

# Association Between Opioid Prescribing Patterns and Overdose-Related Deaths

## ABSTRACT

Over the past ten years, the rate of prescription opioids-related overdose death has increased substantially in the United States. This cohort study seeks to determine if there is a relationship between prescribed daily opioids dosage and risk of unintentional overdose mortality. Records from the Veterans Health Administration, VHA, were examined for a four year period, 2004 through 2008. The records show that 1.8 million individuals met the criteria of being prescribed opioids for chronic pain. A random sampling of these individuals resulted in the selection of 154,684 patient records for the study. Of the 1136 individuals who died of a prescription opioids overdose during the study period, 752 had been treated with prescription opioids for chronic pain. The study reveals a relationship between opioids prescriptions and opioids overdose.

## BACKGROUND

In the past decade there has been an increase in overdose deaths of opioids in the United States. Between 1999-2007, the total accidental overdose death in the U.S. increased by 124%. This is mostly due to the increase in prescription opioid overdose. Gaining a better understanding of what led to the increase in opioid prescription overdose can help decrease the mortality rate. Evidence shows that there is an increase in risk of drug overdose death in individuals with chronic non-cancer pain because of an increase in prescription dosage. There is a difference in opioid treatment based on patient treatment conditions such as the level of pain being treated. In this study, the relationship between maximum prescribed dose of opioid and the risks of overdosing resulting in death was examined over a 5 year period. Patients that were receiving treatment from the VHA and reported chronic non-cancer pain and pain due to cancer were part of the patients involved in the study. Other sub-groups involved in the study included acute pain and substance abuse disorder.

## METHOD

A study was conducted to test the hypothesis of the increase in opioid prescriptions leading to the increase in opioid overdose. Information was obtained from a VHA's National Database and a VHA's pharmacy service to identify patient criteria that fit the study. Cause of death information was retrieved from the

National Death Index. This study is a cohort study that took place from 2004 to 2008. It included 155,434 individuals being treated with opioids through the VHA. The drugs that were being prescribed are known as opioids and include codeine, morphine, oxycodone, hydrocodone, and hydromorphone. Information was recorded from the time the individuals' first dosage was prescribed to the day of death or the end of 2008, whichever came first. The maximum daily dosage was recorded in one of the following categories: 0 mg, 1mg to less than 20mg, 20mg to less than 50mg, 50mg to less than 100mg, and 100mg or more. The measurement of dosage reflects only the maximum dosage prescribed and unintentional deaths. It did not include the amount actually taken by the patient or any intentional deaths.

## DATA

**Table 1:** Patients with Chronic Non-cancer Pain Diagnoses

| Maximum prescribed daily opioid dose | Overdose deaths | Person-Months |
|--------------------------------------|-----------------|---------------|
| 0                                    | 243             | 2729022.7     |
| 1 to < 20 mg                         | 44              | 395205.0      |
| 20 to < 50 mg                        | 108             | 458296.2      |
| 50 to < 100                          | 86              | 129491.6      |
| ≥100                                 | 125             | 100479.3      |

**Table 2:** Patients with Cancer Diagnoses

| Maximum prescribed daily opioid dose | Overdose deaths | Person-Months |
|--------------------------------------|-----------------|---------------|
| 0                                    | 32              | 859278.3      |
| 1 to < 20 mg                         | 7               | 91108.9       |
| 20 to < 50 mg                        | 14              | 96778.6       |
| 50 to < 100                          | 14              | 28809.7       |
| ≥ 100                                | 24              | 24380.1       |

**Table 3: Risk of Death by Prescription Opioid Overdose**

| Maximum prescribed daily opioid dose | Chronic Pain  | Cancer        | Acute Pain    | Substance Use Disorders |
|--------------------------------------|---------------|---------------|---------------|-------------------------|
| 1 to < 20 mg                         | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference)           |
| 20 to < 50 mg                        | 1.88          | 1.74          | 1.58          | 1.42                    |
| 50 to < 100                          | 4.63          | 6.01          | 4.73          | 2.76                    |
| ≥ 100                                | 7.18          | 11.99         | 6.64          | 4.54                    |

**RESULTS**

The findings of this study indicate there is a relationship between maximum daily prescribed dose of opioids and risk of overdose. Out of the 1136 individuals who died of a prescription opioid overdose from 2004-2008, 752 were treated with prescription opioids for pain during the same time and resulted in a fatal overdose. The prescribed dosage of 0 mg actually resulted in the most accidental overdoses. In both the cancer and chronic non-cancer subgroups, the patients with the least risk of overdose resulting in death was 1 to less than 20 mg per dose. In the cancer subgroup that had a maximum dose of 100mg per dose or more were 12 times more likely to accidentally overdose resulting in death compared to someone taking a low dose (1 to less than 20mg). Among those patients with chronic non-cancer pain, they were 7 times more likely to accidentally overdose resulting in a death compared to someone taking 1 to less than 20mg per dose.

**DISCUSSION**

Compared to a previous study, the results of this study were similar. The risk of an unintentional fatal overdose increases as higher dosages are prescribed. This study included patients that had cancer which the previous study did not. There are some factors not examined in the study but could impact the results. For example, patients may get opioids from non-VHA sources and non-clinicians. A non-clinician is someone who is not authorized to prescribe medications. Patients could also save medication to use later or for recreation. The study was not able to measure the actual dosage taken. Only the prescribed amounts were recorded in the study. Cancer patients were prescribed “as needed” dosages, which means patients can adjust dosage according to their pain level, as well as their regular prescribed dosage. This resulted in an increase to the risk in overdose to cancer patients. Although the study indicates that opioid fatal overdose represents an important outcome, it is important to know that overdoses are rare. The study recommends getting patient history of substance use and dependence, using treatment contracts, and scheduling frequent follow-up visits with toxicology screening.

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