Improving the Quality of Care: Legislative Impact on the Use of Naloxone

December 31, 2021 (Table 2 Updated March 31, 2022)

Learning Objectives:

- Identify risk factors for opioid-induced respiratory depression
- Review California legislation regarding naloxone
- Summarize best practices for responsible prescribing and furnishing of naloxone for the complete or partial reversal of opioid-induced respiratory depression

Key Points:

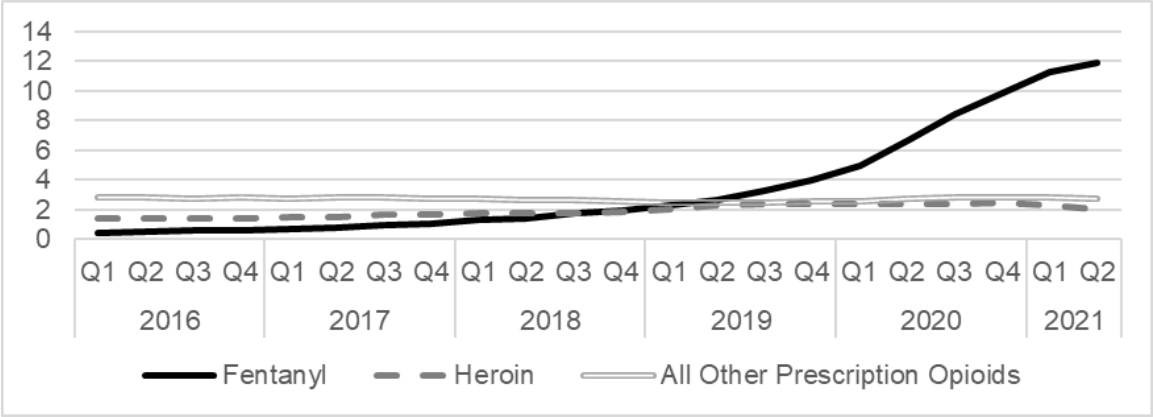
- The age-adjusted opioid-related overdose death rate in California has significantly increased over the last two years, driven primarily by highly potent opioids such as illicitly manufactured fentanyl.
- Naloxone, a potentially life-saving medication for opioid overdose, may be offered to individuals at risk for opioid overdose. Naloxone prescriptions can also be written directly to third party individuals who might be likely to witness and assist a person at risk of an opioid overdose.
- In recent years, California has passed legislation to expand access to naloxone, including a bill allowing pharmacists to furnish naloxone and Assembly Bill (AB) 2760 (Wood, Chapter 324), which requires California providers to offer a prescription for naloxone (or similar) as a rescue medication under certain conditions.
- After AB 2760 became effective on January 1, 2019, there was a 250% increase in overall paid claims for naloxone in the Medi-Cal program between the fourth quarter of 2018 and the first quarter of 2019. Of note, there was also a 150% increase in paid claims for pharmacist-furnished naloxone observed during this same time period, despite no additional requirements for pharmacists in the legislation.
- Health care providers should have ongoing conversations with patients, caregivers, and the community about the changing illicit drug supply and increased risk for overdose.

Background:

Between 2011 and 2020, the United States experienced ten consecutive years of decreasing opioid prescriptions, with a 44% decrease in the total number of opioid prescriptions during this time period.[1] Despite both this overall reduction in opioid prescribing and a corresponding increase in the use of state prescription drug monitoring programs (PDMPs), drug-related mortality continues to rise.[1,2] Provisional data from the Centers for Disease Control (CDC) and Prevention's National Center for Health Statistics indicate that there were an estimated 75,673 opioid-related overdose deaths in the 12-month period ending in April 2021, up from 56,064 the year before.[3]

According to data published on the California Opioid Overdose Surveillance Dashboard, the age-adjusted opioid-related overdose death rate has increased significantly in California over the last two years (**Figure 1**).[4] Of note, the data for 2020 was finalized on November 30, 2021, while the 2021 data are still considered preliminary.[4]

Figure 1. Age-adjusted opioid-related overdose death rate in California between January 1, 2016, and June 30, 2021 (per 100,000 residents).



California experienced 5,502 opioid-related overdose deaths in 2020, a 128% increase from 2018 despite a 25% decrease in opioid prescriptions during this timeframe.[4,5] The majority (71.7%) of the opioid-related overdose deaths in California during 2020 involved fentanyl.[4,5] During the fourth quarter of 2018, fentanyl-related overdose deaths in California surpassed all other opioid-related deaths combined, and since then the age-adjusted death rate per 100,000 residents increased almost 500%, from the fourth quarter of 2018 (1.95) to the second quarter of 2021 (11.89).[4,5] These data are consistent with national reports from the CDC that

showed the largest relative increase in synthetic opioid-involved death rates occurred in the western United States during 2018–2019.[6,7]

On December 17, 2020, the CDC published a Health Alert Network (HAN) Advisory reporting that the increase in drug overdose mortality began in 2019, driven primarily by synthetic opioids, accelerated during the coronavirus disease 2019 (COVID-19) pandemic.[2] Risk factors that may increase the likelihood of overdose include high cumulative dose from all sources of opioids (such as multiple prescriptions, providers or unprescribed sources), concomitant medications with respiratory depressant effects and certain comorbid conditions (**Table 1**).[2,8-10] Medication obtained without a prescription and recreational drugs may also be contaminated with fentanyl, so the use of these products increases overdose risk.[6-10]

Table 1. Risk factors for opioid-induced respiratory depression [2,8-10]

Category	Risk Factors		
Opioid Use	≥90 morphine milligram equivalents (MME)/day)	≥4 overlapping opioid prescriptions	Long-acting opioid use
	Injectable opioid use	Recent period of opioid abstinence	Excessive doses when switching opioids
	Opioid prescriptions from multiple prescribers	Opioid prescriptions filled at multiple pharmacies	
Behavioral Health	Mental health disorder history (undiagnosed or undertreated)	Past substance use or dependence	Concurrent use of benzodiazepines or sedatives
	Actively taking an antidepressant	Using an opioid with CNS depressants combined with alcohol	Using opioids prescribed to someone else
Comorbid Conditions	Liver, lung, or renal disease	Respiratory condition (i.e., asthma, sleep apnea)	

Naloxone

Naloxone is an opioid antagonist used for the complete or partial reversal of opioid-induced respiratory depression. When naloxone is available and utilized quickly by trained members of the community, many opioid-related overdose deaths can be avoided. Naloxone has no potential for abuse and has been used in opioid overdose management for more than 40 years, with minimal adverse effects beyond the induction of opioid withdrawal symptoms.[9,10] While health care providers have an important role in assuring all populations at risk have access to naloxone, a recent study in a national commercial-payer population found that 98.5% of eligible patients with opioid misuse, dependence, or prior overdose diagnoses were not prescribed naloxone despite numerous interactions with the health care system during which they could have received naloxone.[11] Naloxone products currently available on the Medi-Cal Rx Contract Drugs List are listed in **Table 2**.

Table 2. Naloxone Products Available on the Medi-Cal Rx Contract Drugs List *

Dosage Form	Strength	Billing Unit
Injection	0.4 mg/ml	milliliter
Injection	1.0 mg/ml	milliliter
Intranasal Spray	4.0 mg/0.1 ml	each
Intranasal Spray	8.0 mg/0.1 ml	each

* For current information on covered naloxone products, check the Medi-Cal Rx Contract Drugs List page on the Department of Health Care Services (DHCS) website.

Improving Access to Naloxone through Legislation

Every state has now passed at least one law designed to increase access to naloxone.[12] In recent years, the following legislation to improve access to life-saving naloxone has passed in California:

- Effective January 25, 2016, AB 1535 (Bloom, Chapter 326) authorizes trained pharmacists to furnish naloxone products. The full legislation outlining the regulations of the Protocol for Pharmacists Furnishing Naloxone Hydrochloride can be found on the California State Board of Pharmacy website.
- Effective January 1, 2019, AB 2760 (Wood, Chapter 324) requires California providers to offer a prescription for naloxone or another drug approved by the U.S. Food and Drug

Administration (FDA) for the complete or partial reversal of opioid-induced respiratory depression, as a rescue medication under certain conditions. For additional information, providers may review the Naloxone Prescription Requirements page on the Medical Board of California website.

- Effective September 5, 2019, AB 714 (Wood, Chapter 231) clarifies that physicians are required to offer a prescription for naloxone (or equivalent) when prescribing an opioid or benzodiazepine and when one or more of the following conditions are present:
  - The prescription dosage for the patient is greater than or equal to 90 morphine milligram equivalents (MME) of an opioid medication per day.
  - An opioid medication is prescribed within a year from the date a prescription for benzodiazepine has been dispensed to the patient.
  - The patient presents with an increased risk for an opioid overdose, including a patient with a history of overdose, a patient with a history of substance use disorder, or a patient at risk for returning to a high dose of opioid medication to which the patient is no longer tolerant.

Naloxone Use in the Medi-Cal Population

A retrospective cohort study was conducted to evaluate the impact of legislation on the use of naloxone within the Medi-Cal population. All paid pharmacy claims for naloxone were reviewed with a date of service between January 1, 2015, and September 30, 2021. There were no additional inclusion or exclusion criteria. The prescriber NPI for each paid claim was reviewed to determine if the naloxone was pharmacist-furnished.

Results

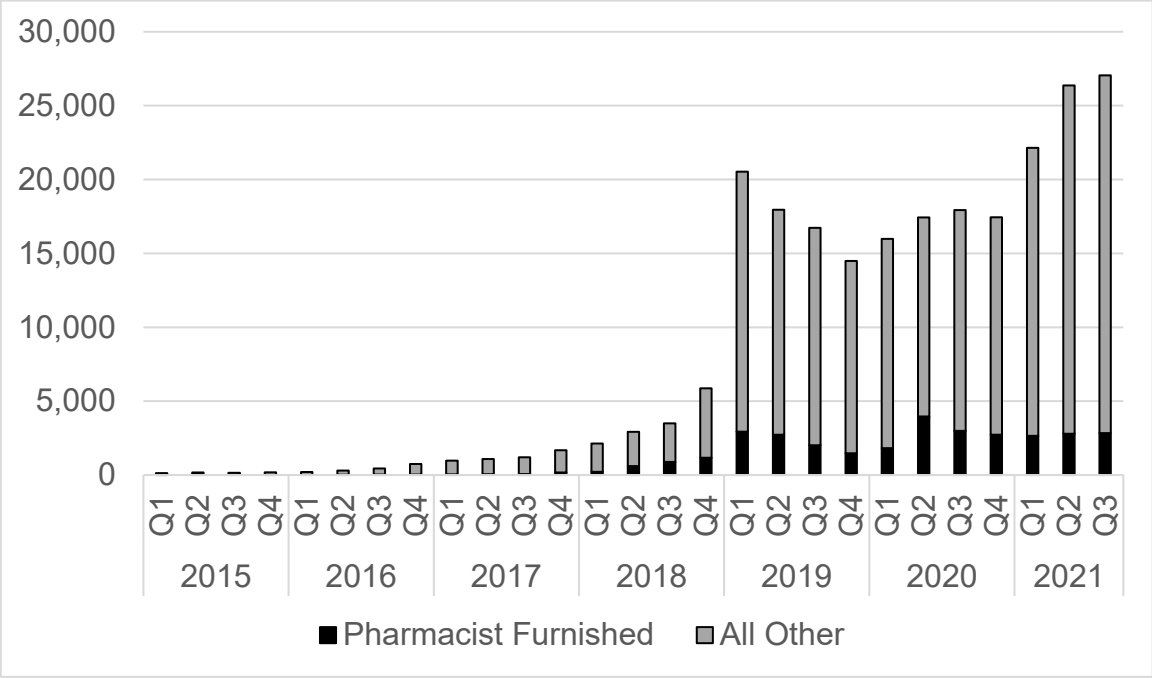
Between January 1, 2015, and September 30, 2021, a total of 171,199 Medi-Cal beneficiaries had 235,790 paid claims for naloxone, with 32% (n = 75,567) of paid claims occurring during the first nine months of 2021. The number of counties in California with at least one paid claim for naloxone in the Medi-Cal program increased from only 29 counties in 2015 to almost all counties (56 out of 58) starting in 2019. While some beneficiaries have received multiple paid claims for naloxone over time, the majority (82%) of beneficiaries had only one paid claim for naloxone between January 1, 2015, and September 30, 2021.

As shown in **Figure 2**, paid claims for naloxone in the Medi-Cal population have increased dramatically over time since California first authorized pharmacists to furnish naloxone

products. Overall paid claims for naloxone increased by 250% between the fourth quarter of 2018 and the first quarter of 2019, when requirements for California providers to offer a prescription for naloxone (or similar) as a rescue medication under certain conditions became effective. Overall paid claims for pharmacist-furnished naloxone also increased 150% during this same period, despite no new requirements for pharmacists outlined under AB 2670.

Since 2019, quarterly paid claims for pharmacist-furnished naloxone in the Medi-Cal program have ranged between 10.2% and 22.8% among all paid claims for naloxone. The highest percentage of pharmacist-furnished naloxone (22.8%) was observed during the second quarter of 2020 (April 2020 – June 2020), which began days after the Stay-at-home Order was issued in California on March 19, 2020. A recent report looking at the impact of COVID-19 on health care access in California found that quarterly use of health care services among all California health plan enrollees declined precipitously with the start of the pandemic, with the most acute decline observed during this quarter (a decrease of 27% compared to the second quarter of 2019).[13]

Figure 2. Total Paid Claims for Naloxone in the Medi-Cal Population between January 1, 2015, and September 30, 2021.



Only outpatient pharmacy paid claims for naloxone billed through the Medi-Cal program are included in **Figure 2**. Naloxone distributed through other mechanisms such as community-

based organizations or administered by emergency response personnel are not included in these data.

Discussion/Conclusion:

Naloxone can be safely administered to prevent opioid-induced respiratory depression outside of a medical setting. Implementation of strategies that remove barriers and increase access to naloxone will be crucial in the fight against the upward trend of opioid-related overdose deaths.

Clinical Recommendations:

General Recommendations:

- Talk to patients, caregivers, and the community about the changing illicit drug supply and risks for overdose and exposure to highly potent opioids such as illicitly manufactured fentanyl.
- Prescribe naloxone to individuals at risk for opioid overdose, such as those with a prior history of overdose, those with opioid use disorder, and individuals using illicit opioids and other drugs that might be mixed with illicitly manufactured fentanyl. Naloxone prescriptions can also be written directly to third party individuals who may be in a position to witness and assist a person at risk of an opioid overdose.
- Co-prescribe naloxone to patients with high morphine milligram equivalents and/or concomitant use of opioids and benzodiazepines.
- Educate patients, caregivers, and the community about the benefits of having naloxone readily available to more people. Individuals experiencing an opioid overdose will not be able to treat themselves so patients will need to be able to educate others about naloxone, demonstrate how to administer the naloxone, and share where the naloxone is stored.
- Counsel patients, caregivers, and the community that multiple doses of naloxone may be needed for a single overdose event because of the potency of illicitly manufactured fentanyl and fentanyl analogs, and that multiple doses of naloxone may be needed over time due to prolonged effects of opioids in some cases.
- Review both AB 2760 (Wood, Chapter 324) and AB 714 (Wood, Chapter 231) for specific legal requirements for prescribers in California.

- For more information and resources about naloxone, including patient-specific materials, practice guidelines, and conversation tips, visit the Prescribe to Prevent website and review the Opioid Overdose Prevention Toolkit developed by the Substance Abuse and Mental Health Services Administration (SAMHSA).
- Become aware of treatment resources in your community and refer patients for medication-assisted treatment (MAT) as needed, including the following:
  - Choose Change California is a DHCS website that provides an easy pathway to get help for people affected by substance use disorder.
  - Non-Emergency Treatment Referral Line (1-800-879-2772) is a DHCS referral line that connects people to local resources and services from their County Alcohol and Other Drugs Program Office.
  - Behavioral Health Treatment Services Locator is a national treatment facility locator from SAMHSA.
- Tailor interventions and outreach to cultural norms of the community to increase naloxone furnishing and reduce opioid-related deaths.

Pharmacy-Specific Recommendations:

- In the pharmacy setting, naloxone prescriptions are treated like any other prescription. However, to furnish naloxone (dispense with the pharmacist as prescriber), pharmacists must follow the §1746.3. Protocol for Pharmacists Furnishing Naloxone Hydrochloride and complete the necessary training in order to furnish naloxone hydrochloride, either through the Naloxone Training Webinar available through the California State Board of Pharmacy website, or an equivalent curriculum-based training program.
- When dispensing naloxone, provide the Naloxone Fact Sheet, which is available on the California State Board of Pharmacy website in multiple languages.
- Notify the patient's primary care provider if the naloxone is provided to the intended patient and consent (either verbal or written) is given by the patient.
- Maintain records of naloxone furnishing for at least three years. If naloxone is furnished to a third party, the patient on record is the third-party recipient.
- Review the Opioid Safety: Focus on Furnishing Naloxone guide for California community pharmacists for guidance on how to talk about opioids, identify patients for naloxone, and educate patients and caregivers about preventing overdose.

- Incorporate a standardized assessment for risk of an opioid use disorder into pharmacy workflow with a simple question such as, "How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?"
- Develop onsite procedures for naloxone requests and proactive criteria for patient selection. Train pharmacy employees to ensure procedures are executed consistently.

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