or females (Table S7a). Claims which were filed during the last 4 months of the year had slightly less protective odds ratios compared to claims that were filed during the first 4 months of the year (Table S7a).

Relationship between Acute Benzodiazepine Use and Risk of Occupational Injury:

Among acute benzodiazepine users with 60 or fewer days of benzodiazepine prescriptions supplied in the 180 days preceding injury, there was no statistically significant increase or decrease in occupational injury risk, even with claims filed by claimants in working in safety sensitive fields (Table 3b). In terms of effect modification, there was no clear difference in odds ratios in the association between acute benzodiazepine use and occupational injury risk between males or females, or between different times of the year (Table S7b).

Relationship between Change in Opioid Dose and Occupational Injury Risk among Chronic opioid users:

Increase in opioid dose of 10% among chronic opioid users was not associated with a statistically significant change in occupational injury risk (Table 4a).

Relationship between Change in Benzodiazepine Dose and Occupational Injury Risk Among Chronic Benzodiazepine users:

Increase in benzodiazepine dose of 10% among chronic benzodiazepine users was not associated with a statistically significant change in occupational injury risk (Table 4b).

DISCUSSION:

This study is one of the first studies to use the case crossover design to assess the relationship between opioid or benzodiazepine use and occupational injury risk. The observed association of decreased occupational injury risk with acute opioid use was unexpected, particularly given the mechanism of action, CNS effects of opioids, and prior literature demonstrating an increased risk of occupational and non-occupational injury associated with opioid use. No statistically significant effect was observed for the association between acute benzodiazepine use and occupational injury risk. Furthermore, dose change in opioids or benzodiazepines did not have a statistically significant association with occupational injury risk. Various elements of the study design, databases used, as well as confounding and misclassification of exposures and outcome may help explain the observed effects.

Study Design:

The case crossover study design may partially explain the association observed between opioid use and occupational injury risk due to biases introduced because of how the control periods were selected. This study design is useful for determining the effects of transient or intermittent exposures on acute events, using only cases. For each individual case, exposure just before the event (hazard or index period) is compared to exposure at other times (control or referent periods)[30,31,41,50]. The case crossover design assumes that there is no exposure trend across the control periods.[31,41,51] Control period selection can

however introduce bias in the statistical determination of risk measures.[41,50] For this study we employed a unidirectional approach to selecting the control periods.

In the air pollution literature in which the case crossover design has been widely used, studies on potential biases associated with the choice of control periods suggest that time-stratified and full-stratum bidirectional control period selection schemes are the least likely to introduce bias, while the (restricted) unidirectional control period selection scheme has a high likelihood of introducing time trend bias and consequently biased effect estimates.[41,51] In time-stratified control period selection, time is divided into separate strata, and the index time used to determine which stratum a given case falls into; all or a sample of the remaining times in the stratum then serve as control or referent periods for the case. [41,51] The full-stratum bidirectional referent selection strategy involves choosing control periods both before and after the index time, such that the control periods encompass all days in the exposure series other than the index day.[41,51] Bidirectional sampling is valid only if cases remain at risk after an event; it cannot for instance be used if cases die as a result of an event of interest.[41,51] With restricted unidirectional design, the controls periods are usually selected close to or on the same day of the week as the index day.[41,51]

In case crossover studies investigating the effects of ambient air pollution, the exposure i.e. air pollution is exogenous or produced independently of the case being investigated.[31,41,50] As such, the short-term distribution of exposure within subjects may be more globally exchangeable.[31,50] In this study, the prescription opioid and benzodiazepine exposures of interest can be considered endogenous exposures since they are influenced by individual indications, behavior and choices. Consequently, the marginal probability of being similarly exposed in the hazard compared to the control periods may differ considerably, particularly since the exposure distribution may not be stationary over time.[50] The unidirectional control period selection approach employed in our study may therefore have introduced both control time selection bias as well as time trend bias.

Control period selection bias occurs when the control period is not selected independently of the exposure; the exposure distribution in the control period therefore does not represent the exposure

distribution of the person-time giving rise to the cases.[31] For instance, selecting a control period when the case is more likely to be exposed can lead to a downward bias in the effect estimate, while selecting a control period when the case is less likely to be exposed can lead to a upward bias of the effect estimate.[31] Time trend bias refers to trends in either exposure or outcome that may introduce non-exchangeability between the hazard and control periods.[31] In this study, there was an observed trend towards a decrease in the number of opioid prescriptions used moving chronologically forward from the fourth control period to the hazard period (Table S6). Based on this observation, it is possible that among opioid users, there is a behavioral tendency towards decreasing opioid use prior to return to work perhaps because of knowledge of opioid side effects. This trend may partly explain the odds ratio obtained for the association between acute opioid use and occupational injury risk. No exposure trend was observed for the distribution of acute benzodiazepine prescriptions across the control and hazard periods (Table S6). An additional critical issue with control period selection in this study was the absence of information on employment status among the cases. Without these data, it was not possible to ascertain whether cases had a similar probability of sustaining an occupational injury across the control and hazard periods. It was only possible to say for certain that they were at work on the date of injury. As such, the control periods selected may have included person-times that did not truly represent the probability of exposure at times when an occupational injury could occur, thereby further introducing bias.[31]

For the secondary goal of the study, change in opioid or benzodiazepine dose between the first control period and hazard period was compared to dose changes between consecutive control periods moving forward chronologically. No statistically significant association was observed between an increase in opioid or benzodiazepine dose of 10% or greater among chronic users and occupational injury risk. Control period selection and time trend biases may have contributed to the absence of statistically significant effect estimates. The chosen size of the difference in opioid or benzodiazepine dose between hazard and control periods may also have been too small to allow a statistically significant effect measure to be observed. Furthermore, it may not have been statistically appropriate to assess for an association between change in dose in only one direction and occupational injury risk.

Based on the biases potentially introduced because of control period selection, and time trends in exposure, repeating the conditional logistical regression analyses using the time-stratified approach for selecting the control periods may help to eliminate these biases. The full-stratum bidirectional approach may however not be appropriate for the study aims, primarily given difference in the prevalence of opioid and benzodiazepine prescriptions use before and after injury.

Completeness and Reliability of Data Sources:

The Washington State Department of Labor and Industries claims database is an administrative database generated as a byproduct of clinical care received by injured workers covered by worker's compensation benefits through the Washington State Fund.[32] This database was used to characterize occupational injuries among cases included in the study analyses. Much of the data in the claims database is obtained from documents such as the 'report of accident' and 'activity prescription form' typically completed at the time the injured worker seeks medical care.[32] Since this data is administrative in nature, and therefore not necessarily developed to support epidemiologic research, it is prone to both random and systematic errors. For instance, the injury dates provided in this dataset are typically based on the report of the injured worker and may as such be subject to recall bias, particularly if medical care is sought some-time after an injury occurs or if the injured worker does not immediately report the injury incident to their employer. Furthermore, systematic errors may be introduced in the process of transferring data from paper records to electronic form, and again in its preparation and de-identification for use in this study. The injury data provided is also incomplete in that it does not include injured workers employed by self-insured companies in Washington state, or workers who may have been injured but did not file a claim, including those who may have been taking opioids or benzodiazepines prior to injury. The injury types, occupations, as well as opioid or benzodiazepine use profiles represented in self-insured claims data or among injured workers who did not file claims may differ from those in the state-funded claims, and could thereby affect effect estimates if included in the study.

The Prescription Monitoring Program (PMP) database provides data on all Schedule II, III, IV, V drugs dispensed in Washington state since October 2011.[34,35] The PMP data was merged with the

administrative claims data prior to performing statistical analyses. In this study, it was assumed that claimants without PMP data had not been prescribed or dispensed any Schedule II, III, IV or V medications after October 2011. This was primarily because populations served by dispensers excluded from reporting e.g. incarcerated populations, populations receiving inpatient care, and populations receiving immediate one day use such as in methadone clinics, are unlikely to be working and therefore at very low risk of sustaining occupational injuries. In terms of completeness of the data for dispensers required to report, review of data and statistical reports available through the Washington State Department of Health did not yield information from which the negative predictive value of not having paired PMP data could be inferred. However, given that licensed dispensers are required by law to report this data and may be subject to disciplinary action for non-compliance, it is likely that the dispenser reporting compliance rates are relatively high.

Confounding:

Because each case serves as their own control in the case crossover study design, self-matching eliminates confounding from time-invariant characteristics. However, there are potential other sources of confounding not controlled for in this study which could have contributed to the effect measures observed. These include confounding by transient or acute indication, transient co-exposure, time trends and unknown or unmeasured time-variant individual characteristics.

In case crossover studies that examine the impact of transient changes in drug use, self-matching removes confounding by indication for chronic health factors, including factors that cannot be measured.[31] However transient indications for a drug can result in lack of exchangeability between hazard and control periods thereby impacting effect estimates.[31] In this study, an opioid or benzodiazepine prescription may have been dispensed for a transient indication that made individuals less likely to be working and therefore at decreased risk of sustaining an occupational injury. In this instance, the person-time represented by the hazard and control periods is not exchangeable; an individual is more likely to be exposed during lower risk of the outcome than during other times leading to a biased estimate of the associations of interest.[31] The likelihood of an individual being dispensed an opioid or benzodiazepine for

a transient indication that made them more likely to return to work is probably much lower, but could also lead to biased effect estimates.

Confounding by transient co-exposures refers to transient co-exposures that may also trigger the outcome.[31] In this study, exposure to other sedating medications such as muscle relaxants, anti-seizure medications, and sedative hypnotic sleep aids which may be associated with opioid or benzodiazepine use and occupational injury risk were not controlled for. Such co-exposures could occur at different levels/frequencies between hazard and control periods thereby yielding biased effect estimates of the association between opioid or benzodiazepine use and occupational injury risk. Additional analyses in which these co-exposures are controlled for, including simultaneous exposure to both opioids and benzodiazepines, could yield more accurate effect estimates for the association between opioid or benzodiazepine use and occupational injury risk.[31]

Confounding by time trends in both exposure and outcome can occur if time trends introduce non-exchangeability between the hazard and control periods.[31] Since the release of the *Washington State Interagency Guideline on Opioid Dosing for Chronic Pain* in 2007, a decrease in opioid prescribing has been demonstrated among certain populations.[52] This decrease in opioid prescribing practices over time, could potentially explain the observed protective effect between opioid use and occupational injury risk. However, this is somewhat unlikely since the time trend in opioid prescribing has occurred over years, while the hazard and control periods in this study are weeks in length. The change in opioid prescribing practices should therefore not significantly impact the measures of risk. Time trends related to occupational injury risk, such as work seasonality, should yield valid results if the probability of exposure remains stable.[31] However, if the distribution of exposure and outcome risk changes between hazard and control periods, as is the likely case in this study, non-exchangeability may arise resulting in biased measures of risk.[31] This type of non-exchangeability between hazard and control periods could be decreased by conditioning on time, selecting control periods that occur on the same day as the index or event day, or comparing control period exposure at the same time of day as the hazard period.[31] There is also the possibility of within-individual time trend bias introduced by the unidirectional selection of the

control periods. [41,51] This type of time trend bias could be addressed by again choosing the time-stratified control period selection approach.[41]

There is also the possibility of confounding by unknown time-variant individual characteristics. The data used in this study did not include information on alcohol or recreational drug use, fatigue-related factors such as restricted sleep duration, or duration of employment or experience on the job. It is possible that such time-variant individual behaviors could be associated with the likelihood of being prescribed an opioid or a benzodiazepine and with occupational injury risk, thereby serving as uncontrolled confounders. [9,14,16,17,53] Furthermore, since individuals with multiple claims were included in the study, there was also the possibility for confounding related to already having an occupational injury; sustaining one occupational injury may be associated with an increased likelihood of being prescribed an opioid or benzodiazepine, as well as increased risk of having subsequent injuries. That said, prior analyses performed (data not shown), in which individuals with more than one claim were excluded, yielded similar effect measures to the present study analyses in which claimants with more than one claim were included. Finally, there may also be autocorrelation, which occurs when the exposure or outcome risk in one time period is correlated with exposure levels in other time periods leading to non-independence.[31] This is again more likely to be an issue in claimants with more than one claim.

Misclassification of Exposure and Outcome

In this study, the exposures were determined using PMP data on prescription dispensation dates. It was assumed that the medications were used as prescribed upon being dispensed. However, the data did not provide information about how the medications were taken and therefore reflects likely but not actual exposure to opioids and benzodiazepines. This likely introduced non-differential exposure misclassification of the control and hazard periods, and is a limitation of the study data in that it likely resulted in bias of the odds ratios towards the null value. Also, because the duration of CNS effects of opioids and benzodiazepines are typically on the order of hours, the study data and consequently the length of control and hazard periods chosen, may not have been granular enough to truly capture the

injury effects of acute opioid or benzodiazepine use or of change in opioid or benzodiazepine use among chronic users.

In terms of outcome misclassification, occupational injury cases were limited to those that were characterized using the Occupational Injury and Illness Classification (OIICS) system as 'traumatic injuries and disorders' under injury nature. These types of injuries were specifically selected with the goal of only including acutely occurring occupational injuries such as fractures, burns, abrasions, intracranial injuries, sprains etc. Of all the claims with Scheduled II, III, IV, and V prescription used before injury, 43.4% had injuries that fell under the subcategory of 'traumatic injuries to muscles, bones, ligaments, joints etc.'; 43.6% of these claims with opioid prescriptions and 47.8% with benzodiazepine prescriptions fell into this injury nature subcategory. This subcategory includes injuries which may be acute in nature, but may also include injuries or occupational musculoskeletal diseases that occur as a result of repetitive work-related activities and are therefore more chronic in nature. The possible inclusion of injuries that did not occur acutely may have introduced non-differential misclassification of the outcome, thereby resulting in bias of the odds ratios obtained towards the null value.

CONCLUSIONS: This study is one of the first to use the case crossover study design to study the association between opioid and benzodiazepine use and occupational injury risk. The study demonstrated that acute opioid use is associated with a statistically significant decreased risk of occupational injury. Given current literature and mechanism of action of opioid medications, this finding was surprising but may have arisen because of bias introduced from unidirectional control period selection, as well as confounding related to observed opioid prescribing time trends. These results should therefore be interpreted with caution. There was no statistically significant association between acute benzodiazepine use and occupational injury risk. There was no statistically significant association between increase in opioid or benzodiazepine dose and occupational injury risk among chronic opioid and benzodiazepine users. Future work should include using the time-stratified approach to selecting the control periods, and also repeating analyses controlling for time-variant individual characteristics as well as time trends.

KEY TABLES AND FIGURES

Table 1. Characteristics of Claims with Prescriptions Before Injury Compared to Claims without Any Prescriptions

Variable	Claims with Any Prescription Before Injury (%)	Claims without Any Prescriptions Before or After Injury (%)	Claims with Any Opioid Before Injury (%)	Claims with Any Benzodiazepine Before Injury (%)
Age (years)				
18 - 24	13,376 (13.5)	21570 (20.1)	12091 (13.2)	2176 (8.5)
25 - 29	12,182 (12.3)	16832 (15.7)	11237 (12.3)	2520 (9.8)
30 - 24	12,284(12.4)	15018 (14.0)	11474 (12.5)	3076 (11.9)
35 - 39	11,326(11.4)	12050 (11.2)	10524 (11.5)	3201 (12.4)
40 - 44	11,192 (11.3)	11002 (10.3)	10382 (11.3)	3203 (12.4)
45 - 49	10,879 (11.0)	9617 (9.0)	10019 (10.9)	3366 (13.1)
50 - 54	11,875 (12.0)	9013(8.4)	10981 (12.0)	3554 (13.8)
55 - 59	9,852 (9.9)	7311 (6.8)	9094 (9.9)	2903 (11.3)
60 - 65	6,325 (6.40)	4928 (4.6)	5785 (6.3)	1756 (6.8)
Total	99291 (100)	107341 (100)	91587 (100)	25755 (100)
Sex				
Female	34,340 (37.5)	32,246 (30.0)	34340 (37.5)	12953 (50.3)
Male	57,246 (62.5)	75,092 (70.0)	57246 (62.5)	12802 (49.7)
Total	91,586 (100)	107,341 (100)	91586 (100)	25755 (100)
Injury Year				
Yr 2013	27992 (28.2)	36059 (33.6)	25650 (28.0)	7639 (29.7)
Yr 2014	34640 (34.9)	35844 (33.4)	31885 (34.8)	9016 (35.0)
Yr 2015	36659 (36.9)	35438 (33.0)	34052 (37.2)	9100 (35.3)
Total	99291 (100)	107341 (100)	91587 (100)	25755 (100)
Claim Status				
Non compensable	70184 (70.7)	90195 (84.0)	63552 (69.4)	16428 (63.8)
Compensable	23575 (23.7)	12809 (11.9)	22715 (24.8)	7915 (30.7)
Fatal	23 (0.02)	69 (0.06)	20 (0.02)	8 (0.03)
Total permanent disability	87 (0.09)	24 (0.02)	87 (0.1)	43 (0.2)
Kept on Salary	4898 (4.93)	3966 (3.7)	4708 (5.1)	1179 (4.6)
Loss of earning power	524 (0.5)	278 (0.3)	505 (0.6)	182 (0.7)
Total	99291 (100)	107341 (100)	91587 (100)	25755 (100)
Injury Nature				
Traumatic injuries and disorders, unspecified	440 (0.4)	378 (0.4)	408 (0.5)	121 (0.5)
Traumatic injuries to bones, nerves,spinal cord	6929 (7.0)	5531 (5.2)	6576 (7.2)	1757 (6.8)
Traumatic injuries to muscles, tendons, ligaments, joints etc	43068 (43.4)	37024 (34.5)	39924 (43.6)	12303 (47.8)
Open wounds	18533 (18.7)	30824 (28.7)	16644 (18.2)	3765 (14.6)
Surface wounds and bruises	14168 (14.3)	18093 (16.9)	13027 (14.2)	3171 (12.3)
Burns	1968 (2.0)	2560 (2.4)	1817 (2.0)	415 (1.6)
Intracranial injuries	1840 (1.9)	1841 (1.7)	1659 (1.8)	587 (2.3)
Multiple traumatic injuries and disorders	7659 (7.7)	7290 (6.8)	7154 (7.8)	2258 (8.8)
Other traumatic injuries and disorders	4686 (4.7)	3800 (3.5)	4378 (4.8)	1378 (5.4)
Total	99291 (100)	107341 (100)	91587 (100)	25755 (100)
Occupational Classification				
Management Occupations	3174 (3.2)	2488 (2.3)	2851 (3.1)	1026 (4.0)
Business and Financial Operations	653 (0.7)	424 (0.4)	572 (0.6)	257 (1.0)
Computer and mathematical occupations	241 (0.2)	264 (0.3)	219 (0.2)	71 (0.3)
Architecture and engineering occupations	385 (0.4)	377 (0.4)	333 (0.4)	114 (0.4)
Life, physical and social science occupations	385 (0.4)	542 (0.5)	331 (0.4)	104 (0.4)
Community and social services occupations	1030 (1.0)	682 (0.6)	911 (1.0)	392 (1.5)
Legal occupations	100 (0.1)	77 (0.1)	88 (0.1)	38 (0.2)
Education, training and library occupations	1295 (1.3)	1145 (1.1)	1130 (1.2)	472 (1.8)
Arts, design, entertainment, sports, media	695 (0.7)	778 (0.7)	609 (0.7)	161 (0.6)
Healthcare practitioners and technical	3437 (3.5)	3502 (3.3)	3007 (3.3)	1327 (5.2)
Healthcare support occupations	6127 (6.2)	4919 (4.6)	5645 (6.2)	2167 (8.4)
Protective services occupations	3256 (3.3)	2199 (2.1)	2979 (3.3)	963 (3.7)
Food preparation and serving related	8062 (8.1)	10622 (9.9)	7378 (8.1)	2043 (4.1)
Building and grounds cleaning	4449 (4.5)	5840 (5.4)	4147 (4.5)	1060 (4.1)
Personal care and service occupations	3733 (3.8)	2989 (2.8)	3434 (3.8)	1280 (5.0)
Sales and related occupations	4266 (4.3)	3610 (3.4)	3859 (4.2)	1347 (5.2)
Office and administrative support occup	4998 (5.0)	3920 (3.7)	4520 (4.9)	1613 (6.3)
Farming, fishing and forestry occupations	3067 (3.1)	9629 (9.0)	2830 (3.1)	459 (1.8)
Construction and extraction occupations	11454 (11.5)	13316 (12.4)	10819 (11.8)	2413 (9.4)
Installation, maintenance and repair	9169 (9.2)	8562 (8.0)	8553 (9.3)	1960 (7.6)
Production occupations	10108 (10.2)	11172 (10.4)	9437 (10.3)	2004 (7.8)
Transportation and material moving	13169 (13.3)	13596 (12.7)	12347 (13.5)	2855 (11.1)
Military specific occupations	3 (0.0)	1 (0.0)	3 (0.03)	1 (0.0)
Not Classified	6040 (6.1)	6687 (6.2)	5585 (6.1)	1628 (6.3)
Total	99291 (100)	107341 (100)	91587 (100)	25755 (100)

Table 2a. Characteristics of Claims with Acute and Chronic Opioid or Benzodiazepine use Before Injury

Variable Components	Any Acute Opioid Before Injury (%)	Any Chronic Opioid Before Injury (%)	Total (%)	Any Acute Benzo Before Injury (%)	Any Chronic Benzo Before Injury (%)	Total (%)
Age (years)						
18 - 24	3383 (13.2)	87 (1.7)	3470 (11.3)	514 (9.6)	105 (3.7)	619 (7.6)
25 - 29	3365 (13.1)	219 (4.3)	3584 (11.7)	584 (10.9)	199 (7.1)	783 (9.6)
30 - 24	3357 (13.1)	453 (9.0)	3810 (12.4)	609 (11.4)	280 (9.9)	889 (10.9)
35 - 39	3112 (12.1)	524 (10.4)	3636 (11.8)	675 (12.6)	325 (11.5)	1000 (12.2)
40 - 44	2880 (11.2)	631 (12.5)	3511 (11.4)	638 (11.9)	357 (12.7)	995 (12.2)
45 - 49	2731 (10.6)	788 (15.6)	3519 (11.5)	669 (12.5)	406 (14.4)	1075 (13.2)
50 - 54	2959 (11.5)	982 (19.5)	3941 (12.8)	714 (13.3)	459 (16.3)	1173 (14.4)
55 - 59	2414 (9.4)	819 (16.3)	3233 (10.5)	579 (10.8)	422 (15.0)	1001 (12.3)
60 - 65	1474 (5.7)	538 (10.7)	2012 (6.6)	369 (6.9)	267 (9.5)	636 (7.8)
Total	25675 (100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)
Sex						
Female	10367(40.4)	2173 (43.1)	12540 (40.8)	3113 (58.2)	1569 (55.6)	4682 (57.3)
Male	15308 (59.6)	2868 (56.9)	18176 (59.2)	2238 (41.8)	1251 (44.4)	3489 (42.7)
Total	25675 (100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)
Injury Year						
Yr 2013	8327 (32.4)	1609 (31.9)	9936 (32.4)	1704 (31.8)	952 (33.8)	2656 (32.5)
Yr 2014	8788 (34.3)	1686 (33.5)	10474 (34.1)	1886 (35.3)	985 (34.9)	2871 (35.1)
Yr 2015	8560 (33.3)	1746 (34.6)	10306 (33.6)	1761 (32.9)	883 (31.3)	2644 (32.4)
Total	25675 (100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)
Claim Status						
Non compensable	17767 (69.2)	2988 (59.3)	20755 (67.6)	3716 (69.4)	1715 (60.8)	5431 966.5)
Compensable	6539 (25.5)	1762 (35.0)	8301 (27.0)	1387 (25.9)	951 (33.7)	2338 (28.6)
Fatal	3 (0.01)	1 (0.02)	4 (0.01)	3 (0.1)	1 (0.04)	4 (0.1)
Total permanent disability	27 (0.1)	15 (0.3)	42 (0.1)	4 (0.1)	8 (0.3)	12 (0.2)
Kept on Salary	1184 (4.6)	244 (4.8)	1428 (4.7)	209 (3.9)	121 (4.3)	330 (4.0)
Loss of earning power	155 (0.6)	31 (0.6)	186 (0.6)	32 (0.6)	24 (0.9)	56 (0.7)
Total	25675(100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)
Injury Nature						
Traumatic injuries and disorders, unspecified	105 (0.4)	26 (0.5)	131 (0.4)	31 (0.6)	17 (0.6)	48 (0.6)
Traumatic injuries to bones, nerves,spinal cord	1692 (6.6)	381 (7.6)	2073 (6.8)	335 (6.3)	192 (6.8)	527 (6.5)
Traumatic injuries to muscles, tendons, ligaments, joints etc	11205 (53.6)	2395 (47.5)	13600 (44.3)	2419 (45.2)	1334 (47.3)	3753 (45.9)
Open wounds	4527 (17.6)	644 (12.8)	5171 (16.8)	867 (16.2)	385 (13.7)	1252 (15.3)
Surface wounds and bruises	3713 (14.5)	681 (13.5)	4394 (14.3)	746 (13.9)	324 (11.5)	1070 (13.1)
Burns	554 (2.2)	65 (1.3)	619 (2.0)	84 (1.6)	44 (1.6)	128 (1.6)
Intracranial injuries	472 (1.8)	85 (1.7)	557 (1.8)	122 (2.3)	79 (2.8)	201 (2.5)
Multiple traumatic injuries and disorders	2120 (8.3)	477 (9.5)	2597 (8.5)	472 (8.8)	300 (10.6)	772 (9.5)
Other traumatic injuries and disorders	1287 (5.0)	287 (5.7)	1574 95.1)	275 (5.1)	145 (5.1)	420 (5.1)
Total	25675 (100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)
Occupational Classification						
Management Occupations	778 (3.0)	165 (3.3)	943 (3.1)	267 (5.0)	119 (4.2)	386 (4.7)
Business and Financial Operations	163 (0.6)	48 (1.0)	211 (0.7)	63 (1.2)	39 (1.4)	102 (1.3)
Computer and mathematical occupations	55 (0.2)	17 (0.3)	72 (0.2)	14 (0.3)	12 (0.4)	26 (0.3)
Architecture and engineering occupations	83 (0.3)	19 (0.4)	102 (0.3)	27 (0.5)	12 (0.4)	39 (0.5)
Life, physical and social science occupations	75 (0.3)	15 (0.3)	90 (0.3)	21 (0.4)	12 (0.4)	33 (0.4)
Community and social services occupations	267 (1.0)	57 (1.1)	324 (1.1)	87 (1.6)	71 (2.5)	158 (1.9)
Legal occupations	23 (0.1)	6 (0.1)	29 (0.1)	11 (0.2)	3 (0.1)	14 (0.2)
Education, training and library occupations	344 (1.3)	57 (1.1)	401 (1.3)	117 (2.2)	56 (2.0)	173 (2.1)
Arts, design, entertainment, sports, media	167 (0.7)	27 (0.5)	194 (0.6)	29 (0.5)	24 (0.9)	53 (0.6)
Healthcare practitioners and technical	864 (3.4)	222 (4.4)	1086 (3.5)	346 (6.5)	187 (6.6)	533 (6.5)
Healthcare support occupations	1783 (6.9)	371 (7.4)	2154 (7.0)	497 (9.3)	254 (9.0)	751 (9.2)
Protective services occupations	740 (2.9)	160 (3.2)	900 (2.9)	188 (3.5)	94 (3.3)	282 (3.5)
Food preparation and serving related	2168 (8.4)	335 (6.7)	2503 (8.2)	440 (8.2)	243 (8.6)	683 (8.4)
Building and grounds cleaning	1156 (4.5)	191 (3.8)	1347 (4.4)	202 (3.8)	123 (4.4)	325 (4.0)
Personal care and service occupations	1038 (4.0)	230 (4.6)	1268 (4.1)	298 (5.6)	162 (5.7)	460 (5.6)
Sales and related occupations	1120 (4.4)	266 (5.3)	1386 (4.5)	295 (5.5)	196 (7.0)	491 (6.0)
Office and administrative support occupations	1325 (5.2)	309 (6.1)	1634 (5.3)	368 (6.9)	206 (7.3)	574 (7.0)
Farming, fishing and forestry occupations	697 (6.7)	72 (1.4)	769 (2.5)	78 (1.5)	29 (1.0)	107 (1.3)
Construction and extraction occupations	2859 (11.1)	581 (11.5)	3440 (11.2)	401 (7.5)	212 (7.5)	613 (7.5)
Installation, maintenance and repair	2190 (8.5)	497 (9.9)	2687 (8.8)	340 (6.4)	195 (6.9)	535 (6.6)
Production occupations	2727 (10.6)	471 (9.3)	3198 (10.4)	386 (7.2)	185 (6.6)	571 (7.0)
Transportation and material moving	3415 (13.3)	565 (11.2)	3980 (13.0)	521 (9.7)	227 (8.1)	748 (9.2)
Military specific occupations	3 (0.01)	0 (0.0)	3 (0.01)	1 (0.02)	0 (0.0)	1 (0.01)
Not Classified	1635 (6.4)	360 (7.1)	1995 (6.5)	354 (6.6)	159 (5.6)	513 (6.3)
Total	25675 (100)	5041 (100)	30716 (100)	5351 (100)	2820 (100)	8171 (100)

Table 2b. Summary of Distribution of Opioid and Benzodiazepine Prescriptions Before Injury

	All Claims		Claims In Safety Sensitive Fields	
Variable	**N**	**% Of Claims with Prescriptions before Injury**	**N**	**% of Claims with Prescriptions before Injury**
Claims with Any Prescriptions before Injury	99291	100.0	67964	100.0
Claims with Any Opioid Before Injury	91587	92.2	63198	93.0
Claims with Any Benzodiazepine Before Injury	25755	25.9	16488	24.3
Claims with Any Other Prescription (not an Opioid or Benzodiazepine) Before Injury	38956	39.2	25649	37.7
Opioids (Acute and Chronic)				
Claims with An Acute Opioid Prescription Before Injury	25675	25.9	17469	25.7
Claims with A Chronic Opioid Prescription Before Injury	5041	5.1	3360	4.9
Benzodiazepines (Acute and Chronic)				
Claims with An Acute Benzodiazepine Prescription Before Injury	5351	5.4	4935.0	7.2
Claims with A Chronic Benzodiazepine Prescription Before Injury	2820	2.8	1668.0	2.5

Table 3a. Association between Acute Opioid Use and Occupational Injury Risk using Conditional Logistic Regression Analysis

	Claims With Acute Opioid Prescriptions Before Injury (N = 25,675)		Claims with Acute Prescriptions Opioid Before Injury in Safety Sensitive Fields (N = 17,469)	
Prescription (Hazard & Control Period Length)	OR	95% CI	OR	95% CI
Opioid (7-day)	0.84*	0.80 - 0.89	0.82*	0.76-0.87
Opioid (14-day)	0.87*	0.82 - 0.89	0.85*	0.80 - 0.89
Opioid (28-day)	0.83*	0.80 - 0.86	0.83*	0.79-0.86

*p <0.05

Table 3b. Association between Acute Benzodiazepine Use and Occupational Injury Risk using Conditional Logistic Regression Analysis

	Claims With Acute Prescriptions Before Injury (N = 5351)		Claims with Acute Prescriptions Before Injury in Safety Sensitive Fields (N = 3257)	
Prescription (Hazard & Control Period Length)	OR	95% CI	OR	95% CI
Benzodiazepine (7-day)	1.03	0.93 - 1.14	1.05	0.91 - 1.20
Benzodiazepine (14-day)	0.97	0.9 - 1.05	0.98	0.88 - 1.08
Benzodiazepine (28-day)	0.97	0.91 - 1.04	0.96	0.88 - 1.04

Table 4a. Association between Dose Change among Chronic Opioid Users and Occupational Injury Risk using Conditional Logistic Regression Analysis

	Claims With Chronic Opioid Prescriptions Before Injury (N = 11,213)	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid (7-day)	1.02	0.96 - 1.08
Opioid (14-day)	1.01	0.96 - 1.06
Opioid (28-day)	0.99	0.94 - 1.04

Table 4b. Association between Dose Change among Chronic Benzodiazepine Users and Occupational Injury Risk using Conditional Logistic Regression Analysis

	Claims With Chronic Prescriptions Before Injury (N = 6261)	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	0.99	0.91 - 1.07
Benzodiazepine (14-day)	1.04	0.97 - 1.12
Benzodiazepine (28-day)	1.04	0.97 - 1.13

Figure 1. Etiologically Relevant Hazard and Control Periods for Occupational Injury Risk Measure Assessment.

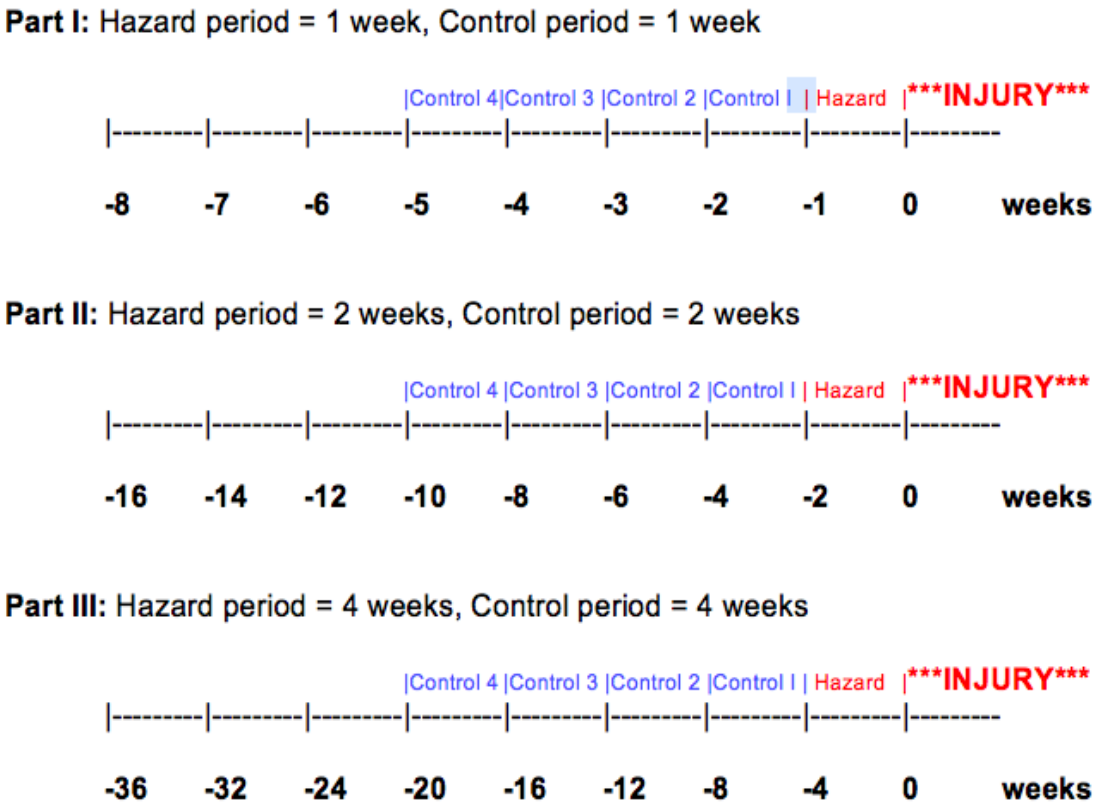


Figure 2. Distribution of Time of Prescription Use Relative to Injury for all Claims

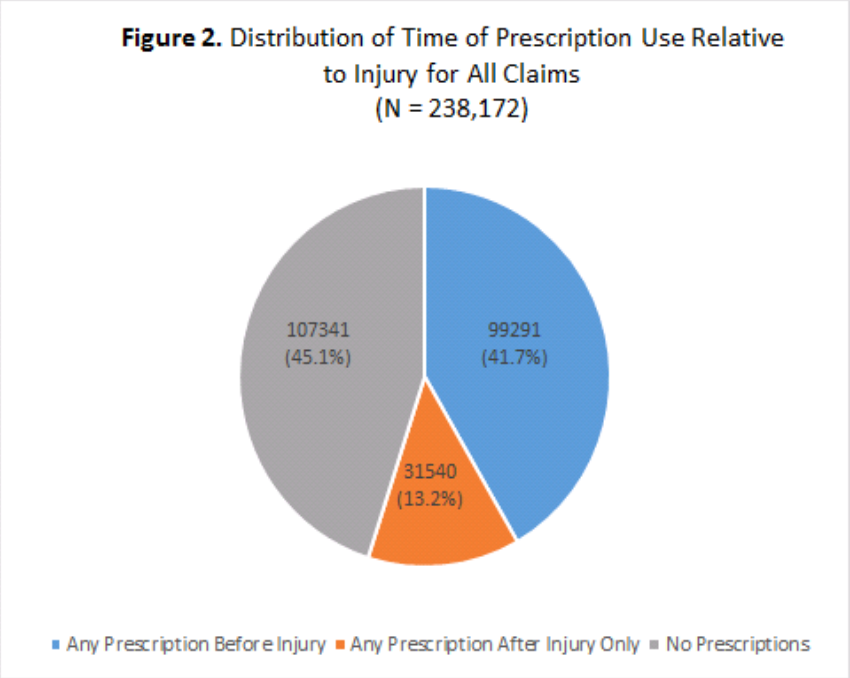


Figure 3. Use of Opioid, Benzodiazepines and Other Prescriptions Before Injury

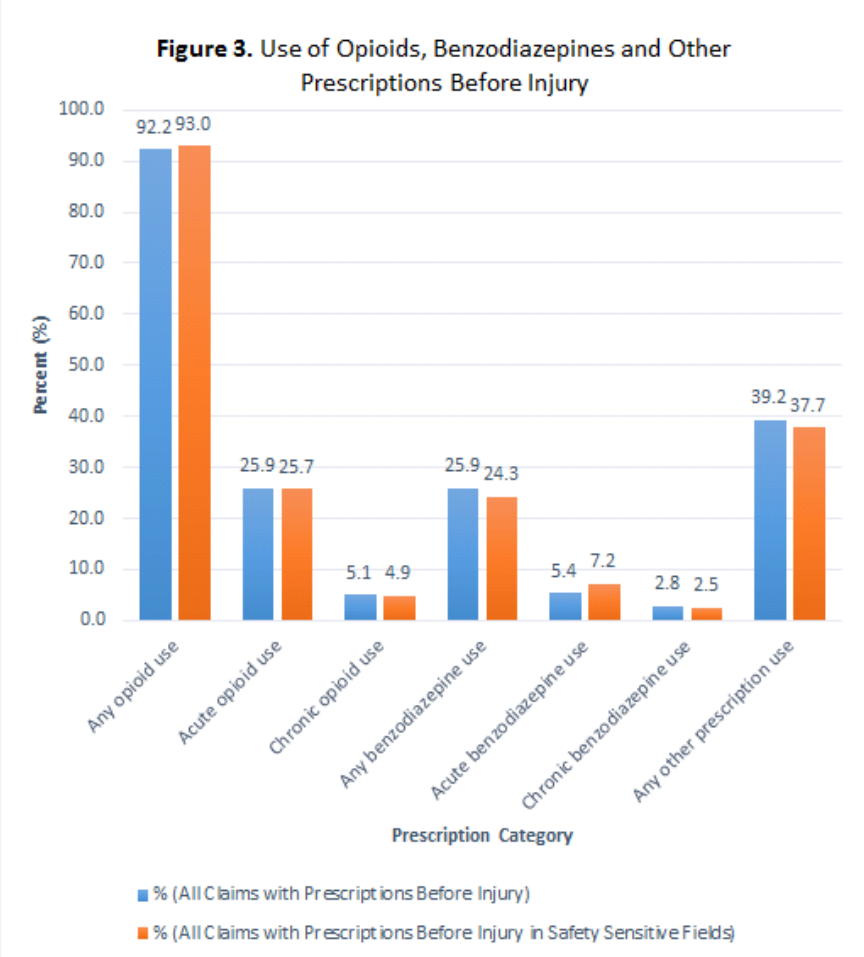


Figure 4. Distribution of Number of Claims per Claimant With Prescriptions Before Injury

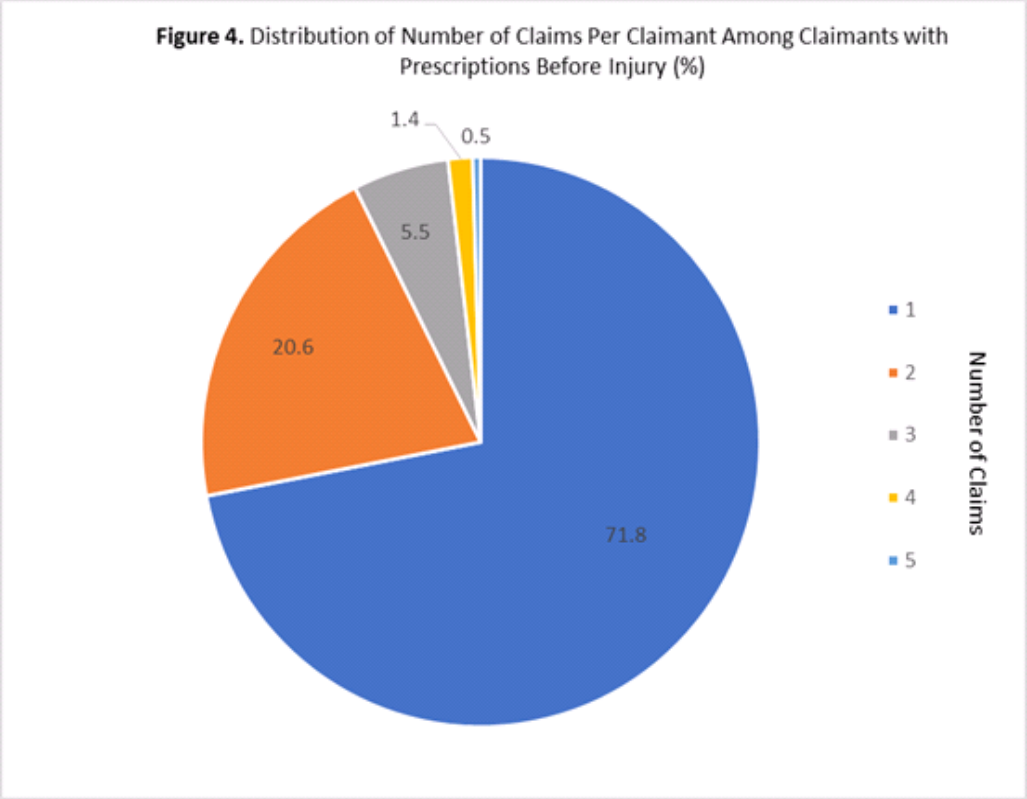


Figure 5a. Distribution of Days of Prescription Supplied Among Acute Opioid Users

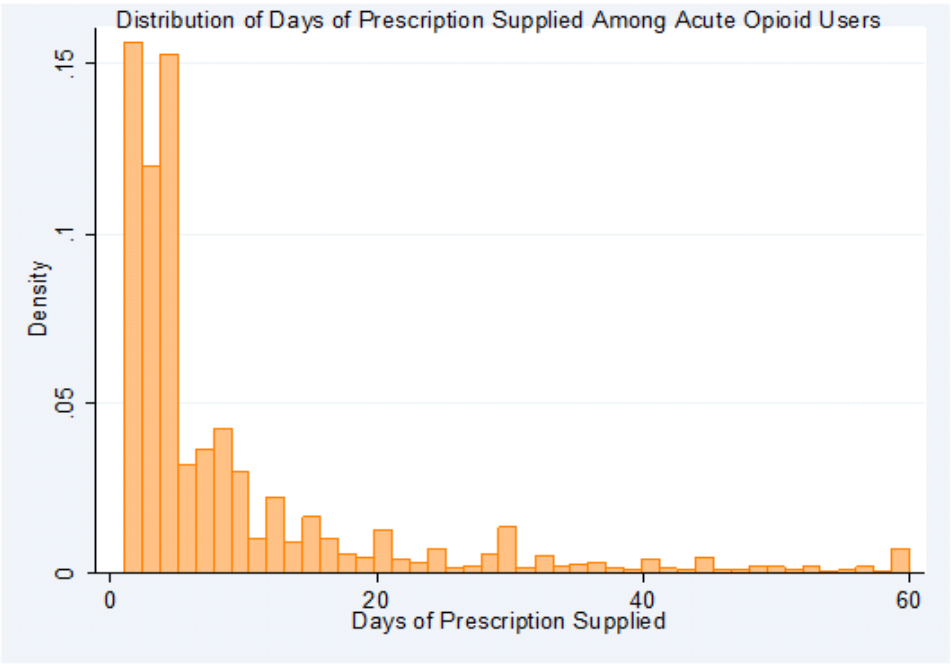


Figure 5b. Distribution of Days of Prescription Supplied Among Acute Benzodiazepine Users

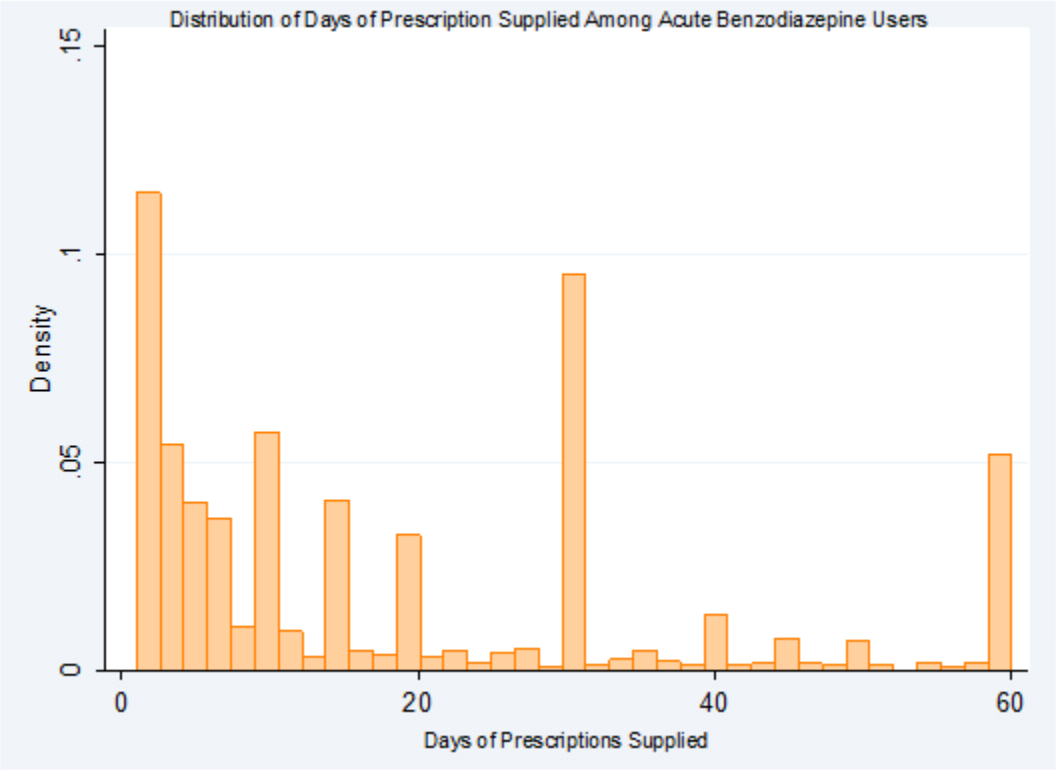


Figure 5c. Distribution of Days of Prescription Supplied Among Chronic Opioid Users

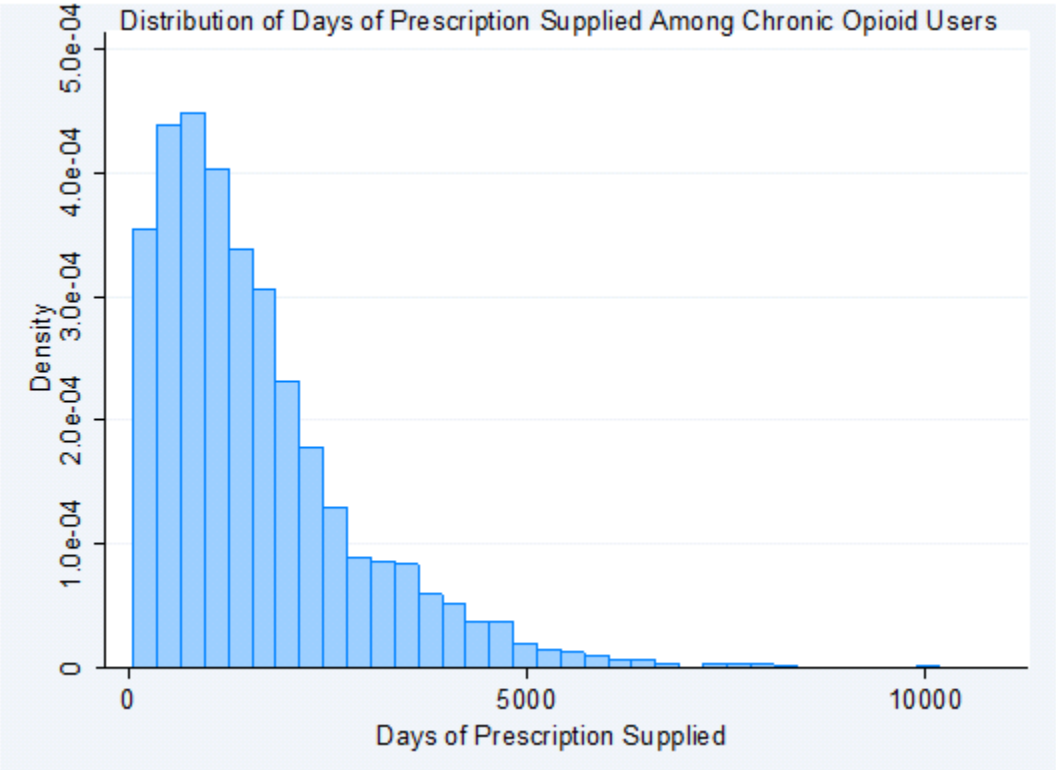
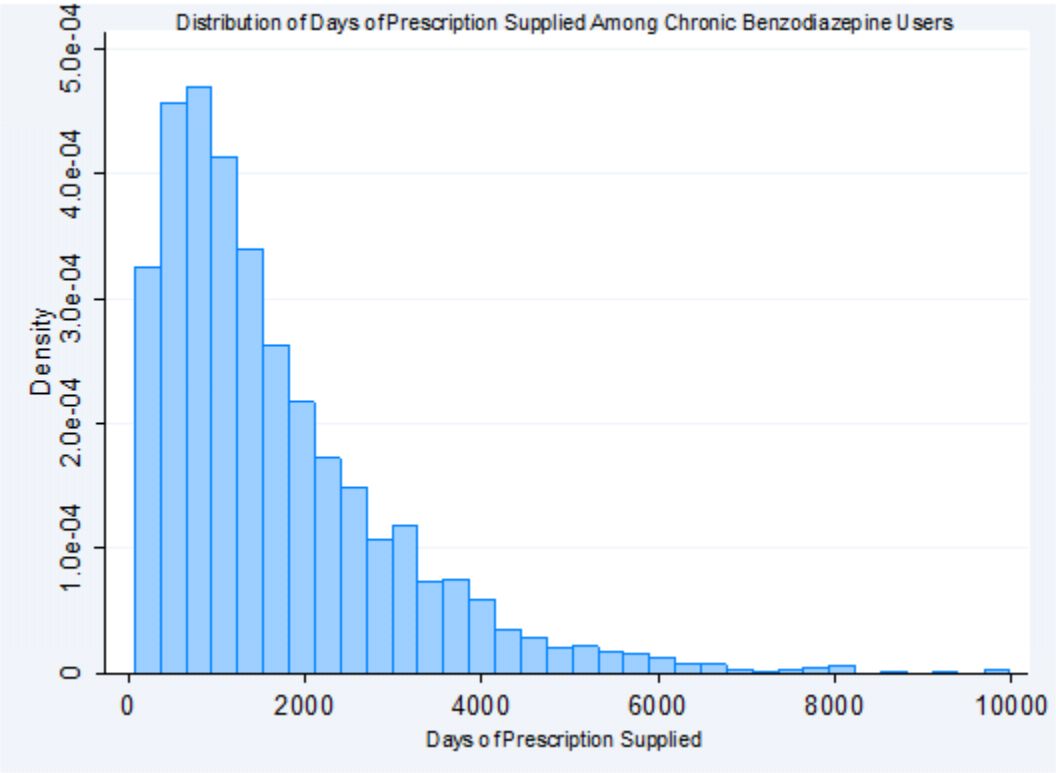


Figure 5d. Distribution of Days of Prescription Supplied Among Chronic Benzodiazepine Users



ADDITIONAL TABLES

Table S1a. Characteristics of All Claims with and without Prescription Data

Variable	Variable Components	Prescription Before Injury (%)	Prescription After Injury (%)	No prescription (%)	Total (%)
All		99291 (41.7)	31540 (13.2)	107341 (45.1)	238172 (100)
Prescription	Any prescription	99291 (75.9)	31,540 (24.1)	*	130831 (100)
	Any Opioid	91587 (75.3)	30,080 (24.7)	*	121667 (100)
	Opioid Alone	47839 (65.1)	25,664 (34.9)	*	73503 (100)
	Any Benzodiazepine	25755 (89.5)	3,022 (10.5)	*	28,777 (100)
	Benzodiazepine Alone	1604 (77.4)	469 (22.6)	*	2073 (100)
	Any Other Rx	38956 (91.8)	3483 (8.2)	*	42439 (100)
	Other Rx Alone	5138 (84.9)	916 (15.1)	*	6054 (100)
Acute Prescriptions (<=60 days supplied in 180 days before injury)	Any Opioid	25675 (28.0) 25676 (21.0)	*	*	91,587 (before injury) 121667 (all)
	Any Benzodiazepine	5351 (21.0) 5351 (18.6)	*	*	25,755 (before injury) 28777 (all)
Chronic Presciptions (>60 days supplied in 180 days before injury)	Any Opioid	5041 (5.5) 5041 (5.2)	*	*	91587 (before injury) 121667 (all)
	Any Benzodiazepine	2820 (10.9) 2820 (9.8)	*	*	25,755 (before injury) 28777 (all)
Age (years)	18 - 24	13,376 (13.5)	4,459 (14.1)	21570 (20.1)	39405 (16.5)
	25 - 29	12,182 (12.3)	4,050 (12.8)	16832 (15.7)	33064 (13.9)
	30 - 24	12,284(12.4)	3,951 (12.5)	15018 (14.0)	31253 (13.1)
	35 - 39	11,326(11.4)	3,603 (11.4)	12050 (11.2)	26979 (11.3)
	40 - 44	11,192 (11.3)	3,604 (11.4)	11002 (10.3)	25798 (10.8)
	45 - 49	10,879 (11.0)	3,557 (11.3)	9617 (9.0)	24053 (10.1)
	50 - 54	11,875 (12.0)	3,610 (11.5)	9013(8.4)	24498 (10.3)
	55 - 59	9,852 (9.9)	2,899 (9.2)	7311 (6.8)	20062 (8.4)
	60 - 65	6,325 (6.40)	1,807 (5.7)	4928 (4.6)	13060 (5.5)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Sex	Female	34,340 (37.5)	7,650 (25.4)	32,246 (30.0)	78,185 (32.8)
	Male	57,246 (62.5)	22,429 (74.6)	75,092 (70.0)	159,985 (67.2)
	Total	91,586 (100)	30,079 (100)	107,341 (100)	238,172 (100)
Injury Year	Yr 2013	27992 (28.2)	13808 (43.8)	36059 (33.6)	77859 (32.7)
	Yr 2014	34640 (34.9)	10558 (33.5)	35844 (33.4)	81042 (34.0)
	Yr 2015	36659 (36.9)	7174 (22.8)	35438 (33.0)	79271 (33.3)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Claim Status	Non compensable	70184 (70.7)	17718 (56.2)	90135 (84.0)	178097 (74.8)
	Compensable	23575 (23.7)	10931 (34.7)	12809 (11.9)	47315 (19.9)
	Fatal	23 (0.02)	5 (0.02)	69 (0.06)	97 (0.04)
	Total permanent disability	87 (0.09)	58 (0.2)	24 (0.02)	169 (0.07)
	Kept on Salary	4898 (4.93)	2611 (8.3)	3966 (3.7)	11475 (4.8)
	Loss of earning power	524 (0.5)	217 (0.7)	278 (0.3)	1019 (0.4)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Injury Nature	Traumatic injuries and disorders, unspecified	440 (0.4)	93 (0.3)	378 (0.4)	911 (0.4)
	Traumatic injuries to bones, nerves, spinal cord	6929 (7.0)	3932 (12.5)	5531 (5.2)	16392 (6.7)
	Traumatic injuries to musdes, tendons, ligaments, joints etc	43068 (43.4)	13069 (41.4)	37024 (34.5)	93161 (39.1)
	Open wounds	18533 (18.7)	5114 (16.2)	30824 (28.7)	54471 (22.9)
	Surface wounds and bruises	14168 (14.3)	3658 (11.6)	18093 (16.9)	35919 (15.1)
	Burns	1968 (2.0)	782 (2.5)	2560 (2.4)	5310 (2.2)
	Intracranial injuries	1840 (1.9)	418 (1.3)	1841 (1.7)	4099 (1.7)
	Multiple traumatic injuries and disorders	7659 (7.7)	3044 (9.7)	7290 (6.8)	17993 (7.6)
	Other traumatic injuries and disorders	4686 (4.7)	1430 (4.5)	3800 (3.5)	9916 (4.2)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)

Injury Source	Chemical and Chemical Products	153 (0.2)	53 (0.2)	263 (0.3)	469 (0.2)
	Containers	10022 (10.1)	3133 (9.9)	10810 (10.1)	23965 (10.1)
	Furniture and fixtures	4024 (4.1)	1048 (3.3)	3680 (3.4)	8752 (3.7)
	Machinery	5113 (5.2)	1976 (6.3)	5937 (5.5)	13026 (5.5)
	Parts and materials	10645 (10.7)	3867 (12.3)	12813 (11.9)	(11.5) 27325
	Persons, plants, animals, and minerals	24884 (25.1)	7022 (22.3)	21409 (19.9)	53315 9224)
	Structures and surfaces	17406 (17.5)	5994 (19.0)	16281 (15.2)	39681 (16.7)
	Tools, instruments and equipment	11516 (11.6)	3297 (10.5)	17823 (16.6)	32636 (13.7)
	Vehicles	7158 (7.2)	2418 (7.7)	7114 (6.6)	16690 (7.0)
	Other Sources & Nondassifiable	8370 (8.4)	2732 (8.7)	11211 (10.4)	22313 (9.4)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Accident Type	Contact with objects and equipment	2378 (2.4)	782 (2.5)	4357 (4.1)	7517 (3.2)
	Falls	24967 (25.2)	7982 (25.3)	27366 (25.5)	60315 (25.3)
	Bodily reaction and exertion	53723 (54.1)	16772 (53.2)	55289 (51.5)	125784 (52.8)
	Exposure to harmful substances or environments	6039 (6.1)	2620 (8.3)	7267 (6.8)	15926 (6.7)
	Transportation accidents	3759 (3.8)	1284 (4.1)	3648 (3.4)	8691 (3.7)
	Fires and explsions	2658 (2.7)	746 (2.4)	4049 (3.8)	7453 (3.1)
	Assaults and violent acts	5178 (5.2)	1094 (3.5)	4625 (4.3)	10897 (4.6)
	Other events/exposures & nonclassifiable	589 (0.6)	260 (0.8)	740 (0.7)	1589 (0.7)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Body Part	Head	9569 (9.6)	3078 (9.8)	8819 (8.2)	21466 (9.0)
	Neck, including throat	4468 (4.5)	1089 (3.5)	4625 (4.3)	10182 (4.3)
	Trunk	30469 (30.7)	10189 (32.3)	26406 (24.6)	67064 (28.2)
	Upper extremities	36365 (36.6)	11060 (35.1)	49214 (45.9)	96639 (40.6)
	Lower extremities	18387 (18.5)	6119 (19.4)	18232 (16.7)	42738 (17.9)
	Other body part, & nondassifiable	33 (0.03)	5 (0.02)	45 (0.04)	83 (0.03)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)
Occupational Classification	Management Occupations	3174 (3.2)	801 (2.5)	2488 (2.3)	6463 (2.7)
	Business and Financial Operations	653 (0.7)	133 (0.4)	424 (0.4)	1210 (0.5)
	Computer and mathematical occupations	241 (0.2)	64 (0.2)	264 (0.3)	569 (0.2)
	Architecture and engineering occupations	385 (0.4)	104 (0.3)	377 (0.4)	866 (0.4)
	Life, physical and social science occupations	385 (0.4)	113 (0.4)	542 (0.5)	1040 (0.4)
	Community and social services occupations	1030 (1.0)	196 (0.6)	682 (0.6)	1908 (0.8)
	Legal occupations	100 (0.1)	23 (0.1)	77 (0.1)	200 (0.1)
	Education, training and library occupations	1295 (1.3)	279 (0.9)	1145 (1.1)	2719 (1.1)
	Arts, design, entertainment, sports, media	685 (0.7)	236 (0.8)	778 (0.7)	1709 (0.7)
	Healthcare practitioners and technical	3437 (3.5)	581 (1.8)	3502 (3.3)	7520 (3.2)
	Healthcare support occupations	6127 (6.2)	1164 (3.7)	4919 (4.6)	12210 (5.1)
	Protective services occupations	3256 (3.3)	825 (2.6)	2199 (2.1)	6280 (2.6)
	Food preparation and serving related	8062 (8.1)	2279 (7.2)	10622 (9.9)	20963 (8.8)
	Building and grounds cleaning	4449 (4.5)	1525 (4.8)	5840 (5.4)	11814 (5.0)
	Personal care and service occupations	3733 (3.8)	832 (2.6)	2989 (2.8)	7554 (3.2)
	Sales and related occupations	4266 (4.3)	1070 (3.4)	3610 (3.4)	8946 (3.8)
	Office and administrative support occup	4998 (5.0)	1156 (3.7)	3920 (3.7)	10074 (4.2)
	Farming, fishing and forestry occupations	3067 (3.1)	2096 (6.7)	9629 (9.0)	14792 (6.2)
	Construction and extraction occupations	11454 (11.5)	4944 (15.7)	13316 (12.4)	29714 (12.5)
	Installation, maintenance and repair	9169 (9.2)	3060 (9.7)	8562 (8.0)	20791 (8.7)
	Production occupations	10103 (10.2)	3456 (11.0)	11172 (10.4)	24731 (10.4)
	Transportation and material moving	13169 (13.3)	4661 (14.8)	13596 (12.7)	31426 (13.2)
	Military specific occupations	3 (0.0)	1 (0.0)	1 (0.0)	5 (0.0)
	Not Classified	6040 (6.1)	1941 (6.2)	6687 (6.2)	14668 (6.2)
	Total	99291 (100)	31540 (100)	107341 (100)	238172 (100)

Table S1b. Characteristics of Claims with Opioid Prescriptions

Variable	Variable Components	Any Opioid Before Injury (%)	Any Opioid After Injury (%)	Total (%)	Any Acute Opioid Before Injury (%)	Any Chronic Opioid Before Injury (%)	Total (%)
All	*	91587 (75.3)	30080 (24.7)	121667 (100)	25675 (83.6)	5041 (16.4)	30716 (100)
	*	*	*	*	25675 (28.0)	5041 (5.5)	91587 (100)
Age (years)	18 - 24	12091 (13.2)	4271 (14.2)	16362 (13.5)	3383 (13.2)	87 (1.7)	3470 (11.3)
	25 - 29	11237 (12.3)	3872 (18.8)	15109 (12.4)	3365 (13.1)	219 (4.3)	3584 (11.7)
	30 - 24	11474 (12.5)	3753 (12.5)	15227 (12.5)	3357 (13.1)	453 (9.0)	3810 (12.4)
	35 - 39	10524 (11.5)	3426 (11.4)	13950 (11.5)	3112 (12.1)	524 (10.4)	3636 (11.8)
	40 - 44	10882 (11.3)	3415 (11.4)	13797 (11.3)	2880 (11.2)	631 (12.5)	3511 (11.4)
	45 - 49	10019 (10.9)	3411 (11.3)	13430 (11.0)	2731 (10.6)	788 (15.6)	3519 (11.5)
	50 - 54	10981 (12.0)	3439 (11.4)	14420 (11.9)	2959 (11.5)	982 (19.5)	3941 (12.8)
	55 - 59	9094 (9.9)	2776 (9.2)	11870 (9.8)	2414 (9.4)	819 (16.3)	3233 (10.5)
	60 - 65	5785 (6.3)	1717 (5.7)	7502 (6.2)	1474 (5.7)	538 (10.7)	2012 (6.6)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100, 83.6)	5041 (100, 16.4)	30716 (100)
Sex	Female	34340 (37.5)	7650 (25.4)	41990 (34.5)	10367 (40.4)	2173 (43.1)	12540 (40.8)
	Male	57246 (62.5)	22429 (74.6)	79675 (65.5)	15308 (59.6)	2868 (56.9)	18176 (59.2)
	Total	91586 (100)	30079 (100)	121665 (100)	25675 (100)	5041 (100)	30716 (100)
Injury Year	Yr 2013	25650 (28.0)	13144 (43.7)	38794 (31.9)	8327 (32.4)	1609 (31.9)	9936 (32.4)
	Yr 2014	31885 (34.8)	10053 (33.4)	41,938 (34.4)	8788 (34.3)	1686 (33.5)	10474 (34.1)
	Yr 2015	34052 (37.2)	6883 (22.9)	40935 (33.7)	8560 (33.3)	1746 (34.6)	10306 (33.6)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)
Claim Status	Non compensable	63552 (69.4)	16650 (55.4)	80202 (65.9)	17767 (69.2)	2988 (59.3)	20755 (67.6)
	Compensable	22715 (24.8)	10593 (35.2)	33308 (27.4)	6539 (25.5)	1762 (35.0)	8301 (27.0)
	Fatal	20 (0.02)	4 (0.01)	24 (0.02)	3 (0.01)	1 (0.02)	4 (0.01)
	Total permanent disability	87 (0.1)	58 (0.2)	145 (0.1)	27 (0.1)	15 (0.3)	42 (0.1)
	Kept on Salary	4708 (5.1)	2566 (8.5)	7274 (6.0)	1184 (4.6)	244 (4.8)	1428 (4.7)
	Loss of earning power	505 (0.6)	209 (0.7)	714 (0.6)	155 (0.6)	31 (0.6)	186 (0.6)
	Total	91587 (100)	30080 (100)	121667 (100)	25675(100)	5041 (100)	30716 (100)
Injury Nature	Traumatic injuries and disorders, unspecified	408 (0.5)	89 (0.3)	497 (0.4)	105 (0.4)	26 (0.5)	131 (0.4)
	Traumatic injuries to bones, nerves, spinal cord	6576 (7.2)	3840 (12.8)	10416 (8.6)	1692 (6.6)	381 (7.6)	2073 (6.8)
	Traumatic injuries to muscles, tendons, ligaments, joints etc	39924 (43.6)	12357 (41.1)	52281 (43.0)	11205 (53.6)	2395 (47.5)	13600 (44.3)
	Open wounds	16644 (18.2)	4901 (16.3)	21545 (17.7)	4527 (17.6)	644 (12.8)	5171 (16.8)
	Surface wounds and bruises	13027 (14.2)	3494 (11.6)	16521 (13.6)	3713 (14.5)	681 (13.5)	4394 (14.3)
	Burns	1817 (2.0)	759 (2.5)	2576 (2.1)	554 (2.2)	65 (1.3)	619 (2.0)
	Intracranial injuries	1659 (1.8)	388 (1.3)	2047 (1.7)	472 (1.8)	85 (1.7)	557 (1.8)
	Multiple traumatic injuries and disorders	7154 (7.8)	2908 (9.7)	10062 98.3)	2120 (8.3)	477 (9.5)	2597 (8.5)
	Other traumatic injuries and disorders	4378 (4.8)	1344 (4.5)	5722 (4.7)	1287 (5.0)	287 (5.7)	1574 95.1)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)
Injury Source	Chemical and Chemical Products	133 (0.2)	51 (0.2)	184 (0.2)	47 (0.2)	3 (0.1)	50 (0.2)
	Containers	9249 (10.1)	2941 (9.8)	12190 (10.0)	2647 (10.3)	474 (9.4)	3121 (10.2)
	Furniture and fixtures	3672 (4.0)	982 (3.3)	4654 (3.8)	1063 (4.1)	209 (4.2)	1272 (4.1)
	Machinery	4778 (5.2)	1906 (6.3)	6684 (5.5)	1349 (5.3)	234 (4.6)	1583 (5.2)
	Parts and materials	9902 (10.8)	3728 (12.4)	13630 (11.2)	2700 (10.5)	449 (8.9)	3149 (10.3)
	Persons, plants, animals, and minerals	22890 (25.0)	6628 (22.0)	29518 (24.3)	6524 (25.4)	1339 (26.6)	7863 (25.6)
	Structures and surfaces	16218 (17.7)	5772 (19.2)	21990 (18.1)	4625 (18.0)	1127 (22.4)	5752 (18.7)
	Tools, instruments and equipment	10452 (11.4)	3148 (10.5)	13600 (11.2)	2861 (11.1)	489 (9.7)	3350 (10.9)
	Vehicles	6582 (7.2)	2308 (7.7)	8890 (7.3)	1786 (7.0)	367 (7.3)	2153 (7.0)
	Other Sources & Nonclassifiable	7711 (8.4)	2616 (8.7)	10327 (8.5)	2073 (8.1)	350 (6.9)	2423 (7.9)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)
Accident Type	Contact with objects and equipment	2147 (2.3)	752 (2.5)	2899 (2.4)	587 (2.3)	112 (2.2)	699 (2.3)
	Falls	23055 (25.2)	7658 (25.5)	30713 (25.2)	6519 (25.4)	1467 (29.1)	7986 (26.0)
	Bodily reaction and exertion	49591 (54.2)	15916 (52.9)	65507 (53.8)	13812 (53.8)	2663 (52.8)	16475 (53.6)
	Exposure to harmful substances or environments	5621 (6.1)	2555 (8.5)	8176 (6.7)	1618 (6.3)	217 (4.3)	1835 (6.0)
	Transportation accidents	3469 (3.8)	1209 (4.0)	4678 (3.8)	972 (3.8)	195 (3.9)	1167 (3.8)
	Fires and explsions	2460 (2.7)	724 (2.4)	3184 (2.6)	638 (2.5)	91 (1.8)	729 (2.4)
	Assaults and violent acts	4695 (5.1)	1016 (3.4)	5711 (4.7)	1376 (5.4)	263 (5.2)	1639 (5.3)
	Other events/exposures & nonclassifiable	549 (0.6)	250 (0.8)	799 (0.7)	153 (0.6)	33 (0.7)	186 (0.6)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)
Body Part	Head	8858 (9.7)	2913 (9.7)	11771 (9.7)	2595 (10.1)	598 (11.9)	3193 (10.4)
	Neck, including throat	4066 (4.4)	998 (3.3)	5064 (4.2)	1133 (4.4)	232 (4.6)	1365 (4.4)
	Trunk	28409 (31.0)	9630 (32.0)	38039 (31.3)	7982 (31.1)	1766 (35.0)	9748 (31.7)
	Upper extremities	33176 (36.2)	10620 (35.3)	43796 (36.0)	9262 (36.1)	1478 (29.3)	10740 (35.0)
	Lower extremities	17047 (18.6)	5914 (19.7)	22961 (18.9)	4695 (18.3)	965 (19.1)	5660 (18.4)
	Other body part, & nonclassifiable	31 (0.03)	5 (0.02)	36 (0.03)	8 (0.03)	2 (0.04)	10 (0.03)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)

Occupational Classification	Management Occupations	2851 (3.1)	743 (2.5)	3594 (3.0)	778 (3.0)	165 (3.3)	943 (3.1)
	Business and Financial Operations	572 (0.6)	120 (0.4)	692 (0.6)	163 (0.6)	48 (1.0)	211 (0.7)
	Computer and mathematical occupations	219 (0.2)	59 (0.2)	278 (0.2)	55 (0.2)	17 (0.3)	72 (0.2)
	Architecture and engineering occupations	333 (0.4)	99 (0.3)	432 (0.4)	83 (0.3)	19 (0.4)	102 (0.3)
	Life, physical and social science occupations	331 (0.4)	103 (0.3)	434 (0.4)	75 (0.3)	15 (0.3)	90 (0.3)
	Community and social services occupations	911 (1.0)	174 (0.6)	1085 (0.9)	267 (1.0)	57 (1.1)	324 (1.1)
	Legal occupations	88 (0.1)	22 (0.1)	110 (0.1)	23 (0.1)	6 (0.1)	29 (0.1)
	Education, training and library occupations	1130 (1.2)	257 (0.9)	1387 (1.1)	344 (1.3)	57 (1.1)	401 (1.3)
	Arts, design, entertainment, sports, media	609 (0.7)	214 (0.7)	823 (0.7)	167 (0.7)	27 (0.5)	194 (0.6)
	Healthcare practitioners and technical	3007 (3.3)	518 (1.7)	3525 (2.9)	864 (3.4)	222 (4.4)	1086 (3.5)
	Healthcare support occupations	5645 (6.2)	1076 (3.6)	6721 (5.5)	1783 (6.9)	371 (7.4)	2154 (7.0)
	Protective services occupations	2979 (3.3)	776 (2.6)	3755 (3.1)	740 (2.9)	160 (3.2)	900 (2.9)
	Food preparation and serving related	7378 (8.1)	2170 (7.2)	9548 (7.9)	2168 (8.4)	335 (6.7)	2503 (8.2)
	Building and grounds cleaning	4147 (4.5)	1454 (4.8)	5601 (4.6)	1156 (4.5)	191 (3.8)	1347 (4.4)
	Personal care and service occupations	3434 (3.8)	775 (2.6)	4209 (3.5)	1038 (4.0)	230 (4.6)	1268 (4.1)
	Sales and related occupations	3859 (4.2)	999 (3.3)	4858 (4.0)	1120 (4.4)	266 (5.3)	1386 (4.5)
	Office and administrative support occup	4520 (4.9)	1078 (3.6)	5598 (4.6)	1325 (5.2)	309 (6.1)	1634 (5.3)
	Farming, fishing and forestry occupations	2830 (3.1)	2043 (6.8)	4873 (4.0)	697 (6.7)	72 (1.4)	769 (2.5)
	Construction and extraction occupations	10819 (11.8)	4812 (16.0)	15631 (12.9)	2859 (11.1)	581 (11.5)	3440 (11.2)
	Installation, maintenance and repair	8553 (9.3)	2935 (9.8)	11488 (9.4)	2190 (8.5)	497 (9.9)	2687 (8.8)
	Production occupations	9437 (10.3)	3317 (11.0)	12754 (10.5)	2727 (10.6)	471 (9.3)	3198 (10.4)
	Transportation and material moving	12347 (13.5)	4487 (14.9)	16834 (13.8)	3415 (13.3)	565 (11.2)	3980 (13.0)
	Military specific occupations	3 (0.03)	1 (0.03)	4 (0.03)	3 (0.01)	*	3 (0.01)
	Not Classified	5585 (6.1)	1848 (6.1)	7433 (6.1)	1635 (6.4)	360 (7.1)	1995 (6.5)
	Total	91587 (100)	30080 (100)	121667 (100)	25675 (100)	5041 (100)	30716 (100)

Table S1c. Characteristics of Claims with Benzodiazepine Prescriptions

Variable	Variable Components	Any Benzo Before Injury	Any Benzo After Injury (%)	Total (%)	Any Acute Benzo Before	Any Chronic Benzo	Total (%)
All	*	25755 (89.5)	3022 (10.5)	28777 (100)	5351 (65.5)	2820 (34.5)	8171 (100)
	*	*	*	*	5351 (20.8)	2820 (10.9)	25755 (100)
Age (years)	18 - 24	2176 (8.5)	296 (9.8)	2472 (8.6)	514 (9.6)	105 (3.7)	619 (7.6)
	25 - 29	2520 (9.8)	334 (11.1)	2854 (9.9)	584 (10.9)	199 (7.1)	783 (9.6)
	30 - 24	3076 (11.9)	366 (12.1)	3442 (12.0)	609 (11.4)	280 (9.9)	889 (10.9)
	35 - 39	3201 (12.4)	385 (12.7)	3586 (12.5)	675 (12.6)	325 (11.5)	1000 (12.2)
	40 - 44	3208 (12.4)	379 (12.5)	3582 (12.5)	638 (11.9)	357 (12.7)	995 (12.2)
	45 - 49	3366 (13.1)	367 (12.1)	3733 (13.0)	669 (12.5)	406 (14.4)	1075 (13.2)
	50 - 54	3554 (13.8)	400 (13.2)	3954 (13.7)	714 (13.3)	459 (16.3)	1173 (14.4)
	55 - 59	2903 (11.3)	316 (10.5)	3219 (11.2)	579 (10.8)	422 (15.0)	1001 (12.3)
	60 - 65	1756 (6.8)	179 (5.9)	1935 (6.7)	369 (6.9)	267 (9.5)	636 (7.8)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Sex	Female	12953 (50.3)	1110 (36.7)	14063 (48.9)	3113 (58.2)	1569 (55.6)	4682 (57.3)
	Male	12802 (49.7)	1912 (63.3)	14714 (51.1)	2238 (41.8)	1251 (44.4)	3489 (42.7)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Injury Year	Yr 2013	7639 (29.7)	1560 (51.6)	9199 (32.0)	1704 (31.8)	952 (33.8)	2656 (32.5)
	Yr 2014	9016 (35.0)	985 (32.6)	10001 (34.8)	1886 (35.3)	985 (34.9)	2871 (35.1)
	Yr 2015	9100 (35.3)	477 (15.8)	9577 (33.3)	1761 (32.9)	883 (31.3)	2644 (32.4)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Claim Status	Non compensable	16428 (63.8)	1459 (48.3)	17887 (62.2)	3716 (69.4)	1715 (60.8)	5431 966.5)
	Compensable	7915 (30.7)	1356 (44.9)	9271 (32.2)	1387 (25.9)	951 (33.7)	2338 (28.6)
	Fatal	8 (0.03)	1 (0.03)	9 (0.03)	3 (0.1)	1 (0.04)	4 (0.1)
	Total permanent disability	43 (0.2)	12 (0.4)	55 (0.2)	4 (0.1)	8 (0.3)	12 (0.2)
	Kept on Salary	1179 (4.6)	170 (5.6)	1349 (4.7)	209 (3.9)	121 (4.3)	330 (4.0)
	Loss of earning power	182 (0.7)	24 (0.8)	206 (0.7)	32 (0.6)	24 (0.9)	56 (0.7)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Injury Nature	Traumatic injuries and disorders, unspecified	121 (0.5)	7 (0.2)	128 (0.4)	31 (0.6)	17 (0.6)	48 (0.6)
	Traumatic injuries to bones, nerves,spinal cord	1757 (6.8)	268 (8.9)	2025 (7.0)	335 (6.3)	192 (6.8)	527 (6.5)
	Traumatic injuries to muscles, tendons, ligaments, joints etc	12303 (47.8)	1598 (52.9)	13901 (48.3)	2419 (45.2)	1334 (47.3)	3753 (45.9)
	Open wounds	3765 (14.6)	301 (10.0)	4066 (11.1)	867 (16.2)	385 (13.7)	1252 (15.3)
	Surface wounds and bruises	3171 (12.3)	262 (8.7)	3433 (11.9)	746 (13.9)	324 (11.5)	1070 (13.1)
	Burns	415 (1.6)	34 (1.1)	449 (1.6)	84 (1.6)	44 (1.6)	128 (1.6)
	Intracranial injuries	587 (2.3)	55 (1.8)	642 (2.2)	122 (2.3)	79 (2.8)	201 (2.5)
	Multiple traumatic injuries and disorders	2258 (8.8)	313 (10.7)	2571 (8.9)	472 (8.8)	300 (10.6)	772 (9.5)
	Other traumatic injuries and disorders	1378 (5.4)	184 (6.1)	1562 (5.4)	275 (5.1)	145 (5.1)	420 (5.1)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Injury Source	Chemical and Chemical Products	33 (0.1)	0 (0.0)	33 (0.1)	5 (0.1)	0 (0.0)	5 (0.1)
	Containers	2666 (10.4)	354 (11.7)	3020 (10.5)	539 (10.1)	271 (9.6)	810 (9.9)
	Furniture and fixtures	1197 (4.7)	119 (3.9)	1316 (4.6)	267 (4.0)	121 (4.3)	388 (4.8)
	Machinery	1111 (4.3)	140 (4.6)	1251 (4.4)	237 (4.4)	109 (3.9)	346 (4.2)
	Parts and materials	2137 (8.3)	295 (9.8)	2432 (8.5)	363 (6.8)	226 (8.0)	589 (7.2)
	Persons, plants, animals, and minerals	7424 (28.8)	796 (26.3)	8220 (28.6)	1545 (28.9)	828 (29.4)	2374 (29.1)
	Structures and surfaces	5051 (19.6)	575 (19.0)	5626 (19.6)	1062 (19.9)	648 (23.0)	1710 (20.9)
	Tools, instruments and equipment	2562 (10.0)	256 (8.5)	2818 (9.8)	596 (11.1)	260 (9.2)	856 (10.5)
	Vehicles	1828 (7.1)	249 (8.2)	2077 (7.2)	368 (6.9)	188 (6.7)	556 (6.8)
	Other Sources & Nonclassifiable	1746 (6.8)	238 (7.9)	1984 (6.9)	368 (6.9)	169 (6.0)	537 (6.6)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)
Accident Type	Contact with objects and equipment	494 (1.9)	64 (2.1)	558 (1.9)	113 (2.1)	58 (2.1)	171 (2.1)
	Falls	6794 (26.4)	674 (22.3)	7468 (26.0)	1453 (27.2)	844 (30.0)	2297 (28.1)
	Bodily reaction and exertion	14026 (54.5)	1798 (59.5)	15824 (55.0)	2834 (53.0)	1435 (50.9)	4269 (52.3)
	Exposure to harmful substances or environments	1212 (4.7)	138 (4.6)	1350 (4.7)	247 (4.6)	113 (4.0)	360 (4.4)
	Transportation accidents	1027 (4.0)	159 (5.3)	1186 (4.1)	219 (4.1)	100 (3.6)	319 (3.9)
	Fires and explsions	409 (1.6)	39 (1.3)	448 (1.6)	82 (1.5)	34 (1.2)	116 (1.4)
	Assaults and violent acts	1642 (6.4)	121 (4.0)	1763 (6.1)	370 (6.9)	222 (7.9)	592 (7.3)
	Other events/exposures & nonclassifiable	151 (0.6)	29 (1.0)	180 (0.6)	33 (0.6)	14 (0.5)	47 (0.6)
	Total	25755 (100)	3022 (100)	28,777.00	5351 (100)	2820 (100)	8171 (100)
Body Part	Head	2955 (11.5)	400 (13.2)	3355 (11.7)	641 (12.0)	397 (14.1)	1038 (12.7)
	Neck, including throat	1417 (5.5)	159 (5.3)	1576 (5.5)	295 (5.5)	170 (6.0)	465 (5.7)
	Trunk	9069 (35.2)	1371 (45.4)	10440 (36.3)	1744 (32.6)	969 (34.4)	2713 (33.2)
	Upper extremities	7820 (30.4)	683 (22.6)	8503 (29.6)	1714 (32.0)	790 (28.0)	2504 (30.6)
	Lower extremities	4484 (17.4)	408 (13.5)	4892 (17.0)	954 (17.8)	493 (17.5)	1447 (17.7)
	Other body part, & nonclassifiable	10(). 04)	1 (0.03)	11 (0.04)	3 (0.1)	1 (0.04)	4 (0.1)
	Total	25755 (100)	3022 (100)	28777 (100)	5351 (100)	2820 (100)	8171 (100)

Occupational Classification	Management Occupations	1026(4.0)	90(3.0)	1116(3.9)	267(5.0)	119(4.2)	386(4.7)
	Business and Financial Operations	257(1.0)	18(0.6)	275(1.0)	68(1.2)	39(1.4)	102(1.3)
	Computer and mathematical occupations	71(0.3)	8(0.3)	79(0.3)	14(0.3)	12(0.4)	26(0.3)
	Architecture and engineering occupations	114(0.4)	8(0.3)	122(0.4)	27(0.5)	12(0.4)	39(0.5)
	Life, physical and social science occupations	104(0.4)	8(0.3)	112(0.4)	21(0.4)	12(0.4)	33(0.4)
	Community and social services occupations	392(1.5)	38(1.3)	430(1.5)	87(1.6)	71(2.5)	158(1.9)
	Legal occupations	38(0.2)	2(0.1)	40(0.1)	11(0.2)	3(0.1)	14(0.2)
	Education, training and library occupations	472(1.8)	29(1.0)	501(1.7)	117(2.2)	56(2.0)	173(2.1)
	Arts, design, entertainment, sports, media	161(0.6)	19(0.6)	180(0.6)	29(0.5)	24(0.9)	53(0.6)
	Healthcare practitioners and technical	1327(5.2)	89(3.0)	1416(4.9)	346(6.5)	187(6.6)	533(6.5)
	Healthcare support occupations	2167(8.4)	199(6.6)	2366(8.2)	497(9.3)	254(9.0)	751(9.2)
	Protective services occupations	963(3.7)	104(3.4)	1067(3.7)	188(3.5)	94(3.3)	282(3.5)
	Food preparation and serving related	2043(4.1)	204(6.8)	2247(7.8)	440(8.2)	243(8.6)	683(8.4)
	Building and grounds cleaning	1060(4.1)	134(4.4)	1194(4.2)	202(3.8)	123(4.4)	325(4.0)
	Personal care and service occupations	1280(5.0)	113(3.7)	1393(4.8)	298(5.6)	162(5.7)	460(5.6)
	Sales and related occupations	1347(5.2)	131(4.3)	1478(5.1)	295(5.5)	196(7.0)	491(6.0)
	Office and administrative support occup	1613(6.3)	139(4.6)	1752(6.1)	368(6.9)	206(7.3)	574(7.0)
	Farming, fishing and forestry occupations	459(1.8)	135(4.47)	594(2.1)	78(1.5)	29(1.0)	107(1.3)
	Construction and extraction occupations	2413(9.4)	399(13.2)	2812(9.8)	401(7.5)	212(7.5)	613(7.5)
	Installation, maintenance and repair	1960(7.6)	272(9.0)	2232(7.8)	340(6.4)	195(6.9)	535(6.6)
	Production occupations	2004(7.8)	285(9.4)	2289(8.0)	386(7.2)	185(6.6)	571(7.0)
	Transportation and material moving	2855(11.1)	415(13.7)	3270(11.4)	521(9.7)	227(8.1)	748(9.2)
	Military specific occupations	1(0.0)	0(0.0)	1(0.0)	1(0.02)	*	1(0.01)
	Not Classified	1628(6.3)	183(6.1)	1811(6.3)	354(6.6)	159(5.6)	513(6.3)
	Total	25755(100)	3022(100)	28777(100)	5351(100)	2820(100)	8171(100)

Table S2. Characteristics of Opioid Prescriptions

Variable	Variable Components	Any Opioid Rx Before Injury (%)	Any Opioid Rx After Injury (%)	Total (%)	Acute Opioid Rx Before Injury (%)	Chronic Opioid Rx Before Injury (%)	Total (%)
Prescription	All	535020 (44.5)	666987 (55.5)	1202007 (100)	*	*	*
Rx within 180 days before injury	Acute	114198 (99.7)	*	114198 (99.7)	*	*	*
	Chronic	299 (0.3)	*	299 (0.3)	*	*	*
	Total	114492 (100)	*	114492 (100)	114198 (99.7)	299 (0.3)	114492 (100)
Rx any time before injury	Acute (any time before)	533836 (99.8)	*	533836 (99.8)	*	*	
	Chronic (any time before)	1184 (0.2)	*	1184 (0.2)	*	*	
	Total	535020 (100)	*	535020 (100)	533836 (99.8)	1184 (0.2)	535020 (100)
Age (years)	18 - 24	36354 (6.8)	37876 (5.7)	74230 (6.2)	8305 (7.3)	1 (0.33)	8306 (7.3)
	25 - 29	48548 (9.1)	56924 (8.5)	105472 (8.8)	10964 (9.6)	0 (0.0)	10964 (9.6)
	30 - 24	63113 (11.8)	76877 (11.5)	139990 (11.7)	13865 (12.1)	15 (5.0)	13880 (12.1)
	35 - 39	64194 (12.0)	77505 (11.6)	141699 (11.8)	13303 (11.7)	30 (10.0)	13333 (11.7)
	40 - 44	65627 (12.3)	86483 (13.0)	152110 (12.7)	13808 (12.1)	15 (5.0)	13823 (12.1)
	45 - 49	70661 (13.2)	96212 (14.4)	166873 (13.9)	15181 (13.3)	26 (8.7)	15207 (13.3)
	50 - 54	81672 (15.3)	110896 (16.6)	192568 (16.0)	17286 (15.1)	73 (24.4)	17359 (15.2)
	55 - 59	65772 (12.3)	82618 (12.4)	148390 (12.4)	13483 (11.8)	88 (29.4)	13571 (11.9)
	60 - 65	39079 (7.3)	41596 (6.2)	80675 (6.7)	7998 (7.0)	51 (17.1)	8049 (7.0)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Sex	Female	221567 (41.4)	231814 (34.8)	453381 (37.70	48736 (42.7)	153 (51.2)	48889 (42.7)
	Male	313451 (58.6)	435168 (65.2)	748619 (62.3)	65457 (57.3)	146 (48.8)	65603 (57.3)
	Unknown	2 (0.0)	5 (0.0)	7 (0.0)	*	*	*
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Injury Year	Yr 2012	52278 (9.8)	238600 (35.8)	290878 (24.2)	29097 (25.5)	85 (28.4)	29182 (25.5)
	Yr 2013	112102 (21.0)	185892 (27.9)	297994 (24.8)	28084 (24.6)	60 (20.1)	28144 (24.6)
	Yr 2014	166502 (31.1)	146107 (21.9)	312609 (26.0)	28958 (25.4)	65 (21.7)	29023 (25.0)
	Yr 2015	204138 (38.2)	96388 (14.5)	300526 (25.0)	28054 (24.6)	89 (29.8)	28143 (25.0)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Rx Dispense Year	Yr 2011	77784 (14.5)	0.00	77784 (6.5)	6173 (5.0)	24 (8.0)	6197 (5.0)
	Yr 2012	205274 (38.4)	73523 (11.0)	278797 (23.2)	30077 (26.0)	77 (26.0)	30154 (26.0)
	Yr 2013	137210 (26.7)	117888 (17.7)	255098 (21.2)	27501 (24.0)	57 (19.1)	27558 (24.1)
	Yr 2014	86725 (16.2)	160997 (24.1)	247722 (20.6)	29639 (26.0)	73 (24.4)	29712 (26.0)
	Yr 2015	28027 (5.2)	179972 (27.0)	207999 (17.3)	20803 (18.0)	68 (22.7)	20871 (18.2)
	Yr 2016	0.00	119112 (17.9)	119112 (9.9)	0 (0.0)	0 (0.0)	0 (0.0)
	Yr 2017	0.00	15495 (2.3)	15495 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Claim Status	Non compensable	343898 (64.3)	300473 (45.1)	644,371	73385 (64.3)	165 (55.2)	73550 (64.2)
	Compensable	161131 (30.1)	318611 (47.8)	479,742	34958 (30.6)	127 (42.5)	35085 (30.6)
	Fatal	125 (0.02)	114 (0.02)	239	24 (0.02)	0 (0.0)	24 (0.02)
	Total permanent disability	805 (0.2)	5691 (0.9)	6,496	287 (0.3)	0 (0.0)	287 (0.3)
	Kept on Salary	25902 (4.8)	37152 (5.6)	63,054	4958 (4.3)	7 (2.3)	4965 (4.0)
	Loss of earning power	3159 (0.6)	4946 (0.7)	8,105	581 (0.5)	0 (0.0)	581 (1.0)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Injury Nature	Traumatic injuries and disorders, unspecified	2888 (0.5)	3506 (0.5)	6394 (0.5)	565 (0.5)	0 (0.0)	565 (0.5)
	Traumatic injuries to bones, nerves, spinal cord	36003 (6.7)	63774 (9.6)	99777 (8.3)	7547 (6.6)	29 (9.7)	7576 (6.6)
	Traumatic injuries to muscles, tendons, ligaments, joints etc	248326 (46.4)	332635 (49.9)	580961 (48.3)	52083 (45.6)	146 (48.8)	52179 (45.7)
	Open wounds	80904 (15.1)	65240 (9.8)	146144 (12.2)	16908 (14.8)	37 (12.4)	16945 914.8)
	Surface wounds and bruises	74727 (14.0)	70947 (10.6)	145674 (12.1)	16200 (14.2)	26 (8.7)	16226 (14.2)
	Burns	8979 (1.7)	8808 (1.3)	17787 (1.5)	2000 (1.8)	3 (1.0)	2003 (1.8)
	Intracranial injuries	9541 (1.8)	8687 (1.3)	18228 (1.5)	1916 (1.7)	2 (0.7)	1918 (1.7)
	Multiple traumatic injuries and disorders	45199 (8.5)	74040 (11.1)	119239 (9.9)	10924 (9.6)	34 (11.4)	10958 (9.6)
	Other traumatic injuries and disorders	28453 (5.3)	39350 (5.9)	67803 (5.6)	6100 (5.3)	22 (7.4)	6122 (5.4)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)
Injury Source	Chemical and Chemical Products	669 (0.1)	709 (0.1)	1378 (0.1)	146 (0.1)	0 (0.0)	146 (0.1)
	Containers	54512 (10.2)	66375 (10.0)	120887 (10.1)	11139 (9.8)	29 (9.7)	11168 (9.8)
	Furniture and fixtures	22313 (4.2)	24993 (3.8)	47306 (3.9)	4736 (4.2)	10 (3.3)	4746 (4.2)
	Machinery	26896 (5.0)	33168 (5.0)	60064 (5.0)	5638 (4.9)	5 (1.7)	5643 (4.9)
	Parts and materials	53046 (9.9)	64261 (9.6)	117307 (9.8)	10764 (9.4)	19 (6.4)	10783 (9.4)
	Persons, plants, animals, and minerals	138138 (25.8)	174590 (26.2)	312728 (26.0)	29674 (26.0)	103 (34.5)	29777 (26.0)
	Structures and surfaces	105167 (19.7)	135604 (20.3)	240771 (20.0)	22878 (20.0)	66 (22.1)	22944 (20.0)
	Tools, instruments and equipment	55762 (10.4)	56548 (8.5)	112310 (9.3)	11600 (10.2)	24 (8.0)	11624 (10.2)
	Vehicles	37089 (6.9)	50285 (7.5)	87374 (7.3)	7839 (6.9)	26 (8.7)	7865 (6.9)
	Other Sources & Nonclassifiable	41428 (7.7)	60454 (9.1)	101882 (8.5)	9779 (8.6)	17 (5.7)	9796 (8.6)
	Total	535020 (100)	666987 (100)	1202007 (100)	114198 (100)	299 (100)	114492 (100)

Accident Type	Contact with objects and equipment	11582 (2.2)	12618 (1.9)	24200 (2.0)	2732 (2.4)	2 (0.7)	2734 (2.4)
	Falls	142302 (26.6)	171869 (25.8)	314171 (26.1)	30922 (27.1)	82 (27.4)	31004 (27.1)
	Bodily reaction and exertion	289969 (54.2)	371591 (55.7)	661560 (55.0)	60228 (52.7)	165 (55.2)	60393 (52.8)
	Exposure to harmful substances or environments	28629 (5.4)	33891 (5.1)	62520 (5.2)	6177 (5.4)	8 (2.7)	6185 (5.4)
	Transportation accidents	19179 (3.6)	25827 (3.9)	45006 (3.7)	4058 (3.6)	15 (5.0)	4073 (3.6)
	Fires and explsions	11134 (2.1)	12424 (1.9)	23558 (2.0)	2555 (2.2)	1 (0.3)	2556 (2.2)
	Assaults and violent acts	28497 (5.3)	28373 (4.3)	56870 (4.7)	6358 (5.6)	25 (8.4)	6383 (5.6)
	Other events/exposures & nonclassifiable	3728 (0.7)	10394 (1.6)	14122 (1.2)	1163 (1.0)	1 (0.3)	1164 (1.0)
	Total	535020 (100)	666987 (100)	1202007 (100)	114193 (100)	299 (100)	114492 (100)
Body Part	Head	57866 (10.8)	86967 (13.0)	144833 (12.1)	13147 (11.5)	51 (17.1)	13198 (11.5)
	Neck, including throat	24558 (4.6)	26249 (3.9)	50807 (4.2)	4982 (4.4)	12 (4.0)	4994 (4.4)
	Trunk	177912 (33.3)	257860 (38.7)	435772 (36.3)	37860 (33.2)	106 (35.5)	37966 (33.2)
	Upper extremities	173135 (32.4)	170204 (25.5)	343339 (28.6)	36697 (32.1)	86 (28.8)	36783 (32.1)
	Lower extremities	101402 (19.0)	125532 (18.8)	226934 (18.9)	21462 (18.8)	44 (14.7)	21506 (18.8)
	Other body part, & nonclassifiable	147 (0.03)	175 (0.03)	322 (0.03)	45 (0.04)	0 (0.0)	45 (0.04)
	Total	535020 (100)	666987 (100)	1202007 (100)	114193 (100)	299 (100)	114492 (100)
Occupational Classification	Management Occupations	17110 (3.2)	19566 (2.9)	36676 (3.1)	3602 (3.2)	11 (3.7)	3613 (3.2)
	Business and Financial Operations	4283 (0.8)	3862 (0.6)	8145 (0.7)	840 (0.7)	0 (0.0)	840 (0.7)
	Computer and mathematical occupations	1511 (0.3)	1256 (0.2)	2767 (0.2)	306 (0.3)	-0.3	307 (0.3)
	Architecture and engineering occupations	2115 (0.4)	2524 (0.4)	4639 (0.4)	456 (0.4)	0 (0.3)	456 (0.4)
	Life, physical and social science occupations	1562 (0.3)	1950 (0.3)	3512 (0.3)	351 (0.3)	0 (0.0)	352 (0.3)
	Community and social services occupations	5991 (1.1)	7027 (1.1)	13018 (1.1)	1356 (1.2)	7 (2.3)	1363 (1.2)
	Legal occupations	758 (0.1)	806 (0.1)	1564 (0.1)	157 (0.1)	0 (0.0)	157 (0.1)
	Education, training and library occupations	6671 (1.3)	6383 (1.0)	13054 (1.1)	1454 (1.3)	5 (1.7)	1459 (1.3)
	Arts, design, entertainment, sports, media	2933 (0.6)	3376 (0.5)	6309 (0.5)	604 (0.5)	0 (0.0)	604 (0.5)
	Healthcare practitioners and technical	19772 (3.7)	22151 (3.3)	41923 (3.5)	4476 (3.9)	20 (6.7)	4496 (3.9)
	Healthcare support occupations	36501 (6.8)	40378 (6.1)	76879 (6.4)	8227 (7.2)	41 (13.7)	8268 (7.2)
	Protective services occupations	17694 (3.3)	22110 (3.3)	39804 (3.3)	3621 (3.2)	11 (3.7)	3632 (3.2)
	Food preparation and serving related	41526 (7.8)	40734 (6.1)	82260 (6.8)	8752 (7.7)	20 (6.7)	8772 (7.7)
	Building and grounds cleaning	23030 (4.3)	28857 (4.3)	51887 (4.3)	4706 (4.1)	4 (1.3)	4710 (4.1)
	Personal care and service occupations	22723 (4.3)	23946 (3.6)	46669 (3.9)	5066 (4.4)	10 (3.3)	5076 (4.4)
	Sales and related occupations	26324 (4.9)	27460 (4.1)	53784 (4.5)	5583 (4.9)	13 (4.4)	5596 (4.9)
	Office and administrative support occup	29341 (5.5)	29907 (4.5)	59248 (4.9)	6701 (5.9)	25 (8.4)	6726 (5.9)
	Farming, fishing and forestry occupations	9700 (1.8)	17287 (2.6)	26987 (2.3)	1939 (1.7)	0 (0.0)	1939 (1.7)
	Construction and extraction occupations	60111 (11.2)	90059 (13.5)	150170 (12.5)	12104 (10.6)	18 (6.0)	12122 (10.6)
	Installation, maintenance and repair	50003 (9.4)	66104 (.9)	116107 (9.7)	10126 (8.9)	34 (11.4)	10160 (8.9)
	Production occupations	51435 (9.6)	65340 (9.8)	116775 (9.7)	11172 (9.8)	15 (5.0)	11187 (9.8)
	Transportation and material moving	68108 (12.7)	94714 (14.2)	162822 (13.6)	13581 (11.9)	40 (13.4)	13621 (11.9)
	Military specific occupations	8 (0.0)	21 (0.0)	29 (0.0)	7 (0.01)	0 (0.0)	7 (0.01)
	Not Classified	35810 (6.7)	51169 (7.7)	86979 (7.2)	9,006	23 (7.7)	9029 (7.9)
	Total	535020 (100)	666987 (100)	1202007 (100)	114193 (100)	299 (100)	114492 (100)

Table S3. Characteristics of Benzodiazepine Prescriptions

Variable	Variable Components	Any Benzodiazepine Rx Before Injury (%)	Any Benzodiazepine Rx After Injury (%)	Total (%)	Acute Benzodiazepine Rx Before Injury (%)	Chronic Benzodiazepine Rx Before Injury (%)	Total (%)
Prescription	All	130893 (54.7)	108285 (45.3)	239178 (100)	*	*	*
Rx within 180 days before injury	Acute	29993 (98.1)	*	29993 (98.1)	*	*	*
	Chronic	583 (1.9)	*	583 (1.9)	*	*	*
	Total	30576 (100)	*	30576 (100)	29993 (98.1)	583 (1.9)	30576 (100)
Rx any time before injury	Acute (any time before)	128420 (98.1)	*	128420 (98.1)	*	*	*
	Chronic (any time before)	2473 (1.9)	*	2473 (1.9)	*	*	*
	Total	130893 (100)	*	130893 (100)	128420 (98.1)	2473 (1.9)	130893 (100)
Age (years)	18 - 24	6272 (4.8)	4437 (4.1)	10709 (4.5)	1614 (5.4)	15 (2.6)	1629 (5.3)
	25 - 29	10530 (8.0)	7761 (7.2)	18291 (7.7)	2653 (8.9)	13 92.2)	2666 (8.7)
	30 - 24	13465 (10.3)	10746 (9.9)	24211 (10.1)	3330 (11.1)	23 (4.0)	3353 (11.0)
	35 - 39	15817 (12.1)	12770 (11.8)	28587 (12.0)	3617 (12.1)	29 (5.0)	3646 (11.9)
	40 - 44	16298 (12.5)	14474 (13.4)	30772 (12.9)	3649 (12.2)	66 (11.3)	3715 (12.2)
	45 - 49	18695 (14.3)	16331 (15.1)	35026 (14.6)	4326 (14.4)	72 (12.4)	4398 (14.4)
	50 - 54	21364 (16.3)	19110 (17.7)	40474 (16.9)	4809 (16.0)	102 (17.5)	4911 (16.1)
	55 - 59	17595 (13.4)	15124 (14.0)	32719 (13.7)	3816 (12.7)	135 (23.2)	3951 (12.9)
	60 - 65	10857 (8.3)	7532 (7.0)	18389 (7.7)	2179 (2.3)	128 (22)	2307 (7.6)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Sex	Female	72798 (55.6)	52,183 (48.2)	124981 (52.3)	16825 (56.1)	350 (60.0)	17175 (56.2)
	Male	58,095 (44.4)	56102 (51.8)	114197 (47.8)	13168 (43.9)	233 (40.0)	13401 (43.8)
	Unknown	*	*	*	*	*	
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Injury Year	Yr 2012	13266 (10.1)	40504 (37.4)	53770 (22.5)	7589 (25.3)	190 (32.6)	7779 (25.4)
	Yr 2013	27231 (20.8)	31016 (28.6)	58247 (24.4)	7398 (24.7)	161 (27.6)	7559 (24.7)
	Yr 2014	40921 (31.3)	23066 (21.3)	63987 (26.8)	7864 (26.2)	130 (22.3)	7994 (26.1)
	Yr 2015	49475 (37.8)	13699 (12.7)	63174 (26.4)	7142 (23.8)	102 (17.5)	7244 (23.7)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Rx Dispense Year	Yr 2011	16796 (12.8)	0 (0.0)	16796 (7.0)	1537 (5.1)	46 (7.9)	1583 (5.2)
	Yr 2012	49144 (37.6)	9619 (8.9)	58763 (24.6)	7738 (25.8)	175 (30.0)	7913 (25.9)
	Yr 2013	35484 (27.1)	17952 (16.6)	53436 (22.3)	7526 (25.1)	165 (28.3)	7691 (25.2)
	Yr 2014	22411 (17.2)	27063 (25.0)	49474 (20.7)	7876 (26.3)	126 (21.6)	8002 (26.2)
	Yr 2015	7058 (5.4)	29422 (27.2)	36480 (15.3)	5316 (17.7)	71 (12.2)	5387 (17.6)
	Yr 2016	0 (0.0)	21549 (19.9)	21549 (9.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Yr 2017	0 (0.0)	2680 (2.5)	2680 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Claim Status	Non compensable	83678 (63.9)	52513 (48.5)	136191 (56.9)	19053 (63.5)	386 (66.2)	19439 (63.6)
	Compensable	40544 (31.0)	49429 (45.7)	89973 (37.6)	9474 (31.6)	182 (31.2)	9656 (31.6)
	Fatal	62 (0.1)	12 (0.01)	74 (0.03)	16 (0.1)	0 (0.0)	16 (0.1)
	Total permanent disability	263 (0.2)	1247 (1.2)	1510 (0.6)	84 (0.3)	0 (0.0)	84 (0.3)
	Kept on Salary	5392 (3.1)	4175 (3.9)	9567 (4.0)	1170 (3.9)	11 (1.9)	1181 (3.9)
	Loss of earning power	954 (0.7)	909 (0.8)	1863 (0.8)	196 (0.7)	4 (0.7)	200 (0.7)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Injury Nature	Traumatic injuries and disorders, unspecified	972 (0.7)	554 (0.5)	1526 (0.6)	202 (0.7)	4 (0.7)	206 (0.7)
	Traumatic injuries to bones, nerves, spinal cord	8247 (6.3)	8052 (7.4)	16299 (6.8)	1850 (6.2)	54 (0.3)	1904 (6.2)
	Traumatic injuries to muscles, tendons, ligaments, joints etc	62324 (47.6)	55300 (51.1)	117624 (49.2)	13889 (46.3)	286 (49.1)	14175 (46.4)
	Open wounds	19116 (14.6)	10825 (10.0)	29941 (12.5)	4418 (14.7)	85 (14.6)	4503 (15.7)
	Surface wounds and bruises	16222 (12.4)	10653 (9.8)	26875 (11.2)	3728 (12.4)	61 (10.5)	3789 (12.4)
	Burns	1970 (1.5)	1101 (1.0)	3071 (1.3)	418 (1.4)	7 (1.2)	425 (1.4)
	Intracranial injuries	3332 (2.6)	2468 (2.3)	5800 (2.4)	797 (2.7)	11 (1.9)	808 (2.6)
	Multiple traumatic injuries and disorders	12446 (.5)	13523 (12.5)	25969 (10.9)	3217 (10.7)	48 (8.2)	3265 (10.7)
	Other traumatic injuries and disorders	6264 (4.8)	5809 (5.4)	12073 (5.1)	1474 (4.9)	27 (4.6)	1501 (4.9)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Injury Source	Chemical and Chemical Products	96 (0.1)	47 (0.04)	143 (0.1)	11 (0.04)	0 (0.0)	11 (0.04)
	Containers	12953 (9.9)	10791 (10.0)	23744 (9.9)	2886 (9.6)	40 (6.9)	2926 (9.6)
	Furniture and fixtures	5689 (4.4)	4686 (4.3)	10375 (4.3)	1406 (5.0)	37 (6.4)	1443 (4.7)
	Machinery	5435 (4.2)	4250 (3.9)	9685 (4.1)	1208 (4.0)	16 (2.7)	1219 (4.0)
	Parts and materials	9708 (7.4)	7783 (7.2)	17491 (7.3)	2085 (7.0)	46 (7.9)	2131 (7.0)
	Persons, plants, animals, and minerals	38068 (29.1)	32655 (30.2)	70723 (29.6)	8663 (28.9)	187 (32.1)	8850 (28.9)
	Structures and surfaces	28559 (21.8)	22339 (20.6)	50898 (21.3)	6551 (21.8)	122 (20.9)	6673 (21.8)
	Tools, instruments and equipment	12594 (9.6)	8911 (8.2)	21505 (9.0)	2944 (9.8)	58 (10.0)	3002 (9.8)
	Vehicles	9088 (6.9)	8042 (7.4)	17080 (7.1)	2060 (6.7)	37 (6.4)	2097 (6.8)
	Other Sources & Nonclassifiable	8753 (6.7)	8781 (8.1)	17534 (7.3)	2184 (7.3)	40 (6.9)	2224 (7.3)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)

Accident Type	Contact with objects and equipment	3089 (2.4)	1958 (1.8)	5047 (2.1)	708 (2.3)	19 (3.3)	722 (2.4)
	Falls	37708 (28.8)	28431 (26.3)	66139 (27.7)	8752 (29.2)	148 (25.4)	8900 (29.1)
	Bodily reaction and exertion	67620 (51.7)	58378 (53.9)	125998 (52.7)	15236 (50.8)	305 (52.3)	15541 (50.8)
	Exposure to harmful substances or environments	5465 (4.2)	3930 (3.6)	9395 (3.9)	1238 (4.1)	21 (3.6)	1259 (4.1)
	Transportation accidents	4738 (3.6)	4577 (4.2)	9315 (3.9)	1084 (3.6)	24 (4.1)	1108 (3.6)
	Fires and explsions	1814 (1.4)	1733 (1.6)	3547 (1.5)	472 (1.6)	8 (1.4)	480 (1.6)
	Assaults and violent acts	9561 (7.3)	7641 (7.1)	17202 (7.2)	2253 (7.5)	52 (8.9)	2305 (7.5)
	Other events/exposures & nonclassifiable	898 (0.7)	1637 (1.5)	2535 (1.1)	255 (0.9)	6 (1.0)	261 (0.9)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Body Part	Head	17318 (13.2)	17110 (15.8)	34428 (14.4)	4157 (13.9)	74 (12.7)	4231 (13.8)
	Neck, including throat	7633 (5.8)	6839 (6.3)	14472 (6.1)	1834 (6.1)	32 (5.5)	1866 (6.1)
	Trunk	43584 (33.3)	41160 (38.0)	84744 (35.4)	9871 (32.9)	198 (34.0)	10069 (32.9)
	Upper extremities	38318 (29.3)	25417 (23.5)	63735 (26.7)	8731 (29.1)	181 (31.1)	8912 (29.2)
	Lower extremities	24000 (18.3)	17704 (16.4)	41704 (17.4)	5391 (18.0)	98 (16.8)	5489 (18.0)
	Other body part, & nonclassifiable	40 (0.03)	55 (0.1)	95 (0.04)	9 (0.03)	0	9 (0.03)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)
Occupational Classification	Management Occupations	5544 (4.2)	3973 (3.7)	9517 (4.0)	1284 (4.3)	19 (3.3)	1303 (4.3)
	Business and Financial Operations	1411 (1.1)	864 (0.8)	2275 (1.0)	326 (1.1)	(2.4)14	340 (1.1)
	Computer and mathematical occupations	518 (0.4)	221 (0.2)	739 (0.3)	98 (0.3)	2 (0.3)	100 (0.3)
	Architecture and engineering occupations	698 (0.5)	586 (0.5)	1284 (0.5)	151 (0.5)	2 (0.3)	153 (0.5)
	Life, physical and social science occupations	491 (0.4)	365 (0.3)	856 (0.4)	116 (0.4)	0 (0.0)	116 (0.4)
	Community and social services occupations	2677 (2.1)	2243 (2.1)	4920 (2.1)	656 (2.2)	25 (4.3)	681 (2.2)
	Legal occupations	231 (0.2)	160 (0.2)	391 (0.2)	38 (0.1)	2 (0.3)	40 (0.1)
	Education, training and library occupations	2406 (1.8)	1263 (1.2)	3669 (1.5)	506 (1.7)	21 (3.6)	527 (1.7)
	Arts, design, entertainment, sports, media	1057 (0.8)	662 (0.6)	1719 (0.7)	237 (0.8)	4 (0.7)	241 (0.8)
	Healthcare practitioners and technical	7813 (6.0)	6251 (5.8)	14064 (5.9)	1854 (6.2)	63 (10.8)	1917 (6.3)
	Healthcare support occupations	11797 (9.0)	9397 (8.7)	21194 (8.9)	2761 (9.2)	44 (7.6)	2805 (9.2)
	Protective services occupations	4346 (3.3)	4492 (4.2)	8838 (3.7)	975 (3.3)	24 (4.1)	999 (3.3)
	Food preparation and serving related	10945 (8.4)	7257 (6.7)	18202 (7.6)	2505 (8.4)	39 (6.7)	2544 (8.3)
	Building and grounds cleaning	5997 (4.5)	4933 (4.6)	10930 (4.6)	1285 (4.3)	10 (1.7)	1295 (4.2)
	Personal care and service occupations	8434 (6.4)	5392 (5.0)	13826 (5.8)	1772 (5.9)	36 (6.2)	1808 (5.9)
	Sales and related occupations	8508 (6.5)	5926 (5.5)	14434 (6.3)	1900 (6.3)	29 (5.0)	1929 (6.3)
	Office and administrative support occup	9062 (6.9)	5914 (5.5)	14976 (6.3)	2184 (7.3)	50 (8.6)	2234 *7.3)
	Farming, fishing and forestry occupations	1540 (1.2)	1709 (1.6)	3249 (1.4)	386 (1.3)	3 (0.5)	389 (1.3)
	Construction and extraction occupations	9710 (7.4)	10094 (9.3)	19804 (8.3)	2103 (7.0)	48 (8.2)	2151 (7.0)
	Installation, maintenance and repair	8977 (6.9)	8090 (7.5)	17067 (7.1)	2088 (7.0)	28 (4.8)	2116 (6.9)
	Production occupations	8823 (6.7)	8070 (7.5)	16893 (7.1)	2040 (6.8)	30 (5.2)	2070 (6.8)
	Transportation and material moving	11732 (9.0)	11720 (10.8)	23452 (9.8)	2535 (8.5)	33 (5.7)	2568 (8.4)
	Military specific occupations	2 (0.0)	0 (0.0)	2 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)
	Not Classified	8174 (6.2)	8703 (8.0)	16877 (7.1)	2192 (7.3)	57 (9.8)	2249 (7.4)
	Total	130893 (100)	108285 (100)	239178 (100)	29993 (100)	583 (100)	30576 (100)

Table S4. Distribution of Opioid Prescriptions Included in the Study

All (Sorted)		
Opioid Name	Freq.	Percent
HYDROCODONE-ACETAMINOPHEN	646,687	53.8
OXYCODONE-ACETAMINOPHEN	210,903	17.55
OXYCODONE HCL	147,696	12.29
TRAMADOL HCL	49,418	4.11
ACETAMINOPHEN-CODEINE	30,813	2.56
MORPHINE SULFATE ER	24,355	2.03
HYDROMORPHONE HCL	20,717	1.72
METHADONE HCL	18,029	1.5
OXYCONTIN	13,636	1.13
ENDOCET	12,734	1.06
FENTANYL	5,035	0.42
MORPHINE SULFATE	3,771	0.31
HYDROCODONE-IBUPROFEN	3,487	0.29
ROXICET	1,910	0.16
VICODIN	1,737	0.14
BUTRANS	1,585	0.13
NUCYNTA	1,305	0.11
MEPERIDINE HCL	868	0.07
OPANA ER	850	0.07
BUTORPHANOL TARTRATE	693	0.06
NORCO	651	0.05
TRAMADOL HCL ER	599	0.05
TRAMADOL HCL-ACETAMINOPHEN	575	0.05
VICODIN ES	568	0.05
OXYMORPHONE HCL ER	432	0.04
NUCYNTA ER	398	0.03
OXYMORPHONE HCL	380	0.03
CODEINE SULFATE	366	0.03
OXYCODONE HCL ER	335	0.03
DEMEROL	191	0.02
HYDROMORPHONE ER	150	0.01
EXALGO	124	0.01
KADIAN	104	0.01
OXYCODONE HCL-ASPIRIN	77	0.01
HYSINGLA ER	69	0.01
LEVORPHANOL TARTRATE	68	0.01
DILAUDID	66	0.01
AVINZA	61	0.01
OXYCODONE-ASPIRIN	56	0
PENTAZOCINE-NALOXONE HCL	55	0
VICODIN HP	55	0
DURAGESIC	53	0
ZOHYDRO ER	53	0
PERCOCET	47	0
XARTEMIS XR	41	0
BELLADONNA-OPIUM	32	0
LORTAB	30	0
ROXICODONE	19	0
OPANA	16	0
PENTAZOCINE-ACETAMINOPHEN	16	0
ENDODAN	12	0
FENTANYL CITRATE	11	0
ULTRAM	10	0
IBUDONE	9	0
TYLENOL-CODEINE NO.3	9	0
BUPRENEX	7	0
FENTORA	6	0
VICOPROFEN	6	0
SUBSYS	4	0
METHADOSE	3	0
OXYCODONE HCL-IBUPROFEN	3	0
BELBUCA	2	0
CO-GESIC	2	0
EMBEDA	2	0
PERCODAN	2	0
REPREXAIN	2	0
MS CONTIN	1	0
Total	1,202,007	100

Before Injury (Sorted)		
Drug Name	Freq.	Percent
HYDROCODONE-ACETAMINOPHEN	312,084	58.33
OXYCODONE-ACETAMINOPHEN	91,914	17.18
OXYCODONE HCL	52,307	9.78
ACETAMINOPHEN-CODEINE	16,154	3.02
MORPHINE SULFATE ER	10,814	2.02
METHADONE HCL	10,657	1.99
HYDROMORPHONE HCL	7,991	1.49
OXYCONTIN	6,727	1.26
TRAMADOL HCL	6,693	1.25
ENDOCET	6,484	1.21
FENTANYL	2,181	0.41
HYDROCODONE-IBUPROFEN	2,103	0.39
MORPHINE SULFATE	1,616	0.3
ROXICET	1,186	0.22
BUTRANS	910	0.17
VICODIN	730	0.14
NUCYNTA	724	0.14
BUTORPHANOL TARTRATE	450	0.08
NORCO	446	0.08
MEPERIDINE HCL	443	0.08
OPANA ER	415	0.08
VICODIN ES	281	0.05
CODEINE SULFATE	207	0.04
OXYMORPHONE HCL	159	0.03
NUCYNTA ER	156	0.03
OXYMORPHONE HCL ER	151	0.03
TRAMADOL HCL ER	138	0.03
DEMEROL	95	0.02
KADIAN	92	0.02
TRAMADOL HCL-ACETAMINOPHEN	88	0.02
EXALGO	83	0.02
AVINZA	56	0.01
DILAUDID	51	0.01
DURAGESIC	51	0.01
OXYCODONE-ASPIRIN	48	0.01
OXYCODONE HCL-ASPIRIN	46	0.01
LEVORPHANOL TARTRATE	37	0.01
PERCOCET	33	0.01
HYDROMORPHONE ER	26	0
VICODIN HP	22	0
BELLADONNA-OPIUM	21	0
LORTAB	17	0
OPANA	16	0
ROXICODONE	16	0
XARTEMIS XR	13	0
ENDODAN	12	0
FENTANYL CITRATE	11	0
PENTAZOCINE-NALOXONE HCL	11	0
OXYCODONE HCL ER	9	0
ZOHYDRO ER	9	0
FENTORA	6	0
PENTAZOCINE-ACETAMINOPHEN	6	0
TYLENOL-CODEINE NO.3	6	0
BUPRENEX	5	0
IBUDONE	5	0
VICOPROFEN	4	0
PERCODAN	2	0
CO-GESIC	1	0
OXYCODONE HCL-IBUPROFEN	1	0
Total	535,020	100

Table S5. Distribution of Benzodiazepine Prescriptions Included in the Study

All (Sorted)				Before Injury (Sorted)		
Benzodiazepine Name	**Freq.**	**Percent**		**Benzodiazepine Name**	**Freq.**	**Percent**
ALPRAZOLAM	77,177	32.27		ALPRAZOLAM	43,543	33.27
CLONAZEPAM	59,407	24.84		CLONAZEPAM	33,530	25.62
LORAZEPAM	55,962	23.4		LORAZEPAM	32,365	24.73
DIAZEPAM	42,392	17.72		DIAZEPAM	18,921	14.46
ALPRAZOLAM ER	1,552	0.65		ALPRAZOLAM ER	895	0.68
CHLORDIAZEPOXIDE HCL	1,215	0.51		CHLORDIAZEPOXIDE HCL	703	0.54
CLORAZEPATE DIPOTASSIUM	492	0.21		CLORAZEPATE DIPOTASSIUM	347	0.27
ALPRAZOLAM XR	316	0.13		ALPRAZOLAM XR	181	0.14
OXAZEPAM	236	0.1		OXAZEPAM	143	0.11
ALPRAZOLAM ODT	148	0.06		ALPRAZOLAM ODT	104	0.08
KLONOPIN	99	0.04		XANAX	51	0.04
XANAX	85	0.04		KLONOPIN	48	0.04
VALIUM	39	0.02		MEPROBAMATE	32	0.02
MEPROBAMATE	34	0.01		VALIUM	21	0.02
LORAZEPAM INTENSOL	12	0.01		LORAZEPAM INTENSOL	3	0
ATIVAN	7	0		XANAX XR	3	0
XANAX XR	3	0		DIASTAT ACUDIAL	2	0
DIASTAT ACUDIAL	2	0		ATIVAN	1	0
Total	239,178	100		Total	130,893	100

Table S6a. Distribution of Prescriptions Among Hazard Periods and Control Periods for Opioids and Benzodiazepines

Length of Hazard and Control Periods	Hazard Period (HP) and Control Periods (CP)	All Prescriptions (N)	All Prescriptions (%)	All Opioids (N)	All Opioids (%)	All Benzos (N)	All Benzos (%)	All Other Prescriptions (N)	All Other Prescriptions (%)
7 days	HP	28,501	19.6	12,406	19.2	5,372	20.0	10,723	19.9
	CP1	29,098	20.0	12,888	20.0	5,350	20.0	10,860	20.1
	CP2	29,218	20.1	13,049	20.2	5,376	20.1	10,793	20.0
	CP3	29,131	20.1	13,061	20.2	5,356	20.0	10,714	19.9
	CP4	29,260	20.2	13,104	20.3	5,345	19.9	10,811	20.1
	Total (35 days before injury)	145,208	100.0	64,508	100.0	26,799	100.0	53,901	100.0
14 days	HP	35,985	19.5	16,491	19.0	6,540	20.0	12,954	20.0
	CP1	36,835	20.0	17,338	19.9	6,552	20.1	12,945	19.9
	CP2	36,950	20.0	17,406	20.0	6,547	20.0	12,997	20.0
	CP3	37,322	20.2	17,804	20.5	6,473	19.8	13,045	20.1
	CP4	37,436	20.3	17,918	20.6	6,553	20.1	12,965	20.0
	Total (70 days before injury)	184,528	100.0	86,957	100.0	32,665	100.0	64,906	100.0
28 days	HP	51,160	19.5	25,009	18.9	8,918	20.1	17,233	20.2
	CP1	52,758	20.1	26,352	19.9	8,938	20.2	17,468	20.5
	CP2	53,390	20.4	27,055	20.4	8,998	20.3	17,337	20.3
	CP3	52,730	20.1	27,047	20.4	8,831	19.9	16,852	19.8
	CP4	52,108	19.9	27,125	20.5	8,600	19.4	16,383	19.2
	Total (140 days before injury)	262,146	100.0	132,588	100.0	44,285	100.0	85,273	100.0

Table S6b. Mean Morphine Equivalent Dose (MED) and Diazepam Equivalent Dose (DED) in Hazard and Control Periods

Length of Hazard and Control Periods		Mean MED per Day (mg/day)	Standard Deviation MED (mg/day)	Mean DED Per Day (mg/day)	Standard Deviation DED (mg/day)
7 day	HP	42.7	49.6	11.8	11.0
	CP1	42.5	49.6	11.8	11.1
	CP2	43.1	52.4	11.6	10.9
	CP3	42.9	52.2	11.8	10.8
	CP4	42.8	49.8	11.7	10.8
14 day	HP	42.2	48.4	11.8	11.0
	CP1	42.5	50.4	11.6	10.8
	CP2	42.3	48.6	11.6	10.7
	CP3	42.6	50.3	11.6	10.7
	CP4	42.7	48.5	11.5	10.5
28 day	HP	41.6	41.6	11.7	10.8
	CP1	41.7	41.7	11.6	10.7
	CP2	42.0	42.0	11.6	10.5
	CP3	42.3	42.3	11.6	10.8
	CP4	42.6	42.6	11.6	10.6
Overall		43.4	39.5	11.1	9.5

Table S7a. Effect Modification by Sex and Time of Year for Association Between Acute Opioid Use and Occupational Injury Risk

Females	**All Claims With Acute Prescriptions Before Injury (N = 10,367)**	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid(7-day)	0.85*	0.78 - 0.93
Opioid (14-day)	0.84*	0.79 - 0.90
Opioid (28-day)	0.80*	0.76 - 0.84

Males	**All Claims With Acute Prescriptions Before Injury (N = 15,308)**	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid(7-day)	0.84*	0.78 - 0.90
Opioid (14-day)	0.87*	0.82 - 0.92
Opioid (28-day)	0.85*	0.82-0.89

Months 1 - 4	**All Claims With Acute Prescriptions Before Injury (N = 8,000)**	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid(7-day)	0.80*	0.72 - 0.88
Opioid (14-day)	0.83*	0.77 - 0.90
Opioid (28-day)	0.80*	0.76 - 0.85

Months 5 - 8	**All Claims With Acute Prescriptions Before Injury (N = 9,184)**	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid(7-day)	0.86*	0.79 - 0.94
Opioid (14-day)	0.85*	0.80 - 0.92
Opioid (28-day)	0.80*	0.76 - 0.85

Months 9 - 12	**All Claims With Acute Prescriptions Before Injury (N = 8,491)**	
Prescription (Hazard & Control Period Length)	OR	95% CI
Opioid(7-day)	0.87*	0.79 - 0.95
Opioid (14-day)	0.88*	0.82 - 0.95
Opioid (28-day)	0.89*	0.84 - 0.94

***p<0.05**

Table S7b. Effect Modification by Sex and Time of Year for Association Between Acute Benzodiazepine Use and Occupational Injury Risk

Females	**All Claims With Acute Prescriptions Before Injury (N = 3113)**	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	1.01	0.88 - 1.15
Benzodiazepine (14-day)	0.93	0.84 - 1.04
Benzodiazepine (28-day)	0.98	0.90 - 1.07

Males	**All Claims With Acute Prescriptions Before Injury (N = 2238)**	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	1.06	0.91-1.23
Benzodiazepine (14-day)	1.04	0.91-1.18
Benzodiazepine (28-day)	0.96	0.87-1.07

Months 1 - 4	**All Claims With Acute Prescriptions Before Injury (N = 1750)**	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	1.02	0.86 - 1.23
Benzodiazepine (14-day)	0.94	0.82 - 1.08
Benzodiazepine (28-day)	1.01	0.90 - 1.14

Months 5 - 8	**All Claims With Acute Prescriptions Before Injury (N = 1877)**	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	1.1	0.93 - 1.31
Benzodiazepine (14-day)	0.98	0.85 - 1.12
Benzodiazepine (28-day)	0.94	0.84 - 1.05

Months 9 - 12	**All Claims With Acute Prescriptions Before Injury (N = 1724)**	
Prescription (Hazard & Control Period Length)	OR	95%CI
Benzodiazepine (7-day)	0.96	0.79 -1.15
Benzodiazepine (14-day)	1.00	0.99 - 1.15
Benzodiazepine (28-day)	0.97	0.87 - 1.09

Table S8a. Opioid Use and Risk of Occupational Injury Determined Using Mcnemar's Test

1. All Occupations

Any Opioids (Acute)	N = 25,675			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	0.81 (0.75 - 0.88)***	0.83 (0.78 - 0.88)***	0.86 (0.81 - 0.92)***	0.88 (0.83 - 0.94)***
14 days	0.84 (0.79 - 0.90)***	0.89 (0.85 - 0.94)***	0.87 (0.83 - 0.92)***	0.84 (0.80 - 0.88)***
28 days	0.90 (0.86 - 0.94)***	0.84 (0.80 - 0.87)***	0.83 (0.79 -0.86)***	0.80 (0.77 - 0.83)***
Any Opioids (Chronic)	N = 5041			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	0.99 (0.81-1.23)	0.94 (0.80 - 1.11)	0.92 (0.79 - 1.06)	0.81(0.69 - 0.94)**
14 days	0.86 (0.71 - 1.06)	0.78 (0.66 - 0.93)*	0.73 (0.63 - 0.86)***	0.79 (0.68 - 0.92)**
28 days	0.62 (0.49 - 0.79)***	0.64 (0.52 - 0.77)*	0.83 (0.70 - 0.98)*	1.09 (0.93 - 1.28)
Any Opioids (All)	N = 30,716			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	0.84 (0.77 - 0.90)***	0.84 (0.90 - 0.90)***	0.87 (0.83 - 0.92)***	0.87 (0.82 - 0.92)***
14 days	0.85(0.80 -0.90)***	0.88 (0.84 - 0.93)***	0.86 (0.82 - 0.90)***	0.84 (0.80 - 0.87)***
28 days	0.88 (0.84 - 0.92)***	0.83 (0.80 - 0.87)***	0.82 (0.79 - 0.85)***	0.82 (0.79 - 0.85)***

2. Safety Sensitive Occupations

Any Opioids (Acute)	N = 17469			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	0.77 (0.69 - 0.85)***	0.81 (0.75 - 0.87)***	0.84 (0.78 - 0.91)***	0.86 (0.80 - 0.92)***
14 days	0.82 (0.76 - 0.88)***	0.88 (0.83 - 0.94)***	0.86 (0.81 - 0.91)***	0.84 (0.79 - 0.89)***
28 days	0.89 (0.84 -0.93)***	0.85 (0.81 - 0 .89)***	0.81 (0.77 -0.85)***	0.80 (0.77 - 0.84)***
Any Opioids (Chronic)	N = 3360			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	1.05 (0.81 -1.37)	0.98 (0.80 - 1.20)	0.94 (0.78 - 1.13)	0.80 (0 .66 - 0.96)*
14 days	0.89 (0.69 - 1.14)	0.73 (0.59 - 0.91)**	0.67 (0.55 - 0.81)***	0.70 (0.58 -0.84)***
28 days	0.53 (0.40 - 0.71)***	0.54 (0.42 - 0.68)***	0.78 (0.64 - 0.96)*	1.05 (0 .87 - 1.26)
Any Opioids (All)	N = 20829			
Length of HP/CP	CP1 OR (95% CI)	CP2 OR (95% CI)	CP3 OR (95% CI)	CP4 OR (95% CI)
7 days	0.80 (0.73 - 0.88)***	0.83 (0.77 - 0.89)***	0.86 (0.80 - 0.92)***	0.85 (0.79 - 0.91)***
14 days	0.83 (0.77 - 0 .89)***	0.87 (0.82 - 0.92)***	0.84(0.79 - 0.89)***	0.82 (0.78 - 0.87)***
28 days	0.87 (0.82 - 0.92)***	0.83 (0 .80 - 0.87)***	0.81 (0.77 - 0.84)***	0.82 (0.78 - 0.85)***
* p<0.05				
**p<0.005				
*** p<0.0005				

Table S8b. Benzodiazepine Use and Risk of Occupational Injury Using Mcnemar's Test

1. All Occupations

Benzos (Acute)	**N = 5351**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	1.04 (0 .87 - 1.25)	1.04 (0.91 - 1.18)	1.01(0.90 - 1.14)	1.03 (0 .92 - 1.14)
14 days	0.95 (0.84 - 1.08)	0.96 (0 .87 - 1.06)	0.96 (0.88 - 1.06)	1.01 (0.92 - 1.10)
28 days	0.93 (0.85 - 1.02)	0.98 (0.91 - 1.06)	1.00 (0.93 - 1.08)	0.97 (0.90 -1.049)
Benzos(Chronic)	**N = 2820**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	0.95 (0.74 - 1.22)	0.95 (0.78 - 1.16)	1.08 (0.91 - 1.28)	1.08 (0.92 - 1.28)
14 days	1.15 (0.90 -1.46)	1.09 (0.90 -1.32)	1.07 (0.90 -1.29)	0.98 (0.82 -1.18)
28 days	1.03 (0.79 -1.34)	0.82 (0.66 - 1.03)	0.98 (0.80 - 1.21)	1.51(1.24 -1.82) ***
Benzos (All)	**N = 8171**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	1.02 (0.93 -1.13)	1.00 (0.91 -1.11)	0.95 (0.86 -1.05)	0.90 (0.80 -1.01)
14 days	0.99 (0.89 -1.11)	0.99 (0.91 -1.08)	0.99 (0.91 -1.07)	1.00 (0.92 -1.09)
28 days	0.96 (0.89 -1.03)	0.99 (0.92 -1.06)	0 .99 (0 .92 - 1.07)	0.97 (0.90 -1.04)

2. Safety Sensitive Occupations

Benzos (Acute)	**N = 3257**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	1.01(0.79 -1.29)	1.08 (0.91 - 1.29)	1.05 (0.91 - 1.22)	1.03 (0.89 -1.18)
14 days	0.97 (0.82 - 1.14)	0.97 (0.85 - 1.10)	0.96 (0 .85 - 1.08)	1.01 (0.89 - 1.14)
28 days	0.94 (0.83 - 1.06)	0.96 (0 .87 -1.07)	0.99 (0.89 - 1.09)	0.95 (0.86 - 1.05)
Benzos(Chronic)	**N = 1668**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	0.92 (0.66 - 1.29)	0.88 (0.68 - 1.15)	0.99 (0.79 - 1.25)	0.99 (0.80 -1.23)
14 days	0.96 (0.70 - 1.32)	0.97 (0.75 -1.25)	0.97 (0.76 - 1.24)	0.96 (0.74 - 1.23)
28 days	1.07 (0.74 - 1.54)	0.84 (0.62 - 1.15)	1.08 (0.82 - 1.43)	1.67 (1.29 - 2.17)***
Benzos (All)	**N = 4925**			
Length of HP/CP	**CP1 OR (95% CI)**	**CP2 OR (95% CI)**	**CP3 OR (95% CI)**	**CP4 OR (95% CI)**
7 days	0.98 (0.80 - 1.19)	1.02 (0 .88 - 1.17)	1.03 (0.91 - 1.17)	1.02 (0.91 - 1.14)
14 days	0.97 (0.84 - 1.12)	0.97 (0.87 - 1.09)	0.96 (0.86 - 1.07)	1.0 (0.90 - 1.11)
28 days	0.95 (0.85 - 1.07)	0.95 (0.86 -1.05)	1.0 (0.91 -1.10)	1.02 (0.93 -1.12)
* p<0.05				
**p<0.005				
*** p<0.0005				

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