A narrative review of risk mitigation strategies in the management of opioids for chronic pain and palliative care in older adults: interprofessional collaboration with the pharmacist

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Background and Objective: The prevalence of chronic non-cancer pain (CNCP) in older adults is high. Opioids carry significant risk for harm in older adults. Yet, many older adults are established on long-term opioid therapy for the treatment of CNCP despite limited documented efficacy. Many of the non-opioid options to treat pain present challenges in this population. Since challenges with tapering patients off of opioids exist, older adults may remain established on long-term opioid therapy for CNCP. While opioid use is less scrutinized for older adults receiving palliative care, significant safety concerns exist. Therefore, efforts to mitigate risks for older adults receiving long-term opioids for CNCP and for palliative care are essential. Pharmacists as members of the interprofessional team are equipped to improve safety among older adults on chronic opioid therapy. Among patients receiving palliative care, collaboration with palliative care specialists is also key. The purpose of this narrative review is to describe risk mitigation strategies for opioid use among older adults with CNCP and those receiving palliative care.

Methods: Data were identified by searching PubMed (January 1, 1990 to February 21, 2024) using the following search terms: older adults, opioids, chronic pain, palliative care, and pharmacist. The search was repeated using terms geriatric, elderly, opiates, narcotics, and controlled substances. Non-English articles and observational studies with fewer than 100 patients were excluded. Major North American and European guidelines were reviewed. Additional literature was obtained through review of relevant references of identified articles.

Key Content and Findings: A variety of risk mitigation strategies to improve safety for older adults using opioids exist. They include risk assessment, tapering opioids, reducing high-risk concomitant medications, utilizing non-opioid therapies, screening for and treatment of opioid use disorder (OUD), toxicology testing, co-prescribing naloxone, utilizing controlled substance agreements, reviewing prescription drug monitoring program data, prescriber and patient education, and collaboration with pharmacists and palliative care specialists.

Conclusions: There are many opioid risk mitigation strategies for older adults. Collaboration with pharmacists and palliative care specialists can be an effective means for implementing strategies to optimize opioid safety for older adults with CNCP and those receiving palliative care.

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Introduction

The prevalence of chronic pain in older adults, defined as individuals aged 65 years and above, is as high as 45% to 85% in the United States (1,2). Chronic pain, defined as pain on most days or every day over 3 months, may impact independence, social activities, mental distress, and cognitive decline among older adults, often requiring pharmacologic management (1,2). There has been increased emphasis on limiting the use of opioids for chronic noncancer pain (CNCP) due to lack of established efficacy, increased risk of adverse effects, and overdose deaths, particularly among high-risk populations such as older adults (3,4). Despite this, millions of older adults are treated with opioids for CNCP annually (4,5). In 2018, 15% of the U.S. population filled at least one opioid prescription, with opioid prescribing highest in patients 65 years of age and older at 25% (6). Older adults, along with females, are more likely to use long-term opioids as compared with other patients (5). Among older adults receiving palliative care, opioid use is a mainstay therapy, with evidence demonstrating effectiveness for pain, dyspnea, and cough (7). While opioid safety has historically been less emphasized in patients receiving palliative care, the current consensus is that risk mitigation is essential among all patients receiving opioids regardless of their life expectancy (7,8). The risks of opioids, despite indication, are more pronounced among older adults, even when used at recommended doses and durations. Such risks include cognitive impairment, altered drug metabolism, falls and fractures, polypharmacy, and increased all-cause mortality (9). It should be noted that older adults with pulmonary and cardiovascular comorbidities may have compounded risk of respiratory depression causing overdose compared with their younger counterparts. Furthermore, older adults are likely to experience decreased clearance of opioid active metabolites (10). In 2019, older adults accounted for the highest number of hospitalized patients due to opioidrelated poisonings (6). Although the risk of opioid overdose death historically has been the lowest among patients 65 years and older, older adults have had the sharpest increase in overdose deaths in recent years (11). In

2021, 57% of overdoses among older adults involved an opioid, and 1 in 5 unintentional overdoses involved both prescription and illicit drugs (12). Similarly, most intentional drug overdoses involved prescription opioids and benzodiazepines (12). There has also been a greater than three-fold increase in opioid use disorder (OUD) diagnosis among older adults since 2013 (13). These trends expose the need for care optimization among older adults managed on long-term opioids for pain.

While a variety of non-opioid pharmacologic options exist for pain management, many of them present challenges for use in older adults (5). Additionally, while tapering off of opioids is an option for patients who meet certain criteria for potential benefit of this approach, this may not be possible in all patients and significant risks may exist (3). This highlights the need for action and risk mitigation among the ageing population established on long-term opioids for CNCP. Risk mitigation strategies are ways to reduce adverse outcomes including opioid overdose, OUD, illicit drug use, and prescription opioid misuse (4). Pharmacists working within an interprofessional team are positioned favorably to help reduce risks for older adults on opioid therapy. Pharmacists can assist in monitoring safety and implementing risk mitigation strategies for patients with non-cancer chronic pain and patients receiving palliative care (2,7). The purpose of this narrative review is to describe risk mitigation opportunities, including interprofessional collaboration with pharmacists and palliative care specialists, to improve safety of opioid use among older adults for CNCP and those receiving palliative care. We present this article in accordance with the Narrative Review reporting checklist (available at https://apm.amegroups.com/article/ view/10.21037/apm-23-488/rc).

Methods

Data for this narrative review were identified by searching the PubMed database (January 1, 1990 to February 21, 2024) using the following search terms: older adults, opioids, chronic pain, palliative care, and pharmacist. The above search was repeated using the following terms

Table 1 Search strategy summary

Items	Specification
Date of search	June 1, 2023; repeated February 21, 2024
Databases and other sources searched	PubMed
Search terms used	older adults, geriatric, elderly, opioids, opiates, narcotics, controlled substances, chronic pain, palliative care, pharmacist
Timeframe	January 1, 1990 to February 21, 2024
Inclusion and exclusion criteria	Clinical trials, observational studies, systematic reviews and meta-analyses. Major North American and European guidelines were included. Articles with animal data and articles in languages other than English were excluded
Selection process	Search and selection of articles were conducted independently by investigators. Any discrepancies related to inclusion or exclusion were resolved through discussion and consensus
Any additional considerations, if applicable	Reference lists of identified articles were manually reviewed to locate additional relevant references

in place of older adults: geriatric and elderly. The search was repeated using combinations of the above terms for opioids: opiates, narcotics, and controlled substances. Nonhuman articles and articles not published in English were excluded. Major North American and European guidelines were reviewed. Additional literature was obtained through a review of relevant references of the identified articles. Observational studies with fewer than 100 patients were excluded. The search strategy is outlined in *Table 1*.

Risk mitigation strategies

A variety of risk mitigation strategies exist to improve safety for older adults taking opioids. Such strategies include risk and functional assessment, tapering therapy, reducing use of high-risk concomitant medications, utilizing alternative non-opioid therapies, screening for and treatment of OUD, toxicology testing, co-prescribing naloxone, utilizing controlled substance agreements (CSAs), reviewing prescription drug monitoring program (PDMP) data, prescriber and patient education, and collaboration with the interprofessional team, including pharmacists and palliative care specialists as necessary, across care settings. These efforts are deemed valuable for older adults receiving opioids for CNCP as well as those receiving palliative care (4,7,8,14).

Risk and functional assessment with opioid use

Identification of high-risk or problematic opioid use is a

critical step in managing patients on these therapies (4). There are several available evidence-based instruments that can be used to help identify or predict problematic opioid use either in advance of initiation or during therapy (*Table 2*). Results of screening tools can be used to educate on opioid use and implement risk mitigation strategies. Furthermore, they can be used to facilitate care coordination with addiction professionals, primary care, and social support services (15). Of note, sensitivity and specificity of the tools vary, and therefore clinicians must cautiously interpret their results; some tools were not studied in patients receiving palliative care and extrapolation of findings may be problematic for these patients (15).

Evaluating the effects of pain on function and independence is essential for elderly patients on opioids (4). While functional assessment tools for patients with pain are not specific to opioid use, they may help prevent overuse of opioids, support the need to taper opioids if benefit is not demonstrated, or identify need for additional non-opioid and/or non-pharmacologic therapy (4). Clinicians may find that scales that are relatively easy to use and quickly administered may be most beneficial. The Pain, Enjoyment, General Activity (PEG) scale asks three questions assessing average pain score, interference of pain with enjoyment of life, and pain interference with general activity (16). A score of 30% improvement from baseline on the PEG is considered clinically meaningful (17). The Functional Pain Scale is a tool that has been determined to be a reliable and valid tool in older adults. This tool assesses tolerability of

Tool	Purpose	Prior or during therapy
Brief Risk Questionnaire	Identify misuse	Prior
Current Opioid Misuse Measure	Aberrant behaviors	During
Leeds Dependence Questionnaire	Identify dependence	During
Mini International Neuropsychiatric Interview-Patient Rated	Diagnose opioid dependence	During
National Institute on Drug Abuse Modified Alcohol, Smoking, and Substance Involvement Screening Test	Identify risky opioid use	Prior or during
Opioid Risk Tool	Identify risk of aberrant use	Prior
Pain Medication Questionnaire	Identify risk of aberrant use	Prior
Prescription Opioid Misuse Index	Identify opioid misuse	During
Rapid Opioid Dependence Screen	Identify dependence	During
Severity of Dependence Scale	Identify dependence	During
Screener and Opioid Assessment for Patients with Pain-Revised	Identify risk of aberrant use	Prior
Tobacco, Alcohol, Prescription, and Other Substance Tool	Identify risky opioid use	During

Table 2 Tools for identification of problematic opioid use (15)

pain and interference with specific functions and activities, with a lower score equating to less severe pain and less interference with functional abilities (18).

Tapering opioids and reducing use of risky concomitant medications

Tapering off of opioids and switching to alternative therapies may be of benefit to some, but not all, patients. Clinicians should consider tapering or reducing the dose of opioids when the risk of opioids outweigh the benefits, such as in situations of addiction/diversion, adverse effects, tolerance, reduced function, reduced quality of life, comorbidities increasing risks, age over 65 years, and concomitant medications that increase risk of opioidrelated harm (4). Both the Centers for Disease Control and Prevention (CDC) Clinical Practice Guideline for Prescribing Opioids for Pain - United States 2022 and the United States Department of Health and Human Services Guide for Clinicians on Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics recommend reducing the dose of opioids by 10% or less of the original dose per month to prevent withdrawal symptoms (4,19). Strategies for successful opioid tapering include (I) provisions for taper failure; (II) addressing "unmasked" underlying psychiatric issues exposed during the taper; (III) collaborating with the patient on the taper;

(IV) avoiding taper mandates; (V) avoiding dismissing patients from care due to lack of agreeability to starting or adhering to taper plan; and (VI) avoiding misinterpreting cautionary dosage thresholds (19). Nevertheless, significant risks exist with tapering, particularly in situations where patients are left unsupported without alternative pain support or adjunct medications to manage withdrawal symptoms, or when opioids are tapered too quickly (4). Additional risks of tapering include unmasking untreated mental health conditions, poor coping skills without proper adjuvant pain and withdrawal symptom management, increased pain, dropout of the tapering plan which may lead to use of more easily attainable illicit substances, and reduced function (19). Some patients may relapse to previous opioid usage following an unsuccessful taper plan (3). Others may experience negative consequences. In one retrospective cohort study in which older adults comprised approximately 28% of the study population, tapering of long-term opioids was associated with an increase in emergency department visits and hospitalizations (20).

It is also important to reduce concomitant use of medications that may increase risk of harm for patients on opioids. Half of Medicare beneficiaries take four or more prescription medications daily, and therefore the risk of dangerous combinations of medication with opioids may be particularly concerning in this group (12). Opioids in combination with benzodiazepines, muscle relaxants,

Medication class	Challenges in older adults	Consideration for use
NSAIDs	Gastrointestinal toxicity, cardiovascular adverse effects, nephrotoxicity, drug-drug interactions (24)	Consider risk vs. benefit of lowest dose for shortest duration (21)
Acetaminophen	Limited evidence for chronic pain; cardiovascular and renal adverse effects in a systematic review (21)	Likely reasonable for use; monitor relevant labs with long-term treatment (21)
Tramadol	Sedation, serotonin syndrome, hyponatremia, seizures, hypoglycemia, increased risk of falls and fractures, drug- drug interactions (25-27); associated with same dose- dependent risks as other opioids (4,21)	Avoid use (28)
Topical therapies	Transdermal absorption limited in patients 85 years and older or frail; fewer systemic adverse effects (21); access issues may exist	Consider use of topical agents when accessible and affordable to patient (21)
Antidepressants	Central nervous system side effects; may have benefits for neuropathic pain (21,23)	Caution advised especially for highly anticholinergic agents such as amitriptyline and paroxetine; introduce gradually and monitor carefully (21)
Antiepileptics	Limited evidence in chronic primary pain and increased risk of adverse effects	Avoid initiation; monitor adverse effects closely for patients established on therapy (23)

Table 3 Considerations for non-opioid therapies in the older adult

NSAIDs, non-steroidal anti-inflammatory medications.

z-hypnotic agents, alcohol, and other opioids increases risk for sedation, respiratory depression, as well as overdose and death (4). The 2022 CDC pain guidelines raise caution about co-prescribing opioids and benzodiazepines, recommending a careful risk assessment evaluating whether the benefits outweigh the risk of concurrent prescriptions (4). Concerns for opioid-related harm are similarly expressed for patients receiving palliative care (7,8). When possible, efforts should be made to appropriately taper off benzodiazepine or other high-risk therapies when used concomitantly with opioids, using safer evidence-based pharmacologic agents as alternatives.

Alternative treatments

The long-term efficacy of opioids in older adults continues to have limited evidence for CNCP, although some literature may support short-term use with regular monitoring (21). However, given adverse effects such as central nervous system depression, respiratory depression, constipation, delirium, risk of falls and fractures, and potential for overdose, caution is advised for chronic use (4,21). While clinicians strive to prevent negative consequences of untreated pain, risks for older adults exist with opioid and non-opioid analgesics including non-steroidal anti-inflammatory medications (NSAIDs), acetaminophen, and other adjuvant medications (9).

Among the available risk mitigation strategies include determining if the patient's pain may be better and more safely managed on alternative treatment options. Alternative options may include non-opioid and non-pharmacologic therapies. Non-pharmacologic alternatives for chronic pain include cognitive behavioral therapy, acupuncture, spinal manipulation therapy, relaxation therapy, biofeedback, and exercise (22,23). However, access and insurance coverage is often limited for many of these options (21,22). The evidence to inform international guideline recommendations for use of pain medications in older adults is limited and the populations studied have significant heterogeneity. Therefore, most guidance on pharmacologic pain management is driven by expert opinion (21). A number of considerations should be made when weighing use of alternative pharmacologic treatments for pain (Table 3). Due to the heightened risks for both opioid and non-opioid therapies in the older adult population, careful evaluation of the patient for potential of experiencing adverse effects is essential. Evaluation of current and longitudinal trends of renal and hepatic function is a necessary component of risk evaluation for pain management. Older adults have an increased potential for accumulation of all medications, including pain medications, and a narrower therapeutic window of safety particularly in the presence of renal or

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hepatic impairment.

Use of NSAIDs for CNCP in older adults has long been suggested to be avoided, particularly in patients with impaired liver or kidney function, comorbidities such as hypertension and cardiovascular disease, patients taking concomitant medications such as anticoagulants, and patients at increased risk for gastrointestinal bleeding (4). Therefore, initiation among older adults is generally not recommended unless for short-term use at the lowest effective dose when the benefits outweigh the risks (21,23).

While acetaminophen continues to have limited evidence for efficacy for CNCP in older adults, its use is reasonable considering lower adverse effect profile (5,21). It should be noted that studies examining acetaminophen for chronic pain in adults over the age of 65 are few, and some literature demonstrates significant adverse effects including an increased risk of cardiovascular, gastrointestinal, and renal adverse effects (21,29). However, limitations of these findings include low number of studies, limited quality of evidence due to observational data, and limited generalizability (29).

Usage of tramadol, which is a weak and mixed centrally acting opioid analgesic, has increased among older adults due to the perceived safety advantages over other opioids, however recent guidance advises against use of tramadol in this population due to potential risks of serotonergic excess, seizures, falls, and drug-drug interactions (25,30). Evidence demonstrates that older adults account for 33% of tramadol-associated emergency department visits and 50% of subsequent hospitalizations (30).

The National Institute for Health and Care Excellence (NICE) guidelines recommend antidepressants, including amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine or sertraline as alternative options for chronic primary pain in adults (23). However, highly anticholinergic medications such as amitriptyline and paroxetine are to be avoided in older adults due to risk for harm (28). Furthermore, antiepileptic medications should not be initiated in older adults due to adverse effects that outweigh potential benefit (23).

Lastly, topical therapies such as ketoprofen and diclofenac are recommended for first-line treatment of osteoarthritis, although cost and accessibility may be restrictive. Due to limited evidence, these agents are not recommended for chronic primary pain (21,23). Topical capsaicin and lidocaine are considered second-line for neuropathic pain due to limited efficacy. Transdermal products may have advantages in older adults due to fewer systemic adverse effects (21). However, absorption is influenced by subcutaneous tissue and therefore such agents may lose efficacy among individuals older than 85 years or in frail patients (21).

Another alternative for pain management that has increased in use over recent years among older adults is marijuana, or cannabis (31). Cannabis contains two major active ingredients (cannabinoids)-delta-9tetrahydrocannabinol (THC) and cannabidiol (CBD). Both THC and CBD have efficacy for pain, however THC causes euphoria while CBD does not. The pharmacokinetics of THC and CBD vary based on administration route (32). A systematic review of 28 studies (2,454 patients) for chronic pain including neuropathic pain, cancer pain, and fibromyalgia examined the effects of cannabis (primarily THC products) on pain. Eight studies reported reduced pain of at least 30% compared with placebo (33). While multiple studies have shown that marijuana is commonly used among older adults, a small number of older adults are included in large studies evaluating its efficacy for chronic pain (31). Therefore, little evidence exists for its safety and efficacy in this population. Differences in studied formulations and concentrations of THC versus CBD must also be noted (31). Additional concerns in the older adult include side effects. The most common adverse drug reactions of cannabis products include dizziness, dry mouth, and nausea which can be problematic for older adults, especially for those who may have polypharmacy and are using medications that also promote these side effects. Other concerns among older adults include driving risks, cognition, and THC euphoria (31,34).

With so many limitations surrounding the use of opioids and non-opioids in older adults, *Table 3* can help the clinician determine how to weigh the risks versus benefits of alternatives to opioids with monitoring.

Medications for opioid use order

Another risk mitigation strategy includes appropriate screening, identification, and management of OUD given the increasing prevalence in the general population but also specifically in the ageing population (13). OUD is often underdiagnosed and undertreated in older adults and is characterized by a problematic pattern of opioid use that causes impairment or distress, with defined criteria within a 12-month period (10,35). The 2022 CDC pain guidelines recommend treatment with evidence-based medications for OUD and advises against detoxification alone without medications due high risk for resuming

Table 4 Medications for opioid use disorder

Medication	Mechanism of action	Phase of treatment	Considerations
Methadone (PO)	Agonist	Medically supervised withdrawal, maintenance	Only available at federally certified OTPs and acute inpatient setting; risk of QT prolongation, drug interactions, and respiratory depression
Buprenorphine (SL, buccal, SD implant, SQ ER)	Partial agonist	Medically supervised withdrawal, maintenance	DEA "X" waiver requirements removed; can be dispensed by pharmacy or OTP; preferred for older adults due to better safety and accessibility
Naltrexone (PO, IM ER)	Antagonist	Maintenance, must be abstinent for 7–10 days	Office-based treatment, not a controlled substance

DEA, drug enforcement agency; ER, extended release; IM, intramuscular; PO, by mouth; OTP, opioid treatment program; QT, QT phase of the cardiac cycle; SD, subdermal; SL, sublingual; SQ, subcutaneous.

opioids and for opioid overdose (4). Among patients receiving palliative care, screening and treatment of OUD is also recommended (7). The available medications to treat opioid use disorder (MOUD), methadone, buprenorphine, and naltrexone, can help mitigate risk for patients when a diagnosis is confirmed (*Table 4*).

While MOUD has been shown to reduce illicit opioid use, retain people in treatment, and reduce risk of opioid overdose death better compared with placebo, over 70% of patients with OUD are not on MOUD (36,37). Nevertheless, access to MOUD is improving, particularly as the Drug Addiction Treatment Act (DATA 2000) "X-waiver", which was a federal requirement for practitioners to apply for a waiver prior to prescribing buprenorphine for OUD treatment, is no longer required for prescribing buprenorphine for OUD; other former federal requirements for prescribing buprenorphine for OUD such as limits on the number of patients a prescriber may treat simultaneously have also been lifted (38). However, little research exists for MOUD among older adults given the lack of their inclusion in randomized controlled trials. Therefore, recommendations for treatment are based on data from younger adults. Observational data suggests that older adults are more adherent to MOUD and experience positive outcomes comparable to, if not better than, their younger counterparts (10). There is a preference for buprenorphine over methadone among this population due to a better safety profile and accessibility (10). Methadone also has increased risk of QT prolongation, drug interactions, and respiratory depression as compared with buprenorphine (39).

In the setting of chronic pain without OUD, there are benefits of using transdermal buprenorphine, which has a labeled indication for severe chronic pain (40,41). Other formulations of buprenorphine can also be used off-label (42). Buprenorphine benefits for chronic pain without OUD include analgesic effect with favorable safety profile, including low risk of consequences such as respiratory depression (42). Clinicians may consider switching a patient to buprenorphine when there has been a lack of pain control, presence of tolerance or hyperalgesia with full opioid agonists, adverse events with the full opioid agonist, or concern for addiction, misuse, and/or overdose death (40).

Toxicology testing

Clinicians may consider the benefits and risks of toxicology testing for patients before starting opioids and periodically (at least annually) during long-term opioid therapy (4). Evidence demonstrates that fewer than 15% of primary care providers report toxicology testing (43). While evidence of effectiveness is lacking in the literature, toxicology testing, such as urine drug screening (UDS), offers an opportunity to provide additional clinical information to improve patient care and should not be used in a punitive manner (4). It may provide information about drug use not reported by the patient, may help identify when opioids are not taken as prescribed, and may help identify diversion or patient challenges such as adverse effects (4). Toxicology testing may also help identify concurrent use of other substances that may increase risk of harm. This may be particularly beneficial for older adults due to polypharmacy, in which other medications used may not be prescribed or documented in the electronic medical record.

When UDS is utilized, the clinician must consider the

type of test used—particularly as immunoassay tests are less sensitive and specific as compared with gas chromatography and may result in false negative results. Therefore, unexpected results should be discussed both with the patient and the laboratory or toxicologist (4). Following toxicology testing, when non-prescribed substances are identified, education regarding the risks of concomitant use of such substances should occur. Further, referral to OUD care may be needed.

Naloxone

Clinicians should offer naloxone to patients at increased risk for opioid overdose, including those who have a history of overdose, patients with substance use disorder (SUD), patients taking high-risk concomitant medications such as benzodiazepines, or patients taking ≥ 50 morphine milligram equivalent per day (4). Despite this recommendation, naloxone remains under-prescribed and underused particularly among high-risk patients; data shows that only one naloxone prescription was dispensed for every 69 highdose opioid prescriptions (44). While a high predictor of inappropriate opioid prescribing in advanced age, a cross sectional study of primary care clinics revealed low naloxone co-prescribing among this population (45). The Food and Drug Administration (FDA) updated labeling for all opioids and MOUD recommending routine co-prescribing of naloxone with every new and refilled prescription (46). Most recently, the FDA approved intranasal naloxone for over-the-counter, non-prescription use (47).

CSAs

A CSA outlines prescriber and patient responsibilities while prescribed long-term-controlled substances. Most CSAs highlight risks versus benefits of therapy, goals of therapy, stipulations for refills, frequency of toxicology testing, and PDMP review (48). CSAs are recommended by clinical practice guidelines as a risk mitigation strategy for patients managed on controlled substances (49). Yet, there is mixed evidence of their effectiveness and best practices for CSA adherence are not clearly defined (48,50,51). Some systematic reviews found that effectiveness of CSAs may be weak in reducing opioid misuse (50,51). While mixed evidence on the use of CSAs exists, benefits include facilitating open communication regarding patient adherence, education on the benefits and risks of opioid therapy, and improved patient safety (48,50,51).

PDMPs

PDMPs are statewide electronic databases that track and report all controlled substance prescriptions (15). PDMPs provide information regarding controlled substance prescribers, dispensing pharmacies, doses, and number of prescriptions (2). Clinicians should use the PDMP when prescribing initial opioid therapy and during chronic opioid therapy to determine whether dosages or combinations of controlled substances exist that may increase risk for overdose (4). States with more robust PDMP programs have been shown to have fewer prescription opioid overdose deaths compared to states with weaker programs (52). Despite conflicting evidence on whether or not PDMPs prevent harmful medication prescribing and opioidassociated mortality, older adults may benefit from their review due to polypharmacy, fragmented care, and having multiple healthcare providers (2). Among older adults receiving more than one opioid prescription, 60% to 70% receive them from multiple providers (2). While there are some limitations to use of PDMPs, such as lack of consistent integration into the electronic medical record, limited time for physicians to review the database, and different requirements for physician and pharmacist review across different states, they still provide important information that can improve safety among older adults on opioids (2).

Patient evaluation and education

Proper history, evaluation, and patient education is a key risk mitigation strategy for patients on long-term opioids, including older adults. Older adults who may have comorbidities and receive more medications are at increased risk for drug-drug and drug-disease interactions. Before prescribing opioid therapies, clinicians should conduct a thorough medication history, including prescription medications, over-the-counter medications, and natural or herbal remedies. Medication review should occur prior to prescribing new medications and at every encounter, especially as older adults commonly have changing health conditions and consequently frequent updates in medication therapies. Furthermore, evaluation of medication adherence is important. Additionally, patients may have saved old mediations that are still on hand, creating potential for medication errors. Patients should be educated on proper storage and disposal of all medications, particularly opioids.

Patients should be educated on the expected benefits, goals of therapy, common side effects and serious risks with

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Strategy	Community pharmacy	Ambulatory clinic	Acute care
Assessing risk		Utilize screening tools	
PDMP	Check on each dispense Check before new and chronic prescribing		
CSA	Ask patients	Initiate	Uphold
UDS	Call prescriber to ask	Order	Order
Reducing risky combinations	Discuss with prescribers	Initiate taper; prescribe alternatives	Communicate with PCP
Medications for OUD	Remove stigma at dispensing	Initiate/refer	Initiate/refer
Naloxone		Co-prescribe and reiterate	
Education		Counsel on each fill	

PDMP, prescription drug monitoring program; CSA, controlled substance agreement; UDS, urine drug screening; OUD, opioid use disorder; PCP, primary care provider.

opioids before initiating or continuing therapy, and risk reduction strategies while on therapy (4). Clinicians also should implement education and interventions directed towards reducing common risks of opioid therapy among older adults, such as monitoring for cognitive impairment, assessment for fall risk, exercise, and bowel regimens to prevent constipation (4,9).

Prescribers should screen for and treat comorbid conditions such as mental health disorders or SUD, defined as recurrent use of alcohol and/or drugs causing clinically significant impairment, including health problems, disability, and failure to meet major responsibilities at work, school, or home (2,53). A thorough review of personal and family history of SUD is key, and patients should be educated on the difference between physical dependence, tolerance, and addiction. An initial assessment and ongoing reassessment of pain level and functional status is key, with comparison to baseline pain assessment as treatment continues (54). Lastly, clinicians should be mindful of disparities in access to pain management based on race and ethnicity, lower income and education, sex and gender, and geographic location (22). Clinicians should be mindful of reducing stigma among patients with pain and OUD, while recognizing the impact of word choice that may perpetuate stigma and discrimination, given that negative terms such as "addict", "abuse", and "abuser" lead to lower likelihood of appropriate care (53,55).

Collaboration with the interprofessional team

Interprofessional collaboration is essential for risk

mitigation among older adults on opioids for CNCP and those receiving palliative care (2,7,8,14). Pharmacists in the primary care setting, community setting, and acute care settings have distinct opportunities to promote the use of risk mitigation strategies with opioid use. Further, risk mitigation of opioid use involves time and expertise, which may be leveraged through collaboration with pharmacists (Table 5). Pharmacist collaboration with prescribers is essential in the current landscape of fragmented care among older adults. Community pharmacists particularly, as the most accessible health care professionals, have multiple opportunities to prevent opioid harm. Their frequent interactions with patients allow for more closely monitored opioid usage, review of PDMPs, patient education, and facilitation of communication between the patient and prescriber (2). Compliance with risk mitigation strategies such as CSAs, UDS, and PDMP review has been found to be less than 50% across primary care practices (56-58). Interprofessional collaboration with a clinical pharmacist may improve use of risk mitigation strategies for patients with CNCP and those receiving palliative care (2).

A variety of pharmacist-led initiatives have been described in the literature, including education on best-practice standards and guidelines, safe opioid tapering and discontinuation, PDMP review, toxicology testing, educating patients on opioid safety, storage, disposal, as well as providing resources for addiction treatment (59-63). A reduction in opioid morphine milligram equivalents and increase in completion of UDS and CSA reviews has been demonstrated from this literature (61,62). A model of pharmacist-physician collaboration in the management of patients with chronic pain resulted in more

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non-opioid use, switching to buprenorphine for pain, and opioid tapering (63).

Among older adults receiving palliative care, collaboration among the interprofessional team is key to implement risk mitigation strategies across care settings (7,8,14). Health care professionals that add value to the patient-centered team include palliative care specialists, cancer specialists, psychologists, addiction medicine, pain specialists, pharmacists, nurses, and social workers, among others (7,8,14).

Conclusions

Older adults commonly have chronic pain, and management of pain is complicated by comorbidities, polypharmacy, and adverse effects associated with opioid therapies. There are a myriad of risk mitigation strategies to improve safe opioid use in older adults among patients with CNCP and those receiving palliative care. A multifaceted, comprehensive approach should be utilized, particularly as not all older adults established on long-term opioids will be able to practically manage their pain without them or safely discontinue their use. Interprofessional collaboration, including with pharmacists and palliative care specialists, can be an effective means for implementing such strategies to optimize safety of older adults on opioid therapy.

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References

- Guerriero F. Guidance on opioids prescribing for the management of persistent non-cancer pain in older adults. World J Clin Cases 2017;5:73-81.
- Kakatkar S, Narayan A, Balkrishnan R. Prescription analgesic overuse in older adults: Can we mitigate this growing problem? Aging Med (Milton) 2022;5:294-6.
- Berna C, Kulich RJ, Rathmell JP. Tapering Long-term Opioid Therapy in Chronic Noncancer Pain: Evidence and Recommendations for Everyday Practice. Mayo Clin Proc 2015;90:828-42.
- Dowell D, Ragan KR, Jones CM, et al. CDC Clinical Practice Guideline for Prescribing Opioids for Pain -United States, 2022. MMWR Recomm Rep 2022;71:1-95.
- Gazelka HM, Leal JC, Lapid MI, et al. Opioids in Older Adults: Indications, Prescribing, Complications, and Alternative Therapies for Primary Care. Mayo Clin Proc 2020;95:793-800.
- Centers for Disease Control and Prevention. 2019 Annual Surveillance Report of Drug-Related Risks and Outcomes

 United States Surveillance Special Report. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Published November 1, 2019. Available online: https://www.cdc.gov/drugoverdose/ pdf/pubs/2019-cdc-drug-surveillancereport.pdf. Accessed

January 28, 2024.

- Lau J, Mazzotta P, Whelan C, et al. Opioid safety recommendations in adult palliative medicine: a North American Delphi expert consensus. BMJ Support Palliat Care 2022;12:81-90.
- Gaertner J, Boehlke C, Simone CB 2nd, et al. Early palliative care and the opioid crisis: ten pragmatic steps towards a more rational use of opioids. Ann Palliat Med 2019;8:490-7.
- Zullo AR, Danko KJ, Moyo P, et al. Prevention, Diagnosis, and Management of Opioids, Opioid Misuse, and Opioid Use Disorder in Older Adults. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Nov. Report No.: 21-EHC005.
- Dufort A, Samaan Z. Problematic Opioid Use Among Older Adults: Epidemiology, Adverse Outcomes and Treatment Considerations. Drugs Aging 2021;38:1043-53.
- Hedegaard H, Miniño AM, Warner M. Drug Overdose Deaths in the United States, 1999-2019. NCHS Data Brief 2020;(394):1-8.
- Humphreys K, Shover CL. Twenty-Year Trends in Drug Overdose Fatalities Among Older Adults in the US. JAMA Psychiatry 2023;80:518-20.
- Shoff C, Yang TC, Shaw BA. Trends in Opioid Use Disorder Among Older Adults: Analyzing Medicare Data, 2013-2018. Am J Prev Med 2021;60:850-5.
- National Consensus Project for Quality Palliative Care. Clinical Practice Guidelines for Quality Palliative Care, 4th edition. Richmond, VA: National Coalition for Hospice and Palliative Care; 2018. Available online: https://www.nationalcoalitionhpc.org/ncp. Accessed February 21, 2024.
- Lindley B, Cox N, Cochran G. Screening tools for detecting problematic opioid use and potential application to community pharmacy practice: a review. Integr Pharm Res Pract 2019;8:85-96.
- Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. J Gen Intern Med 2009;24:733-8.
- US Department of Health and Human Services Centers for Disease Control. Checklist for prescribing opioids for chronic pain. Available online: https://www.cdc.gov/ drugoverdose/pdf/pdo_checklist-a.pdf. Accessed January 28, 2024.
- Gloth FM 3rd, Scheve AA, Stober CV, et al. The Functional Pain Scale: reliability, validity, and responsiveness in an elderly population. J Am Med Dir

Assoc 2001;2:110-4.

- HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. 2019. Available online: https://www.cms.gov/ About-CMS/Story-Page/CDCs-Tapering-Guidance.pdf. Accessed on January 28, 2024.
- Magnan EM, Tancredi DJ, Xing G, et al. Association Between Opioid Tapering and Subsequent Health Care Use, Medication Adherence, and Chronic Condition Control. JAMA Netw Open 2023;6:e2255101.
- 21. Schofield P, Dunham M, Martin D, et al. Evidence-based clinical practice guidelines on the management of pain in older people a summary report. Br J Pain 2022;16:6-13.
- 22. Tick H, Nielsen A, Pelletier KR, et al. Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care: The Consortium Pain Task Force White Paper. Explore (NY) 2018;14:177-211.
- National Institute for Health Care Excellence. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain (NG193). Available online: www.nice.org.uk/guidance/ ng193. Accessed on January 28, 2024.
- Wongrakpanich S, Wongrakpanich A, Melhado K, et al. A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drug Use in The Elderly. Aging Dis 2018;9:143-50.
- 25. Musich S, Wang SS, Schaeffer JA, et al. Safety Events Associated with Tramadol Use Among Older Adults with Osteoarthritis. Popul Health Manag 2021;24:122-32.
- Bush DM. Emergency Department Visits for Drug Misuse or Abuse Involving the Pain Medication Tramadol. 2015 May 14. In: The CBHSQ Report. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2013.
- 27. Fournier JP, Azoulay L, Yin H, et al. Tramadol use and the risk of hospitalization for hypoglycemia in patients with noncancer pain. JAMA Intern Med 2015;175:186-93.
- 28. By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2023;71:2052-81.
- Roberts E, Delgado Nunes V, Buckner S, et al. Paracetamol: not as safe as we thought? A systematic literature review of observational studies. Ann Rheum Dis 2016;75:552-9.
- 30. American Society of Consultant Pharmacists. Choosing Wisely Recommendations: Don't prescribe tramadol

for older adults without considering the potential risks and harms related to serotonergic excess, seizures, falls, and drug-drug interactions. American Family Physician (519). Available online: https://www.aafp.org/pubs/afp/ collections/choosing-wisely/519.html. Accessed on January 28, 2024.

- Abuhasira R, Ron A, Sikorin I, et al. Medical Cannabis for Older Patients-Treatment Protocol and Initial Results. J Clin Med 2019;8:1819.
- Romero-Sandoval EA, Kolano AL, Alvarado-Vázquez PA. Cannabis and Cannabinoids for Chronic Pain. Curr Rheumatol Rep 2017;19:67.
- Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA 2015;313:2456-73.
- Carr D, Schatman M. Cannabis for Chronic Pain: Not Ready for Prime Time. Am J Public Health 2019;109:50-1.
- American Psychiatric Association DSM-5 Task Force. Diagnostic and statistical manual of mental disorders: DSM-5[™]. 5th ed. Arlington, VA: American Psychiatric Publishing, Inc., 2013.
- Mauro PM, Gutkind S, Annunziato EM, et al. Use of Medication for Opioid Use Disorder Among US Adolescents and Adults With Need for Opioid Treatment, 2019. JAMA Netw Open 2022;5:e223821.
- 37. U.S. Department of Health & Human Services Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. 2018. Available online: https://www. samhsa.gov/data/report/2017-nsduh-annual-nationalreport. Accessed on January 28, 2024.
- 38. U.S Department of Health & Human Services Substance Abuse and Mental Health Services Administration. Waiver Elimination (MAT Act). 2023. Available online: https:// www.samhsa.gov/medications-substance-use-disorders/ waiver-elimination-mat-act. Accessed on January 28, 2024.
- LaGrotta C. Treatment of Opioid Use Disorder in the Elderly. Curr Treat Options Psych 2020;7:531-543.
- Webster L, Gudin J, Raffa RB, et al. Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion. Pain Med 2020;21:714-23.
- Lazaridou A, Paschali M, Edwards RR, et al. Is Buprenorphine Effective for Chronic Pain? A Systematic Review and Meta-analysis. Pain Med 2020;21:3691-9.
- 42. Provider CLinical Support System: PCCS Guidance. The Off-Label Use of Sublingual Buprenorphine and

Buprenorphine/Naloxone for Pain. Available online: https://pcssnow.org/wp-content/uploads/2014/02/PCSS-MATGuidanceOff-label-bup-for-pain.Gordon.pdf. Accessed on January 28, 2024.

- 43. Mahajan G. Role of Urine Drug Testing in the Current Opioid Epidemic. Anesth Analg 2017;125:2094-104.
- Guy GP Jr, Haegerich TM, Evans ME, et al. Vital Signs: Pharmacy-Based Naloxone Dispensing — United States, 2012–2018. MMWR Morb Mortal Wkly Rep 2019;68:679-86.
- Luther CD, Hughes TD, Ferreri SP. Naloxone prescribing to older adults in primary care. J Am Geriatr Soc 2021;69:3681-3.
- 46. U.S Food and Drug Administration. FDA Requiring Labeling Changes for Opioid Pain Medicines, Opioid Use Disorder Medicines Regarding Naloxone. 2020. Available online: https://www.fda.gov/news-events/pressannouncements/fda-requiring-labeling-changes-opioidpain-medicines-opioid-use-disorder-medicines-regarding. Accessed on January 28, 2024.
- 47. U.S. Food and Drug Administration. FDA Approves First Over-the-Counter Naloxone Nasal Spray: Agency Continues to Take Critical Steps to Reduce Drug Overdose Deaths Being Driven Primarily by Illicit Opioids. 2023. Available online: https://www.fda.gov/ news-events/press-announcements/fda-approves-firstover-counter-naloxone-nasal-spray Accessed on January 28, 2024.
- Irwin AN, Braden-Suchy N, Hartung DM. Exploring Patient Perceptions of Opioid Treatment Agreements in a Community Health Center Environment. Pain Med 2021;22:970-8.
- Nuckols TK, Anderson L, Popescu I, et al. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. Ann Intern Med 2014;160:38-47.
- McAuliffe Staehler TM, Palombi LC. Beneficial opioid management strategies: A review of the evidence for the use of opioid treatment agreements. Subst Abus 2020;41:208-15.
- 51. Starrels JL, Becker WC, Alford DP, et al. Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. Ann Intern Med 2010;152:712-20.
- Pardo B. Do more robust prescription drug monitoring programs reduce prescription opioid overdose? Addiction 2017;112:1773-83.
- 53. Substance Abuse and Mental Health Services

Administration. Mental Health and Substance Use Disorders Available online: https://www.samhsa.gov/findhelp/disorders. Accessed on January 28, 2024.

- Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. Pain Med 2005;6:107-12.
- 55. Ashford RD, Brown AM, Curtis B. Substance use, recovery, and linguistics: The impact of word choice on explicit and implicit bias. Drug Alcohol Depend 2018;189:131-8.
- Hariharan J, Lamb GC, Neuner JM. Long-term opioid contract use for chronic pain management in primary care practice. A five year experience. J Gen Intern Med 2007;22:485-90.
- 57. Lasser KE, Shanahan C, Parker V, et al. A Multicomponent Intervention to Improve Primary Care Provider Adherence to Chronic Opioid Therapy Guidelines and Reduce Opioid Misuse: A Cluster Randomized Controlled Trial Protocol. J Subst Abuse Treat 2016;60:101-9.
- 58. Freeman PR, Curran GM, Drummond KL, et al.

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- Thakur T, Frey M, Chewning B. Pharmacist Services in the Opioid Crisis: Current Practices and Scope in the United States. Pharmacy (Basel) 2019;7:60.
- 60. Tewell R, Edgerton L, Kyle E. Establishment of a pharmacist-led service for patients at high risk for opioid overdose. Am J Health Syst Pharm 2018;75:376-83.
- Hellier Y, Wilson M, Leahy A, et al. Pharmacy multidisciplinary stewardship program for high-risk patients prescribed opioids in an academic clinic. J Opioid Manag 2020;16:341-50.
- 62. Boren LL, Locke AM, Friedman AS, et al. Team-Based Medicine: Incorporating a Clinical Pharmacist into Pain and Opioid Practice Management. PM R 2019;11:1170-7.
- 63. Lagisetty P, Smith A, Antoku D, et al. A physicianpharmacist collaborative care model to prevent opioid misuse. Am J Health Syst Pharm 2020;77:771-80.