NIH
HEAL
INITIATIVE

HEALing Communities Study
Kentucky

Opioid Safety:
Pharmacy at the forefront

A Guide for Pharmacists and Pharmacy Technicians

Helping to End Addiction Long-term

The HEALing Communities Study utilizes a community engaged process to develop a comprehensive, data-driven community response plan to deploy evidence-based practices across multiple sectors and reduce opioid overdose deaths within highly affected communities by 40% over 3 years.

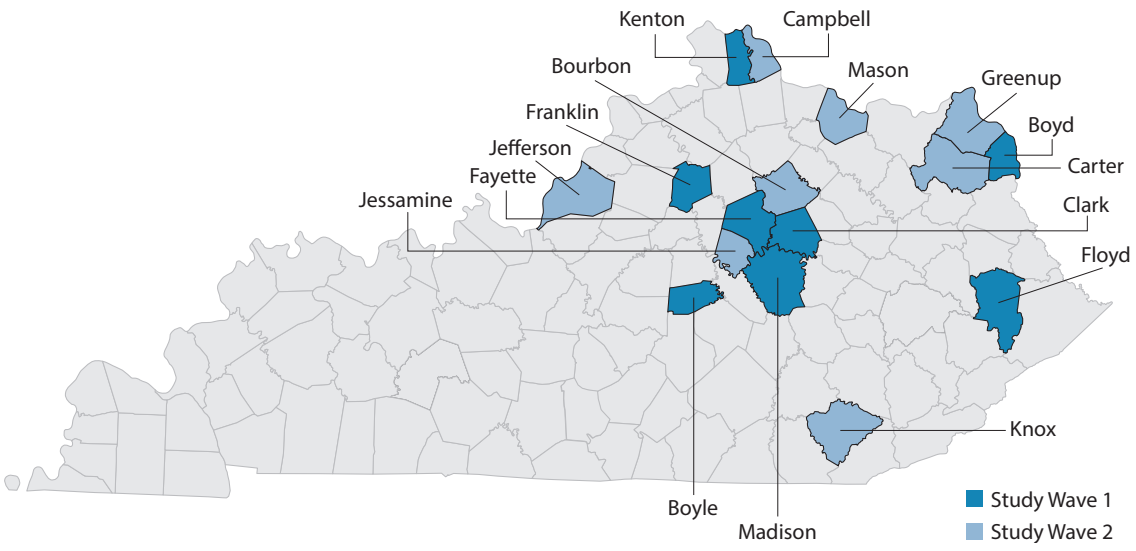
HEALing Communities Study

Ambitiously aiming to reduce opioid overdose deaths by 40 percent over three years

The HEALing Communities Study at the University of Kentucky is a 4-year, $87 million project funded by the National Institute on Drug Abuse.

Researchers will work with 16 Kentucky counties to leverage existing resources and develop a collaborative model for ending the opioid overdose crisis. Intervention strategies focus on expanding treatment for opioid use disorder, ensuring naloxone availability, and improving prescription opioid safety.

As we implement an integrated set of evidence-based practices, we seek to better understand the unique needs of each community. What we learn will help guide efforts to increase support for patients and families and improve lives throughout Kentucky and across the country.



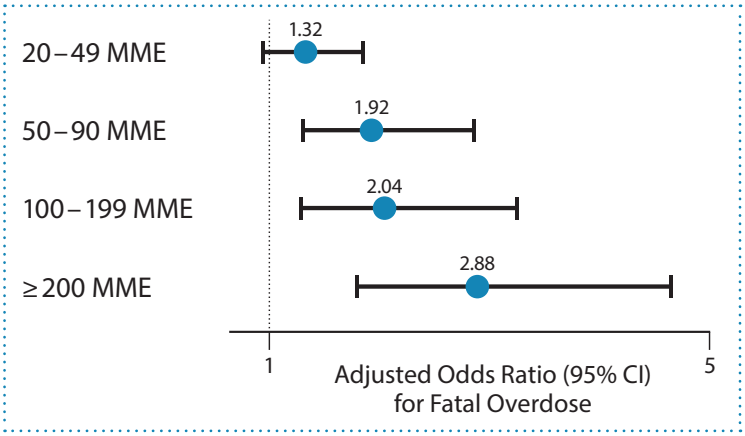
Learn more at www.healingcommunitiesstudy.org

Address high-risk opioid prescriptions with patients and prescribers

Overdose risk is dose-dependent

Compared to daily doses less than 20 MME, the odds of a fatal overdose double with a daily dose greater than 50 MME and nearly triple with a daily dose greater than 200 MME.[2]

Non-fatal overdoses also increase with higher doses.[3] Patients taking more than 100 MME daily had a 1.8% annual overdose rate, nearly 9 times the rate of patients taking 1 to 20 MME daily.[3]



Adapted from Gomes, et al.[2]

Short-acting opioids are safer than long-acting agents for initial therapy

Patients who initiated opioid therapy with long-acting agents (morphine ER, fentanyl patches, methadone, and oxycodone ER) were at significantly higher risk of unintentional overdose compared to those who received short-acting agents.[4] Risk of overdose was 5-fold higher in the 2 weeks after treatment initiation.[4] Patients who initiated therapy with long-acting opioids were also more likely to develop chronic opioid use.[5]

Methadone poses unique challenges: Although methadone accounted for approximately 1% of all opioid analgesic prescriptions, methadone-related deaths accounted for 22.9% of all opioid-related mortality in 2014.[6]

High-Risk Prescription Features

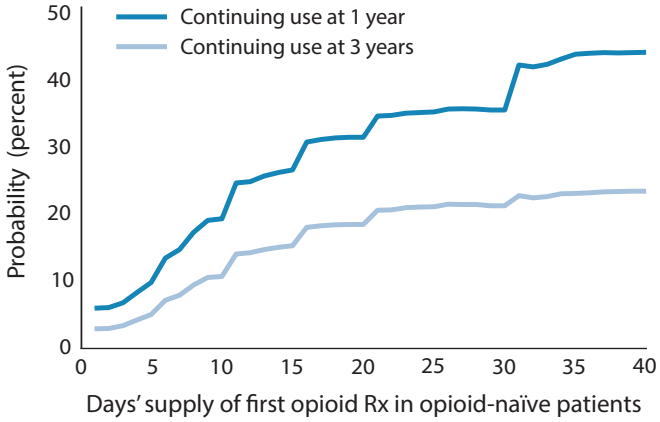
- High daily dose (≥50 MME/day)
- Initiating therapy with a long-acting or extended-release formulation
- Initial duration more than 7 days
- Concurrent benzodiazepine or gabapentinoid
- Methadone for chronic pain
- Patient younger than 18 y/o
- High-risk comorbidity
  - Age ≥65 years
  - Sleep-disordered breathing (sleep apnea, CHF, obesity)
  - Renal or hepatic insufficiency
  - Mental health condition (anxiety, depression, PTSD)
  - Substance use disorder
  - Prior overdose

A prescription with a high-risk feature may be appropriate based on the patient's situation. When a high-risk element is identified, seek and document additional information rather than refusing the prescription outright. **Start a conversation with the patient or prescriber about how to safely and effectively treat the patient's pain.**

Longer duration of initial opioid therapy correlates to increased probability of long-term opioid use[5]

CDC Guidelines recommend that prescribers limit the use of opioids for acute pain to the lowest effective dose and smallest quantity needed for the expected duration of severe pain. The guidelines note that ***"3 days or less will often be sufficient; more than 7 days will rarely be needed."***[1]

201 KAR 9:260 restricts acute treatment with Schedule II opioids to 3 days or less. Exceptions include major surgery, cancer pain, significant trauma, and end-of-life care.



Adapted from Shah, et al.[5]

Use caution with medication combinations: Rates of overdose death are 10 times higher in patients prescribed both a benzodiazepine and an opioid than in those prescribed only an opioid.[7] Concomitant gabapentin and opioid exposure has been associated with a 49% higher risk of fatal opioid overdose compared to opioid exposure alone.[8]

Limit opioid exposure in adolescence: Individuals who have an opioid prescription by 12th grade are 33% more likely to misuse prescription opioids after high school than those with no opioid prescription. Risk triples in otherwise low-risk individuals.[9]

KASPER is crucial: KASPER contains key information for keeping patients safe. Check KASPER with ***every*** opioid prescription.

For help with KASPER, visit https://ekasper.chfs.ky.gov or call 502-564-2703.

Consider the Risk of Rx Refusal

Overdose death and suicide are more common in patients whose chronic opioid therapy is stopped than in those maintained on opioids, so tapering and discontinuation require careful planning.[10,11] The FDA warns against abrupt discontinuation in physically dependent patients.[12] Consider the following suggestions to improve care and advocate for patients before refusing to fill an opioid prescription:

- Request a diagnosis and treatment, tapering, or risk-mitigation plans from the prescriber.
- Dispense naloxone and educate the patient on its use.
- Fill a short days' supply to allow time for communication.
- Provide advance notice of refusal when possible so the patient is not at risk of running out of medication.

Remember to document the details of your decision-making, counseling, and communication.

Tips for talking about opioids with a prescriber, nurse, or medical assistant

Tip	Example Statements
Stay clinical and neutral	I'm concerned that the patient's sleep apnea may contribute to opioid-induced respiratory depression. Could you walk me through your risk assessment?
Focus on the evidence	I'm calling because the patient was prescribed an opioid. Were you aware that he is also taking a benzodiazepine? Studies have shown a significant risk of overdose death with this combination.
Take a balanced approach	I want to ensure our patient's pain is addressed, but I have concerns about her safety. Can we discuss alternatives? What other therapies has the patient tried?
Offer alternatives	There is evidence for duloxetine in neuropathic pain conditions like fibromyalgia. Maybe we can avoid this opioid dose increase by adding a co-analgesic. I'd like to dispense a 5-day supply and then reassess for continuing therapy or tapering. If needed, we can fill the remainder of the prescription for up to 30 days from its written date.
Acknowledge difficulty	I know treating patients with chronic pain can be tough. I don't specialize in pain management, but I'm happy to contribute what I know to help our patients.
Be part of the team	I'm happy to work with you and the patient on a taper plan. Because he is in my pharmacy often, I can help track his progress and let you know if it isn't working. I'd like to document details of your diagnosis and treatment plan so I can better assess the patient's medications. It will also help me counsel, monitor for side effects, and reinforce your treatment goals with the patient.
Speak directly with the prescriber	Given the risks involved with this medication, I'd like to discuss the details with [prescriber]. I'll hold this prescription until she has a moment to call me back.

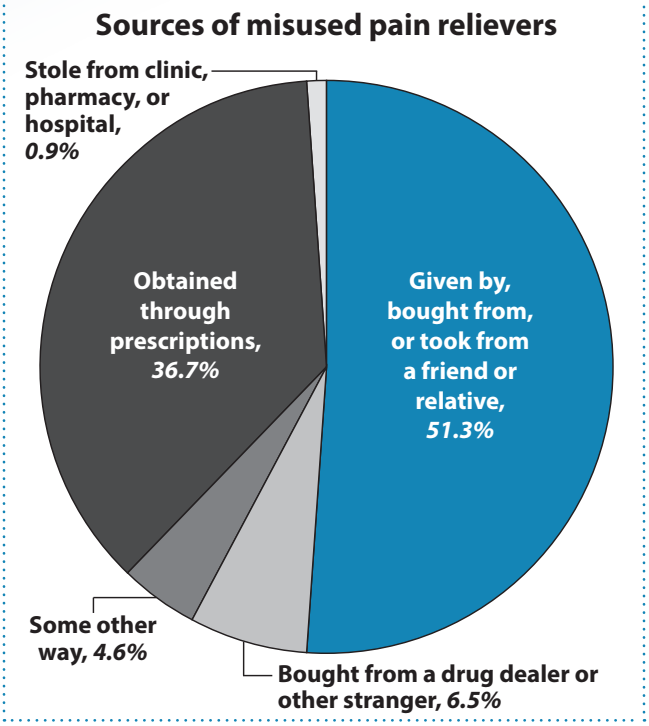
Counsel all patients on safe storage and disposal

Child and adolescent mortality from opioid poisoning nearly tripled between 1999 and 2016, resulting in almost 9,000 deaths.[13]

Safe storage tips to share with patients

- Keep medicine out of sight and out of reach of children and guests.
- Use a lock box or other device to store high-risk medications such as opioids.
- Store medicine in the original vial with the lid securely closed; use safety lids when possible.
- Keep a list of all medicine in the house and be aware of how much you should have left.

More than half of people who misused pain relievers in the past year obtained them from a friend or relative.[14]



Adapted from SAMHSA[14]

A survey of patients with an opioid prescription found that only one-third had disposed of unused medication. An important driver of disposal was instruction from a healthcare provider.[15]

The FDA recommends immediate disposal of unused medication and suggests the following means of disposal, in preference order:[16]

1. Drop off the medicine promptly at a drug take-back event or permanent disposal kiosk in a pharmacy or law enforcement agency.
2. Review the FDA Flush List for medications that are appropriate to dispose of in the toilet.
3. Discard medications in the household trash:
   - Mix medication with an unpalatable substance (e.g., cat litter, coffee grounds).
   - Place the mixture in a sealed container.
   - Throw the container in household trash.
   - Destroy or disguise personal information and dispose of prescription vial.

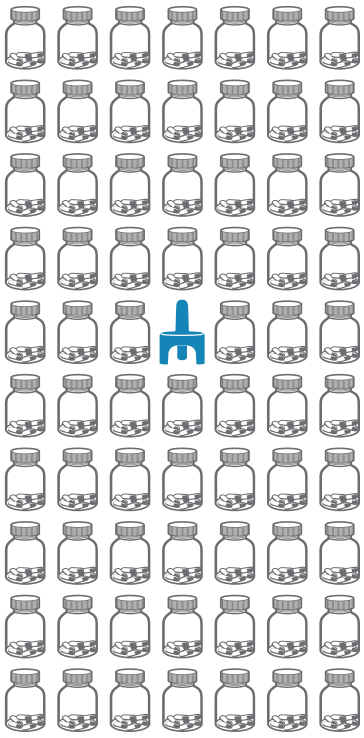
Recommend & dispense naloxone to all patients at risk of overdose

Nationally, only 1 naloxone prescription was dispensed for every 69 high-dose (≥50 MME) opioid prescriptions dispensed in 2018.[17]

Laws providing direct authority to pharmacists for naloxone provision are associated with reductions in opioid-related mortality.[18]

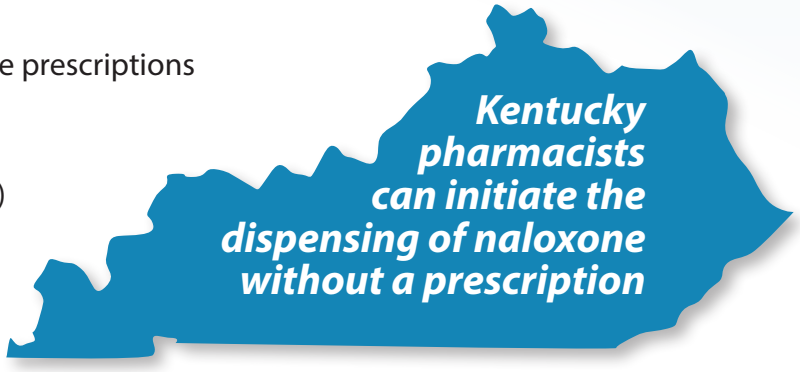
With certification and a physician-approved protocol, pharmacists in Kentucky can initiate the dispensing of naloxone without a patient-specific prescription. (See 201 KAR 2:360 for details.)

All KY Medicaid programs cover Narcan Nasal Spray. To find agencies offering free naloxone, visit healtogetherky.org and select your county.



FDA recommends discussing the availability of naloxone with all patients who are prescribed opioids.[19] Proactively dispense naloxone to patients at high risk:[1]

- Total daily opioid dose ≥ 50 MME
- Concomitant opioid and benzodiazepine prescriptions
- History of opioid overdose
- History of substance use disorder (e.g., patient on buprenorphine therapy)
- Decreased tolerance (e.g., gap in opioid therapy, taper, incarceration)
- Other high-risk patient factors:
  - ≥65 years old
  - Sleep-disordered breathing (e.g., sleep apnea, CHF, obesity)
  - Mental health conditions (depression, anxiety, PTSD)
  - Renal or hepatic insufficiency



Tips for talking about naloxone

Adapted from American Pharmacists Association[20]

Tip	Example Statements
Focus on adverse effects	A serious side effect of this medication is that it can slow down or stop your breathing. Naloxone can help your [spouse, caretaker, etc.] save your life if you have a bad reaction.
Talk about the individual	I know you have been taking this medication for a while, but breathing emergencies can occur unexpectedly, especially [at this dose, because you've had a gap in therapy, with your other medications or health conditions, etc.].
Emphasize safety	While accidental overdose may be unlikely when you use this medication as prescribed, a serious accident might occur if you unintentionally take too much or if a child or other person gets access to your medication.
Use analogies	Naloxone is like a fire extinguisher. You take precautions and hope you won't ever need to use it, but you keep it on hand just in case something bad happens.
Make it routine	We recommend naloxone to all of our patients taking opioid pain medicine.
Gauge interest	Has anyone discussed naloxone with you? Would you like to learn how it improves safety?

Other tips

- Approach the conversation as a routine medication consultation; discuss overdose as you would any serious but rare adverse drug reaction.
- Be professional and neutral, and avoid stigmatizing language (e.g., addict, abuser, OD, drug habit).
- If the patient is offended or defensive, express concern for their health and safety and return to the conversation at another time.
- Script out language you feel comfortable using and practice counseling with a friend or coworker.

Key Best Practices

- ☑ *Address high-risk opioid prescriptions with prescribers and patients*
- ☑ *Counsel patients on safe storage and disposal of unused medications*
- ☑ *Recommend and dispense naloxone to patients at risk*

NIH
HEAL
INITIATIVE

HEALing Communities Study
Kentucky

The information in this document is intended to be general and educational in nature. Clinical and dispensing decisions should be made by a pharmacist based on individual patient and prescription circumstances. This document is not legal advice. Licensed professionals are individually responsible for complying with all laws and regulations related to their practice. *This publication was supported by the National Institutes of Health through the NIH HEAL Initiative under award number UM1DA049406. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or its NIH HEAL Initiative.*

References: [1]Dowell D, et al. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep*. 2016. [2]Gomes T, et al. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011. [3]Dunn KM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Annals of Internal Medicine*. 2010. [4]Miller M, et al. Prescription opioid duration of action and the risk of unintentional overdose among patients receiving opioid therapy. *JAMA Intern Med*. 2015. [5]Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006-2015. *MMWR Morb Mortal Wkly Rep*. 2017. [6]Faul M, et al. Methadone Prescribing and Overdose and the Association with Medicaid Preferred Drug List Policies — United States, 2007-2014. *MMWR Morb Mortal Wkly Rep*. 2017. [7]Dasgupta N, et al. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. *Pain Med*. 2016. [8]Gomes T, et al. Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case-control study. *PLoS Med*. 2017. [9]Miech R, et al. Prescription opioids in adolescence and future opioid misuse. *Pediatrics*. 2015. [10]James JR, et al. Mortality after discontinuation of primary care-based chronic opioid therapy for pain: A retrospective cohort study. *Journal of General Internal Medicine*. 2019. [11]Oliva EM, et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ*. 2020. [12]U.S. Food and Drug Administration. FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering. https://www.fda.gov/ drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes. Accessed 5/5/2020. [13]Gaither JR, et al. US national trends in pediatric deaths from prescription and illicit opioids, 1999-2016. *JAMA Network Open*. 2018. [14]Substance Abuse and Mental Health Services Administration. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health*. Rockville, MD: Center for Behavioral Health Statistics and Quality, 2019. [15]Buffington DE, et al. Understanding factors that contribute to the disposal of unused opioid medication. *J Pain Res*. 2019. [16]U.S. Food & Drug Administration. Safe Disposal of Medicines. https://www.fda.gov/drugs/ensuring-safe-use-medicine/safe-disposal-medicines. Accessed 10/14/2019. [17]Guy GP, Jr., et al. Vital signs: pharmacy-based naloxone dispensing — United States, 2012-2018. *MMWR Morb Mortal Wkly Rep*. 2019. [18]Abouk R, et al. Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. *JAMA Intern Med*. 2019. [19]U.S. Food and Drug Administration. FDA recommends health care professionals discuss naloxone with all patients when prescribing opioid pain relievers or medicines to treat opioid use disorder. https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-health-care-professionals-discuss-naloxone-all-patients-when-prescribing-opioid-pain. Accessed 7/30/2020. [20]American Pharmacists Association. *Let's Talk About Naloxone — It Saves Lives*. https://www.pharmacist.com/sites/default/files/audience/LetsTalkAboutNaloxone.pdf. Accessed 5/28/2020.