



Understanding Opioid use Among Adults with Chronic Spinal Cord Injury Living in the United States: An Issue Brief

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- What are Opioids?
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- Opioid prescriptions and use after SCI
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- Clinical perspectives
- Next steps

OVERVIEW OF THE PROBLEM

This issue brief is part of the first phase of a 5-year National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) funded project. The purpose of this issue brief is to summarize the state of the science of opioid use, misuse, and OUD among individuals with spinal cord injuries (SCI). We begin by describing opioids and their use within the general population, followed by a description of use, perspectives, and risks for people with SCI living in the United States. We summarize with considerations for future research and clinical directions.

What are Opioids?

Opioids are a class of drugs that include licit (legal) prescription analgesics often prescribed to treat moderate to severe pain, illicitly produced synthetic opioids (e.g. fentanyl), and illicit drugs such as heroin. In addition to providing pain relief, prescription opioids can make people feel very relaxed/calm and have euphoric effects. When taken as directed, and for short periods of time, prescription opioids are generally safe. But, serious risks exist, including numerous side effects (even when taken as prescribed) and risks of misuse, addiction, overdose, and death.

| Prescription Opioids | |
|----------------------|--|
| Medication | Brand names |
| Hydrocodone | Vicodin [®] , Lortab [®] , Norco [®] , Zohydro [®] ER |
| Oxycodone | OxyContin [®] , Percocet [®] , Percodan [®] , Roxicodone [®] |
| Tramadol | Ultram [®] , Ultram [®] ER, Ultracet [®] |
| Codeine | Tylenol [®] with codeine 3 or 4 |
| Morphine | Avinza [®] , Kadian [®] , MS Contin [®] |
| Fentanyl | Duragesic [®] , Fentora [®] |
| Buprenorphine | Suboxone [®] |
| Oxymorphone | Opana [®] , Opana [®] ER |
| Meperidine | Demerol [®] |
| Hydromorphone | Dilaudid [®] , Exalgo [®] |
| Methadone | Dolophine [®] , Methadose [™] , Diskets [®] |
| Tapentadol | Nucynta [®] |

The United States Opioid Epidemic

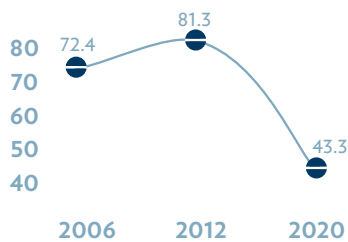
The United States is in the midst of an opioid epidemic.¹ Stemming from the rise in opioid prescriptions beginning in the 1990s,² there has been an alarming increase in licit and illicit opioid use, prescription opioid misuse, opioid use disorder (OUD), opioid-related overdose, and deaths.^{3,4} Although data from recent years suggest improvements in opioid prescription rates⁵ and misuse,⁶ opioid related overdose and deaths increased in 2019, driven by increases in synthetic fentanyl related deaths and have remained elevated over the course of the COVID-19 pandemic.^{4,7} The opioid crisis remains a public health emergency.⁸

Opioid Prescriptions Quick Facts

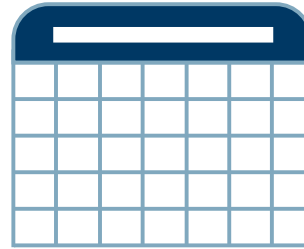
The number of written opioid prescriptions peaked in 2012 and has decreased annually, owing in part to heightened awareness and changes in prescribing practices.⁹

In 2020 (the latest year with data), there were still more than 142 million prescriptions for opioids.⁵ Despite the significant reductions in the number of prescriptions, there has been an increase in the average days of supply of prescriptions filled, and the average daily morphine milligram equivalent (MME) per prescription remains high, at more than 42.9 MME.⁹

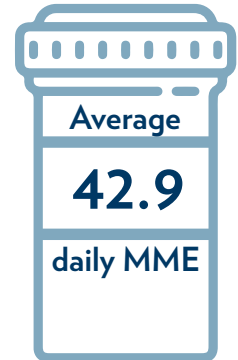
US Opioid Dispensing Rate per 100 persons



142 Million Opioid Rx in 2020



The average daily supply of prescriptions filled has increased despite fewer prescriptions written



Opioid Misuse and Use Disorders

Opioid misuse is classified as use of illegal opioids (e.g. heroin) and/or the use of prescription drugs in a manner other than as directed by a doctor, such as use in greater amounts, more often, or longer than told to take a drug, or using someone else's prescription.^{11,12} Based on results from the National Survey on Drug Use and Health (NSDUH), since 2015, there has been decrease in reported opioid misuse in the United States. In 2019, an estimated 10.1 million people (3.7%) aged 12 or older reported misuse of opioids in the past year. Specifically, 9.7 million people reported misuse of prescription pain relievers and 745,000 people used heroin.⁶

Pain is the leading risk factor for opioid misuse¹³ and is reported to be the primary reason for misuse (62.3%), followed by taking to feel good or get high (13%), to relax or relieve tension (10.8%), and to help with feelings and emotions (4%).¹⁴

Opioid Use Disorders (OUD) are defined by the DSM-IV¹⁵ as a problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of 11 criteria occurring within a 12-month period, such as taking larger amounts or over a longer time than intended, persistent desire or unsuccessful efforts to cut down or control opioid use, or craving. In 2019, 1.6 million (0.6%) Americans 12 and older reported an OUD, defined by the NSDUH as meeting DSM-IV criteria for heroin use disorder and/or pain reliever use disorder. The 2019 estimate was lower than each year prior (2015-2018).

Opioid Overdose & Death

Drug overdose is the leading cause of accidental (injury-related) death in the United States. Between 1999-2019, there was over a 4-fold increase in opioid overdose deaths in the US. Although the data suggested slight declines in opioid-involved overdose deaths from 2017 to 2018, from 2018-2019 there was a significant 6% increase in opioid related overdose deaths, and from 2019-2021, there was a 30% increase. The increase in overdose deaths are driven by synthetic opioids. Opioids contribute to roughly 80% of all drug related overdose deaths.

<https://www.cdc.gov/drugoverdose/prevention/index.html>



Recent impact of the COVID-19 Pandemic

Nearly every state has reported an outbreak or sustained increase in opioid- and other drug-related mortality—particularly from illicitly manufactured fentanyl and fentanyl analogs.¹⁶ For the first time ever, the US experienced 100,000 overdose deaths over a one year period.

<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

<https://www.whitehouse.gov/briefing-room/statements-releases/2021/11/17/statement-by-president-joe-biden-on-surpassing-100000-american-overdose-deaths-in-the-past-year/>

SPINAL CORD INJURY

An estimated 252,000 to 373,000 Americans are living with spinal cord injury (SCI).¹⁷ Nearly 18,000 Americans per year experience a SCI; the annual incidence is approximately 54 cases per million.¹⁷ Motor vehicle collisions are the primary cause of SCI (38.2%), followed by falls (32.3%) and violence (14.3%).¹⁷

Individuals with SCI often live with significant motor and sensory impairments and experience high rates of secondary and chronic health conditions. Pain is one of the most common and complex conditions after SCI. Based on a recent meta-analysis, the prevalence of chronic and neuropathic pain were 68% and 58%, respectively.¹⁸ The management of pain after SCI often requires a multi-modal approach including pharmacological treatment with prescription analgesics including opioids, psychotropic medications, or “off-label” prescription medication use, as well as non-pharmacological relief strategies.¹⁹⁻²⁵ The use of marijuana (cannabis), although controversial, has also been advocated for.²⁶

Opioids Are Frequently Prescribed after SCI

In 2016, the Centers for Disease Control and Prevention (CDC) published guidelines for prescribing opioids for chronic pain,¹⁰ advising providers to use caution when prescribing opioids at any dosage, to carefully reassess evidence of risks and benefits when considering ≥ 50 MME/day, and avoid increasing to ≥ 90 MME/day or carefully justify a decision to do so.¹⁰ Dosages exceeding 50 MME/day are associated with a twofold risk of opioid overdose, compared to 20 MME or less per day. Concurrent prescriptions for opioids and benzodiazepines should be also avoided when possible due to an increased risk of serious adverse outcomes including overdose, and death.

The use prescription opioids after SCI is a significant and controversial issue posing a unique risk. Several studies have noted the heightened risks of polypharmacy and treatment with high-risk medications after SCI, and the risks of adverse health outcomes associated with long-term opioid therapy.^{23,27-32} Opioids are generally not recommended as a first-line therapy after SCI, and some say they should only be used as a last resort, but still, they are commonly prescribed, and often continued long term.^{21,23,24,33,34} Estimates for opioid use vary and depend on the data source assessed.

How are opioid prescriptions different among those with SCI?

Individuals with SCI living in the United States have been found to have higher rates of prescription opioid use, longer durations of coverage, and higher MME dosages compared to the general population.^{35,36} Among Veterans with SCI, opioids have been identified as the most frequently filled class of drugs.^{37,38} Estimates from the Veterans Affairs Spinal Cord Dysfunction Registry suggest that upwards of 70% of the population are prescribed opioids for pain.³⁷

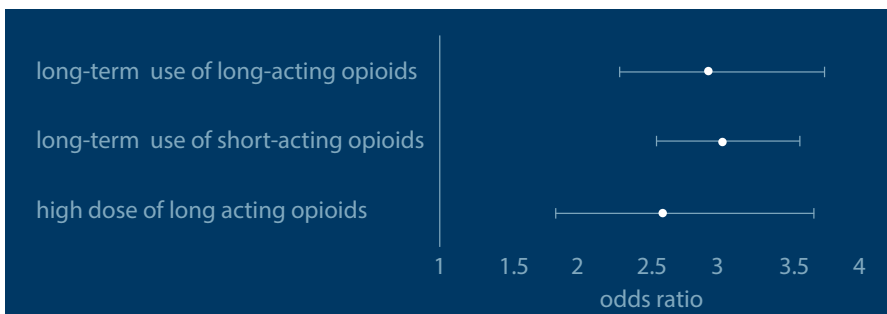
In an analysis of opioid dosage and duration using medical and pharmacy claims from 2012-2013, Hand and colleagues found that individuals with SCI were more likely to receive opioids for longer durations and at higher morphine-equivalent dosages than propensity-score matched controls.³⁵ The study, which included 1,454 individuals with SCI, found that among those with an opioid prescription claim, 81.8% received low-dose, long-acting opioids for less than



90 days (short-term), compared to 92.6% without SCI. Conversely, a larger percentage of adults with SCI received low-dose, long-acting opioids for greater than 90 days (10.2% vs 4.1%). A greater percentage of individuals with SCI received high-dose, long-acting opioids for both the short-and long-term. Examining short-acting opioids, fewer individuals with SCI received low-dose for less than 90 days (59.4% vs 81.4%) and a greater percentage received low-dose, short-acting opioids for more than 90 days (40.6% vs 18.6%). After controlling for age, sex, and medical comorbidities, those with SCI were significantly more likely to receive long-acting opioids for more than 90 days.

Opioid prescriptions for persons with SCI

Compared to propensity score matched controls, individuals with SCI were significantly more likely to be prescribed high average daily morphine equivalents of long-acting opioid prescriptions (OR=2.59, $p<0.0001$), more likely to be long-term users of short-acting opioids (OR=3.02, $p<0.0001$), and more likely to use long-acting opioids long-term (OR=2.92, $p<0.0001$).



More recent data from a state-based prescription drug monitoring program suggested that a greater percentage of adults with SCI filled opioid prescriptions, and at higher morphine milligram equivalents than state residents.³⁶ In a sample of 503 adults with chronic SCI (>1 year post injury), 53.5% filled at least one opioid prescription in years 2 or 3 post injury. In the two-year study timeframe, there were total of 3,386 opioid fills, and the average daily MME per prescription fill was 58.9. The average coverage period was 389 ± 290 days and the average daily MME during the coverage period was 41 ± 70 MME.

Additional analyses looked more in depth at high-risk prescription fills, defined by the duration, dosage, and concurrent prescriptions for opioids and benzodiazepines, sedatives, or hypnotics (BSH).³⁹ Among the 269 individuals who filled an opioid prescription in years 2-3 after injury, 38% had a concurrent BSH fill, 76% of which were for benzodiazepines. In any given quarter over the two-year timeframe, over half of the opioid prescriptions were for 60 days or more (chronic opioid prescriptions). Of those with chronic prescriptions, roughly 40% had high-dose chronic opioid prescriptions ≥ 50 MME/d and 25% had daily dosages ≥ 90 MME/d. Over 33% had a concurrent BSH prescription for ≥ 60 days. Despite the small sample size, these findings provide a more complete look at high-risk opioid use after SCI, and suggest a need for more cautious opioid prescribing and monitoring in adults with chronic SCI.

Are prescribing patterns changing?

Since the release of opioid prescribing guidelines,^{10,40} several clinical perspectives have been published addressing the use of opioids and changing prescribing practices for those with SCI.^{28,41,42} However, there is limited published data on the effectiveness of interventions to reduce use and risk.

Some argue that opioids should not be used for chronic pain after SCI and clinicians should slowly taper use.²⁸ Others acknowledge the problematic nature of opioids, and urge caution on the use of forced tapers and suggest an informed consent when changing opioid use involves meaningful risk.⁴¹ In one SCI system of care in Ohio, an interdisciplinary approach to reduce opioid use was shown to be beneficial. The quality improvement project resulted in a reduction in the percentage of individuals receiving opioids, the number of prescriptions, and the MME being prescribed. ⁴³

In 2018, researchers conducted an international survey of 128 clinicians providing care for individuals with SCI.⁴² They found that some providers haven't changed their prescribing patterns, despite the epidemic and new practice



guidelines, and many do not feel influenced in their prescribing patterns by regulatory bodies. When asked about opioids for the treatment of chronic pain, 67% of providers reported that opioids were indicated at any time, and of those providers, 46% thought there should be no upper limit for the dosage. Given a case scenario, 86% of providers indicated they would continue prescribing opioids at high dosages (>250MME/day) if they were effective.

How are individuals with SCI at risk?

Despite the growing national efforts to address the opioid epidemic, limited research exists regarding the prevalence rates and risks of opioid use, misuse, OUD, and adverse opioid-related outcomes in individuals with SCI.

Substance use, including the use of psychoactive substances (i.e., psychotropic medications, alcohol, and illicit drugs), and substance use disorders are high among those with SCI.^{44,45} Although a number of earlier studies addressed substance use, findings from more recent reviews highlight the sparsity of research regarding opioid use, misuse, and OUD.⁴⁴⁻⁴⁶ In a small early study, the reported rate of opioid use was around 4%.⁴⁷ Another early study of 30 participants from the SCIMS found 20% of individuals with SCI reported illicit drug use in the past 6-12 months; among those, 12.5% reported heroin/opiate use.⁴⁸ However, in the wake of the current epidemic, these prevalence rates should be interpreted with caution.

In a recent analysis of psychoactive substance (PAS) use, among 4,577 adults with chronic SCI, 24% reported using at least one PAS in the past three months for which they did not have a prescription. Illicit opioid use specifically was reported by 3.5% of participants.^{DiPiro, 2022 #4959}

Several studies from the SCI Longitudinal Health Study have identified relationships between prescription pain medication use (though not specifically identified as opioids) and mortality. In 2017, a study found the frequency of pain medication use was associated with a significant increase in mortality, above and beyond demographic, injury-related, socioeconomic, and health characteristics.⁴⁹ In a longitudinal analysis analysis, a 35% increase in pain medication use was observed over a 10-year timeframe, and among those who reported daily pain medication use at time 1, there was a 229% increase in the likelihood of death at time 2. Controlling for covariates, those who reported increased pain medication usage were 95% more likely to be deceased at the 10 year follow-up.⁵⁰

In 2018, Krause et al. published findings highlighting how risk factors for unintentional death due to drug poisoning differ from the risks associated with deaths from other causes.⁵¹ Of 690 deaths, 24 were unintentional deaths due to drug poisoning. Risk factors for these deaths included binge drinking, medication use total score, and impulsive-sensation seeking, compared to risk factors for all other causes which were: older age, greater injury severity, non-ambulatory, smoking regularly, medication use total score, and greater neuroticism-anxiety scale scores. The unintentional deaths due to prescription drug overdose were associated with a set of risk factors that differed in meaningful ways from risk of death due to other causes after SCI, and those differences may hold the key to prevention strategies.

What about alternatives to Opioid Therapy?

There are several pain management therapies that could be considered, including alternative medications and non-opioid pain medications, physical therapy, massage, acupuncture, injections and surgical procedures, and relaxation and biofeedback techniques. In recent years the use of medical marijuana (cannabis) has risen as an alternative. Cannabis is a PAS that is frequently used and perceived by individuals with SCI as an effective alternative;⁵²⁻⁵⁵ however there is insufficient evidence to support the efficacy of cannabis on pain intensity.⁵⁶ Furthermore, based on the limited SCI literature, it is not clear if cannabis use is associated with a reduction in opioid use.

In a self-reported study of cannabis use, a greater percentage of cannabis users (38%) than non-users (23%) reported having a prescription for at least one opioid medication, suggesting that cannabis use does not mitigate opioid



use.⁵⁷ In a recent yet to be published analysis of self-reported non-prescription substance use, the findings suggest that cannabis use is not associated with a reduction in opioid use, as a larger percentage of those who endorsed usage of cannabis and other substances indicated non-prescription opioid use (33%) compared to those who reported only use of other substances (no cannabis), with 27% reporting opioid use. There is a need for continued research to assess whether the use of cannabis is associated with reduced opioid usage after SCI.

Is there a flip side?

When considering the high rates of opioid use and the associated increased risk of adverse outcomes including misuse, overdose, and death, it is logical to recommend following guidelines for decreasing or stopping opioid use, but considerations should be given to the flip side. In reality, opioids may play an important role in pain management after SCI, as several clinical perspectives have addressed.^(CITE)

NEXT STEPS

What is needed is continued evaluation of opioid use, risk factors, and consequences, and tools to help clinicians identify high-risk individuals and modifiable factors that may become the focus of clinical interventions and prevention strategies.

There are several questions that remain unanswered and should be considered:

- What if opioids are the only effective treatment for pain relief?
- May the benefit of opioid therapy outweigh the risks?
- Will alternative therapies result in similar risks? Or even provide effective relief?
- What are the unexpected consequences of altering (tapering or abruptly stopping) opioid prescriptions among those with SCI?
- Will individuals with SCI experience increased risk of adverse outcomes after tapering or cessation of opioid use?

We may make erroneous assumptions that changing prescribing practices to reduce the risk of overdose and other complications will not also introduce new problems, particularly in the absence of alternative treatments. There is a need for continued study of opioid use and safe strategies for reducing risky use.

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