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## Causes of death in the 12 months after hospital discharge among patients with opioid use disorder

Caroline King, PhD, MPH<sup>1,2</sup>, Ryan Cook, PhD, MSPH<sup>2</sup>, P. Todd Korthuis, MD, MPH<sup>2</sup>, Cynthia D. Morris, PhD, MPH<sup>3</sup>, Honora Englander, MD<sup>2,4</sup>

<sup>1</sup>Dept. of Biomedical Engineering, School of Medicine, Oregon Health & Science University, Portland, OR

<sup>2</sup>Department of Medicine, Section of Addiction Medicine, Oregon Health & Science University, Portland, OR

<sup>3</sup>Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, OR

<sup>4</sup>Department of Medicine, Division of Hospital Medicine, Oregon Health & Science University, Portland, OR

### Abstract

**Background:** Patients with substance use disorders are seven times more likely hospitalized than the general population. However, causes of death for recently hospitalized patients with Opioid Use Disorder (OUD) are not well described. This study describes causes of death in the year post-discharge among hospitalized patients with OUD.

**Methods:** We analyzed data from participants who were at least 18 years old, with Medicaid insurance, and had a diagnosis of OUD during a general hospital admission in Oregon between April 2015 and December 2017.

**Results:** During the study window, 6,654 Oregon Medicaid patients with an OUD diagnosis were hospitalized. Patients were predominately female (56.7%) and White (72.2%), an average age of 44.2 years (SD=15.4 years) and average hospital length of stay of 6.5 days (SD=10.9 days). In the 12 months post-discharge, 522 patients died (7.8%); 301 patients from a drug or substance related cause (4.5%), including 71 from drug overdose (1.1%). Stated another way, of those who died within 12 months, 58% of deaths were attributed to drug-related causes, including 13.6% of deaths attributed to overdose; 42% died of non-drug related causes. Drug-related death was the most frequent cause of mortality.

**Conclusions:** Hospitalized patients with OUD are at high risk of death, from drug and non-drug related causes, in the year after discharge. Future research should consider not only overdose, but a more comprehensive definition of drug-related death in understanding post-discharge mortality

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**Corresponding Author:** Caroline King, PhD, MPH, 3181 Sam Jackson Park Road, Portland, OR 97207, kingca@ohsu.edu, p. 503.494.8311.

Conflicts of Interest:

No authors have financial conflicts of interest. Dr. Korthuis serves as principal investigator for NIH-funded trials that accept donated study medications from Alkermes (extended-release naltrexone) and Indivior (buprenorphine-naloxone).

among hospitalized patients with OUD, and care systems should work to mitigate the risk of death in this population.

## Keywords

Medicaid; Oregon; Cause of Death; Opioid-Related Disorders; Drug Overdose; Hospitalization; Inpatients

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## 1. Introduction

Patients with substance use disorders are seven times more likely hospitalized than the general population<sup>1</sup> and hospitalizations among patients with opioid use disorder (OUD) are rising<sup>2</sup>. Hospitalization is a critical time to engage, treat, and support patients with OUD<sup>3</sup>. Support for these patients impacts not only OUD care, but also care for any illness both in and out of the hospital. Patients with OUD face high mortality from a variety of causes<sup>4</sup>. However, to date, causes of 12-month mortality for hospitalized patients with OUD are not well described, nor are the causes of death in this population beyond the immediate post-discharge period. Understanding causes of mortality among these patients is essential to identifying and addressing healthcare system gaps. The objective of this study was to describe causes of death in the year post-discharge among patients hospitalized with OUD.

## 2. Methods

### 2.1 Study setting and design

This analysis is part of a larger project modeling care trajectories for hospitalized patients with OUD in Oregon<sup>5</sup>. We used data from all Oregon Medicaid patients who were admitted to one of 62 Oregon hospitals at least once between April 2015 and December 2017. Encrypted IDs from these patients were linked to encrypted Oregon Vital Statistics mortality data through December 2018 by Medicaid Health Service Delivery in Oregon. All persons who die in Oregon are required to have death information submitted to Vital Statistics. Information is submitted by many sources, including by hospitals, nursing homes, counties and families<sup>6</sup>. The Oregon Health & Science University's Institutional Review Board approved this study (#00010846).

### 2.2 Participants

This study included patients age 18 years old and older and had an ICD-9 (304.\*) or ICD-10 (F11\*) diagnosis code of OUD during a general hospital admission during the study window.

### 2.3 Measures

We extracted the following variables from Oregon Medicaid claims data: age (years), sex (male/female), race (white/Black/Asian/Other), ethnicity (Not Hispanic/Hispanic or Other), length of stay (days), concurrent Alcohol Use Disorder (yes/no), Amphetamine Use Disorder (yes/no), Sedative Use Disorder, including benzodiazepines (yes/no), and Chronic Illness and Disability Payment System Score, a surrogate estimate of comorbid burden

available in Oregon Medicaid data. We selected these additional Use Disorders because of their high prevalence in Oregon<sup>7</sup>.

## 2.4 Outcome

We classified deaths using categories defined by ICD-10 codes from the National Center for Health Statistics<sup>8</sup>. We categorized drug-related deaths as all unintentional, intentional, and undetermined intent deaths from drug poisoning (ICD-10 codes X40-X49; X60-X69; Y10-Y19) and deaths attributed to mental and behavioral disorders because of substance use (F10-F19)<sup>8</sup>. Separately, we identified patients who had at least a code for a drug overdose. Participants were classified in each category of death for which they had codes; for example, a person with a code for drug-related death and for respiratory death was counted in both categories. Similarly, a patient who died from a drug overdose is counted as both a drug overdose death and drug-related death. A patient who died from endocarditis would be included as a drug-related death if a code for mental and behavioral disorders because of substance use (F10-F19) was also listed on their death certificate.

## 2.5 Data analysis

We calculated the cumulative monthly mortality rate and overall percentage of patients who died by different causes within 12-months of hospital discharge.

## 3. Results

From April 2015 to December 2017, 6,654 Oregon Medicaid patients with an OUD diagnosis were hospitalized. Patients were predominately female (56.7%) and white (72.2%), with an average age of 44.2 years (SD=15.4 years) and average length of stay of 6.5 days in the hospital (SD=10.9 days). In the month after hospital discharge, 130 (2%) patients died. Sixty-five (1%) died from drug-related causes, including 0.2% who died from drug overdose. Sixty-five (1%) died from non-drug-related causes.

In the 12 months post-discharge, 522 patients died (7.8%); 301 patients died from a drug or substance related cause other than drug overdose (4.5%), and 71 died from a drug overdose (1.1%). Stated another way, of those who died within 12 months, 58% of deaths were attributed to drug-related causes, including 13.6% of deaths attributed to overdose; 42% of deaths were attributed to non-drug-related causes. After drug-related deaths, diseases of the circulatory system (39.5%), respiratory system (33.5%), other causes of death (24.3%), neoplasms (18.5%), endocrine, nutritional, and metabolic diseases (18.1%), and certain infectious and parasitic diseases (17.8%) were the next most frequently identified causes of death in the cohort at 12 months. Figure 1 displays cumulative mortality, by cause.

Among patients who died from drug-related causes, the most common ICD-10 codes listed on death certificates in order of prevalence were F17.9 (Nicotine Dependence, n=182, 60.5%), J44.9 (Chronic obstructive pulmonary disease, unspecified, n=99, 32.9%), X42 (Accidental poisoning by and exposure to narcotics or hallucinogens, n=32, 10.6%), B182 (Chronic viral hepatitis C, n=32, 10.6%), and T401 (Opioid overdose, n=31, 10.3%). Among patients who were classified as not dying from drug-related causes, the most common ICD-10 codes listed on their death certificates in order of prevalence were

A419 (Sepsis, unspecified organism, n=23, 10.4%), I50 (Heart failure, n=22, 10.0%), I10 (Essential primary hypertension, n=20, 9.0%), J44.9 (Chronic obstructive pulmonary disease, unspecified, n=15, 6.8%), and B18.2 (Hepatitis C, n=14, 6.3%). In unadjusted analyses, there were differences in rates among patients who died from non-drug related deaths, drug-related non-overdose deaths, and overdose deaths by gender, age and co-occurring substance use disorder (Table 1).

#### 4. Discussion

Patients with OUD are at high-risk of death from a myriad of causes in the year after hospital discharge. Overdose deaths represent the tip of the iceberg; causes of death spanned nearly every medical specialty, reflecting the burden of comorbid medical conditions among people with OUD. Mortality in our study is similar to acute coronary syndrome (estimated 5–9% one-year mortality), a condition which has garnered enormous attention from providers, policy-makers, and payers to achieve high quality care<sup>9</sup>. And yet, most hospitals do not offer medication for OUD (MOUD)<sup>10</sup>, patients with OUD frequently have stigmatizing healthcare experiences, providers receive little training to address OUD<sup>11, 12</sup>, and there are no widely accepted hospital standards or metrics for OUD. This underscores key needs: first, healthcare providers in many disciplines should learn about and offer OUD treatment, regardless of whether the patient's illness is attributable to their substance use. Healthcare providers can support increased treatment engagement in OUD treatment<sup>3</sup>, and MOUD reduces overdose risk<sup>13</sup>. Second, healthcare systems and policymakers must create systems that destigmatize OUD and better care for patients at risk of death. This might include implementing inpatient addiction consult services<sup>3</sup>; integrating OUD care in primary care<sup>14</sup>; and removing barriers to methadone that limit access for people with serious medical illness<sup>15</sup>. Finally, we must invest in broad program and policy solutions that drive integration across hospital and community settings for people with OUD, including hospital-quality metrics.

There are some limitations to this work. First, our study only uses death data from Oregon Vital Statistics and ICD-10 codes which likely underestimate mortality incidence and causes of death. Second, OUD may be underdiagnosed in patient data. Third, Oregon has low racial and ethnic diversity, and may not be generalizable to other populations.

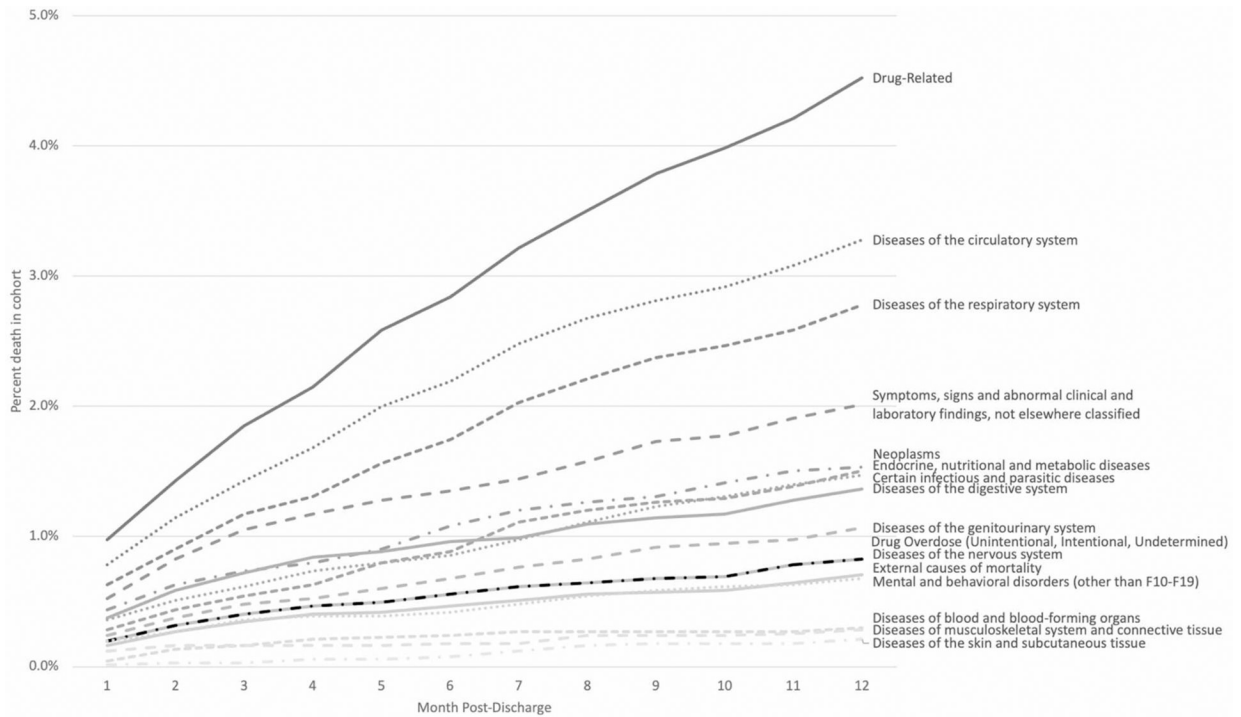
Hospitalized patients with OUD are at high risk of death in the year after discharge. Care systems must work to mitigate the risk of death in this population.

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**Figure 1.** Cumulative mortality by cause among people hospitalized with OUD in Oregon, 2015–2018

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**Table 1.** Demographics of patients with OUD who died within 12 months of hospital discharge in Oregon, 2015–2018

	Non-drug related death (n=221)	Non-overdose drug-related death (n=230)	Overdose death (n=71)	p-value**
<b>Sex</b>	Male	123 (53.5%)	41 (57.7%)	0.012
	Female	107 (46.5%)	30 (42.3%)	
<b>Age (years)</b>		58.0 (12.4)	43.2 (13.2)	0.0012
		9 (3.9%)	*	
<b>Race</b>	Black	9 (4.1%)		0.80
	White	176 (79.6%)	55 (77.5%)	
	Asian	6 (2.7%)	0	
	Other	30 (13.6%)	13 (18.3%)	
<b>Ethnicity</b>	Not Hispanic	205 (89.1%)	56 (78.9%)	0.083
	Hispanic/Other	29 (13.1%)	15 (21.1%)	
<b>Length of stay (days)</b>	10.1 (14.0)	9.7 (17.3)	7.7 (13.9)	0.39
<b>Alcohol use disorder</b>	Yes	14 (6.1%)	6 (8.5%)	0.004
<b>Amphetamine use disorder</b>	Yes	10 (4.5%)	13 (18.3%)	<0.001
<b>Sedative use disorder</b>	Yes	*	*	0.042
<b>Chronic Illness &amp; Disability Payment System Score</b>	4.3 (2.0)	4.1 (1.8)	3.0 (1.5)	<0.0001

\* Cells suppressed if n<=5

\*\* Assessed using Chi-squared tests, Fisher's exact test, or Analysis of Variance