



## Use of a prescription opioid registry to examine opioid misuse and overdose in an integrated health system



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### ABSTRACT

Strategies are needed to identify at-risk patients for adverse events associated with prescription opioids. This study identified prescription opioid misuse in an integrated health system using electronic health record (EHR) data, and examined predictors of misuse and overdose. The sample included patients from an EHR-based registry of adults who used prescription opioids in 2011 in Kaiser Permanente Northern California, a large integrated health care system. We characterized time-at-risk for opioid misuse and overdose, and used Cox proportional hazard models to model predictors of these events from 2011 to 2014. Among 396,452 patients, 2.7% were identified with opioid misuse and 1044 had an overdose event. Older patients were less likely to meet misuse criteria or have an overdose. Whites were more likely to be identified with misuse, but not to have an overdose. Alcohol and drug disorders were related to higher risk of misuse and overdose, with the exception that marijuana disorder was not related to opioid misuse. Higher daily opioid dosages and benzodiazepine use increased the risk of both opioid misuse and overdose. We characterized several risk factors associated with misuse and overdose using EHR-based data, which can be leveraged relatively quickly to inform preventive strategies to address the opioid crisis.

### 1. Introduction

The misuse and abuse of prescription opioid medications and related overdose is a critical U.S. public health issue. While opioid prescribing has decreased nationally since 2012 (Guy Jr et al., 2017; Schuchat et al., 2017), opioid misuse and overdose continue to increase (Rudd et al., 2016a). In 2016, nearly half of all U.S. opioid overdose deaths involve a prescription opioid (Rudd et al., 2016a). Approximately 2 million people had a prescription opioid use disorder in 2015 (Substance Abuse and Mental Health Services Administration, 2016), and > 15,000 people had a fatal overdose related to prescription opioids (Centers for Disease Control and Prevention, 2017a), higher than in 2014 (Centers for Disease Control and Prevention, 2017b). In addition, misuse of prescription opioids is a risk factor for heroin use, which is a key contributor to the increasing rate of overdoses (Compton et al., 2016). It is essential that policymakers and healthcare providers can identify factors that predispose some individuals to misuse of prescribed opioids and overdose in order to address the opioid crisis

(Centers for Disease Control and Prevention, 2017c).

Data from large health systems allow for optimal study of opioid misuse, abuse, and related overdose, given that these events are relatively infrequent. While much of this research has been conducted with administrative data and has used varying definitions and algorithms to identify prescription opioid misuse (Cochran et al., 2015), similar risk factors have emerged (i.e., male sex, younger age, substance use disorder, medical and psychiatric comorbidities, and using opioids > 100 mg/day in morphine equivalents) (Edlund et al., 2007; Rice et al., 2012; Sullivan et al., 2010; White et al., 2009). Individuals at risk for opioid misuse are also likely to have multiple complex health needs, which not only increase the risk of medical harms associated with opioid misuse but also result in substantial burdens on society and health systems (Cochran et al., 2015).

Several studies have shown opioid-related overdose deaths increase proportionally with the prescribed dose, with significant increases at doses > 100 mg/day in morphine equivalents (Bohnert et al., 2010; Dunn et al., 2010). Other factors placing patients at high risk of

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overdose include long-term opioid use, concurrent benzodiazepine use (Brady et al., 2016; Park et al., 2015), depression, substance use diagnoses, and poor overall health (Rice et al., 2012; Sullivan et al., 2010; White et al., 2009).

Understanding predictors of misuse and overdose is critical so that health policy and healthcare systems can effectively target high risk opioid prescribing practices, and identify at-risk patients, as recommended by the Centers for Disease Control Guidelines (Dowell et al., 2016). Using electronic health record (EHR) data can provide clinicians and health systems with timely clinical information and drive health system prevention strategies, such as prescribing initiatives (Compton et al., 2016), naloxone distribution, surveillance, and disease management approaches to prevent misuse and overdose.

We build on previous literature by developing an EHR-based prescription opioid registry to examine misuse and overdose within a large, integrated health care system. EHR data based on encounters have been found to have more comprehensive diagnostic data relative to claims data (Devoe et al., 2011; Heintzman et al., 2014; Angier et al., 2014; Bailey et al., 2016), particularly in integrated systems where specialty care is provided internally. In addition, some data elements available in EHR data are not available in claims data (e.g. smoking status). We characterize individuals at risk of misuse and overdose among patients prescribed opioid medications from 2011 to 2014. Specifically, we (1) identify opioid misuse using EHR data; (2) describe time-at-risk for patients identified with misuse and overdose; and (3) examine the socio-demographic, clinical (e.g. medical and mood/anxiety comorbidity, alcohol and other drug use disorder), and pharmacological risk factors (e.g. concurrent benzodiazepine use) associated with misuse and overdose (non-fatal and fatal).

## 2. Methods

### 2.1. Study setting

Kaiser Permanente Northern California (KPNC) is a nonprofit, integrated healthcare system with approximately 4 million members. The population represents the region; however, as an insured population, it underrepresents those with low levels of education and income (Gordon, 2012). All patients were selected from the KPNC membership, and approval was obtained from the Kaiser Foundation Research Institute Institutional Review Board.

### 2.2. Data sources and study population

The study population was adult members from a prescription opioid registry developed using KPNC's EHR data. The registry represents all patients with an opioid fill from a KPNC outpatient pharmacy during 2011 ( $n = 396,452$ ), with follow-up data through 2014 (Ray et al., 2017). The patient's index date was the first opioid fill made during 2011. Encounters outside of KPNC were captured through claims. More than 90% of enrollees obtain their prescription medications through KPNC pharmacies (Selby et al., 2005). We excluded patients diagnosed with cancer. The detailed methodology used to create the opioid registry has been reported elsewhere (Ray et al., 2017).

### 2.3. Data elements

The registry contains patient demographics (age, sex, race/ethnicity: Asian, African American, Hispanic, Native American, Multi-racial, white, and other/unknown), KPNC membership status, health service utilization, clinical International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses, pharmacy data, and mortality. As a proxy for socio-economic status (SES), it includes a neighborhood deprivation index (NDI) based on home address and census tract variables (e.g. households in poverty) from the U.S. Census Bureau's 2006–2010 American Community Survey (Census Bureau,

2008; Messer et al., 2006).

#### 2.3.1. Comorbid health conditions and mortality

The registry contains baseline comorbidities for each patient, based on all ICD-9-CM diagnoses documented during healthcare encounters. As in prior research with complex patient populations (Young et al., 2015), we identified whether persons received a diagnosis for any of the following chronic medical conditions in the year prior to their index date: arthritis; hypertension; chronic pain; diabetes mellitus; asthma; ischemic heart disease; congestive heart failure; stroke/cerebrovascular accident; epilepsy; Parkinson's Disease; end-stage renal disease; osteoporosis; chronic obstructive pulmonary disease (Ray et al., 2017). We categorized the number of conditions into 4 groups: 0, 1–2, 3–4, and  $> 5$ . Based on their prevalence in this population (Scherrer et al., 2014; Barry et al., 2016), we also created a combined dichotomous indicator for mood/anxiety disorder diagnoses representing depression, anxiety, and bipolar disorder (Young et al., 2015). Substance use disorder measures were dichotomous, reflecting ICD-9-CM abuse/dependence diagnoses for: alcohol, opioid, marijuana, and other non-opioid drug disorders (e.g. cocaine, methamphetamine). Smoking status indicated current tobacco smoker, former, or neither, gathered through annual universal screening in primary care.

Non-fatal opioid overdoses were identified by ICD-9-CM codes of opioid overdose or poisoning (Supplemental Table 1). Fatal overdoses were identified by state death certificates (underlying cause of death was listed as opioid overdose or poisoning).

#### 2.3.2. Daily opioid and benzodiazepine use

All outpatient prescriptions of opioid and benzodiazepine (Supplemental Tables 2 and 3) fills from 1/1/11 to 12/31/14 are included. The registry contains one record/person/day from 1/1/11 to 12/31/14. For each day, variables indicate: 1) whether an opioid prescription was filled, 2) days supply; 3) the prescribing provider; 4) whether the person was assumed to be using opioids that day; 5) short- or long-acting opioid, and; 6) the morphine daily dose equivalent (MDDE) categories of: 0, 1– $< 20$ , 20– $< 50$ , 50– $< 100$ , 100+ mg. We assumed persons used according to provider instructions (for additional detail, see Ray, 2017) (Ray et al., 2017). If a person had  $\geq 7$  days remaining on a prior fill at dispensation time, the new fill was assumed to be used concurrently, otherwise, the new fill was assumed to be used consecutively. We also created number of days of benzodiazepine use in six groups: 0, 1– $< 30$ , 30– $< 60$ , 60– $< 120$ , 120– $< 180$ , and 180 days.

#### 2.3.3. Opioid misuse algorithm and score

Our measure of opioid misuse followed the method developed by Sullivan et al. (2010). First, opioid misuse scores were computed using three variables: days supplied of short-acting opioids, days supplied of long-acting opioids, and number of prescribers. (We did not include the number of different pharmacies, as originally done by Sullivan et al. (2010), since within the closed KPNC system, pharmacies are electronically connected and all dispensations are observable across the system. In addition, most patients fill their prescriptions at 1–2 KPNC pharmacies and would have received a “0” for this component). Scores were computed for each 180-day period between the patient's index date and 12/31/2014 (Sullivan et al., 2010; Edlund et al., 2014). For long-acting and short-acting days supplied, 186–240 days = “1”, and  $> 240$  days = “2” for 6-month periods. Prescribers were categorized as: 3–4 prescribers = ‘1’, and  $> 4$  prescribers = ‘2’; Scores for days supplied of short- and long-acting opioids, and number of prescribers were summed, with a possible range from 0 to 6. Higher misuse scores reflect a greater probability of misuse. Similarly, for each 180-day period, we created an indicator for whether the person received an ICD-9 opioid use disorder diagnosis (Supplemental Table 1). A period was classified as a misuse period if the misuse score was  $\geq 3$ , (suggesting “possible” misuse) (Sullivan et al., 2010) or if the person had an ICD-9

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