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Opioid Safety:
Pharmacy at the Forefront

A Guide for Pharmacists and Pharmacy Technicians

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This activity is designed to meet the Kentucky Board of Pharmacy requirement for pharmacists to complete 1 hour of CPE on the opioid epidemic or opioid use disorder as outlined in 201 KAR 2:015.

University of Kentucky

Opioid Safety: Pharmacy at the Forefront

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Learning Objectives

Upon completion of this educational activity, learners will be able to:

- Discuss key themes of the *CDC Clinical Practice Guideline for Prescribing Opioids for Pain* with an emphasis on multimodal pain care and opioid tapering
- Recognize high-risk opioid prescriptions
- Review strategies for addressing opioid risks, including safe medication disposal
- Describe why and how pharmacies should dispense naloxone

HEALing Communities Study

The HEALing Communities Study (HCS) at the University of Kentucky is a 4-year, $87 million effort to reduce opioid overdose deaths. Researchers work with 16 Kentucky counties to develop a collaborative model for increasing naloxone availability, expanding treatment for opioid use disorder, and improving prescription opioid safety. For additional continuing education activities from HCS, visit **http://healky.learningexpressce.com**

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Disclaimer

The information in this document is intended to be general and educational in nature. Clinical and dispensing decisions should be made 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.

Understand and apply the 2022 CDC Guideline

In 2022, the CDC issued an updated clinical practice guideline for prescribing opioids.[1]

The major concepts are consistent with the 2016 guideline. Key themes and notable changes in the new edition include:

Focus on risks and benefits: A foundational principle of the guideline is assessment of realistic benefits and known risks of opioids. Initiation and adjustment of opioid therapy are only appropriate when benefits outweigh risks and the clinician and patient have engaged in shared decision-making.

Downplayed duration and dose details: The 2022 guideline still advises limiting days' supply and careful consideration before increasing opioid doses. However, the recommendations no longer provide the specific thresholds for duration or dose that were included in the 2016 guideline.

New guidance on tapering: The 2022 guideline includes a section related to patients already on opioid therapy. It recommends continuing opioids when benefits outweigh risks. Detailed advice is provided for gradual, patient-centered tapering when risks outweigh benefits.

Call for multimodal pain care: The 2022 guideline continues to emphasize nonpharmacologic and non-opioid therapies and to call for increased reimbursement for and access to multimodal care.

Emphasis on flexibility: The CDC acknowledged misapplication of the 2016 guideline. The 2022 guideline emphasizes clinical judgment and cautions against rigid policy or over-application by organizations or governments.

Expanded scope: The 2022 guideline applies to acute, subacute, and chronic pain care for adult outpatients. It continues to exclude pain related to sickle cell disease or cancer and to palliative and end-of-life care.

Guiding Principles

Pain needs to be appropriately assessed and treated, whether or not opioids are prescribed.

Recommendations are ***voluntary*** and support individualized, person-centered care. Flexibility to meet patient needs is critical.

Pain management requires a multimodal, multidisciplinary approach.

Special attention should be given to avoid misapplying the guideline or implementing policies that unintentionally cause harm to patients.

All health care entities should attend to health inequities, provide culturally appropriate and accessible communication, and ensure access to effective pain management regimens for all persons.

Adapted from the 2022 CDC Guideline[1]

Read the CDC's 12 recommendations in Box 3 of the full guideline:

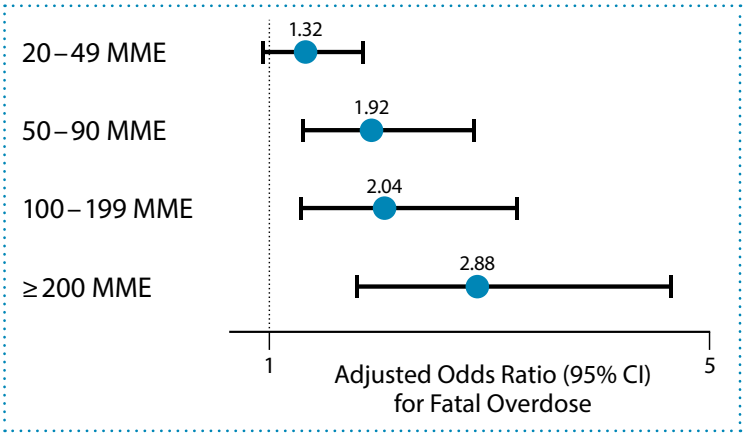
Dowell D, et al. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. *MMWR Recomm Rep.* 2022;71. doi:10.15585/mmwr.rr7103a1

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 about 1% of opioid analgesic prescriptions, methadone-related deaths accounted for 22.9% of opioid-related mortality in 2014.[6] This imbalance prompted a reevaluation of methadone use and calls for closer monitoring.

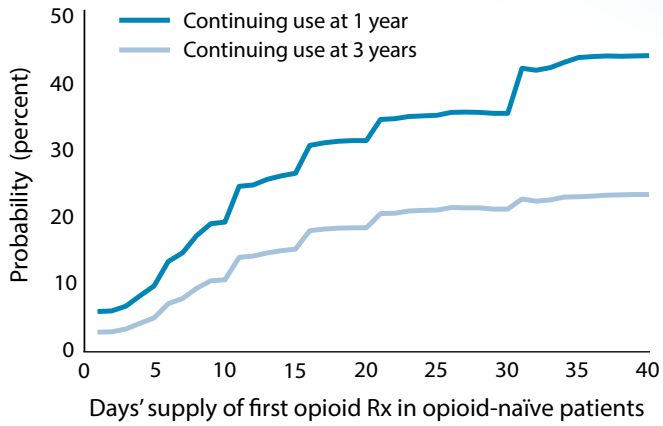
High-Risk Prescription Features

- 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]

The CDC recommends limiting opioids for acute pain to the lowest effective dose and smallest quantity needed for the expected duration of severe pain. Opioid regimens should be individualized, but a few days or less are often sufficient for nontraumatic, nonsurgical pain.[1] Kentucky law limits acute treatment with Schedule II opioids to 3 days, with exceptions based on medical necessity. Pharmacists can presume the validity of an exception when dispensing prescriptions written for greater than a 3-day supply.



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, email eKASPERHelp@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.

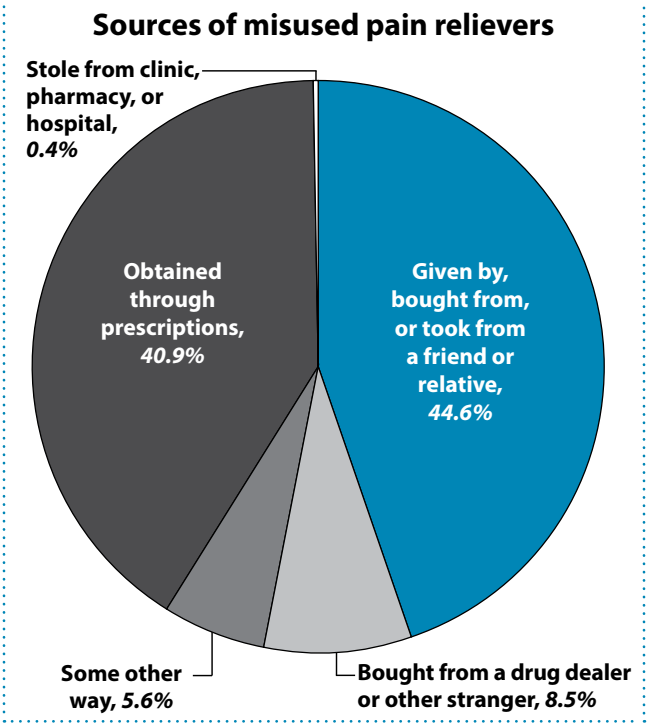
Counsel all patients on safe storage and disposal

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.

Almost 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. Mix medication with an unpalatable substance (e.g., cat litter, coffee grounds), place in a sealed container, and discard in the household trash.

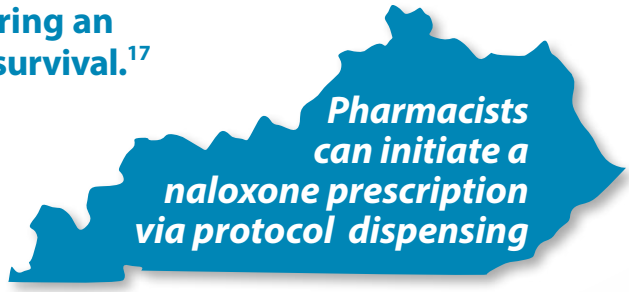
Find the nearest pharmacy with a permanent disposal kiosk using the DEA search tool at https://www.deadiversion.usdoj.gov/drug_disposal

Dispense naloxone to patients at risk of overdose

Naloxone administration by bystanders during an overdose significantly increases the odds of survival.[17]

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

Naloxone products are available over the counter. However, processing naloxone as a prescription provides access to cost savings through insurance, Medicaid, and discount programs. Local health departments and other community programs may also offer free or low-cost naloxone.



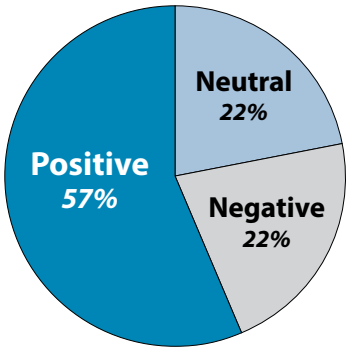
*Read state law **KRS 217.186** and pharmacy regulation **201 KAR 2:360,** available in the list of resources at https://healky.learningexpressce.com*

To access the Kentucky Naloxone Copay Program, visit www.kphanet.org/copay

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
- 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 (e.g., depression, anxiety, PTSD)
  - Renal or hepatic insufficiency

Reaction of patients taking a prescription opioid to a naloxone prescription offer



After education, 95% said they would want naloxone in the future

Adapted from Behar, et al.[20]

Tips for talking about naloxone

Adapted from American Pharmacists Association[21]

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, junkie).
- Script out language you feel comfortable using and practice counseling with a friend or coworker.

Watch one of the Kentucky Opioid Response Effort (KORE) naloxone training videos at https://www.youtube.com/@KORENaloxone1. These videos can be used for staff training or patient education.

Support a biopsychosocial approach to chronic pain

As pain shifts from acute to chronic, it is less connected to an underlying pathology of tissue damage.[22]

Pathways transmitting pain signals become more sensitive, and the contributions from psychosocial factors or secondary pathology can increase.[22] Effectively treating chronic pain requires a biopsychosocial approach that acknowledges the complex interactions among physical health, emotion and perception, and social factors.[22] Multimodal pain management should incorporate nonpharmacologic interventions, self-management education, and medications.

Nonpharmacologic pain management strategies

Physical activity

Increasing physical activity improves pain severity, physical function, and quality of life across a variety of chronic pain conditions.[23,24] No single exercise modality is superior, with evidence supporting land- or water-based aerobic and resistance exercise.[22] Mind-body activities like tai chi and yoga are often similar or superior to other forms of physical activity for chronic pain.[25–27]

Mindfulness-based stress reduction (MBSR)

MBSR is a structured program using meditation and exercise techniques aimed at helping participants develop "nonjudgmental awareness of moment-to-moment experience."[28] Mindfulness-based interventions have been shown to improve outcomes related to quality of life, well-being, and psychological distress in addition to reducing pain intensity.[29]

Cognitive behavioral therapy (CBT)

CBT aims to reduce distress and improve function by decreasing maladaptive thoughts and behaviors and increasing self-efficacy.[30] The use of CBT as an adjunctive therapy for chronic pain has a long history. A 2020 systematic review concluded that CBT has a small beneficial effect on pain, disability, and distress compared to treatment as usual in chronic pain.[31]

Massage

Massage therapy is widely accepted for musculoskeletal disorders and chronic pain conditions.[32] Systematic reviews have shown high heterogeneity and mixed results, with some evidence for improved pain and function in the short-term compared to no treatment or inactive controls.[32,33]

Acupuncture

Acupuncture is a traditional Chinese medicine technique that uses insertion of needles at specific points to promote healing and improve function.[34] A trial of more than 600 patients with chronic low back pain showed a clinically and statistically significant improvement in disability and symptom bothersomeness for individualized, standardized, and simulated acupuncture compared to usual care, but did not show a difference between sham acupuncture and real acupuncture.[35]

Chronic pain self-management

Self-management interventions have shown small but significant improvements in pain intensity, pain disability, catastrophizing, and health-related quality of life.[36] Formal self-management programs are offered in group or individual sessions, via online or telephone courses, or by self-study toolkits.[36] Elements of chronic pain self-management include:

- **Acceptance:** Patient manages pain as a long-term practice rather than seeking a "cure."
- **Continued activity:** Patient performs activities of daily living and engages in physical activity that supports function and quality of life.
- **Goals & action planning**: Patient has specific, measurable, and action-oriented goals.
- **Coping & mental health:** Patient understands the role of psychology in pain and finds ways to thrive and enjoy life despite the chronic pain condition.
- **Social support:** Patient reaches out to others, avoids isolation, and maintains healthy relationships.

Help Patients Learn More

American Chronic Pain Association: www.acpanow.com

Choose PT: www.choosept.com

Self-Management Resource Center: www.selfmanagementresource.com

Non-opioid pharmacotherapy

The landmark SPACE trial found that treatment of chronic back pain and hip or knee osteoarthritis with opioids was ***not*** superior to treatment with non-opioid medications for improving pain-related function. Pain intensity was significantly lower in the non-opioid group, and adverse medication-related symptoms were significantly more common in the opioid group.[37]

Non-opioid medications to consider for select chronic pain conditions[38–45]

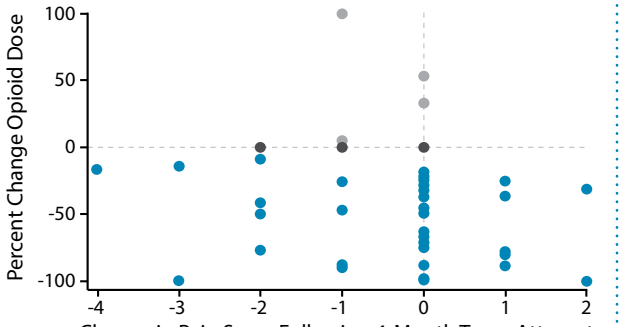
	Low Back Pain	Osteoarthritis	Fibromyalgia	Diabetic Neuropathy
Best Bet	Oral NSAIDs SNRIs	Oral NSAIDs Topical NSAIDs SNRIs	SNRIs TCAs Pregabalin	SNRIs TCAs Gabapentinoids Topical lidocaine
Might Help	Muscle relaxers *(Short-term use only)* Topical capsaicin Acetaminophen TCAs Topiramate	Acetaminophen	SSRIs Low-dose naltrexone Cyclobenzaprine Gabapentin	SSRIs Topical capsaicin
Likely Ineffective	Topical lidocaine SSRIs Gabapentinoids		Acetaminophen Oral NSAIDs	Topiramate

NSAID = Non-steroidal anti-inflammatory drug
SNRI = Serotonin and norepinephrine reuptake inhibitor
TCA = Tricyclic antidepressant
SSRI = Selective serotonin reuptake inhibitor

Collaborate with patients and prescribers to *reduce opioid doses* safely and effectively

Expert guidelines recommend tapering opioids when risks outweigh benefits, but reducing opioid doses can be challenging for patients and prescribers.[1,46]

Pain, function, and quality of life may improve with ***voluntary*** opioid dose reduction.[47] In one study, pain clinic patients were offered a slow taper over 4 months. The results for each individual who completed the study are shown as points on the graph. The median opioid dose was reduced from 288 MME to 150 MME. Reaching a 50% dose reduction was not predicted by starting dose, baseline pain intensity, or years prescribed opioids.[48]



Adapted from Darnall, et al.[48]

When to discuss tapering opioids[46]

- Patient request
- Resolution of pain
- Inadequate analgesia or improvement in function
- Intolerable side effects or poor quality of life
- Evidence of opioid misuse or OUD
- Overdose or other warning sign
- New medications or medical conditions that increase risk of overdose

Use Caution: Overdose death and suicide are more common in patients whose chronic opioid therapy is discontinued than in those maintained on opioids.[10,11]

Rapid tapering or abrupt discontinuation of opioids can cause significant distress and harm.[12] The risk of death after stopping opioids increases with longer treatment duration and is highest immediately after discontinuation.[11]

Opioid discontinuation is not recommended when benefits of opioids outweigh risks.[1]

Slow Tapers Minimize Harm

- A dose reduction of 5% to 20% every 4 weeks is common.
- Long durations of opioid therapy generally require longer tapers.
  - 10% a month or slower for patients on opioids for more than a year.
  - 10% a week may work for patients on opioids for weeks to months.
  - Consider rapid taper only after a serious adverse event.
- Significant withdrawal symptoms signal need to slow or pause taper.
- Extend dosing interval when smallest available dosage form is reached.
- Progress toward a safer dose is a success, no matter how slowly the taper occurs.

Adapted from HHS Guide[46]

Key Best Practices

- ☑ *Understand and apply the 2022 CDC Guideline*
- ☑ *Address high-risk opioid prescriptions with patients and prescribers*
- ☑ *Counsel all patients on safe storage and disposal*
- ☑ *Dispense naloxone to patients at risk of overdose*
- ☑ *Support a biopsychosocial approach to chronic pain*
- ☑ *Collaborate with patients and prescribers to reduce opioid doses safely and effectively*

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For more information about a reference, please email monica.roberts@uky.edu

NIH HEAL INITIATIVE

HEALing Communities Study Kentucky