Evidence-based Practice Center Rapid Review Protocol

Project Title: *Making Healthcare Safer IV: Opioid Stewardship*

Review Questions

1. What is the frequency and severity of harms associated with opioid prescribing and ordering?
2. What patient safety measures or indicators have been used to examine the harms associated with opioids prescribed or ordered by clinicians?
3. What opioid stewardship patient safety practices (PSPs) have been used to prevent or mitigate the harms associated with prescribed or ordered opioid, and in what settings have they been used?
4. What is the rationale for the opioid stewardship practices that have been used to prevent or mitigate the harms associated with prescribed or ordered opioids?
5. What are the effectiveness and unintended effects of opioid stewardship practices, and what new evidence has been published since the search was done for the Making Healthcare Safer (MHS) III report in 2019?
6. What are common barriers and facilitators to implementing opioid stewardship practices?
7. What resources (e.g., cost, staff, time) are required for implementation of opioid stewardship practices?
8. What toolkits are available to support implementation of opioid stewardship practices?

Context and Domain Being Studied

The Agency for Healthcare Research and Quality (AHRQ) Making Healthcare Safer (MHS) reports consolidate information for healthcare providers, health system administrators, researchers, and government agencies about practices that can improve patient safety across the healthcare system—from hospitals to primary care practices, long-term care facilities, and other healthcare settings. In Spring of 2023, AHRQ launched its fourth iteration of the MHS Report (MHS IV). Opioid stewardship as a PSP was identified as high priority for inclusion in the MHS IV reports using a modified Delphi technique by a Technical Expert Panel (TEP) that met in December 2022. The TEP included 15 experts in patient safety with representatives of governmental agencies, healthcare stakeholders, clinical specialists, experts in patient safety issues, and a patient/consumer perspective. See the MHS IV Prioritization Report for additional details.[1]

The treatment of pain and suffering is fundamental to high-quality healthcare, and opioids are often an essential medicine for acute, severe pain. However, opioids also carry well known risks, including for overdose, misuse, and opioid use disorder. [2, 3] [4] In 2016, the Centers for Disease Control and Prevention (CDC) released a Clinical Practice Guideline for Prescribing Opioids for Pain to promote more effective and safe opioid use. In 2022, the CDC released an update to those guidelines, noting a concern that previous guidance had been misapplied, leading to unintended patient harm including untreated or undertreated pain and abrupt tapering of opioids causing withdrawal, distress, and suicidal ideation.[3] Thus, any approach to mitigate risks of prescribed or ordered opioids should be balanced against any unintended harms.

Overview of the PSP

Opioid stewardship can be defined as promoting the appropriate use of prescribed and ordered opioids while reducing the risk of opioid use disorder, misuse, overdose, and other adverse events. The National Quality Forum (NQF) identified fundamental actions to support opioid stewardship in healthcare organizations,[5] six of which are relevant to this report:

- Promote leadership commitment and culture,
- Implement organizational policies,
- Advance clinical knowledge, expertise, and practice,

- Enhance patient and family caregiver education and engagement,
- Track, monitor, and report performance data, and
- Establish accountability.

The updated CDC Clinical Practice Guideline for Prescribing Opioids for Pain provides guidelines for determining whether opioids are appropriate, deciding duration, dosage and followup for prescriptions, and assessing risk and addressing potential harm.[3]

The MHS III report summarized one systematic review and 14 original studies on this topic.[6] According to the report, most studies examined multicomponent interventions consisting of clinical interventions and implementation strategies, with moderate strength of evidence for only one outcome - significant reduction in opioid dosages; no conclusions could be drawn about clinical outcomes or impact on pain.

Purpose of the Review

The overall purpose of this review is to determine the effect of opioid stewardship interventions on key opioid prescribing and clinical outcomes (e.g., opioid dosage, opioid prescriptions, and overdose), and unintended consequences (e.g., increase in pain due to undertreatment), and how these interventions can be effectively implemented.

Methodologic Approach

For this rapid review, strategic adjustments will be made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. We will follow adjustments and streamlining processes proposed by the AHRQ Evidence-based Practice Center Program. Adjustments include being as specific as possible about the questions, limiting the number of databases searched, modifying search strategies to focus on finding the most valuable studies (i.e., being flexible on sensitivity to increase the specificity of the search), restricting the search to studies published in English and performed in the United States, and having each study assessed by a single reviewer except for a randomly selected 10% sample that will be checked by a second reviewer or use the artificial intelligence (AI) feature of DistillerSR (AI Classifier Manager) as a second reviewer at the title and abstract screening stage, as described below in the section on Data Extraction. We will search for recent high quality systematic reviews and will

rely primarily on the findings of any such systematic review that is found. We will not perform an independent assessment of original studies cited in any such systematic review.

For this topic, we will ask our content experts to answer Review Questions 1 and 2, by citing selected references that best answer the questions without conducting a systematic search for all evidence on the targeted harms and related patient safety measures or indicators.

For Review Question 2, we will focus on identifying relevant measures that are included in the Centers for Medicare & Medicaid Services (CMS) patient safety measures, AHRQ's Patient Safety Indicators, or the National Committee for Quality Assurance (NCQA) patient safety related measures.

We will ask our content experts to answer Review Questions 3 and 4 by citing selected references, including PSPs used and explanations of the rationale presented in the studies we find for Review Question 5. For Review Questions 6 and 7, we will focus on the barriers, facilitators, and required resources reported in the studies we find for Review Question 5.

For Review Question 8, we will identify publicly available patient safety toolkits developed by AHRQ or other organizations that could help to support implementation of the PSPs. To accomplish that task, we will review AHRQ's Patient Safety Network (PSNet) (https:/psnet.ahrq.gov) and AHRQ's listing of patient safety related toolkits (https://www.ahrq.gov/tools/index.html?search_api_views_fulltext=&field_toolkit_topics=14170&sort_by=title&sort_order=ASC) and we will include any toolkits mentioned in the studies we find for Review Question 5. We will identify toolkits without assessing or endorsing them.

Eligibility Criteria for Studies of Effectiveness

We will search for original studies and systematic reviews on Review Question 5 according to the inclusion and exclusion criteria presented in Table 1

Table 1. Inclusion and Exclusion Criteria

Study Parameter	Inclusion criteria	Exclusion criteria
Population	Any clinical population (i.e., people receiving care from a health care professional) Given that opioids can have significant harms in all clinical populations, we will include populations not included in the CDC guidelines, such as sickle cell disease, cancer-related pain treatment, palliative care, and end-of-life care.	N/A

Study Parameter	Inclusion criteria	Exclusion criteria
Intervention	• Interventions focused on opioid stewardship involving organizational leadership and policies within a healthcare facility or healthcare system: o Opioid stewardship committees o Clinical decision support or electronic health record interventions o Protocols or care bundles, which may address components such as treatment agreements, urine drug screening, risk assessment, and/or naloxone prescribing • Interventions focused on clinical knowledge, expertise, and behavior related to prescribed or ordered opioids: o Clinician education or academic detailing o Clinical pharmacist consultation o Increased access/ emphasis on non-opioid or multimodal analgesia, and/or limits on opioid prescribing/ordering • Interventions focused on patient and family education or engagement related to use of prescribed or ordered opioids • Interventions focused on tracking, monitoring, and reporting performance data related to prescribed or ordered opioids: o Clinical audits o Dashboards • Interventions focused on clinical accountability related to prescribed or ordered opioids: o Prescriber feedback o Peer comparison • Multi-component interventions focused on opioid stewardship	• Interventions focused on treatment of opioid use disorder (this is a separate topic in MHS) • Interventions or policies established by entities other than healthcare providers, including: o Insurance company restrictions (e.g., limits on pill numbers or prior authorization) o Government restrictions or regulations (e.g., establishment of prescription drug monitoring programs) o Naloxone distribution outside healthcare settings (e.g., by county health departments)
Comparator	Usual care	N/A

Study Parameter	Inclusion criteria	Exclusion criteria

Outcome	Primary outcomes of interest are clinical outcomes. Secondary outcomes of interest are prescribing/ordering outcomes and process outcomes, if they are reported in studies that also report clinical outcomes.
	
	• Clinical outcomes:
	  ○ Health care utilization (focusing on emergency department use and hospitalizations for adverse events)
	  ○ Overdose rates
	  ○ Adverse consequences:
	  ▪ Increase in pain intensity or distress
	  ▪ Increase in opioid refill requests
	  ▪ Patient dissatisfaction
	
	• Opioid prescribing or ordering outcomes:
	  ○ Rates of opioid prescribing or ordering
	  ○ Total morphine milligram equivalents per prescription or per patient
	  ○ Number of pills per prescription
	  ○ Rates of non-opioid analgesic prescribing
	
	• Changes in process outcomes:
	  ○ Urine drug screen ordering or administration
	  ○ Treatment agreement use
	  ○ Risk assessment screening tool use
	  ○ Use of prescription drug monitoring program reports
	  ○ Other referrals relevant to pain management (behavioral health, physical therapy, etc.)
	  ○ Pain management documentation
	
	• Implementation outcomes (Review Questions 6 and 7)
	  ○ Barriers and facilitators
	  ○ Cost, staffing, time
		Studies with prescribing/ordering outcomes or process outcomes or implementation outcomes without clinical outcomes)

Timing	• Systematic reviews published since 2019 • Original studies published since 2016, the year the initial CDC guideline on opioid prescribing was published with resultant shifts in prescribing	N/A
Setting	Healthcare settings in the United States	• Outside of healthcare (e.g., state-level regulation) • Nursing home or prison settings • No site in the United States
Type of studies	Systematic reviews Randomized controlled trials and observational studies with a comparison group, including pre-post studies Studies should include at least 50 pills, prescriptions, or patients or at least 50 clinicians	• Narrative reviews, scoping reviews, editorials, commentaries, and abstracts • Qualitative studies without quantitative data

CDC = Centers for Disease Control and Prevention; MHS = Making Healthcare Safer

Literature Searches for Studies of Effectiveness

Our search strategy will focus on databases expected to have the highest yield of relevant studies,

including PubMed and the Cochrane Library, supplemented by a narrowly focused search for unpublished reports that are publicly available from governmental agencies, professional societies, or membership organizations with a strong interest in the topic, including the CDC, AHRQ, the National Institutes of Health (NIH), NQF, and American Hospital Association (AHA).

Data Extraction

To efficiently identify studies that meet the eligibility criteria, we will distribute citations from the literature search to team members, with plans to have the title and abstract of each citation reviewed by a single team member. We will use the artificial intelligence (AI) feature of DistillerSR (AI Classifier Manager) as a semi-automated screening tool to conduct this review efficiently at the title and abstract screening stage. The title and abstract of each citation will be reviewed by a team member, and then the AI Classifier Manager will serve as a second reviewer of each citation. The full text of each remaining potentially eligible article will be reviewed by a single team member to confirm eligibility and extract data. A second team member will check a randomly selected 10% sample of the articles to verify that important studies were not excluded and confirm the accuracy of extracted data. Information will be organized according to the review questions, and will include author, year, study design, frequency and severity of the harms, measures of harm, characteristics of the PSP, rationale for the PSP, outcomes, implementation barriers and facilitators, resources needed for implementation, and description of toolkits. To streamline data extraction, we will sort eligible studies by specific PSP (if we find studies that report on fundamentally different types of opioid stewardship PSPs), and focus on extracting information about characteristics, outcomes, and barriers/facilitators most pertinent to a specific PSP.

Risk of Bias (Quality) Assessment

For studies that address Review Question 5 about the effectiveness of PSPs, the primary reviewer will use the Cochrane Collaboration's tool for assessing the risk of bias of randomized controlled trials (RCTs) or the ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions.[7,8] When assessing RCTs, we will use the 7 items in the Cochrane Collaboration's tool that cover the domains of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[7] When assessing non-randomized studies, we will

use specific items in the ROBINS-I tool that assess bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported results.[8] The risk of bias assessments will focus on the main outcome of interest in each study.

If we identify a recent eligible systematic review, the primary reviewer will use the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[9]

- **Good** - Recent relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.
- **Fair** - Recent relevant review that is not clearly biased but lacks comprehensive sources and search strategies.
- **Poor** - Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

The Task Leader will review the risk of bias assessments and any disagreements will be resolved through discussion with the team.

Strategy for Data Synthesis

Selected data will be compiled into evidence tables and synthesized narratively. We will not conduct a meta-analysis. For Review Question 5 about the effectiveness of PSPs, we will record information about the context of each study and whether the effectiveness of the PSP differs across patient subgroups. If any of the PSPs have more than one study of effectiveness, we will grade the strength of evidence for those PSPs using the methods outlined in the AHRQ Effective Health Care Program (EHC) Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[10] Evidence grading would not add value for PSPs that do not have more than one available study.

Analysis of Subgroups or Subsets

For this rapid review, no subgroup analyses will be conducted.

Registration

We will submit the protocol to AHRQ and to the PROSPERO international prospective register of systematic reviews.

EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators from participation in the review.

External Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers.

We will ask at least one clinical content expert and one methodological expert to review the draft report. Potential peer reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited peer reviewers may not have any financial conflict of interest greater than $5,000.

Role of the Funder

This project is funded under Contract No. 75Q80120D00003/75Q80122F32009 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The AHRQ Task Order Officer will review contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by AHRQ or the U.S. Department of Health and Human Services.]

Format and Content of Report

The report will follow the most recent template approved by AHRQ at the time of approval of the protocol.

References

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