

Annual Perspective: Topics in Medication Safety

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Introduction

Issues with medication management and errors in medication administration are major threats to patient safety. These topics are among the areas of focus in the Agency for Healthcare Research and Quality (AHRQ) report *Making Healthcare Safer III: A Critical Analysis of Existing and Emerging Patient Safety Practices*.¹ Although medication safety is a broad subject that encompasses many topics, this Annual Perspective addresses three topics—reducing adverse drug events (ADEs) in older adults, reducing harms due to opioids, and reducing nursing-sensitive medication administration errors—that were addressed in the patient safety literature around the prior year. This Annual Perspective was developed in collaboration with Ilene Harris, PharmD, PhD, a subject matter expert in drug policy and program evaluation, gerontology, and medication use and quality. Perspective authors reviewed articles and other materials related to the safety practice areas listed above and that were featured on the [AHRQ Patient Safety Network \(PSNet\)](#) in late 2020 or during 2021. Materials related to medication management issues, including reducing ADEs in older adults, reducing harms due to opioids, and reducing nursing-sensitive medication administration errors are highlighted in the sections that follow.

Medication Safety in Older Adults

High-Risk Medication Use in Older Adults

Prescribing high-risk, potentially inappropriate medications (PIMs) in older adults may result in ADEs, posing serious threats to patient safety. The American Geriatrics Society Beers Criteria® (AGS Beers Criteria®) contain a widely employed list of PIMs that adults 65 years and older should avoid under most circumstances due to the potential for ADEs such as orthostatic hypotension, falls, and mental confusion.²

Computerized clinical decision support (CDS) interventions provide prescribers with medication warning alerts and alternative medications that are safer than PIMs. The [Enhancing Quality of Prescribing Practices for Older Adults Discharged from the Emergency Department \(EQUIPPED\)](#) medication safety program is a CDS that was originally developed by the Veterans Health Administration (VHA). EQUIPPED was designed

to decrease the number of PIMs prescribed to older adults upon discharge from the emergency department.³ EQUIPPED implementation includes three core components: (1) education for providers from an onsite champion, (2) a list of discharge medications produced through an electronic health record (EHR) CDS, and (3) auditing and feedback information for providers with peer benchmarking. The EQUIPPED CDS program is currently being deployed beyond VHA systems as a [model program](#) and it has significantly reduced overall PIM prescribing at one site. Future lessons learned from this project will be valuable for reducing ADEs from PIMs.

An independent study from an academic medical center evaluated the efficacy of CDS in [reducing PIM prescribing rates](#) within two distinct EHR systems. Friebe and colleagues found that PIM prescribing rates decreased by 5.2% when the CDS was first deployed within the Vanderbilt University Medical Center's legacy EHR. An additional 18.8% reduction in PIM prescribing was observed years later when the medical center rebuilt the CDS alert as part of a migration to a new EHR system. These results indicate that CDS interventions are effective at reducing PIM prescribing. However, among prescribers, the overall acceptance rate of an alternative medication suggested by the CDS alert in response to the original PIM was low at 11.1%. The study authors speculated that the low acceptance rate could be due in part to [alert fatigue](#). Future studies could (1) help identify the precise factors that optimize the efficacy of CDS interventions in reducing PIM prescribing rates, including the impact of different EHR systems in enhancing CDS interventions, and (2) determine whether decreased prescribing of PIMs affects patient outcomes.

Polypharmacy

Polypharmacy (taking five or more medications regularly) is common among older adults and is a preventable risk factor for ADEs. With the rising trend in overall prescribing rates, particularly for older adults, the risk of ADEs increases with each new drug added to a medication regimen. Each drug alone has the potential to directly cause an ADE (e.g., benzodiazepines are PIMs for older adults and can directly cause cognitive impairment and increased risk of falls). The issue becomes more complex when two drugs interacting with each other can, in turn, lead to one or more ADEs (e.g., there is a drug-drug interaction [DDI] between opioids and benzodiazepines resulting in an increased risk for fatal respiratory depression). A further complication is a [multidrug interaction](#) (MDI) where one drug interacts with two or more other drugs, resulting in an ADE (e.g., there is a DDI between aspirin and warfarin and a third drug, amiodarone, further exacerbates this interaction, creating an MDI with an increased risk of bleeding). Anand and colleagues screened the medication lists from a sample of older adults and reported that 1.3% of the lists contained MDIs. Among patients who were prescribed amiodarone or methotrexate, the prevalence of MDIs on medication lists was greater than 20%. The most common drugs involved in MDIs were psychotropics (e.g., bupropion, trazodone, escitalopram, sertraline, fluoxetine), which represented more than 35% of all drugs involved in MDIs. Incorporating MDIs into CDS intervention systems along with DDI alerts and other warnings could be an effective strategy for reducing ADEs.

One solution for reducing the prevalence of polypharmacy is [deprescribing](#), which is defined as the process of supervised medication discontinuation or dose reduction to decrease PIM use. Specific programs for organizations, physicians, and pharmacists, such as [Drive to Deprescribe](#), are designed to create a learning network and educational opportunities centered around deprescribing. Several provider tools are available to assist with identifying PIMs, including the AGS Beers Criteria®, the Medication

Appropriateness Index (MAI), and the Screening Tool of Older Persons' Prescriptions (STOPP) criteria. Once PIMs are identified, effective implementation of deprescribing practices includes a shared decision-making approach with close patient involvement. A national survey of older adults found that patients [prefer deprescribing language](#) that includes an explanation of the risk of side effects associated with the medication under discussion. The least preferred language includes reference to the amount of effort required to take the medication. Older adults react negatively to language indicating that a patient may no longer benefit from preventive medications (e.g., cholesterol-lowering statin medications to prevent adverse cardiovascular events). These findings highlight the importance of understanding patient preferences and perceptions when framing deprescribing conversations and to maximize chances for successful interventions.

The concept of deprescribing seems relatively straightforward from a process perspective and when using the tools and practices described above. In reality, though, there are several known barriers to implementing a deprescribing process. A study of providers in VHA primary care clinics found that even though most providers reported having patients who were taking unnecessary medications, [less than one-third of providers recommended deprescribing](#) to their qualifying patients. Several factors were found to increase the likelihood of a provider recommending deprescribing to patients, included having more patients who asked for information about their medication, providers having more familiarity with the deprescribing process, and providers having the resources to monitor patients after deprescribing. Providers also reported being less likely to recommend deprescribing when the indication for a medication was unclear. In another study involving primary care physicians, Hahn and coworkers found that providers perceived the process of [deprescribing as potentially contentious](#), even when considering discussions with patients who experienced ADEs in the form of falls. Patient interviews in this study revealed that patients had little awareness of the potential for serious falls. Addressing these barriers will increase the chances of successful interventions directed at increasing deprescribing.

Opioid Medication Safety

Reducing Opioid Overprescribing

The opioid epidemic in the United States was driven by the improper prescribing of opioids, including excessive dosages or extended use. Prescribing rates between 2006 and 2020 peaked in 2012 with more than 255 million prescriptions dispensed.⁴ In response to improper prescribing and use of opioids, [government action](#) was taken across the country in the form of state regulations which focused on limiting the prescribing of opioids for treating acute pain. In addition, in 2016, the Centers for Disease Control and Prevention (CDC) published the Guideline for Prescribing Opioids for Chronic Pain (hereafter referred to as the "CDC guideline").⁵ The CDC guideline included recommendations to use the lowest effective dose of opioids, to frequently evaluate the benefits and harms of opioid therapy, to prescribe short durations of opioids for acute pain (more than seven days of therapy are rarely needed), and to use nonpharmacologic and nonopioid pharmacologic therapies as first-line treatment for pain. The CDC guideline cited AHRQ-sponsored clinical evidence reviews on the minimal effectiveness of long-term opioid therapy in treating chronic pain.^{6,7} Although the CDC guideline focused on chronic pain, it did not apply to patients diagnosed with cancer or to patients receiving palliative care. An updated version of the CDC guideline was open for

public comment in early 2022.⁸

Between 2012 and 2017, prescriptions for high-dose opioids decreased by almost 50% and overall prescribing of opioids declined; the rate of decline further increased after the CDC guideline was released in 2016.⁹ Similarly, an independent study of commercial prescription claims for [patients with chronic pain](#) from 2014 to 2018 reported a decline in the percentage of patients receiving opioid prescriptions, the percentage of patients receiving prescriptions for high-dose opioids, and the number of days that opioids were supplied. A study of opioid prescribing practices related to workers' compensation in Washington State reported that [safer opioid prescribing](#) was observed after several regulations for state prescribing were put in place. For example, after a policy was implemented to require prior authorization for opioid prescriptions exceeding six weeks of treatment, the prevalence of opioid prescriptions for a 60-day supply dropped to nearly zero. In addition, an analysis of AHRQ's Medical Expenditure Panel Survey (MEPS) data from 2013 to 2017 demonstrated that the CDC guideline reduced the number of opioid prescriptions, increased the number of patients with chronic pain who switched to nonopioid pain analgesics, and increased the number of tapered opioid doses.¹⁰ Patients who discontinued opioids under state regulations and the CDC guideline showed no harms related to work limitations due to pain after one year of discontinuing opioids. The analysis revealed that state regulations appeared to reduce opioid use by limiting the number of new opioid prescriptions, while the CDC guideline reduced opioid use by reducing the number of current opioid users, with no impact on new starts.

Increasing Naloxone Access and Use

In addition to targeting opioid overprescribing, increasing access to the medication that rapidly reverses opioid overdose, naloxone, is a harm-reduction strategy for patients at a high risk of opioid overdose. The CDC guideline recommends that naloxone be offered to patients at risk for opioid overdose when there is a history of overdose or substance use disorder, a higher opioid dosage (≥50 morphine milligram equivalents [MME]), or concurrent benzodiazepine use. In all 50 states, the District of Columbia, and Puerto Rico, people can obtain naloxone without a prescription through various mechanisms (e.g., standing orders, pharmacists' prescriptive authority, or direct authority by statute or administrative order).¹¹ A study of pharmacies in Texas found that, despite having a standing order in place to dispense naloxone, secret shoppers were [unable to access naloxone](#) in nearly one-third of the pharmacies they tested. Although there may still be some barriers to accessing naloxone in certain areas, pharmacies represent a primary distribution point for this medication. Community pharmacists, in particular, are well-positioned to [identify patients at risk for overdose and facilitate access to naloxone](#). Emergency departments can also identify patients at high risk for overdose and are another key distribution point for naloxone. [Increased naloxone prescribing rates](#) were attained in a large, tertiary care academic emergency department after the implementation of electronic medical record-based work-aids, including a naloxone best practice advisory and order set, and staff education. Continuing medical education resources for identifying and [managing patients at high risk for opioid overdose](#) are available for practitioners from various resources.

Other Interventions for Opioid Medication Safety

It seems clear that interventions deployed to limit opioid overprescribing have been successful in steadily decreasing the number, dosage, and duration of opioid prescriptions over time. In addition to state

regulations and guidelines targeting opioid prescribing behavior, [other interventions](#), including prescription drug monitoring programs (PDMPs) and prescriber education initiatives, are currently being tested. A study conducted in an emergency department (ED) reported that combining the use of PDMPs with a [customized educational program for prescribers](#) decreased the percentage of persons who received an opioid prescription when they were discharged from the emergency department, from 19.4% to 7.4%. In another example, a large health system implemented changes to its EHR program to encourage [best practices in opioid prescribing](#). As a result, the health system saw reductions in (1) the total number of opioid prescriptions per 100 patient discharges, (2) the number of opioid prescriptions exceeding a three-day supply, (3) the number of prescriptions exceeding 30 MME, and (4) the number of prescriptions written for opioids that were not on the ED's formulary. In another study, administrative data were used to develop [machine learning models](#) to estimate the risk of adverse outcomes after the receipt of an opioid prescription. Results from this study indicate that machine learning classifiers can better predict adverse outcomes compared with individual approaches that use guidelines or prescription histories alone.

Update on the Opioid Epidemic

Interventions designed to prevent overprescribing of opioids may result in unintended consequences, such as patients suffering from poorly controlled pain, experiencing unpleasant symptoms from forced medication tapers, or turning to illicit sources of opioids.¹ Despite evidence indicating that state drug-control policies have resulted in both reduced misuse of prescription opioids and reduced deaths from prescription opioid overdoses, Lee and colleagues found that some state policies (e.g., mandatory PDMPs and naloxone access) are also associated with an increase in overdose deaths from synthetic opioids and cocaine.¹² The authors concluded that, despite declines in overall opioid prescribing since 2012, deaths due to drug overdoses from illicit drugs continue to rise. In addition, the authors found that state policies may have the unintended consequence of motivating individuals with opioid use disorders to switch to alternative illicit substances (including those laced with fentanyl). Although progress has been made in decreasing opioid overprescribing, the opioid epidemic is a complex, multifactorial issue that requires additional and more focused interventions than those currently in place.

Nursing-Sensitive Medication Safety

Blume and colleagues conducted a literature review and identified “medication error” as 1 of 22 [nursing-sensitive issues](#) that can affect patient safety outcomes. Schroers and colleagues identified the following as [nurses’ perceived causes of medication administration errors](#): lack of knowledge, staffing levels/workload, interruptions, challenging professional relationships/poor communication, lack of support/supervision, physical working conditions, and unsafe standards of practice. A recent report on nursing education curricula examined the [safety and medication administration practice](#) components of nursing education and identified punitive responses for addressing nursing student medication errors. The report recommended transitioning to a “Just Culture” in nursing school programs. The report also identified strategies to include error prevention and safety education in the curricula.

Other strategies to address [nursing-sensitive medication administration errors](#) have been proposed, many of which have been discussed in the field of nursing and are experiencing ongoing development, improvement, and assessment. For example, optimizing nursing workflows to minimize interruptions and to lower the potential for errors is one such strategy. Results from a recent study provided an additional assessment of a bundled intervention that included a [“do not interrupt” vest](#) worn by nurses during medication administration rounds. The study concluded that the vest had no impact on medication administration errors or interruption rates, raising questions about the utility of this intervention. In another example, barcode medication verification technology has been integrated into nursing workflows for many years, and recent studies continue to support the utility and further development of this technology. For example, Kung and colleagues reported that [medication preparation errors decreased](#) in a teaching hospital after barcode technology was implemented. Owens and colleagues found that deploying barcode technology [reduced medication administration errors and improved nurse satisfaction](#) with medication administration systems.

Smart infusion pumps are used frequently to deliver medications. Errors occur when pump users bypass the programmed dosage or infusion rates or the drug library. The Joint Commission released a Sentinel Event Alert that described actions that healthcare organizations can take to reduce the risk of errors caused by the [misuse of smart infusion pumps](#). Examples included the use of dose error reduction software (DERS) and integration of smart infusion pumps with EHR systems. DERS can be programmed with hard and soft stops to facilitate appropriate dosing and data can be collected to study potential safety issues in pump usage patterns. Another distinct software package developed at Cincinnati Children's Hospital Medical Center, called MED.Safe, has been successfully tested in several locations. MED.Safe, which is directed at high-risk medications, uses [medication administration discrepancy detection algorithms](#) to perform an automated comparison of medication orders to medication administration records. [Data from smart pumps](#) are also being compared to medication orders to detect medication administration errors. Expanding the application of software programs like MED.Safe for use as both a rapid detection system and a learning tool may be an effective strategy for preventing errors in medication administration.

Future Research Directions in Medication Safety

The recent advances in medication safety highlighted in this Perspective are promising strategies for reducing adverse medication events among older adults, reducing harms due to opioid medications, and reducing nursing-sensitive medication administration errors. Taking advantage of available data and of developing technology will further advance ongoing efforts in these areas to improve medication safety and overall patient safety. Research on medication safety should promote the use of improved practices that are standardized in addition to reducing errors and preventing harm. Investigating [improvement strategies and tools for medication safety](#) may advance overall patient safety.

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