Opioid Use: Harm Reduction and Treatment for Opioid Use Disorder

In 2017, 2.1 million Americans had an opioid use disorder and on average 130 people die every day from opioid overdose.[1,2] Preventative measures for mitigation of risk in the face of this epidemic are essential. Harm reduction is a strategic set of policies, programs, and actions applied to protect individuals and communities from the negative consequences of potentially risky behaviors. The principles of harm reduction are founded in a social justice perspective of respect for the dignity of all persons.[3] Harm reduction strategies for the potential risks of opioid use include: safe prescribing practices, universal opioid use screening, accessible and timely treatment of opioid use disorder, overdose prevention and reversal, disease prevention and protections for personal safety among persons who use drugs.

Safe Prescribing

A key opioid use disorder (OUD) harm reduction initiative in the U.S. targets opioid prescribing practices and the overall reduction of the quantity of prescribed opioids. Although the rate of opioid prescribing has been declining in the U.S. since 2012, still in 2017, 58 opioid prescriptions were written for every 100 Americans.[4]

An estimated 2 million Americans misused pain medications for the first time in 2017.[1]

Opioids are commonly prescribed for the management of non-cancer related chronic pain[5]. In 2016, the CDC released safe opioid prescribing recommendations for the management of chronic pain aimed at reducing the risk of opioid related harm to individuals and communities including opioid misuse, addiction, and overdose.

Key CDC recommendations for safe opioid prescribing include[5]:

1. Opioids are not first line therapy for the treatment of non-cancer chronic pain, alternatives should be considered
2. Establish pain treatment goals and monitor patient function regularly
3. Discuss risks and benefits of opioids including physical dependence and overdose
4. Use immediate release opioids instead of extended release or long acting formulations
5. Always use the lowest effective dose opioids
6. Prescribe opioids for short durations
7. Evaluate benefits and harms of opioid use within 1-4 weeks of initiating therapy and at least every three months
8. Evaluate risk factors for opioid use related harm. Use strategies to mitigate the risk of overdose including providing naloxone and limiting the dosage of opioids at 50 Morphine Milligram Equivalents (MME)/day or below and avoid concurrent benzodiazepine use
9. Review the CURES prescription drug monitoring program to evaluate for multiple opioid prescriptions or dangerous drug combinations
10. Conduct urine drug tests when prescribing opioids to assess for other controlled prescriptions and illicit drugs
11. Avoid concurrent opioid and benzodiazepine prescribing
12. Offer treatment for opioid use disorder. Consider obtaining a waiver to prescribe buprenorphine to treat patients with opioid use disorder.

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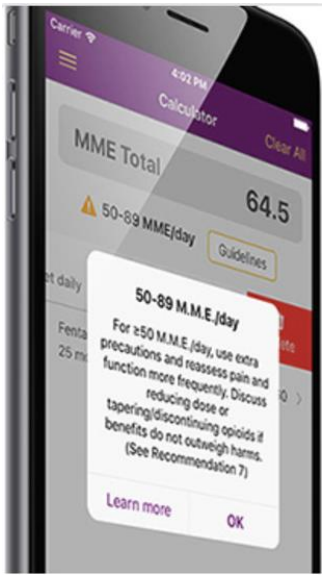
The complete recommendations for opioid prescribing are presented in the **CDC Guidelines for Prescribing Opioids for Chronic Pain** available at https://www.cdc.gov/drugoverdose/prescribing/guideline.html.



A free CDC Opioid Guideline App is available through Google Play (Android) or the Apple Store (iOS). This App provides the guidelines and an MME calculator.

https://www.cdc.gov/drugoverdose/prescribing/app.html

Opioid Use Disorder Screening

An expert panel of the Substance Abuse and Mental Health Services (SAMHSA) Treatment Improvement Protocols (TIP) recommends universal screening for opioid use disorder.[6] Similarly, the U.S. Preventive Services Task Force (USPSTF) released a draft recommendation to routinely screen adults 18 and older for illicit drug use including nonmedical use of prescription drugs.[7]

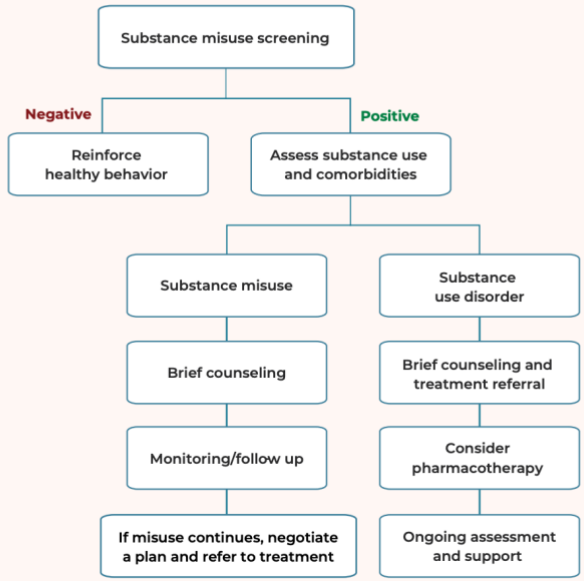
A single question screener can be used to efficiently screen for opioid misuse[6]:

How many times in the past year have you used an illegal drug or a prescription medication for nonmedical reasons?

A positive single question screen for opioid misuse should be followed by a brief assessment using a validated screening instrument such as the Tobacco, Alcohol, Prescription Medications and Other Substance Use (TAPS) tool[6].

In the event of a positive assessment for OUD, the patient should be offered or referred to OUD treatment. Additional opioid use harm reduction measures described below should also be encouraged as appropriate.[6]

EXHIBIT 2.2. Substance Misuse and SUD Screening



SAMHSA TIP 63[6]

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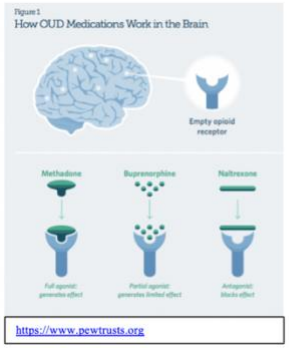
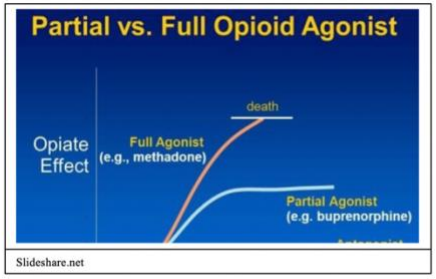
Treatment for Opioid Use Disorder

OUD is a high-risk, chronic disease requiring long term management. Treating OUD **decreases mortality**, **decreases the transmission of disease** (e.g. HIV and hepatitis), **decreases crime** and **improves social functioning** [8-12]

Medications are available to treat opioid use disorder that are safe and effective among medically eligible and motivated patients. [13,14] Pharmacotherapy therapy for OUD is interchangeably referred to as Medication Assisted Treatment (MAT) or Medications for Opioid Use Disorder (MOUD).

Whereas previous medical management for opioid use disorder was highly reliant on methadone treatment dispensed through narcotic treatment programs; office-based opioid treatment appropriate for primary care practice is now available, including **Naltrexone** and **Buprenorphine**. Naltrexone is an opioid antagonist that blocks the effect of opioids at the receptor sites. Buprenorphine is a partial opioid agonist that binds partially at the opioid receptor site reducing opioid cravings and withdrawal symptoms without producing significant euphoria. As a partial opioid agonist, buprenorphine has a drug response ceiling effect that dramatically reduces the risk of opioid overdose, thereby increasing the safety profile.[15,16] Concurrent behavioral therapies for the treatment of OUD are recommended to be delivered in conjunction with medication management.[13]



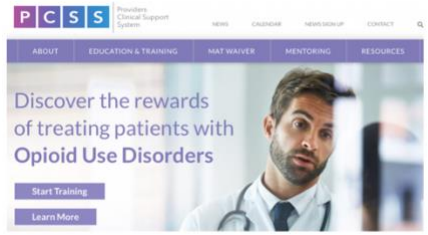


MAT/MOUD Training and Support

Whereas Naltrexone can be provided in the primary care setting without any additional training, buprenorphine prescribing requires a Drug Enforcement Administration (DEA) waiver. To obtain a DEA waiver, physicians are required to complete 8 hours of additional training; nurse practitioners and physician assistants complete 24 hours of training. The training is free through SAMHSA and can be completed online[16]: https://www.samhsa.gov/medication-assisted-treatment/training-materials-resources/buprenorphine-physician-training
During the first year after obtaining the waiver a provider can maintain a panel of 30 buprenorphine patients, increasing to 100 after the first year.

To improve timely access to the treatment of opioid use disorder, the California Bridge program provides support for emergency departments to begin buprenorphine treatment.[17] Up to a 7-day supply of buprenorphine, along with naloxone for the treatment of opioid overdose, can be provided from the emergency department in order to provide treatment until the patient is able to connect with a community MAT provider. Additional information on the California Bridge program can be accessed at: https://www.bridgetotreatment.org.

Provider support for MAT clinical practice is available. Providers Clinical Support Systems offers further education on OUD treatment as well as peer mentorship (**https://pcssnow.org**) and the Clinician Consultation Center through the University of California San Francisco (UCSF) provides a warmline for real time clinician to clinician advice (**http://nccc.ucsf.edu**).



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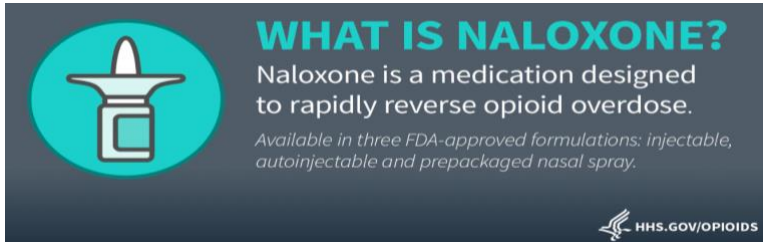
Opioid Overdose Prevention and Reversal

The U.S. Department of Health and Human Services recommends opioid overdose education and opioid antagonist medication (naloxone) be provided to all persons at risk for opioid overdose.[18] Persons at risk for opioid overdose include:

1. Any patients receiving opioid doses greater the 50 MME
2. Patients concurrently using benzodiazepines with opioids
3. Patients with an opioid use disorder
4. Patients in OUD treatment
5. Patients using opioids who have chronic obstructive respiratory symptoms
6. Patients using opioids who have a co-occurring mental health disorder or another non-opioid substance use disorder
7. Patients with a history of opioid misuse who were previously released from incarceration

Education on how to administer naloxone should be provided to all patients and families.



1. Identify unresponsiveness, extreme sleepiness or lack of oxygen (blue fingers or lips)
2. Call 911
3. Administer naloxone
4. If no response in 3 minutes administer a second dose of naloxone
5. Follow the instructions of the 911 operator regarding resuscitation efforts including respiratory support[19]

A video demonstration of naloxone administration can be accessed at: https://www.youtube.com/watch?v=YyDdMdLvdBc&feature=youtu.be

The SAMHSA Opioid Overdose Toolkit including safety advice for patients and families can be accessed at: https://store.samhsa.gov/system/files/sma18-4742.pdf

Disease Prevention and Personal Safety

Persons with an opioid use disorder are at increased risk for infectious disease including hepatitis, HIV, sexually transmitted infections (STI), respiratory infections and skin abscesses.[13] Hepatitis and HIV serology should be conducted when caring for persons with OUD, as well as a complete blood count, liver function tests and a pregnancy test for women of childbearing potential. STI and TB testing should also be considered. Hepatitis A, B, HPV and Tdap vaccinations should be offered as appropriate.[6]

Safer sex practices should be discussed with all persons with an OUD including consistent use of a protective barrier, use of a lubricant during sexual activity, limiting sexual partners, regular STI testing, and obtaining recommended vaccinations.[20] Consider providing safer sex kits when treating persons who use drugs.

Local resources for safe syringe access should be provided for persons who inject drugs. A directory of safe syringe access programs in California compiled by the California Department of Public Health and can be accessed at: https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OA_prev_sep.aspx#

Personal safety precautions should be reviewed with persons with an OUD including: 1) only use drugs from a known source and 2) never use drugs alone or with people you don't know.[21]

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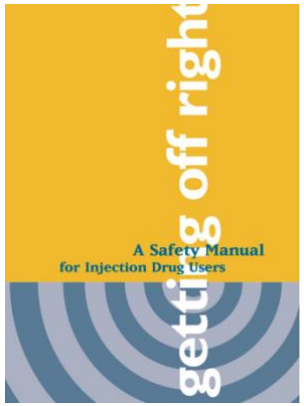
Harmreduction.org is an excellent resource for additional harm reduction materials including the publication Getting Off Right: A Safe Manual for Injection Drug Users



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