Naloxone
for opioid safety

A provider's guide to prescribing naloxone to patients who use opioids

Overdose is the leading cause of injury-related death in the U.S.

100 PEOPLE DIE FROM DRUG OVERDOSE EVERYDAY IN THE UNITED STATES.

FIGURE 1. DEATH BY LEADING CAUSE OF INJURY[1]

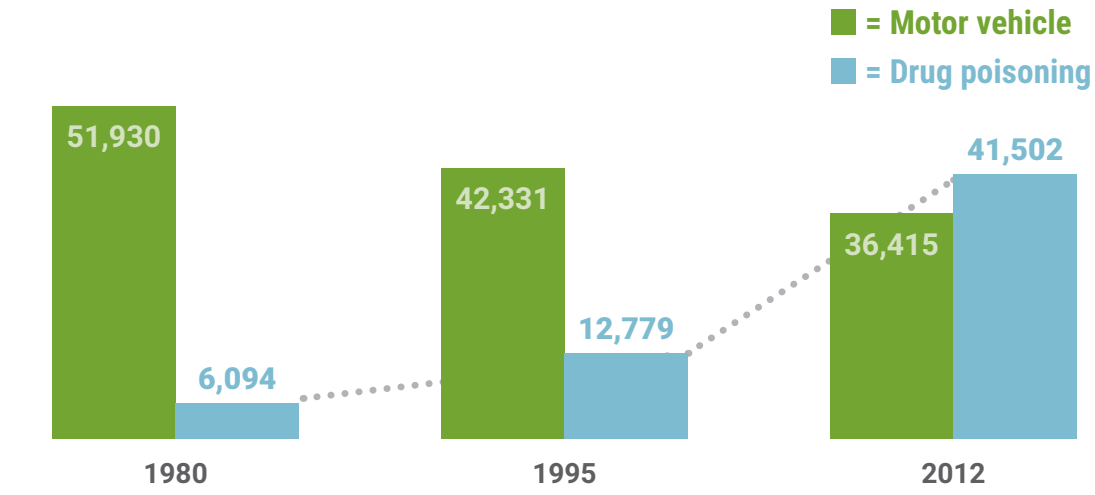
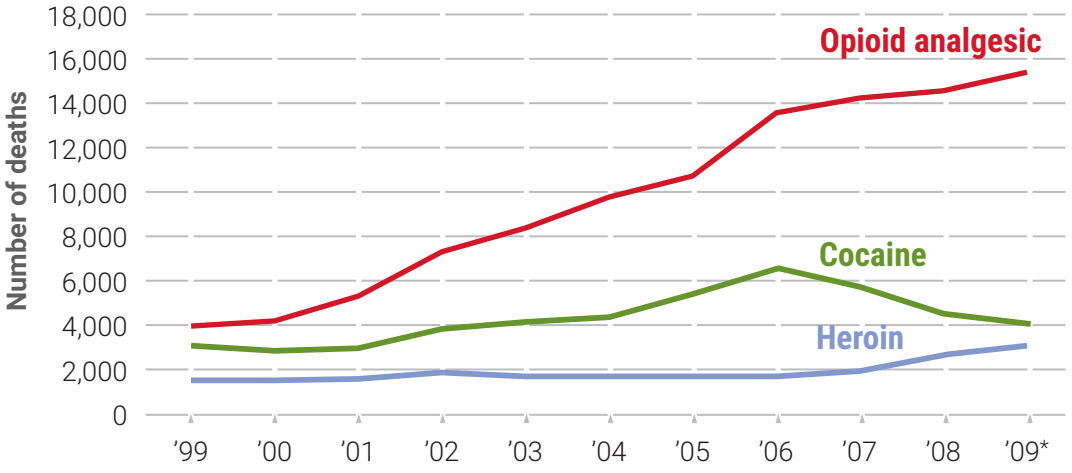


FIGURE 2. OVERDOSE DEATH BY DRUG TYPE[2]



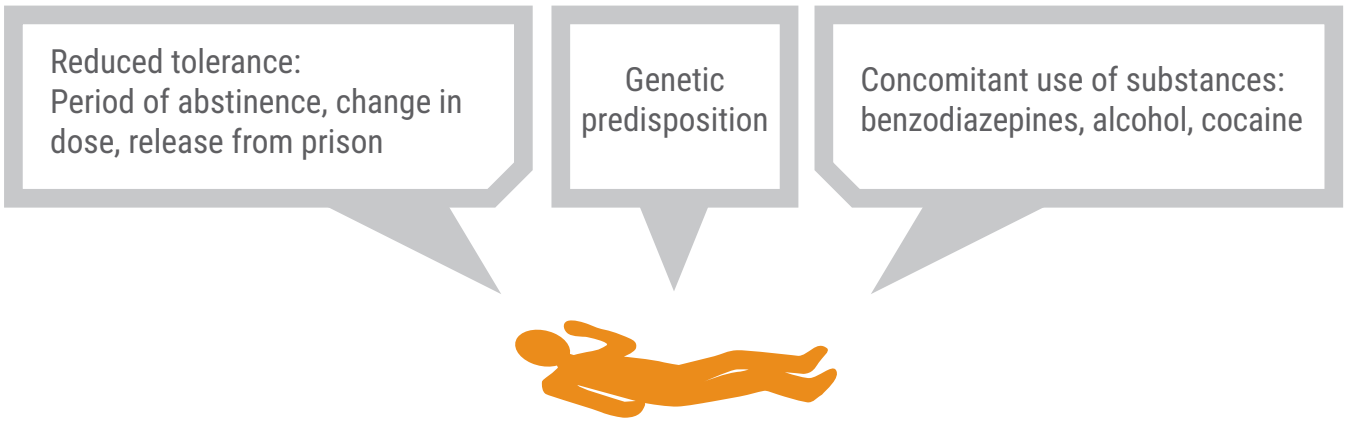
Opioid analgesics accounted for over 16,000 deaths in 2010.

* The reported 2009 numbers are underestimates. Some overdose deaths were not included in the total for 2009 because of delayed reporting of the final cause of death.

Accidental opioid overdose is preventable

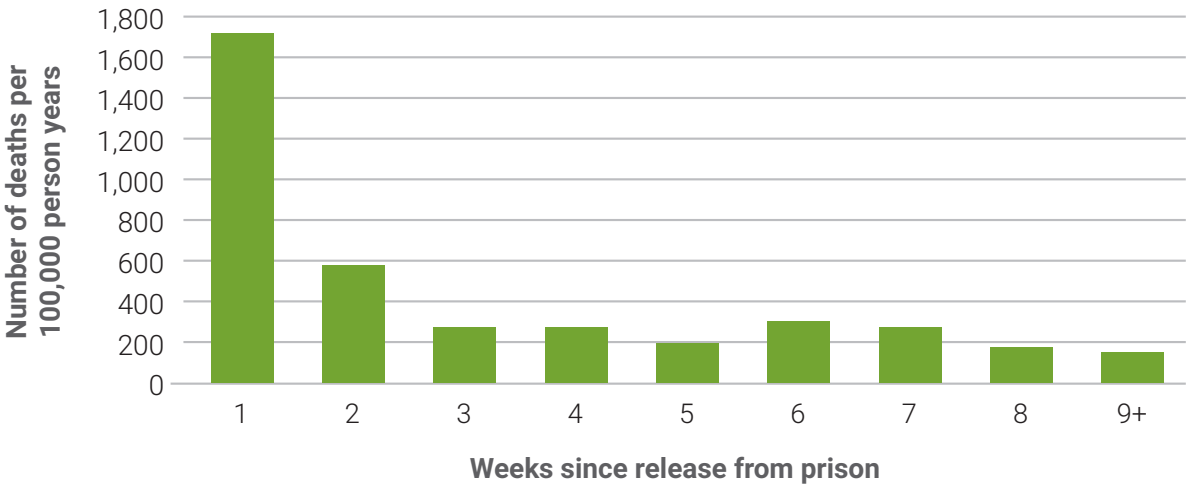
The main risk of death from an opioid overdose is prior overdose. A patient who has previously overdosed is 6 times more likely to overdose in the subsequent year.[3]

OTHER FACTORS THAT INCREASE RISK OF OVERDOSE:



The majority of opioid overdose deaths involve at least one other drug, including benzodiazepines, cocaine or alcohol.[4]

FIGURE 3. OVERDOSE MORTALITY RATE BY WEEK SINCE PRISON RELEASE:
An example of overdose risk if opioids are discontinued and restarted[5]

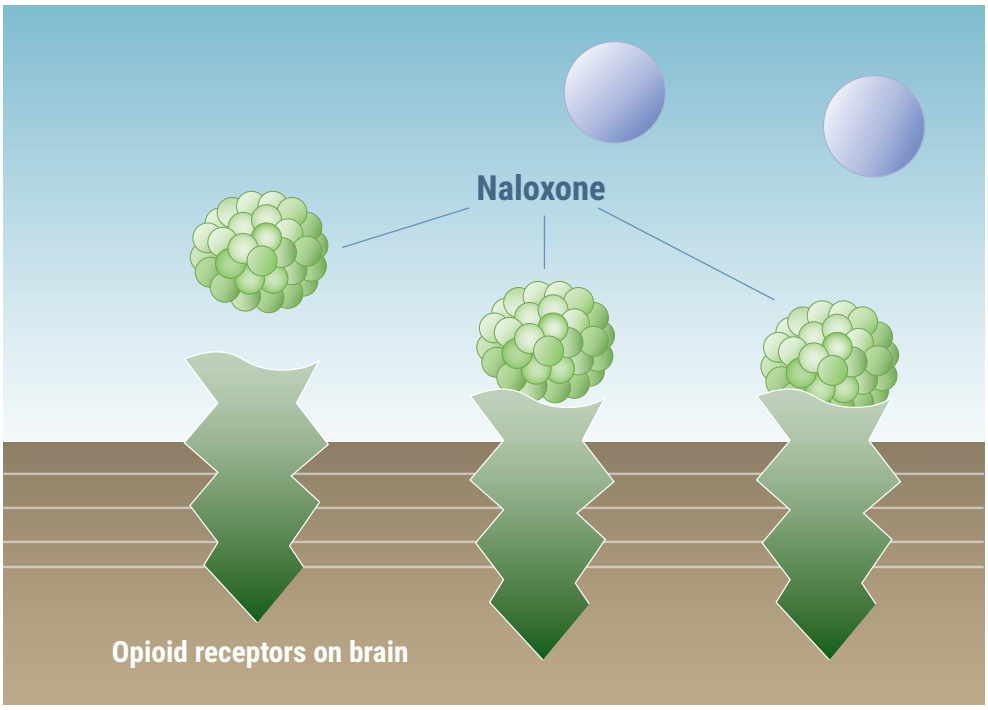


When a patient reduces or stops opioid use, there is an increased risk of overdose death if opioid use increases again.

Naloxone

- Highly specific, high-affinity opioid antagonist used to reverse the effects of opioids.
- Can be safely administered by laypersons via intramuscular or intranasal* routes, with virtually no side effects and no effect in the absence of opioids.
- Effects last 30-90 minutes; usually sufficient for short-acting opioids but help should always be sought.
- While high doses of intravenous naloxone by paramedics have been associated with withdrawal symptoms, lower lay-administered doses produce much more mild symptomatology.[6]

FIGURE 4. NALOXONE MECHANISM OF ACTION[7]



Naloxone has a higher affinity to the opioid receptors than opioids like heroin or oxycodone, so it knocks other opioids off the receptors for 30-90 minutes. This reverses the overdose and allows the person to breathe.

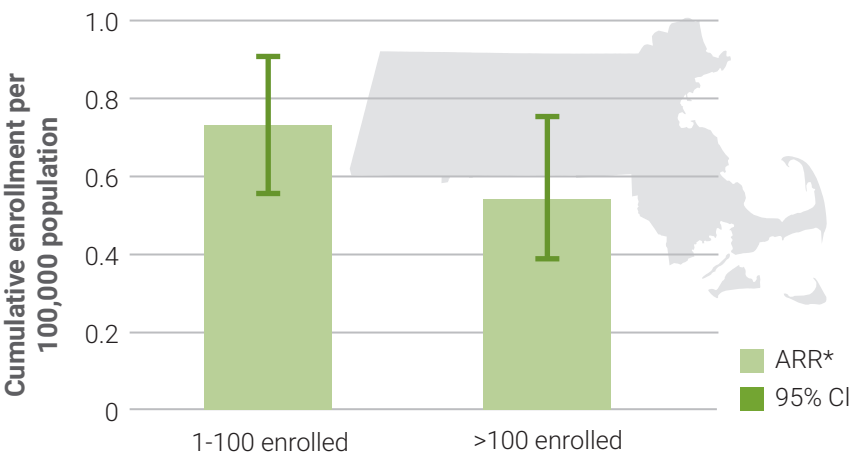
The American Medical Association has endorsed the distribution of naloxone to anyone at risk for having or witnessing an opioid overdose.[8]

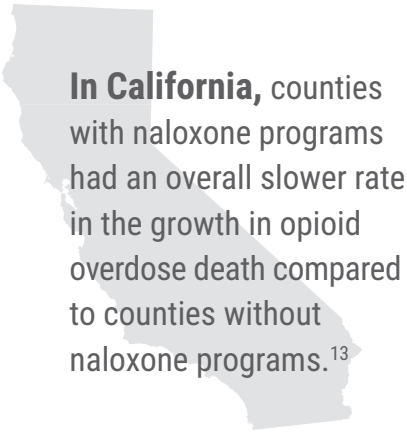
There are 240 sites across 18 states that prescribe or distribute naloxone. Since 1996, naloxone has been distributed to over 53,000 people and more than 10,000 overdose reversals have been reported.[9]

* Intranasal is off-label but is supported by the American Medical Association and has become the preferred route for many emergency responders.[10, 11, 12]

Naloxone is effective

FIGURE 5. FATAL OPIOID OVERDOSE RATES BY NALOXONE IMPLEMENTATION IN MASSACHUSETTS[10]





In California, counties with naloxone programs had an overall slower rate in the growth in opioid overdose death compared to counties without naloxone programs.[13]

* Adjusted Rate Ratios (ARR) adjusted for population age <18, male, race/ethnicity, below poverty level, medically supervised inpatient withdrawal, methadone and buprenorphine treatment, prescriptions to doctor shoppers, year

...and cost-effective[14]

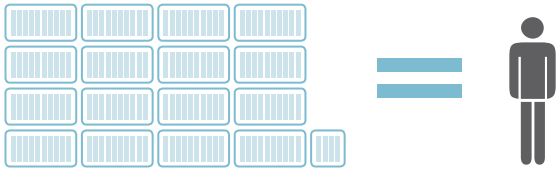
A manuscript in the *Annals of Internal Medicine* indicated that providing naloxone to heroin users is robustly cost-effective and possibly cost-saving. Investigators believe similar results apply to other opioid users.

Cost:

$421 per quality-adjusted life-year gained

Benefit:

164 naloxone scripts = 1 prevented death



Emerging data suggests that providing naloxone may encourage patients to be safer with their opioid use. If this is the case, the intervention would be cost-saving and **36 prescriptions** would prevent one death.

Indications for naloxone prescription

CONSIDER OFFERING A NALOXONE PRESCRIPTION TO:

- All patients prescribed long-term opioids
- Anyone otherwise at risk of experiencing or witnessing an opioid overdose

WHY PRESCRIBE TO ALL PATIENTS ON LONG-TERM OPIOIDS?

It is difficult to predict which patients who take prescription opioids are at risk for overdose.
Many patients do not feel they are at risk for overdose. Prescribing to all patients on opioids will help patients understand naloxone is being prescribed for risky drugs, not risky patients.
About 40% of overdose deaths result from diverted medications.[15] Whether intentional or unintentional, diverted opioids are a serious risk. Co-prescribing naloxone increases the chance that the antidote will remain with the medication.

Potential behavioral impact

Being offered a naloxone prescription may lead to safer opioid use.

U.S. army base Fort Bragg in North Carolina averaged 8 overdoses per month. After initiating naloxone distribution, the overdose rate dropped to zero—with no reported naloxone use.[16]

> *"[W]hen I prescribe naloxone...there's that realization of how important this is and how serious this is in their eyes."* —US army Fort Bragg primary care provider

Selected San Francisco Health Network clinics began co-prescribing naloxone to patients on opioids in 2013.

> *"I had never really thought about [overdose] before...it was more so an eye opener for me to just look at my medications and actually start reading [about] the side effects, you know, and how long should I take them...I looked at different options, especially at my age."*
>
> —San Francisco patient[17]

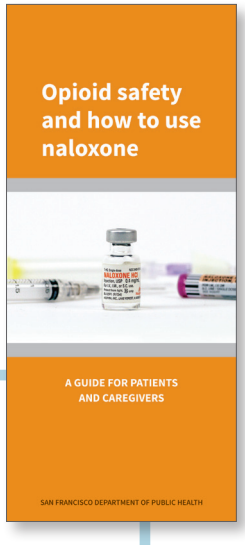
Offering a naloxone prescription can increase communication, trust and openness between patients and providers.

> *"By being able to offer something concrete to protect patients from the danger of overdose, I am given an opening to discuss the potential harms of opioids in a non-judgmental way."*
>
> —San Francisco primary care provider[18]

How to educate patients on naloxone

Clinic staff can educate patients about naloxone. Education generally includes:

- When to administer naloxone
- How to administer naloxone (including demonstration)
- Informing patients to alert others about the medication, how to use it and where it's kept, as it is generally not self-administered



Brochures remind patients and caregivers how to manage an overdose. Example brochures can be found at **www.prescribetoprevent.org**.

OPIOID SAFETY LANGUAGE

The word "overdose" has negative connotations and prescription opioid users may not relate to it.

Patients prescribed opioids (including high-risk persons with a history of overdose) reported their risk of "overdose" was 2 out of 10.[19]

Instead of using the word "overdose," consider using language like "accidental overdose," "bad reaction" or "opioid safety." You may also consider saying:

"Opioids can sometimes slow or even stop your breathing."

"Naloxone is the antidote to opioids—to be [sprayed in the nose/injected] if there is a bad reaction where you can't be woken up."

"Naloxone is for opioid medications like an epinephrine pen is for someone with an allergy."

State law encourages naloxone prescribing

Naloxone is NOT a controlled substance. **Any licensed healthcare provider can prescribe naloxone.** California State law provides additional protections to encourage naloxone prescribing and distribution:

PROVIDER AND PATIENT PROTECTIONS (CA AB635 effective 1/1/14)

- **Providers are encouraged to prescribe naloxone** to patients receiving a chronic opioid prescription.
- **Naloxone prescriptions also can be written directly to third party individuals** (caregivers, family members, friends, etc.) who are in a position to witness and assist a person at risk of an opioid overdose.
- **A licensed healthcare prescriber can issue a standing order** for the dispensing of naloxone by healthcare or community workers to individuals at risk of experiencing or witnessing an overdose.
- **Lay persons can possess and administer naloxone** to others during an overdose situation.

GOOD SAMARITAN PROTECTION (CA AB472 effective 9/17/12)

- **Witnesses of an overdose who seek medical help are provided legal protection** from arrest and prosecution for minor drug and alcohol violations.

PHARMACIST PROVISION OF NALOXONE (CA AB1535 effective 1/1/15*)

- **Pharmacists are allowed to directly prescribe and dispense naloxone** to patients at risk of experiencing or witnessing an opioid overdose.

* Pending pharmacy and medical board agreement on regulations.

Examples of how to prescribe naloxone

INJECTABLE

- Naloxone 0.4mg/1ml IM if overdose. Call 911. Repeat if necessary. #2
- IM syringes (3ml 25g 1" syringes are recommended) #2

INTRANASAL (OFF-LABEL)

- Naloxone 2mg/2ml prefilled syringe, spray ½ into each nostril if overdose. Call 911. Repeat if necessary. #2
- MAD (Mucosal Atomization Device) nasal adapter

Atomizer access is complicated. Select pharmacies now carry the atomizer, but most still have trouble accessing it. Insurers may require a TAR for reimbursement.

AUTO-INJECTOR

- Naloxone auto-injector 0.4mg #1 two pack, use PRN for suspected opioid overdose

SBIRT CODES COVER TRAINING (per 15 min intervals)

MediCare: G0396
MediCal: H0050
Commercial: CPT99408

Please copy or scan and send to your local pharmacist.

Pharmacy access

All pharmacies can fill naloxone prescriptions, but naloxone is new for many pharmacists so some may not know how. If a pharmacist is unsure how to fill a naloxone prescription, the information outlined on this page may be helpful.

ORDERING:

- Injectable: **Hospira** NDC#00409-1215-01; **Mylan** NDC#67457-292-00
- Intranasal: NDC#76329-3369-01
- MAD (atomizer) nasal devices produced by Teleflex*
- Auto-injector: NDC#60842-030-01

BILLING:

- Naloxone is covered by MediCal (as a "carve-out" **so submit directly to FFS MediCal**—do NOT send a PA to the HMO plan), and many other plans
- The MAD does not have an NDC, therefore cannot be billed through usual pharmacy billing routes. Pharmacies may be willing to cover the cost of the MAD or patients may be requested to pay for the cost of the MAD, which is around $5 per atomizer.

COUNSELING:

- Instruct patients to administer if non-responsive from opioid use and how to assemble for administration.
- Include family/caregivers in patient counseling or instruct patients to train others.

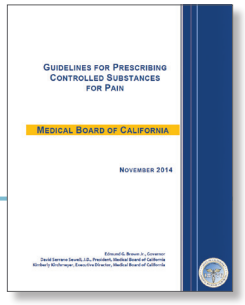
SIDE EFFECTS: Anxiety, sweating, nausea/vomiting or shaking. Talk to your doctor if these occur. This is not a complete list of possible side effects. If you notice other effects not listed, contact your doctor or pharmacist.

*** Contact Michelle Geier, PharmD, with questions or concerns related to pharmacies, at (415) 503-4755 or michelle.geier@sfdph.org**

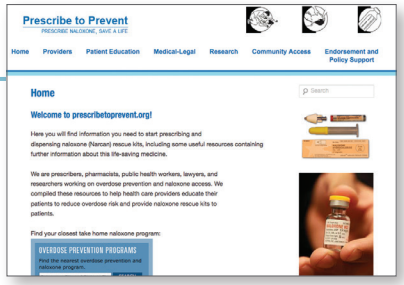
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Resources

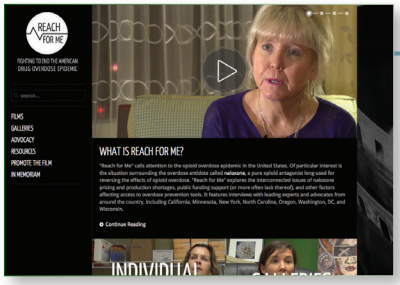
Medical Board of California: Guidelines for Prescribing Controlled Substances for Pain: **www.mbc.ca.gov/Licensees/Prescribing/Pain_Guidelines.pdf**



California Society of Addiction Medicine: Naloxone resources for providers, naloxone legal status, webinars and trainings: **www.csam-asam.org/naloxone-resources**



Prescribe to Prevent: Clinic-based prescribing information and guidelines: **www.prescribetoprevent.org**



Reach for Me: Film and resource materials for advocates, families and providers: **www.reach4me.org**

References

(1) Warner M, Chen LH, Makuc DM, Anderson RN, Minino AM. Drug poisoning deaths in the United States 1980-2008. National Center for Health Statistics. 2011;(81):1-8. Updated with Jones, C.M. Prescription Drug Abuse and Overdose in United States. Presented at: Third Party Payer and PDMP Meeting. 2012. **(2)** National Vital Statistics System. United States Department of Health and Human Services. Center for Disease Control and Prevention, National Center for Health Statistic. Multiple Cause of Death on CDC WONDER Online Database. Released 2012. **(3)** Darke S, Williamson A, Ross J, Teesson M. Non-fatal heroin overdose, treatment exposure and client characteristics: findings from the Australian treatment outcome study (ATOS). *Drug Alcohol Rev.* 2005;24(5):425-32. **(4)** Policy Impact: Prescription Painkiller Overdoses. Center for Disease Control and Prevention website. www.cdc.gov/homeandrecreationalsafety/rxbrief/. Updated Jul 2013. Accessed Dec 2014. **(5)** Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. *Ann Intern Med.* 2013;159(9):592-600. **(6)** Enteen L, Bauer J, McLean R, Wheeler E, Huriaux E, Kral AH, et al. Overdose prevention and naloxone prescription for opioid users in San Francisco. *J Urban Health.* 2010;87(6):931-41. **(7)** Understanding Naloxone. Harm Reduction Coalition website. www.harmreduction.org/issues/overdose-prevention/overview/overdose-basics/understanding-naloxone/. Accessed Dec 2014. **(8)** AMA adopts new policies at annual meeting: promoting prevention of fatal opioid overdose. American Medical Association website. www.ama-assn.org/ama/pub/news/news/2012-06-19-amaadopts-new-policies.page. Jun 2012. Accessed Dec 2014. **(9)** Community-Based Opioid Overdose Prevention Programs Providing Naloxone—United States, 2010. Centers for Disease Control and Prevention website. www.cdc.gov/mmwr/pdf/wk/mm6106.pdf. Feb 2012. Accessed Dec 2014. **(10)** Walley AY, Xuan Z, Hackman HH, Quinn E, Doe-Simkins M, Sorensen-Alawad A, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ.* 2013;346. **(11)** Barton ED, Colwell CB, Wolfe T, Fosnocht D, Gravitz C, Bryan T, et al. Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting. *J. Emerg. Med.* 2005;29(3):265-71. **(12)** Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. *Addiction.* 2009;104(12):2067-74. **(13)** Davidson PJ, Wheeler E, Proudfoot J, Xu R, Wagner K. Naloxone distribution to drug users in California and opioid related overdose death rates. Unpublished manuscript; 2014. **(14)** Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intern Med.* 2013;158(1):1-9. **(15)** Hirsch A, Proescholdbell SK, Bronson W, Dasgupta N. Prescription histories and dose strengths associated with overdose deaths. *Pain Med.* 2014;15(7):1187-95. **(16)** Role of Naloxone in Opioid Overdose Fatality Prevention. Food and Drug Administration website. www.fda.gov/downloads/Drugs/NewsEvents/UCM304621.pdf. 2012;339-340. Accessed Dec 2014. **(17)** Patient Interview. Naloxone for Opioid Safety Evaluation. San Francisco Department of Public Health. Dec 2014. **(18)** Primary Care Provider Interview. Naloxone for Opioid Safety Evaluation. San Francisco Department of Public Health. Jul 2014. **(19)** Patient Interviews. Naloxone for Opioid Safety Evaluation. San Francisco Department of Public Health. Oct 2013—Dec 2014.

About this publication

This publication was produced by the San Francisco Department of Public Health. Support was provided by the National Resource Center for Academic Detailing (NaRCAD). No pharmaceutical company resources were used in the development of these materials and authors (Phillip Coffin MD, Assistant Clinical Professor of HIV/AIDS at University of California San Francisco, and Emily Behar MS) deny any financial conflicts of interest.

The recommendations contained in this brochure are general and informational only; specific clinical decisions should be made by providers on an individual case basis.

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

NaRCAD
National Resource Center for Academic Detailing

This publication is in the public domain and may be copied or reproduced without permission.
Suggested citation: San Francisco Department of Public Health. *Naloxone for opioid safety: a provider's guide to prescribing naloxone to patients who use opioids.* January 2015.

Design and layout: Amy Braddock