Making Healthcare Safer IV

Computerized Clinical Decision Support To Prevent Medication Errors and Adverse Drug Events

Rapid Review

Structured Abstract

Objectives. To assess the evidence on the effects of computerized clinical decision support systems (CDSSs) on the prevention of medication errors and adverse drug events, related implementation outcomes such as rates of medication alert overrides, and unintended consequences of use. We also summarized the literature around the effective implementation of a CDSS.

Methods. We followed the rapid review processes of the Agency for Healthcare Research and Quality Evidence-based Practice Center Program. We queried PubMed and the Cochrane Library to locate relevant systematic reviews and primary studies published from 2015 to April 2023, supplemented by a targeted review of the grey literature. We narratively synthesized the evidence and assessed the overall strength of evidence for the outcomes of interest. The protocol for the review has been registered in PROSPERO (CRD42023449710).

Findings. Our search yielded 1,335 unique abstracts, of which 33 articles met the target criteria and were included in the review (27 systematic reviews, one overview of reviews, and five primary studies). Twenty reviews (out of 22) reporting on effectiveness were rated "good" or "fair" quality. One primary study included in the narrative synthesis was rated as having a "low" risk of bias. The evidence covered the effects of CDSSs across various healthcare settings and specialties. The type of decision support provided by the CDSSs and outcomes were heterogeneous between studies. Overall, computerized provider order entry with medication-related CDSSs were associated with reduced medication errors (moderate strength of evidence) and prevention of adverse drug events (low strength of evidence). Improved or targeted medication-related CDSSs were associated with reductions of medication errors and adverse drug events (moderate strength of evidence). However, alert override rates were high and varied between studies, and the appropriateness of the overrides was largely influenced by the type of alert. Other unintended consequences included CDSS-related errors, overdependence on alerts, alert fatigue, inappropriate alert overrides, and provider burnout. An additional 48 articles focused on barriers and facilitators of CDSS implementation.

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Conclusions. Overall, CDSSs reduce medication errors and adverse drug events, with moderate- and low-certainty evidence, respectively. However, there were several unintended consequences of CDSS implementation and use. The evidence of benefits and harms was generally reported in different studies with varying contexts, making the net benefit difficult to estimate. Future research should focus on measuring these outcomes and unintended consequences in the same study to generate evidence on both the benefits and harms associated with using a CDSS in the same context.

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1. Background and Purpose

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 patient safety practices (PSPs) 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 2023, AHRQ launched its fourth iteration of the Making Healthcare Safer Report (MHS IV). Computerized Clinical Decision Support Systems (CDSSs) 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]

Adverse drug events are defined by the Institute of Medicine as "an injury resulting from medical intervention related to a drug."[2] These include nonpreventable events, such as adverse drug reactions, and preventable events caused by medication errors. Medication errors are defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm."[3]

Adverse drug events are a leading type of healthcare-related harm, accounting for 39 percent of all adverse events in the inpatient setting.[4] Of these events, it is estimated that 27 percent are preventable and 24 percent have a severity level of serious (defined as causing "harm that resulted in substantial intervention or prolonged recovery") or higher. Similarly, these events are also common in the outpatient setting, with an estimated 25 percent of patients experiencing an adverse drug event after an encounter. Of these events, 11 percent are preventable, 28 percent are ameliorable, and 13 percent are serious.[5] There is substantial opportunity to reduce the frequency and severity of adverse drug events and improve patient outcomes.

1.1 Overview of the Patient Safety Practice

CDSSs can provide support for various clinical decisions related to medications, laboratory tests, preventive care, and diagnoses. In the prioritization process, the MHS IV TEP noted that CDSSs is a very broad topic and would likely need narrowing on either specific outcomes or specific clinical contexts. As a result, this rapid review focused on CDSSs providing medication-related alerts, such as reminders or recommendations, to prevent medication errors and ameliorate adverse drug events at the point of care. MHS (2001) addressed "Computerized Physician Order Entry (CPOE) with Clinical Decision Support Systems (CDSSs)" (Chapter 6 in the Adverse Drug Event section) and summarized eight studies as well as potential for harm, and cost and implementation.[6] The report concluded that CDSSs improve the quality and safety of prescribing; however, impact on patient outcomes was limited. It is important to note that both CPOE and CDSSs are not specific to physicians and are now used by several types of providers, including physician assistants, pharmacists, and nursing staff.

MHS II (2013) provided an update focused on "Computerized Provider Order Entry With Clinical Decision Support Systems: Brief Update Review" (Chapter 41), also focused on adverse drug events and medication errors, and summarized three systematic reviews as well as unintended consequences, and implementation and cost.[7] This report stated that "conclusions regarding CPOE+CDSS in the 2001 edition of 'Making Health Care Safer' thus appear to stand largely unchanged a decade later." MHS III (2020) did not address CPOE with CDSSs. The report focused on other PSPs for "Reducing ADEs in Older Adults" (Chapter 9) and covered CDSSs for other health topics but not adverse drug events.[8]

There have been important changes in the landscape of CDSSs since the publication of MHS I (2001) and II (2013). These two reports described the effects of CDSSs developed and integrated within homegrown electronic health record (EHR) systems, where the tools were tailored to the population and largely customizable. In particular, the early publications of the 1990s and 2000s described investigator-initiated interventions that were developed and implemented locally by leaders in this field. This allowed for iterations and testing to develop effective CDSSs, with studies demonstrating substantial reductions in medication errors and adverse drug events (such as the 55% reduction in non-intercepted errors in one early randomized trial).[9]

In 2009, the Health Information Technology for Economic and Clinical Health (HITECH) Act incentivized health systems and providers to adopt a certified EHR and make *meaningful use* of the information and technology to improve the quality and safety of healthcare. The most significant change in EHR uptake occurred from 2013 to 2014, corresponding with Stage 2 of *meaningful use*; adoption of certified EHRs at non-Federal acute care hospitals increased from 59 percent to 97 percent and for office-based physicians from 48 percent to 74 percent, and stayed relatively stable through the end of the study period in 2021.[10, 11] One of the key requirements for *meaningful use* in Stage 2 was use of a CDSS, in particular to "implement 5 clinical decision support interventions related to 4 or more clinical quality measures, if applicable, at a relevant point in patient care for the entire EHR reporting period" and "enable the functionality for drug-drug and drug-allergy interaction checks for the entire EHR reporting period."[12] At this time, CDSSs were not widespread in the United States, creating a need for scalable tools that could be integrated with various certified EHRs. As a result, current CDSSs are largely vendor developed and less tailored to local contexts. Although some EHR vendors develop and integrate CDSSs, most tools are available from companies that are different from the EHR vendors. These substantial changes and incentives have made development, implementation, and evaluation of CDSSs a moving target.

1.2 Purpose of the Rapid Review

The overall purpose of this rapid review is to determine the effect of CDSSs on the key clinical outcomes of medication errors and adverse drug events. We also consider unintended outcomes such as alert fatigue, low-value alerts, and unsubstantiated overrides of alerts, and how CDSSs can be effectively implemented.

1.3 Review Questions

1. What are the frequency and severity of medication errors and adverse drug events?
2. What patient safety measures or indicators have been used to examine the frequency and severity of medication errors and adverse drug events?
3. In what ways is computerized clinical decision support used for preventing medication errors and adverse drug events, and in what settings is it used?
4. What is the reported rationale for using computerized clinical decision support to prevent or mitigate the harms of medication errors or adverse drug events?
5. What are the effectiveness and unintended effects of using computerized clinical decision support on the frequency of medication errors and adverse drug events?
6. What are the most common barriers and facilitators of implementing computerized clinical decision support to reduce the frequency of medication errors and adverse drug events?
7. What resources (e.g., cost, staff, time) are required for implementation of computerized clinical decision support practices?
8. What toolkits are available to support implementation of computerized clinical decision support to reduce the frequency of medication errors and adverse drug events?

2. Methods

We followed processes proposed by the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program.[13] The final protocol for this rapid review is posted on the AHRQ website at https://www.ahrq.gov/research/findings/making-healthcare-safer/mhs4/index.html.

For this rapid review, strategic adjustments were made to streamline traditional systematic review processes and deliver an evidence product in the allotted time. Adjustments included 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), and restricting the search to studies published since 2015 (corresponding with the release of the proposed Meaningful Use Stage 3 criteria), in English and conducted in the United States. For this report, we used independent dual review to screen all titles/abstracts and full text articles. Conflicts were discussed and resolved during team meetings. We searched for recent systematic reviews and relied primarily on the content of any such systematic review that was found. We did not perform an independent assessment of original studies cited in any such systematic review.

We asked 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 focused 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 asked content experts to answer Review Questions 3 and 4 by citing selected references, including patient safety practices (PSPs) used and explanations of the rationale presented in the studies we found for Review Question 5. For Review Questions 6 and 7, we focused on the barriers, facilitators, and required resources reported in the studies we found for Review Question 5, and supplemented this with systematic reviews on implementation. For Review Question 8, we searched for publicly available patient safety toolkits developed by AHRQ or other organizations that could help to support implementation of the PSP. To accomplish that task, we reviewed AHRQ's Patient Safety Network (PSNet) and AHRQ's listing of patient safety-related toolkits and we included any toolkits mentioned in the studies we found for Review Question 5.[14, 15]

2.1 Eligibility Criteria for Studies of Effectiveness

We searched for primary 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	Adult patients (18+ years) receiving care from a healthcare professional	Pediatric patients (under 18 years) because pediatrics is a different patient population with different needs (such as differences in prescribing [e.g., weight-based prescribing], ordering, and preparing medications); involvement of proxy decision makers such as caregivers; and it is a separate literature base.
Intervention	Computerized clinical decision support providing medication-related alerts	Computerized clinical decision support that— • Provides alerts for only one drug (rationale: not scalable), or • Focuses on vaccines
Comparator	Usual care or alternative clinical decision support	N/A

Outcome	• Clinical outcomes
	  ○ Adverse drug event rates
	  ○ Medication error rates
	• Provider outcomes
	  ○ Changes in prescribing behavior
	• Implementation outcomes
	  ○ Rates of valid and/or useful alerts
	  ○ Unsubstantiated override rates
	• Unintended consequences
	  ○ Alert fatigue
		No outcomes of interest

Timing	Studies published since 2015, corresponding with the release of the proposed electronic health record (EHR) Meaningful Use Stage 3 criteria by the Centers for Medicare & Medicaid Services (CMS) focusing on advanced use of EHRs and better health outcomes for patients.	Last year of data used in the analysis was 2014 or earlier for original research
Setting	Inpatient and outpatient healthcare settings in the United States	• Providers not using electronic health record • Nursing home or prison settings • No site in the United States
Type of studies	• Systematic reviews • Randomized trials • Nonrandomized trials • Controlled before-after studies • Interrupted time series studies and repeated measures studies	• Not published in English • Not original research or systematic review • Other study designs (e.g., uncontrolled before-after studies or cross-sectional studies)

N/A = not applicable

2.2 Literature Searches for Studies of Effectiveness

We searched PubMed, and Cochrane Library, supplemented by a narrowly focused search for unpublished reports, primary studies, and systematic reviews that are publicly available from governmental agencies, professional societies, or membership organizations with a strong interest in CDSSs, including AHRQ, National Quality

Forum (NQF), and American Hospital Association (AHA). For details of the search strategy, see Appendix A.

2.3 Data Extraction (Selecting and Coding)

The title and abstract of each citation were screened by two independent team members based on predefined eligibility criteria (Table 1). The full text of each remaining potentially eligible article was reviewed by two independent members to confirm eligibility and extract data. All conflicts were resolved in team meetings. At data extraction, a second team member validated a randomly selected 10 percent sample of the articles to confirm the accuracy of extracted data.

We prioritized our efforts by extracting detailed information from the highest quality studies. We sought to extract information from systematic reviews, randomized controlled trials (RCTs), nonrandomized controlled trials (NRCTs), controlled before-after (CBA) studies, and interrupted time series (ITS) studies and repeated measures studies.

Data extraction is organized according to the review questions, and includes author, publication year, data years, study designs, healthcare setting, intervention, outcomes (e.g., reduction in medication errors or adverse drug events, unintended consequences), key findings and quality assessment.

2.4 Risk of Bias (Quality) Assessment

Our intention was to assess the risk of bias for any included RCTs for Review Question 5 with the Cochrane Collaboration's tool for assessing the risk of bias; and to assess nonrandomized studies for risk of bias using the ROBINS-I tool for assessing the Risk Of Bias In Non-randomized Studies – of Interventions.[16, 17] As it turned out, we did not identify any eligible RCTs or nonrandomized studies for Review Question 5. The one new original study we included in Review Question 5 was an assessment of the sensitivity and specificity of two different methods to trigger medication alerts, and thus to assess risk of bias we used the QUADAS-2 instrument.

For a recent eligible systematic review, the primary reviewer used the criteria developed by the United States Preventive Services Task Force Methods Workgroup for assessing the quality of systematic reviews.[18]

- 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."

2.5 Strategy for Data Synthesis

We did not conduct a meta-analysis; our synthesis was narrative. For Review Question 5 about the effectiveness of CDSSs, we recorded information about the context of each primary study or systematic review and whether the effectiveness of the PSP differed across healthcare settings. If there was more than one systematic review on a specific topic, we selected the best review for inclusion in the narrative synthesis, based on recency, the largest number of studies, and quality of the review.

We graded the strength of evidence for the PSP using the methods outlined in the AHRQ Effective Health Care Program Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[19] To assess the strength of evidence for the included systematic reviews, we either used the strength (or certainty) of evidence reported by the original authors of the systematic review, or if this was not available we assessed it ourselves considering how many original studies were included in the review, whether the included studies were RCTs or observational studies or a mix of both, whether the synthesis of evidence in the systematic review was meta-analytic or narrative, the size of the intervention effect, the heterogeneity of the results, what the authors of the systematic review stated as limitations of their review, and lastly how the authors of the systematic review described their conclusions. The strength of evidence scale used the following overall ratings for each systematic review: "high," "moderate," "low," and "very low."

2.6 Analysis of Subgroups or Subsets

For this rapid review, we intended to assess the effectiveness of clinical decision support across different contexts, such as in-hospital or outpatient settings.

3. Evidence Summary

3.1 Benefits and Harms

- This rapid review identified 27 systematic reviews, one overview of reviews, and five primary studies that described the effects of CDSSs on the clinical outcomes of medication errors and adverse drug events, related implementation outcomes such as rates of medication alert overrides, and unintended consequences of CDSS use.
- 20 reviews (out of 22) reporting on effectiveness were rated "good" or "fair" quality. One primary study included in the narrative synthesis was rated as having a "low" risk of bias using the QUADAS-2 tool.
- The systematic reviews covered the effects of CDSSs across various healthcare settings (e.g., general inpatient, intensive care unit (ICU), emergency department (ED), and ambulatory/outpatient care) and specialties (e.g., allergy, anticoagulation, and oncology), demonstrating the breadth of the literature.
- The type of decision support provided by the CDSSs (e.g., dose checks, drug-disease contraindications) and outcomes (e.g., specific adverse drug events) were heterogeneous between studies.
- The evidence focused on the effects of CPOE with CDSSs compared with usual care or paper-based prescribing on the rates of medication errors and reported significant reductions. However, most of the studies included in the reviews used uncontrolled study designs, such as pre-post comparisons, which are considered lower quality evidence and the findings should be interpreted with caution around causation.
- Only one systematic review conducted meta-analyses focused on RCT and ITS study designs. It showed "moderate" level of certainty of evidence that CPOE with CDSSs reduced medication errors compared with usual care or paper-based prescribing. However, the certainty of evidence that CPOE with CDSSs reduced adverse drug events was considered "very low."
- The same systematic review conducted several meta-analyses evaluating the effect of CPOE with standard versus improved CDSSs and provided "moderate" certainty that improved CDSSs reduced medication errors and adverse drug events.
- Alert override rates were high and varied between studies; the appropriateness of overrides was largely influenced by the type of medication-related alert.
- Alert relevance based on the positive predictive values (PPVs) varied tenfold based on the type of decision support provided and context, with higher PPVs when alerts were informed by patient-level data.

- Several unintended consequences were identified and included CPOE with CDSS-related medication errors, overdependence on alerts, alert fatigue, inappropriate alert overrides, and provider burnout.
- Notably, the estimates of the effect of the CDSSs on medication errors, adverse drug events, related implementation outcomes such as alert overrides, and unintended consequences of use all come from different studies.

3.2 Future Research Needs

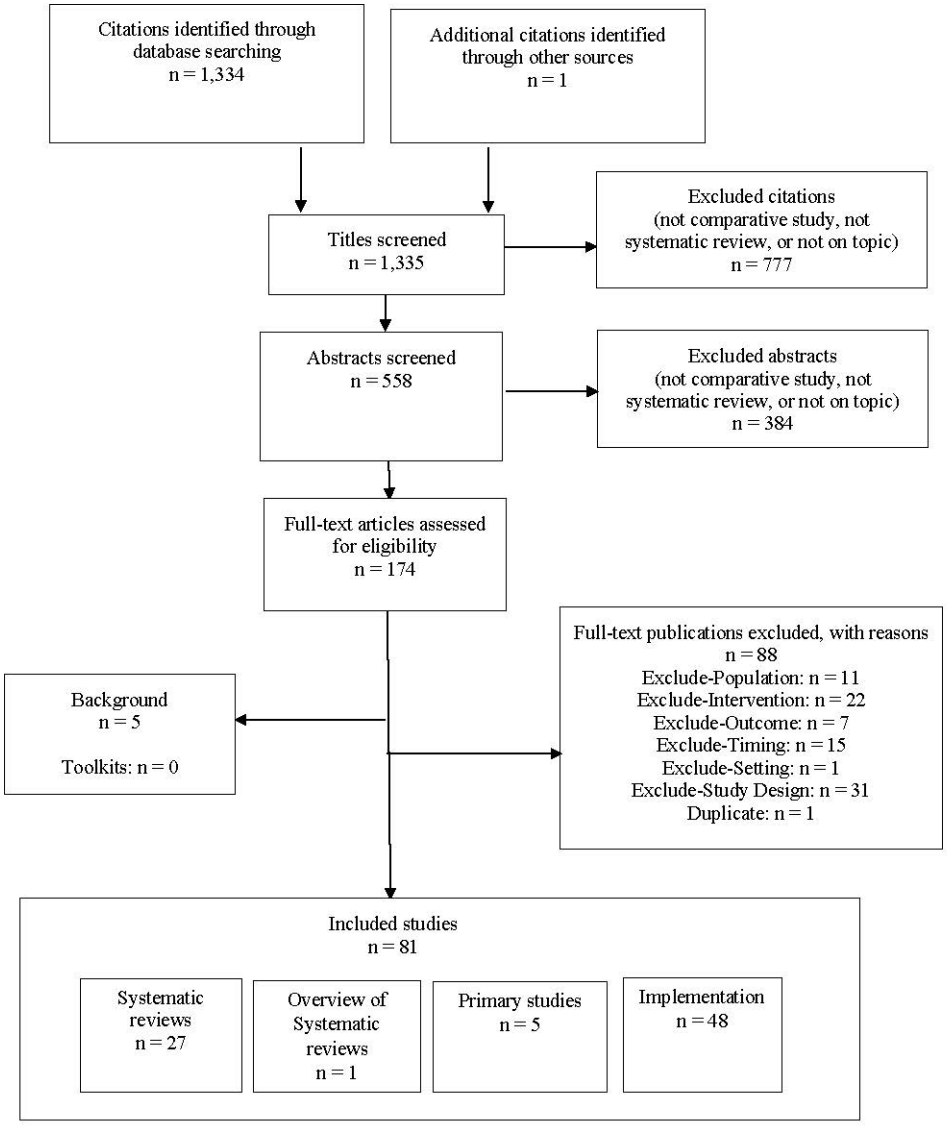
- Current data make it challenging to assess the net benefit of using CDSSs.
- Future research should focus on measuring the effects of CDSSs on all related outcomes (e.g., clinical, implementation, and unintended consequences) in the same study to control for context.
- These studies should employ RCT or controlled quasi-experimental designs to generate stronger evidence around causation.
- Future publications should provide detailed information on the characteristics of the CDSS (e.g., basic versus advanced alerts), type of decision support provided by the CDSS, populations under study, and characteristics of the healthcare organizations to clearly describe the specific context of implementation and use. This information is critical for interpreting the results and assessing generalizability of the findings.
- Future research should also focus on how CDSSs could be made more effective broadly, given that CDSSs are now largely vendor developed. This area of study should also focus on defining successful collaborations between vendors, researchers, and clinicians for developing and evaluating the effects of these vendor-based CDSSs on medication errors and adverse drug events.
- Development of CDSSs leveraging artificial intelligence, such as natural language processing and complex machine learning, could substantially improve the effectiveness of these tools by providing more relevant and tailored alerts at the point of care.
- Future research should also focus on the development of patient safety measures specific to medication errors and adverse drug events to allow for tracking over time and evaluating quality improvement initiatives.
- Studies should also assess disparities in the impact of medication-related alerts on different segments of the population and between different types of health systems.

4. Evidence Base

4.1 Number of Studies

Our searches retrieved 1,335 unique titles and abstracts from which we reviewed 174 full-text articles for eligibility (Figure 1). We found 81 studies that met our eligibility criteria.[20-100] A listing of studies excluded during full-text review is included in Appendix B, List of Excluded Studies, and information abstracted from the systematic reviews is in Table 2.

Figure 1. Results of the search and screening



4.2 Findings for Review Questions

4.2.1 Review Question 1. What Are the Frequency and Severity of Medication Errors and Adverse Drug Events?

Adverse drug events are defined by the Institute of Medicine as "an injury resulting from medical intervention related to a drug."[2] These include nonpreventable events, such as adverse drug reactions, and preventable events caused by medication errors. Medication errors are defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm."[3]

Adverse drug events are a leading type of healthcare-related harm, accounting for 39 percent of all adverse events in the inpatient setting.[4] Of these events, it is estimated that 27 percent are preventable and 24 percent have a severity of serious (defined as causing "harm that resulted in substantial intervention or prolonged recovery") or higher. Similarly, these events are also common in the outpatient setting with an estimated 25 percent of patients experiencing an adverse drug event after an encounter. Of these events, 11 percent are preventable, 28 percent are ameliorable, and 13 percent are serious.[5] There is substantial opportunity to reduce the frequency and severity of adverse drug events and improve patient outcomes.

Medication errors cause the subset of adverse drug events that are preventable. It has been estimated that 1.7 percent of prescriptions from pharmacies in the United States included a medication error; however, only ~0.1 percent were considered to be clinically important.[101] Although medication errors are common, these events may not cause patient harm even if the medication reaches the patient. Errors can occur at any point between medication ordering and administration with ordering errors accounting for ~50 percent of all medication errors.[102]

4.2.2 Review Question 2. What Patient Safety Measures or Indicators Have Been Used To Examine the Frequency and Severity of Medication Errors and Adverse Drug Events?

We did not identify any validated patient safety measures or indicators to report on the frequency or severity of medication errors or adverse drug events that have been endorsed for use in nationally recognized quality measurement programs. We noted great variability in the definitions of medication errors and adverse drug events in the literature described in Review Question 5. There were no standard metrics for these two outcomes, likely because the types of medication errors and adverse drug events targeted by the CDSSs vary depending on the context.

4.2.3 Review Question 3. In What Ways Is Computerized Clinical Decision Support Used for Preventing Medication Errors and Adverse Drug Events, and in What Settings Is It Used?

This rapid review focused on a specific PSP, CDSSs, to reduce medication errors and adverse drug events. CDSSs can provide a wide range of alerts and recommendations for providers at the point of care about:

- Allergies
- Drug-drug interactions
- Drug-disease interactions
- Appropriate dosing, duration, and frequency
- Routes of administration
- Administration scheduling
- Therapeutic monitoring
- Relevant laboratory results
- Potentially inappropriate prescribing
- Wrong medication
- Wrong patient

These types of CDSSs are used across traditional healthcare settings in hospitals (e.g., general and surgical wards, and ICUs), EDs, ambulatory care, outpatient clinics, and specialty care. Although not covered in this review, CDSSs can also be used to reduce medication errors and adverse drug events in other settings where medications are dispensed or administered, such as pharmacies or long-term care.

4.2.4 Review Question 4. What Is the Reported Rationale for Using Computerized Clinical Decision Support To Prevent or Mitigate the Harms of Medication Errors or Adverse Drug Events?

The rationale for CDSSs was perhaps best summed up by Clement J. McDonald, one of the early innovators of health informatics, who wrote in 1976:[103]

"Implicit in currently available remedies for medical errors is the belief that man is perfectable and his errors can be eliminated by training or coercion…. However, man is not perfectable. There are limits to man's capabilities as an information processor that assure the occurrence of random errors in his activities… Given this background, it seems reasonable to hypothesize that many medical errors are due to the physician's intrinsic limits rather than to remediable flaws in his fund of knowledge."

"Information theory states that to eliminate such errors, one must commit more time to the processing of the relevant data. Since many of the physician's informational tasks are rote and repetitive, a computer, given the necessary decision

logic (protocols), could perform them and thereby provide the necessary processing time." In other words, the computer can assess for the possibility of errors or drug-drug interactions with greater speed and reliability than the human mind.

While Dr. McDonald's rationale was framed in terms of male physicians' use of computers to reduce errors, CDSSs are now also used by women and other clinical specialties (nursing, pharmacy, physical therapy, etc.).

4.2.5 Review Question 5. What Are the Effectiveness and Unintended Effects of Using Computerized Clinical Decision Support on the Frequency of Medication Errors and Adverse Drug Events?

We identified 27 systematic reviews, one overview of reviews, and five primary research studies that met the inclusion criteria for this rapid review. We presented the evidence by focusing on the findings of good- or fair-quality systematic reviews and meta-analyses and supplemented these findings with results from individual primary studies that were published more recently (i.e., since 2015) and as a result were not included in the systematic reviews. The evidence for effectiveness is presented by healthcare setting (i.e., general inpatient, ICU, ED, and ambulatory/outpatient care) and by content area (i.e., allergy, anticoagulation, and oncology) for reviews focused on medical specialties.

4.2.5.2 Inpatient – General

We identified six systematic reviews[35, 37, 40, 70, 78, 95] and one overview of systematic reviews[21] that included assessments of CDSSs predominantly in the general inpatient setting published in 2015 or later (Table 2). One of the systematic reviews focused on potentially inappropriate prescribing in older adults;[37] we do not focus on this topic since PSPs for deprescribing is a separate chapter in MHS IV; however, the general findings are summarized in Table 1.

The overview of seven systematic reviews conducted by Abraham et al. (2020) included studies describing the effects of CPOE with or without CDSSs on medication errors and adverse drug events;[21] all systematic reviews included in the overview were published in 2017 or earlier. The overview showed that most studies included in the systematic reviews used uncontrolled pre-post or observational study designs, and that RCTs and controlled quasi-experimental studies were rare. The overview reported significant relative risk reductions in the outcomes of interest with wide variation between systematic review pooled results for medication errors (range: 54% to 92%) and adverse drug events (range: 35% to 53%). Notably, 24 percent of primary studies were only included in one review and only ~2 percent were included in six reviews, impacting the findings and emphasizing the challenges in searching and summarizing evidence in this area.

Our rapid review builds on where the overview left off, with an overlap of only one systematic review.[75] Table 2 shows that most systematic reviews continued to

predominantly include studies using uncontrolled designs, which are considered lower quality evidence and should be interpreted with caution around causation.

Table 2. Characteristics of included systematic reviews by healthcare settings, specialties, and implementation outcomes

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
Inpatient – General	Ciapponi, 2021[35]* inception to 1/2020	6 RCT 7 ITS (2 CBA reanalyzed as ITS)	9 Inpatient 2 Inpatient-ICU 1 ED 1 Inpatient/ Outpatient/ ED	CPOE with a CDSS "Electronic prescribing systems, including computerized physician ordering entry (CPOE) and clinical decision support systems (CDSS). In general, these refer to the process of a medical professional entering and sending medication orders and treatment instructions electronically via a computer application instead of on paper charts. They are computer-based programs that analyse data within electronic health records to provide prompts and reminders to assist healthcare providers in implementing treatments at the point of care."	Medication errors Adverse drug events	"Moderate-certainty evidence shows that CPOE/CDSS probably reduce medication errors compared to paper-based systems (OR 0.74, 95%CI 0.31 to 1.79; 2 studies, n=88)." "Moderate-certainty evidence shows that, compared with standard CPOE/CDSS, improved CPOE/CDSS probably reduce medication errors (OR 0.85, 95%CI 0.74 to 0.97; 2 studies, n=630)." "Low-certainty evidence suggests that prioritised alerts provided by CPOE/CDSS may prevent [adverse drug events] compared to non-prioritised (inconsequential) alerts (MD 1.98, 95%CI 1.65 to 2.31; 1 study; participant numbers unavailable)."	Good
	Gates, 2021[40] 1/2005 to 3/2019	1 RCT 2 ITS 1 CBA 14 Other	13 Inpatient 5 Inpatient-ICU	Electronic medication system with or without a CDSS "We defined an electronic medication	Medication errors Adverse drug events	"Of 10 studies of prescribing error rates, 9 reported a reduction but variable denominators precluded meta-	Good

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				system (EMS) as a computer-based system for electronic prescribing and/or administration of medicines. Systems with or without detailed [clinical decision support] and those integrated or not with larger hospital electronic health record systems were included."		analysis." "Meta-analysis showed a significant reduction in [medication administration error] rates post-[electronic medication system] implementation (pooled RR: 0.77, 95% CI: 0.72–0.83, *P*=.004)" (n=3). "Meta-analysis results indicated that the introduction of [electronic medication systems] had no significant effect on patient harm (pooled RR: 1.22, 95% CI: 0.18–8.38, *P*=.8)." (n=5) "Twelve studies provided qualitative examples of [system-related errors] though only 5 reported on [system-related error] rates."	
	Roumeliotis, 2019[78] 1/2007 to 1/2018	11 RCT 2 ITS 25 Other	11 Inpatient 19 Inpatient-ICU 4 ED 2 OR 2 N/S	CPOE, CDSS, CPOE with a CDSS "Eligible interventions were an electronic prescribing strategy, and these were compared with a control without electronic prescribing support." "Interventions were categorized as stand-alone	Medication errors Adverse drug events	"Meta-analysis for the effect of electronic prescribing on medication error showed a significant reduction in overall medication errors (RR 0.24 (95% CI 0.13, 0.46), I^2 98%, n = 11), with high heterogeneity (0 RCT)." (GRADE quality of evidence: Very low)	Good

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				Clinical Decision Support Systems (CDSS) or Computerized Physician Order Entry (CPOE). CPOE functionality was further defined as without CDSS, embedded with limited CDSS (dosing limits and allergy), or advanced CDSS (decision support for weight-based dosing, renal dosing, or drug-drug interactions).” “Given that the majority of computerized order entry systems had a decision support system of some form built within them, they were regarded as a single category for analyses.”		“Meta-analysis demonstrated a reduction in dosing errors (RR 0.17 (95% CI 0.08, 0.38), I^2 96%, n = 9) with electronic versus no electronic strategy, with very high heterogeneity.” (0 RCT, GRADE quality of evidence: Very low) “Electronic prescribing strategies were associated with reduced [adverse drug events] (RR 0.52 (95% CI 0.40, 0.68), I^2 0%, n = 2), but not preventable [adverse drug events] (RR 0.55 (95% CI 0.30, 1.01), I^2 78%, n = 3), versus no electronic strategy.” (0 RCT, GRADE quality of evidence: Very low)	
	Dalton, 2018[37] inception to 10/2017	2 RCT 2 ITS 4 Other	6 Inpatient 2 ED	Computer-generated recommendations “In four of the studies, the intervention utilised clinical decision support within a CPOE system. In three other studies, the intervention comprised of alerts or reminders embedded into a CPOE system. The remaining study involved the	Medication errors (PIP) Adverse drug events	“Seven studies showed either a statistically significant reduction in the proportion of patients prescribed a potentially inappropriate medicine (PIM) (absolute risk reduction {ARR} 1.3–30.1%), or in PIMs ordered (ARR 2–5.9%).” “It was only possible to include three studies in	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				use of INTERcheck® software, a 'computerised prescription support system' which aimed to reduce potentially inappropriate medicines (PIMs), potentially severe drug-drug interactions and anticholinergic burden."		the meta-analysis—which demonstrated that intervention patients were less likely to be prescribed a PIM (odds ratio 0.6; 95% CI 0.38, 0.93)." "Three of the included studies assessed clinical outcomes. Griffey *et al.* demonstrated a statistically significant reduction in [adverse drug events] (3.4% vs 7.1%; *P* = 0.02) and Peterson *et al.* showed a statistically significant reduction in inpatient falls (0.28 vs 0.64 falls per 100 patient days; *P* = 0.001)." "Four of the included studies have data on acceptance rates or levels of agreement with the computer's recommendations " ranging from 7.5% to 95%.	
	Vélez-Díaz-Pallarés, 2018[95] 1995 to 2016	1 RCT 3 ITS 15 Other	13 Inpatient 6 Inpatient-ICU	CPOE with a CDSS "The research group adopted the definition of CPOE provided by [the Agency for Healthcare Research and Quality], whereby CPOE refers to any system in which clinicians	Medication errors Adverse drug events	"Significant reductions in pre-scription errors were observed only when CPOE was used, with a 71% overall reduction (relative risk [RR], 0.29 [95% CI, 0.10–0.85]; I^2 = 99%), […] whereas no significant	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				directly enter medication orders into a computer system, which then transmits the order directly to a pharmacy with a [clinical decision support] system in place." "It was noteworthy that, together with CPOE implementation, some authors included more complex interventions such as education (seminars and newsletters), pharmacist order checking, and use of interprofessional teams."		differences in rates of validation, dispensing, and administration errors with CPOE versus manual prescribing were observed." "CPOE implementation was associated with an increase in the number of other types of errors (e.g., duplication errors)." (RR, 1.85 [95% CI, 1.08–3.17]; n=7)	
	Page, 2017[70] 1/2000 to 2/2016	3 RCT 3 ITS 17 Other	22 Inpatient 1 Inpatient-ICU	CPOE with a CDSS "Studies must have evaluated the impact of automatic, interruptive alert/s that provide immediate notification of potential errors or safety risks to a prescriber at the time of medication order entry."	Medication errors (prescriber behavior) Adverse drug events	"Half of the studies (53%, n= 17) reported a statistically significant beneficial effect from the intervention alert; 34% (n =11) reported no statistically significant effect, and 6% (n =2) reported a significant detrimental effect. Two studies also evaluated the effect of alerts on patient outcome measures; neither finding that patient outcomes significantly improved following alert implementation (6%, n=2)."	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
Inpatient – Intensive Care Unit (ICU)	Prgomet, 2017[75]* 1/2000 to 1/2016	1 RCT 9 Other	10 Inpatient-ICU	Commercial CPOE, CPOE with a CDSS, CPOE with a targeted CDSS "Studies were eligible for inclusion if they: […] evaluated the impact of moving from paper-based ordering to CPOE or evaluated the addition of a targeted CDSS to an existing CPOE system." "We defined CPOE as computer-based systems used for entering orders, including laboratory tests, imaging, nutrition, blood products, and medication prescriptions. Almost all CPOE systems have some level of decision support to assist ordering decisions; however, the degree of sophistication of CDSSs can vary from basic duplicate order alerts to complex algorithms based on patient-specific data. Where studies evaluated the addition of a specific CDSS to an existing CPOE system, such as algorithms developed in response to identified medical errors or quality	Medication errors	"There was evidence that the introduction of CPOE was associated with a significant reduction in the medication error rate by 85% (pooled RR: 0.15, 95% confidence interval (CI), 0.03–0.80, P=.03)." " Subgroup analysis by ICU type showed no evidence of significant error reduction following CPOE implementation for studies conducted in adult ICUs (pooled RR: 0.11, 95% CI, 0.00–3.41, P=.1) or in pediatric ICUs (pooled RR: 0.21, 95% CI, 0.02–2.65, P=.1)." "Three [of the adult ICU] studies reported new error types arising due to CPOE."	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				improvement initiatives, we defined these as "targeted" CDSSs."			
Emergency Department (ED)	Hajesmaeel Gohari, 2021[41] 2003 to 11/2018	2 RCT 1 CBA 1 ITS 7 Other	11 ED	CPOE, CDSS, CPOE with a CDSS "CDSS is a computerized system that aids health care providers to make evidence-based clinical decisions about a particular patient at the point of care." "Six studies (54.5%) evaluated CPOE with CDSS, 4 studies (36.5%) evaluated only CDSS, and 1 (9%) evaluated only CPOE." "In this review, 10 of 11 studies (91%) used CDSS; 9 studies used dosing guidance, 4 used drug-allergy checking, 3 used formulary decision, 3 used drug interaction, and 2 used duplicate therapy of basic properties of CDSS. Advanced properties were used in 8 studies, of which 4 related to dosing support for renal insufficiency and geriatric patients, 3 related to guidance for medication-related laboratory testing, and 1 related to a drug-disease	Medication errors Adverse drug events	"Generally, the percentage of reduction in the rate of prescribing errors, [adverse drug events], excessive doses, and inappropriate prescribing in 6 articles was from 2% to 31%. Also, the percentage of increase in the rate of appropriate prescribing and dosing and compliance with established guidelines was from 5.2% to 21.5%."	Good

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				contraindication."			
Ambulatory and Outpatient Care	Cerqueira, 2021[32] inception to 12/2020	3 RCT 1 NRCT 1 CBA 4 Other	9 Ambulatory/ Outpatient	CPOE with an interruptive CDSS "This review included [clinical decision support] alerts defined as 'knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and healthcare.'" "Studies must have evaluated the impact of automatic interruptive alerts that provide immediate notification of potential errors or risks at time of order entry."	Medication errors (prescriber behavior)	"Seven of the nine studies demonstrated significant provider behaviour change." "Clinician feedback, rarely solicited, expressed frustration with alerts creating a time delay."	Good
	Scott, 2018[80] inception to 1/2018	10 RCT 2 ITS 8 Other	6 Inpatient 1 ED 1 Inpatient/ Outpatient 9 Ambulatory/ Outpatient 3 LTC	EMR-enabled CDSS "Articles were selected […] if they described electronic prescribing software integrated or interfaced with EMR (or its CPOE or e-prescribing components) and using CDSS in some form that enables prescribers to make changes at the time of prescribing in adults. Studies describing stand-alone e-prescribing systems or EMR-linked systems devoid of CDSS	Medication errors (PIP) Adverse drug events	"The totality of evidence favours EMR-enabled CDSS as being effective in reducing the prescribing of [potentially inappropriate medications] in hospitals by up to 50%, but less effective in ambulatory care settings (up to 23%) and borderline effective in [residential aged care facilities]." "While absolute effects in most positive studies were modest, they suggest EMR-enabled CDSS are feasible and	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				targeting [potentially inappropriate medications] (i.e. offering only medication reconciliation, dose checks, monitoring for medication errors, or basic formulary information) were excluded."		acceptable to clinicians, and if certain design features are adhered to, there is potential for even greater impact."	
	Nabovati, 2017[64] inception to 03/2014	5 RCT 5 ITS 9 Other	7 Inpatient 11 Ambulatory/ Outpatient 1 Inpatient/ Outpatient	Information Technology (IT)-based interventions "An IT-based intervention was broadly defined as a strategy that employs any IT-based system such as CDSS and CPOE." "We defined an IT-based intervention as a system which generated advice and delivered it to either the prescriber or another (non-prescriber) care provider, and thus excluded studies wherein IT solutions were used only to support the intervention (e.g. to collect data)."	Medication errors (potential DDIs) Adverse drug events (DDIs)	"Sixty-four percent of prescriber-directed interventions, and all non-prescriber interventions, were effective." "Most studies that measured surrogate outcomes (e.g. potential DDIs) and other outcomes (e.g. adherence to alerts) showed improvements." "Only two studies measured clinical outcomes: an RCT that showed no significant improvement and an [observational study with controls] that showed improvement, but did not statistically assess the effect." "The possible harm (i.e. unintended consequences) resulting from IT-based interventions was reported only in one study."	Poor
Laboratory	Whitehead,	3 RCT7	4 Inpatient	CDSS	Medication	"We found	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
Alerts – Across Healthcare Settings	2019[97]* 1/1990 to 4/2016	Other	2 Inpatient-ICU 1 Outpatient 1 Inpatient/ Ambulatory 1 Ambulatory pharmacy 1 LTC	"[Clinical decision support] tools designed for use in clinical care to detect patients who are at risk of or have experienced a medication-related adverse event that included 2 or more pieces of information, at least 1 of which was a laboratory test result."	errors Adverse drug events	moderate and consistent evidence that [clinical decision support] tools applied at medication ordering or dispensing can increase prescriptions of appropriate medications or dosages [6 results, pooled risk ratio (RR), 1.48; 95% CI, 1.27–1.74]." "The evidence that [clinical decision support] tools reduced adverse drug events was inconsistent (5 results, pooled RR, 0.69; 95% CI, 0.46–1.03)." "We did not find studies that investigated potential harms or unintended consequences of [clinical decision support] tools."	
Allergy	Légat, 2018[53]* inception to 02/2016	7 Other	6 Inpatient 1 Inpatient-ICU	CPOE with a CDSS "When a prescription poses a threat to the patient, the clinical decision support system (CDSS) warns the user by providing an alert message." "We focused on searching for articles related to CDSS and associated alerts in the domain of [drug allergies]."	Medication errors Adverse drug events (drug allergy)	"CPOE systems can help in making fewer [prescribing errors], although not all studies quantify this improvement." Five studies demonstrated significant reductions in medication errors or adverse drug events using CPOE with a CDSS. "We found only one study specifically	Poor

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
						reporting outcomes related to CDSS for drug allergies. It showed that adverse drug events resulting from overridden drug allergy alerts do not occur frequently."	
	Bassir, 2022[26]* 1/2000 to 6/2021	1 CBA 3 Other	3 Inpatient 1 Inpatient/ Outpatient	General use of EHRs, including CDSSs "Automated [clinical decision support] in EHRs."	Medication errors (premedication) Adverse drug events (hypersensitivity reactions)	"Two studies evaluated clinician behavior after reducing allergy alerts for beta-lactam antibiotics […] both studies noted that the reduction and even the elimination of allergy alerts did not lead to a significant increase in [drug hypersensitivity reactions]. "[Two] other studies created [clinical decision support] alerts [for] premedication alerts for when patients were prescribed radiocontrast media" and found that "there was a significant increase in premedication rates; however, only [one study] noticed a significant reduction in breakthrough reactions."	Fair
Anticoagulation	Austin, 2020[24]* inception to 09/2018	3 RCT 11 Other	14 Inpatient	EMR interventions, including CPOE and CDSSs	Medication errors Adverse drug events	"Evidence suggests that CPOE in conjunction with	Good

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				"We defined CPOE as 'the provider's use of computer assistance to directly enter medication orders from a computer or mobile device.' Where any additional strategies or functionality of the EMR were utilised, they were classified according to the type of CDSS."		CDSS is needed to effectively manage therapeutic anticoagulation." "Different alert-based CDSS demonstrated varying degrees of success." "Studies evaluating drug interaction alerts suggest a hard-stop alert is superior to a soft 'acknowledgment alert'."	
Oncology	Rahimi, 2019[76]* inception to 05/2017	2 ITS 25 Other	7 Inpatient 4 Ambulatory/ Outpatient 10 Inpatient/ Outpatient 6 N/S	CPOE with a CDSS, CDSS "For the purposes of this study CDSSs are defined as systems that help prescriber to make better clinical decisions at the prescription stage." **"**Studies that examined CPOE systems but did not report on CDSS features […] were excluded."	Medication errors Adverse drug events	"In most of the studies, the use of CDSSs in chemotherapy prescription has reduced medication errors, especially dosage errors." "However, in a few studies, the system has not been effective in reducing medication errors, has increased certain type of errors or has introduced new errors."	Fair
	Pawloski, 2019[71]* 01/1995 to 12/2016	1 ITS 9 Other	1 Inpatient 1 Outpatient 6 Inpatient/ Outpatient 2 N/S	CDSS "We defined a [CDSS] as any electronic system in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians to aid in	Medication errors Adverse drug events	"The rate of prescription errors was the primary study outcome in 9 studies. Although errors were defined differently across studies, prescription errors were reduced in each of the 9 studies. One study evaluated medication-related safety events,	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				clinical decision making."		demonstrating fewer events with use of [clinical decision support]." "One study evaluated prescriber alerts with [clinical decision support] tools and demonstrated that hard stops for hepatitis B screening prior to chemotherapy treatment were associated with increased screening (99.3% vs. 40.2%, P<.001) and chemoprophylaxis rates (95.8% vs. 39.2%, P<.001) and a reduction in severe exacerbations of liver disease."	
	Srinivasamurthy, 2021[86] 01/1995 to 08/2019	1 ITS 10 Other	8 Inpatient/ Outpatient 3 N/S	CPOE, CPOE with a CDSS	Medication errors Adverse drug events	"The meta-analysis of eight studies with a random effects model showed a risk ratio of 0.19 (95% confidence interval: 0.08–0.44) favouring CPOE (I^2 = 99%)." "Studies with quality scores below the lower limit of 95% CI (≤ 6) were excluded from the meta-analysis." "Seven studies reported clinical implications of CPOE on the occurrence of serious or fatal events among [chemotherapy-related medication	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
						errors] […]. The major, fatal, or serious adverse events (SAEs) that ranged from 0.8 to 36.5% of CMEs pre-CPOE were reduced from 0% to 20% post-CPOE."	
	Setareh, 2022[82]* inception to 06/2020	1 ITS 10 Other	2 Outpatient 6 Inpatient/ Outpatient 3 N/S	Guideline-based CPOE, CPOE with a CDSS "Studies examining the effect of guideline-based CPOEs on the chemotherapy order process were included." "We appreciate that almost all of the recent COPEs utilize a form of clinical decision support system, so the focus of this review was the utilization of guidelines in the development of [CPOEs]."	Medication errors	"The results showed that most CPOEs lead to a significant reduction in chemotherapy-related errors […]. Although chemotherapy improvement and error reduction were reported by all these studies, and most of them only used systems with a basic CDSS."	Fair
Implementation Outcomes – Alert Relevance & Overrides	Carli, 2018[31] 02/2009 to 03/2015	1 Systematic review 16 Other	16 Inpatient 1 Inpatient-ICU	CPOE with a CDSS "We targeted publications evaluating clinically relevant alert in computerized patient records implementing CPOE." "The third pillar is the decision support capability during the ordering process, such as the provision of extensive information on the drugs being	Alert relevance	"The results demonstrate massive variations in [positive predictive values] ranging from 8% to 83% according to the object of the decision support, with most results between 20% and 40%. The best results were observed when patients' characteristics, such as comorbidity or laboratory test results, were taken into	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				prescribed or the links made between the current order and other elements of the patient's record such as problems, laboratory results, and other drugs or diagnoses."		account. There was also an important variation in sensitivity, ranging from 38% to 91%."	
	Poly, 2020[74] 1/2000 to 4/2019	23 Other	15 Inpatient 4 Inpatient-ICU 1 Outpatient 1 Inpatient/ED 1 Inpatient/Outpatient 1 Ambulatory/Outpatient	CPOE with medication-related CDSS alerts	Alert override rates Override appropriateness Adverse drug events (due to overrides)	"The range of average override alerts was 46.2%-96.2%. An average of 29.4%-100% of the overrides alerts were classified as appropriate, and the rate of appropriateness varied according to the alert type (drug-allergy interaction 63.4%-100%, drug-drug interaction 0%-95%, dose 43.9%-88.8%, geriatric 14.3%-57%, renal 27%-87.5%)." "Inappropriate overrides were associated with an increased risk of [adverse drug events] when compared with appropriately overridden alerts."	Fair
	Luri, 2022[55] Inception to 03/2020	1 CBA 27 Other	17 Inpatient 3 Inpatient-ICU 1 ED 7 Inpatient/Ambulatory	Drug allergy CDSS alerts "The electronic drug allergy alert systems (DAAS) refer to a system that generates drug allergy alerts (DAA) in order to assist providers/users when	Alert override rates (drug allergy) Adverse drug events (due to overrides)	"The [override rate] ranged from 43.7% to 97%." "Clinical consequences of overriding [drug allergy alerts] were only analyzed in four studies, with an [adverse drug event] incidence between 0% and	Fair

Main Healthcare Context	Author, Year, Search Dates	Included Study Designs	Study Setting(s)	Interventions	Outcomes of Interest	Key Findings	Quality of Review
				ordering/signing/prescribing/administering a drug to a patient with a previously recorded theoretical allergy." "Studies analyzing electronic DAAS that consider both drug allergies and other aspects, such as drug interactions, dose adjustments, etc. were included only if the study provided a specific description on the electronic DAAS."		6%."	

*Information about selected studies focusing on medication-related CDSSs to prevent medication errors or adverse drug events extracted.

Abbreviations: CBA = controlled before-after; CDSS = clinical decision support system; CPOE = computerized provider order entry; DDI = drug-drug interaction; ED = emergency department; EMR = electronic medical record; ICU = intensive care unit; IT = information technology; ITS = interrupted time series; LTC = long-term care; PIP = potentially inappropriate prescribing; N/S = not specified; NRCT = nonrandomized controlled trial; RCT = randomized controlled trial.

Our rapid review focuses on the findings of one good quality systematic review that aligns with the inclusion criteria for experimental or controlled quasi-experimental study designs outlined in Table 1. The systematic review and meta-analyses conducted by Ciapponi et al. (2021) explored a broad scope of interventions focused on "reducing medication errors for adults in hospital settings," including CPOE/CDSSs, medication reconciliation, and barcoding.[35] The study was conducted according to the methods outlined by Cochrane and the Effective Practice and Organisation of Care (EPOC) Group. As one of many interventions, the systematic review assessed the impact of CPOE with CDSSs on both medication errors and adverse drug events based on results from RCTs and ITS studies. The search queried ten databases from inception to January 2020 and identified six RCTs and seven ITS studies for inclusion.

The meta-analysis that compared CPOE with CDSSs to usual care without CDSSs showed a nonsignificant reduction in medication errors (OR = 0.74; 95% CI = 0.31 to 1.79). The finding was assigned a GRADE certainty rating of "moderate," indicating that the authors believed that "the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different." Similarly, a meta-analysis of two RCTs showed a non-significant effect of CPOE with CDSSs on adverse drug events (OR = 0.24; 95% CI = 0.04 to 1.50). The authors assigned a GRADE of "very low," meaning that "the true effect is likely to be substantially different from the estimate of effect." Both RCTs reported a significant reduction; however, the heterogeneity of the studies resulted in an overall nonsignificant effect.

Additional meta-analyses compared CPOE with standard versus improved CDSSs, such as patient verification, e-prescribing with barcoding, or enhanced clinical pharmacist surveillance with existing CDSSs for medication errors. A meta-analysis of two RCTs demonstrated a significant reduction in medication errors using improved CDSSs (OR = 0.85; 95% CI = 0.74 to 0.97). A meta-analysis of two ITS studies also showed a reduction in medication errors; however, the effect was not significant (OR = 0.77; 95% CI = 0.37 to 1.62). Overall, the authors assigned a GRADE of 'moderate' to these findings. For effect on adverse drug events, a meta-analysis of two ITS studies provided the authors with "moderate" certainty that improved CDSSs significantly reduced events (OR = 0.82; 95% CI = 0.71 to 0.94). Furthermore, one ITS study showed positive effects of prioritized alerts compared with non-prioritized alerts on resolving potential adverse drug events (mean difference = 1.98; 95% CI = 1.65 to 2.31).[27] The authors assigned a "low" GRADE indicating that "the true effect may be substantially different from the estimate of the effect."

We identified four primary studies published since 2015 conducted in the United States that evaluated medication-related CDSSs and met the inclusion criteria for this rapid review.[27, 39, 60, 73] Bhakta et al. (2019) was included in the good-quality systematic review described in this section.[27] Two ITS studies focused on CDSSs for opioid prescribing[60, 73] and another ITS study described a CDSS for

potentially inappropriate prescribing in older adults.[39] We did not cover these topics in detail since there are separate chapters on opioid stewardship and medication deprescribing in MHS IV, but summarize their findings below.

Briefly, the MHS IV rapid response on deprescribing included eight (of 21) systematic reviews and two (of 11) primary studies that included CDSSs as one of the interventions. Overall, the results showed that deprescribing PSPs including CDSSs generally reduced the number of medications or potentially inappropriate medications; however, related clinical outcomes were more variable.[104]

For opioid stewardship, the MHS IV rapid review included five systematic reviews published since 2019 and three new primary studies published since 2016.[105] The results showed that opioid stewardship PSPs involving CDSSs, EHRs, or multicomponent interventions reduced rates of opioid prescribing and dosing without increasing pain, ED visits, or hospitalizations.

4.2.5.3 Inpatient – Intensive Care Unit (ICU)

Our search identified one systematic review and meta-analysis focused on the ICU setting[75] and another review that predominantly included studies conducted in the ICU.[78] Both systematic reviews indicated that the target interventions were CPOE with or without a CDSS on medication errors and patient outcomes (e.g., adverse drug events, length of hospital stay, mortality). Half of the studies (19 out of 38) in the Roumeliotis et al. (2019) systematic review were conducted in the ICU setting.[78] However, only two were included in the meta-analysis for medication errors, making the findings more applicable to the general inpatient setting.

Prgomet et al. (2017) conducted a meta-analysis of the five studies reporting on the effects of implementing commercial CPOE with or without a CDSS on medication errors in adult patients and showed a non-significant reduction in the relative risk (RR) of errors (RR = 0.11; 95% CI = 0.00 to 3.41). The interventions varied from simple CPOE to CDSSs with duplicate, allergy, and interaction alerts. The effect and wide confidence intervals were driven by one large pre-post study testing CPOE only, which accounted for 78 percent of the medication orders included in the analysis and demonstrated a 39 percent increase in medication errors post-implementation of CPOE. The investigators documented that two of the studies included in the meta-analysis (1 RCT and 1 uncontrolled pre-post design) provided medication-related alerts as part of the CDSSs.[106, 107] Both studies found a significant reduction in medication errors compared with paper-based prescribing. We assessed the strength of the evidence as very low based on the heterogeneity of the included studies.

4.2.5.4 Emergency Department (ED)

We identified one systematic review published by Hajesmaeel Gohari et al. (2021) focused on the effects of CPOE and CDSSs on medication errors and adverse drug events in the ED.[41] The results were narratively summarized, and no

meta-analyses or quantitative assessments were performed. The type of decision support provided by the CDSSs varied from simple (e.g., dose checking) to advanced alerts (e.g., dosing for renal insufficiency). Ten studies, including two RCTs, one CBA study, and one ITS design, generally demonstrated statistically significant reductions in various types of medication errors (range: 2% to 31%; n=5) and improvements in appropriate prescribing or guideline concordance (range: 5.2% to 21.5%; n=5). One crossover study showed a significant decrease in adverse drug events when the CDSS was activated (7.1% to 3.4%; p-value=0.02).[108] We rated the strength of the evidence as very low based on the heterogeneity of the included studies.

4.2.5.5 Ambulatory and Outpatient Care

Our search located three systematic reviews focused on the effects of CDSSs in the ambulatory and outpatient care settings.[32, 64, 80] One review was about potentially inappropriate prescribing,[80] which is covered in a separate chapter of MHS IV. Another review was of poor quality and covered a limited scope (focused on potential drug-drug interactions) and less recent timeframe compared with the review described.[64]

One good quality systematic review conducted by Cerqueira et al. (2021) focused on CPOE with interruptive CDSS alerts in the outpatient setting.[32] The results were narratively summarized, and no quantitative assessments were performed. Five out of six studies that focused on medication errors found a significant improvement with interruptive CDSSs. One pre-post study reported reduced prescribing errors in adopters versus non-adopters (1.5-fold decrease, $p<0.001$), and one CBA study demonstrated greater reductions in potential drug-drug interactions after CDSS implementation (RR = 0.81, 95% CI = 0.60 to 0.99) compared with controls (RR = 0.91, 95% CI = 0.32 to 1.29). One RCT showed a relative increase in appropriate drug dosing based on creatinine clearance in the CDSS group (OR = 1.89, $p<0.0001$), and two pre-post studies showed reductions in inappropriate medication use (antibiotic prescribing for acute respiratory infection decreased from 22% to 3%, $p=0.0001$; glyburide prescribing in older adults decreased from 3.3% to 1.2%, $p<0.001$). However, one RCT showed a non-significant effect of interruptive alerts compared with an on-demand CDSS in reducing prescribing errors (odds ratio [OR] = 1.31, 95% CI = 0.89-1.92).[109] Four of these studies also reported alert acceptance rates or compared outcomes between providers who used the CDSSs versus those who did not. We assessed the certainty of the evidence for the conclusion of this review that there is "a clear indication that many categories of alerts are effective at changing prescriber behavior" as low given that the synthesis was narrative and included observational studies.

4.2.5.6 Laboratory Alerts – Across Healthcare Settings

We identified one systematic review of fair quality conducted by Whitehead et al. (2019) focused on the effects of CDSSs with laboratory-related alerts, such as appropriate dosing for patients with renal insufficiency or avoidance of specific medications when laboratory results are abnormal (e.g., potassium, liver enzyme levels).[97] The search queried six databases for studies published from January 1990 to April 2016 and included various healthcare settings. A meta-analysis of five studies that assessed the impact on appropriate medication and dose included two RCTs, two crossover designs, and one uncontrolled pre-post design, and found an effect size of 1.48 (95% CI = 1.27 to 1.74). The authors of the systematic review rated the strength of this evidence as moderate and consistent. The meta-analysis of five studies that evaluated the effect of laboratory alerts on adverse drug events, based on one RCT, one crossover design, and three uncontrolled pre-post designs,

found a non-significant reduction (RR = 0.69; 95% CI = 0.46-1.03). The authors of the systematic review judged the body of the evidence as "too inconsistent to support a recommendation on this outcome."

4.2.5.7 Allergy

We identified two systematic reviews covering a wide range of topics related to CDSSs for medication-related allergies.[26, 53] One review was considered poor quality and is not discussed in this narrative.[53] A fair quality systematic review was conducted by Bassir et al. (2022).[26] The search queried five databases from January 2000 to June 2021. The search identified four relevant studies. Two studies (CBA and observational designs) assessed the effect of either removing or modifying inappropriate alerts for beta-lactam antibiotics and demonstrated safer prescribing without increased risk of anaphylaxis in the intervention arms.[110, 111] Two other studies (pre-post designs) evaluated the impact of CDSSs on premedication regimens for radiocontrast agents; both studies showed a significant increase in appropriate premedication rates, and one study reported a significantly lower rate of breakthrough reactions (6.7% vs. 15.2%).[112, 113] We rated the strength of the evidence as very low based on the heterogeneity of the included studies.

4.2.5.8 Anticoagulation

Our search located one good quality systematic review conducted by Austin et al. (2020) that included studies assessing the impact of CDSSs for anticoagulation on medication errors and adverse drug events in the inpatient setting.[24] The search queried four databases from inception to September 2018. The review included three RCTs, 10 pre-post studies, and one uncontrolled cohort study on CDSS alerts, and demonstrated mixed effects; however, only a subset assessed impacts on medication errors, adverse drug events or appropriate prescribing. Two of the RCTs focused on assessing the impact of alerts on prescribing medications contraindicated with warfarin; soft-stop alerts were not found to be effective while near-hard-stop alerts significantly reduced concomitant prescribing (OR = 0.12; 95% CI = 0.045 to 0.33).[114, 115] The third RCT reported higher rates of anticoagulant prescribing at hospital discharge in patients with atrial fibrillation in the alert group compared with the control group (22% vs. 16%, p-value=0.02).[116] We assessed the strength of the evidence as low that "CPOE in conjunction with CDSSs is needed to effectively manage therapeutic anticoagulation" given that the synthesis was narrative and included observational studies.

4.2.5.9 Oncology

We identified four systematic reviews related to oncology.[71, 76, 82, 86] The reviews did not focus on CDSSs for medication errors or adverse drug events, but had subsections covering these outcomes. Two reviews focused on the effects of

CPOE with or without a CDSS and are not covered in detail.[82, 86] The systematic review conducted by Pawlowski et al. (2019) was fair quality; however, the search covered a similar timeframe but was less comprehensive and yielded a subset of the studies included in the systematic review discussed.[71]

Rahimi et al. (2019) conducted a fair quality systematic review that queried two databases from inception to May 2017.[76] The search located 27 studies evaluating the effects of CPOE with a CDSS on chemotherapy-related medication errors or adverse drug events, which predominantly used pre-post or observational designs. Twenty studies focused on the prescribing process and 75 percent found a significant reduction in prescribing errors ranging from 12 percent to 98 percent. However, in a few studies, new types of errors were introduced through CDSS implementation. Three of the four studies that evaluated the effect on medication errors across all phases of the chemotherapy process showed significant reductions; the other study did not assess for improvements. Of the three studies that investigated effects on adverse drug events in adults, all reported reductions or no adverse drug events post-implementation; however, one study only showed a decrease after a 4 percent increase in the first year. We assessed the strength of the evidence as low that "the use of CDSSs in chemotherapy prescription has reduced medication errors" given that the synthesis was narrative and included observational studies.

4.2.5.10 Implementation Outcomes – Alert Relevance & Overrides

Our search identified six systematic reviews reporting on implementation outcomes.[26, 31, 37, 53, 55, 74] Four of these reviews are not covered in detail; three focused on allergy alerts[26, 53, 55] and the other review only provided medication-related alert acceptance rates for studies meeting the inclusion criteria for the primary focus of the review.[37]

Poly et al. (2020) conducted a fair quality systematic review to quantify the magnitude of medication-related alert overrides in CPOE systems and assess the appropriateness of the overrides.[74] The search queried five databases from January 2000 to April 2019 and identified 23 studies for inclusion. Reported override rates varied between studies from 46 percent to 96 percent, and the appropriateness of overrides ranged from 29 percent to 100 percent, influenced by the type of medication-related alert. We rated the strength of the evidence for a precise rate of overrides as very low based on the heterogeneity of the included studies; however, the strength of evidence that there is a clinically important high rate of alert overrides is moderate, as all reported override rates exceeded 46 percent. The most common reasons for overrides were patient tolerated the medications, benefits outweighed the risks, no reasonable alternatives, provider planned to monitor, provider planned to adjust dose as recommended, provider approved or aware, and clinically irrelevant or inaccurate alert.

Carli et al. (2018) conducted a fair quality systematic review to assess the clinical relevance of medication-related CDSS alerts in CPOE.[31] The search queried

PubMed from February 2009 to March 2015 and identified 17 studies for inclusion. The positive predictive values (PPVs) of alerts ranged from 8 percent to 83 percent, and sensitivities ranged from 38 percent to 91 percent. Higher PPVs were associated with alerts informed by the patient-level data, such as comorbidities and laboratory results.

Our search also identified one primary study conducted by Shah et al. (2021) that reported on implementation outcomes, which compared the clinical relevance of medication-related alerts from two commercial CDSSs.[83] The evaluation was controlled by testing both applications on the same sample of patients. We assessed the study as having a low risk of bias using QUADAS-2 (see Appendix C). The study found that the platform providing targeted and personalized alerts based on information documented in the patient record resulted in 93 percent fewer alerts with substantially and significantly improved sensitivity, specificity, PPV, and negative predictive values across inpatient and outpatient settings.

4.2.5.11 Unintended Consequences

We identified five systematic reviews that described or summarized the potential unintended consequences of implementing CPOE with CDSSs.[29, 38, 47, 49, 51] Notably, none of the studies included in these reviews meet the study design inclusion criteria outlined in Table 1.

Korb-Savoldelli et al. (2018) conducted a good quality systematic review to quantify the magnitude of CPOE-related medication prescribing errors for inpatient and outpatient settings.[51] The search queried six databases from March 1982 to August 2017 and identified 14 studies for inclusion. The study found that CPOE system-related medication errors occurred in 0.3 percent to 6.3 percent of all prescriptions across studies, accounting for 6.1 percent to 77.7 percent of all prescribing errors. The authors developed a comprehensive list of types of errors caused by CPOE. The types related to medication-related alerts are provided in Box 1.

Elshayib & Pawola (2020) conducted a fair quality systematic review to identify studies describing CPOE-related medication errors that occur in the hospital setting.[38] The search queried two databases from 2007 to 2019. The study identified and summarized several unintended consequences and factors contributing to errors from medication-related CDSS alerts in CPOE systems (Box 1). Brown et al. (2017) conducted a fair quality systematic review for primary and secondary care settings.[29] They searched three databases from January 2004 to June 2015 and identified 34 articles for inclusion. They summarized various user and system issues related to implementation of medication-related CDSSs (Box 1). Kinlay et al. (2021) conducted a fair systematic review primarily focused on CPOE-related medication errors.[49] They identified only one broad unintended consequence related to CDSSs, which was inconsistent or poor configuration.

Jankovic & Chen (2020) conducted a fair systematic review focused on the implications of CDSSs on provider burnout.[47] The study identified four key harmful

factors contributing to clinician burnout from systematic reviews and RCTs: use of interruptive or hard-stop alerts, lack of relevant or "right information," and inadequate CDSS integration.

Box 1. Unintended consequences

Increased provider workload[38]
Lack of knowledge about types of CDSS alerts being used[29]
Overdependence on alerts[38]
Alert fatigue
- High rate of false positive alerts[38]
- Inappropriate or erroneous alerts[29, 38]
- Low priority or low clinical significance alerts[38]
- Confusing or difficult to interpret alerts[38]

Alert overrides[51]
Inconsistent or insufficient use of alerts to mitigate errors[29]
Lack of alert[51]
Alert failure or dysfunction[38, 51]
Provider burnout[47]

4.2.5.12 Disparities

Our literature search identified one study assessing the potential for disparities in CDSS implementation or use.[36] It did not meet our standard inclusion criteria because there is no assessment of the effect of the alerts on outcomes of interest, but as it was the only such study we found we include it here. The investigator compared the alert override rate at a single academic medical center using a commercial EHR. The number of alerts and the overrides were compared between patient self-designated race, along with reasons for overrides for common alerts (only one of which was drug-drug interaction). Among 169 types of alerts triggered more than 5 million times, Black patients had about a 1 percent greater override rate compared with White patients (82.27% versus 81.30%) a difference that was statistically significant. Override patterns varied greatly among individual clinicians. The author concluded that "if racist behavior is present, it is not widely systemic. However, the great variability in individual clinician behavior suggests that deeper analysis is warranted."

4.2.5.13 Overall Strength of Evidence

All the strength of evidence assessments are based on the included systematic reviews. We assessed most of the reviews as providing low or very low strength of evidence. Our overall assessments of the strength of evidence for each outcome was based on the directionality of the association, and not precise estimates of the magnitude of the effect (Table 3). These effects were contextually dependent and will vary from application to application. The provider outcomes, specifically changes in prescribing behavior, were used to support assessment of the impact of CDSSs on medication errors, since the two outcomes are highly correlated.

Overall, four outcomes had moderate strength of evidence, three had low, and two had very low. We rated alert fatigue as very low based on the evidence from

our rapid review. Other observational studies not included in our review may provide stronger evidence of this unintended consequence.

Table 3. Overall assessments of the strength (certainty) of evidence

Outcomes	Conclusion	Strength of Evidence
Medication Errors	CDSSs are associated with reduced medication errors	Moderate
	Improved or targeted CDSSs are associated with reduced medication errors	Moderate
Adverse Drug Events	CDSSs are associated with reduced adverse drug events	Low
	Improved or targeted CDSSs are associated with reduced adverse drug events	Moderate
Unintended Consequences	CDSSs are associated with high override rates	Moderate
	CDSSs are associated with high inappropriate overrides	Low
	CDSSs are associated with low alert relevance	Low
	CDSSs are associated with high degrees of alert fatigue	Very low
	CDSSs are associated with increased provider burnout	Very low

4.2.6 Review Question 6. What Are the Most Common Barriers and Facilitators of Implementing Computerized Clinical Decision Support To Reduce the Frequency of Medication Errors and Adverse Drug Events?

Our literature search identified a large number of studies potentially relevant to barriers and facilitators and implementation. Studies of barriers and facilitators are fundamentally different than studies of effectiveness, and thus the evidence in these reviews includes data from surveys, case studies, focus groups, and other study designs that would not be relevant to a review question about effectiveness. We identified nine systematic reviews about various aspects of implementation,[25, 46, 58, 61, 69, 77, 90-92] four reports of expert recommendations about aspects of implementation,[59, 72, 81, 89] six studies that were case reports of CDSS malfunctions or unintended consequences,[22, 84, 87, 94, 98, 99] six qualitative studies of alert malfunctions or unintended consequences,[20, 23, 48, 52, 62, 65] six idiosyncratic interventions to improve alert appropriateness,[30, 44, 48, 63, 79, 88] two studies of costs associated with aspects of a specific CDSS implementation,[43, 96] one modeling study of the societal benefits of CDSS,[67] a study assessing the potential for disparities,[36] and then eight studies of idiosyncratic topics (a tool to evaluate alert appropriateness,[100] a study of alert appropriateness,[66] a study of how clinicians think about alerts,[45] a study about "evidence based usability design principles,"[56] a study of training doctors in e-prescribing,[93] a review of "usability aspects,"[42] a review of "modulators influencing alert acceptance,"[28] and a review of "alert stewardship"[33]). We focused on the systematic reviews of implementation, and the three most relevant to our key questions[61, 91, 92] (the other eight were less relevant because: they

were older than one of the included three,[56, 57] they had a more narrow focus,[25, 46] or they were insufficiently reported.[68, 69, 77, 90]). One of the reviews was about implementation of CDSSs in general,[61] another of the reviews was about medication-related CDSSs that also included antimicrobial prescribing,[91] while seven of the eight included studies in the third review were specifically about medication alert CDSSs.[92] The three reviews were about different levels of implementation: interface and information design of the CDSS itself,[61] prescriber perceptions of medication-related CDSS,[91] and strategies used by hospitals to implement medication alerts.[92]

The first review searched for studies through 2016 and focused on interface, information, and interaction features.[61] This review, which we judged to be of fair quality, identified 14 eligible studies that provided data on 42 design recommendations, based on evidence of either improved provider usability or satisfaction, improved process of care or knowledge of guidelines, or knowledge and attitudes; or improved fit with workflow and cognitive processes; or through improvements in patient outcomes or efficiency. The authors identified 11 interface features (Box 2), 9 information features (Box 3), and 21 interaction features (Box 4). The authors concluded that human factors, usability, and human-computer interaction principles are fundamental to successful CDSSs.

Box 2. Interface features categorized as presentation, placement, positioning, and provision of multiple presentation layers

Interface (Presentation)
Presentation • Make it simple • Use appropriate font sizes • Use meaningful colors • Ensure acceptable contrast between text and background • Keep presentation consistent • Deploy space-filling techniques • Make icons bold or bigger in size
Placement and positioning • Display information in prominent positions to ensure that it is seen • Allow for reading left to right • Localize information
Provision of multiple presentation layers • Avoid using only text

Miller K, Mosby D, Capan M, et al. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc. 2018 May 1;25(5):585-92. doi: 10.1093/jamia/ocx118. PMID: 29126196[61] Adapted with permission.

Box 3. Information features categorized as clean and concise, content guidance, and consistency

Information (Content)
Clean and concise • Standardize terminology • Use concise and effective language
Content guidance • Provide a recommendation, not an assessment • Justify recommendations • Suggest alternative recommendations

• Provide additional resources • Make evidence-based recommendations the default • Keep recommendations up to date
Consistency • Recommendations should come from the same place • Have the same display of basic CDSS for all members of the healthcare team

Miller K, Mosby D, Capan M, et al. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc. 2018 May 1;25(5):585-92. doi: 10.1093/jamia/ocx118. PMID: 29126196[61] Adapted with permission.

Box 4. Interaction features categorized as fast, fit, feedback, forgiveness, and flexible design Interaction (Function)

Interaction (Function)
Fast • Provide timely feedback • Reduce the amount of time the user is required to interact with the CDSS
Fit • Minimize cognitive load (reduce the number of mouse clicks and amount of free-text typing; use selection tools, sort options) • Minimize cognitive load (request information from the provider only when necessary; reduce manual input of values) • Reduce screens to facilitate navigation and to promote efficient interactions • Automatically pull data from the EHR/integrate into the charting system • Navigate to appropriate locations • Initiate intervention and take advantage of interactivity (system provides corollary action) • Provide a route to get to provider-specific info • Adapt its behavior according to a subset of relevant actions taken by clinicians • Incorporate functions supporting the dialog between the CDSS and the clinician
Feedback • Provide decision support automatically as part of clinician workflow • Automate alerting • Request documentation of reasons for not following system recommendations
Forgiveness • Allow the user to be able to modify orders • Integrate a reset button
Flexible design • Involve the patient • Utilize adaptive design and feedback • Provide an indication for all professionals of the availability of information; the designers may choose the most appropriate way of indicating the information in the interface • Incorporate functions to support team awareness about alert management and its evolution over time (e.g., visible access to how the alert was handled and the reasons for alert override or rule deactivation if any has been documented) • Give access upon request to extended information (e.g., justification for the rule, attached scientific documentation) that should be structured depending on the user profile

Miller K, Mosby D, Capan M, et al. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc. 2018 May 1;25(5):585-92. doi: 10.1093/jamia/ocx118. PMID: 2912619661 Adapted with permission.

The second review searched from 2003 through March 2018 for studies of provider perceptions of medication related CDSSs in order to identify key factors that prevent and promote uptake.[91] This review, which we judged as good quality, identified 13 studies meeting the inclusion criteria. Five studies came from North America, 4 studies were from Europe, 3 studies were from Australasia, and 1 study was from Asia. Two studies focused on antimicrobial prescribing, 1 study on acute

kidney injury, and the remainder did not have a specific focus on a health condition or drug class. Reported barriers to medication alert uptake included irrelevant alerts, mistrust of alert information, too many alerts, alerts being ignored in favor of senior staff or departmental preferences, outdated alerts, and the perception that alerts encroached on physician autonomy. Facilitators to medication alert uptake included convincing providers that the use of alerts improves patient safety, user involvement in implementation of alerts, the use of alerts that are non-interruptive to workflow, alerts that target cases of uncertainty, having trust in alert information, and viewing alerts as being complementary to clinicians' competencies and skills. The authors concluded that to promote medication-CDSS uptake, "providers perspectives on CDSS usability and integration be sought at the design phase, that evidence of effectiveness…for safety be provided to prescribers, and that system information be kept up to date."

The third review, which we judged to be of good quality, searched from January 2010 through April 2020 for studies describing the internal governance processes for selecting CDSS alerts for implementation or for optimizing CDSS alerts in the hospital setting.[92] The authors identified 8 studies meeting eligibility criteria, of which 5 were conducted in the United States, all used commercial EHR systems, and 7 of which were specifically about medication alerts (5 of these were about drug-drug interaction alerts). In these 8 studies, all of them described the use of a committee, which could include physicians, pharmacists, other clinicians, an informaticist, and others, to oversee implementation/optimization. In four studies, there was a mechanism for clinician feedback, where suggestions from staff were sent to committees to decide what alerts should be implemented or modified. In four studies, data on alert overrides and firing rate were extracted from the EHR and used when considering changes to alerts. Two studies described use of dashboards to monitor and evaluate alert data, and 4 studies described the use of literature to inform their changes to alerts. All included studies used more than one method; the median was 2.5. The authors concluded that a multidisciplinary committee, combined with other approaches, was the most frequently reported strategy to implement and optimize their CDSS medication alerts; and that there were too few studies to compare the effectiveness of different strategies.

4.2.7 Review Question 7. What Resources (e.g., Cost, Staff, Time) Are Required for Implementation of Computerized Clinical Decision Support Practices?

Our literature search identified three studies reporting data on resource use,[43, 67, 96] but only one study was based on U.S. data.[67] This study was a cost effectiveness analysis using a societal perspective of implementing CPOE, which in their analysis specifically included a CDSS, "with checks for allergies and drug-drug interactions." In order to estimate the costs of CPOE, the author performed a systematic review (search through 2013) for studies reporting data on multiple hospitals and including capital and maintenance costs (such as hardware and

software, training hospital staff members, technical support, and consulting charges) and selected those articles they judged most relevant. Cost estimates were then constructed based on hospital bed size and categorized by equally sized quintiles of hospitals. An example estimate is given for the middle quintile of U.S. hospitals, with a mean of 100 beds, which showed implementation costs estimated at $5,618,000, physician costs as $2,576,000, nonphysician providers savings of $13,532,000, and ordering of medications and laboratory tests savings of $1,834,000. Incremental effectiveness went down as implementation costs went up. The authors concluded that on average implementing CPOE with a basic CDSS would be cost saving at a societal level, although individual hospital results might vary.

4.2.8 Review Question 8. What Toolkits Are Available To Support Implementation of Computerized Clinical Decision Support To Reduce the Frequency of Medication Errors and Adverse Drug Events?

No U.S. toolkits were identified for this review.

5. Discussion

5.1 Summary and Interpretation of Findings

Most of the literature published since 2015 has focused on summarizing the evidence, rather than strengthening the evidence by conducting methodologically stronger studies using RCT or controlled quasi-experimental designs. The systematic reviews described in this rapid review were generally of good or fair quality and demonstrated reductions in medication errors or adverse drug events across various healthcare settings (i.e., general inpatient, ICU, ED, and ambulatory/outpatient care). Most reviews predominantly included uncontrolled observational studies and provided narrative summaries; as a result, these reviews provided low or very low certainty of evidence. Only one review conducted meta-analyses using RCTs and controlled quasi-experimental designs to estimate the overall effect of CDSSs on reduction of medication errors and adverse drug events in the hospital setting. These meta-analyses included comparatively low numbers of primary studies that demonstrated significant or non-significant reductions and provided a moderate level of certainty around the evidence. These findings align with the results from previous editions of MHS reports.

Most of the primary studies included in the reviews focused on the effect of CPOE with a CDSS compared with usual care or paper-based prescribing. However, there was substantial heterogeneity between studies with regard to the quality of the CDSSs (basic versus advanced features and alerts), type of decision support provided by the CDSSs (e.g., drug-drug interactions, contraindications, laboratory results), populations under study, outcomes under investigation, and characteristics of the healthcare organizations, leading to heterogeneous results across studies and making it inappropriate to summarize the evidence into an overall effect. As a result, there are likely a very large number of effects that are context specific, and the key is to optimize the CDSSs and implementation to maximize and realize the potential benefits in each context. Further complicating interpretation, most CDSSs are integrated directly with CPOE as a combination of interventions and the contribution of medication-related alerts to any improvements is not possible to estimate.

The systematic reviews primarily included studies focused on the effect of CDSSs on medication errors, rather than adverse drug events. Medication errors are considered preventable and have the potential to lead to adverse drug events. Focusing on what is preventable allows for more opportunity to improve process and systems. From a methodological standpoint, medication errors are more easily identified through data that can be extracted from the CPOE system or from errors reported during the medication use process; as a result, it is easier to demonstrate effectiveness of CDSSs on improving medication errors. Since only a subset of medication errors cause adverse drug events, it is critical to estimate the effect of CDSSs on actual patient harm, especially given the wide range of documented unintended negative consequences associated with misuse of medication-related alerts, such as increased provider workload, alert fatigue, and provider burnout. As a result, there are very high

rates of medication-related alert overrides when using these systems, depending on the type of alert. This includes overrides of appropriate alerts, marking missed opportunities to prevent medication errors and adverse drug events. It is important to note, that the estimates of the effects of the CDSSs on medication errors, adverse drug events, related implementation outcomes such as alert overrides, and unintended consequences of use all come from different studies with unique contexts, which makes understanding the net benefit extremely challenging.

Since CPOE is now the standard across U.S. healthcare systems, the literature is moving toward evaluating and optimizing the quality of CDSSs and alerts integrated within CPOE. A recent systematic review by Chien et al. (2022) conducted a bibliometric analysis that showed a shift over the last decade from "patient safety to system utility."[117] One meta-analysis identified through our rapid review showed significant reductions with moderate certainty in both medication errors and adverse drug events when using improved CDSSs compared with standard versions, as well as a significant positive effect of using prioritized alerts over nonprioritized alerts with a low level of certainty around the evidence.[35]

5.2 Limitations and Strengths

This rapid review had limitations related to the review process. It is possible that there were additional relevant studies that we did not identify using our search strategy and querying specific databases (i.e., PubMed and Cochrane Library).

There were several limitations related to the sources of evidence that were located through the search. This rapid review relied heavily on evidence from systematic reviews, which predominantly included uncontrolled study designs, such as pre-post comparisons. As a result, most of the reviews were assessed as providing low or very low strength of evidence. Most of the reviews did not include statements around the strength of the evidence, which had to be assessed by the authors of this rapid review.

Many of the studies using RCTs and controlled quasi-experimental studies that were included in the systematic reviews were conducted over 10 years ago, making the findings less relevant or generalizable to IT-focused medical practice today. The capabilities of EHRs and algorithms behind medication-related alerts have dramatically improved, and CDSSs have also evolved as a result.

Another limitation was the multicomponent nature of most interventions, which evaluated the effects of CPOE with a CDSS, making it impossible to disentangle the effects of the CPOE from the effects of the CDSS and medication-related alerts. However, a limited number of studies demonstrated the positive effects of using improved CDSSs over standard versions and prioritized over non-prioritized alerts.

Primarily relying on the summaries and meta-analyses from systematic reviews limited our ability to report on the effectiveness of specific domains of CDSSs. Proxy measures described in this report were alert relevance and override rates which varied greatly based on the type of medication-related alert.

A limitation of the results was the lack of literature around disparities. Our review only identified one study that addressed disparities in CDSS implementation and use,

which compared alert overrides between Black and White patients. The results did not show a clinically significant difference overall and further assessments are necessary.

A key strength of this review was the inclusion of a broad scope of literature across various healthcare settings (i.e., general inpatient, ICU, ED, and ambulatory/outpatient care) and specialties (i.e., allergy, anticoagulation, and oncology). Despite the low certainty of evidence provided by most of the systematic reviews, this rapid review showed that CDSSs have demonstrated reductions in medication errors and adverse drug events in many different contexts.

5.3 Implications for Clinical Practice and Future Research

The findings of this report need to be interpreted in the context of the major shift from investigator-initiated development and implementation of medication-related CDSSs in the late 1990s to the largely vendor-based tools available today. Currently, CDSSs are generally purchased separately and integrated with EHRs to provide alerts at the point of care. These tools vary widely in targets, scope, and effectiveness. Given the current requirements for meaningful use of EHRs and implementation of CDSSs to improve patient outcomes, it is critical to understand the effects of CDSSs on the prevention of medication errors and adverse drug events and be able to balance the evidence with potential harms and unintended consequences of use. The findings from randomized studies 20 or more years ago of homegrown, investigator-initiated CDSSs may not necessarily be generalizable to the current multiple vendor-driven landscape today.

There are several implications for clinical practice. Clinicians should be aware of the strengths and weaknesses of any CDSS that is employed in their practice, including the scope of the medication-related alerts, new errors potentially introduced by the system, risks of accepting inappropriate alerts, and risks of overriding high-value alerts. All alerts must be considered in the context of the specific patient, since the CDSS may not be optimized to provide tailored information based on patient-level information documented in the patient record.

Future research should focus on a few key areas. Studies should be conducted where the effects of a CDSS on all related outcomes (e.g., clinical, implementation, and unintended consequences) are measured and interpreted within the same context. This type of assessment would allow for stronger evidence around benefits and unintended consequences of CDSS use and help guide optimization of medication-related alerts and implementation to minimize unintended consequences, while maintaining high-value and critical alerts. This approach has worked well in other areas of medicine, such as RCTs evaluating new medications or surgical procedures, which report both benefits and harms of the interventions. Future CDSS studies should also be conducted using RCT or controlled quasi-experimental designs to provide stronger evidence around causation. It is also important for future publications and reports to provide detailed information about the context of the study to inform

interpretation of the results and assessments around the generalizability of the findings.

Given that CPOE and CDSSs are ubiquitous, future research should also focus on how CDSSs can be made to work well. The lessons learned from cases where CDSSs have demonstrated substantial reductions in medication errors and adverse drug events should be applied across CDSSs with different targets. This area of research is particularly valuable given that CPOE and CDSSs are now largely vendor-developed, less modifiable, and not tailored to specific health systems, and as a result evidence from homegrown CDSSs is less applicable to today's landscape. Future research should also focus on defining successful collaborations between vendors, researchers, and clinicians for developing and evaluating the effects of these vendor-based CDSSs.

The field of artificial intelligence is rapidly expanding and leveraging these algorithms and tools could substantially improve the effectiveness of medication-related CDSSs.[118] For example, natural language processing could be used to access and extract data routinely stored in unstructured fields, such as reports or free-text notes, providing substantially more information about the patient and the context. This information coupled with structured data analyzed using complex algorithms (such as neural networks that can manage high-dimensional data) could provide more relevant and tailored alerts at the point of care.

We did not identify any patient safety measures or indicators for Review Question 2, future research should also focus on the development of these types of standardized, nationally endorsed measures to report on the rates of medication errors and adverse drug events. Such measures would allow for tracking progress over time and help with evaluating quality improvement initiatives aimed at optimizing medication-related CDSSs.

Finally, two forms of equity should be considered in future research. Studies should assess the impact of medication-related alerts on different segments of the population within health systems, as well as potential disparities between different types of health systems, such as safety-net or rural hospitals which may have less effective CDSSs or less sophisticated implementation compared with large urban integrated delivery networks.

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118. Syrowatka A, Song W, Amato MG, et al. Key use cases for artificial intelligence to reduce the frequency of adverse drug events: a scoping review. Lancet Digit Health. 2022 Feb;4(2):e137-e48. doi: 10.1016/S2589-7500(21)00229-6. PMID: 34836823.

Authors

Ania Syrowatka, Ph.D.
Aneesa Motala, B.A.
Emily Lawson, M.S.
Paul Shekelle, M.D., Ph.D.

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Peer Reviewers

The list of Peer Reviewers follows:

David W. Bates, M.D., M.Sci
Medical Director, Clinical and Quality Analysis, Mass General Brigham
Professor of Medicine, Harvard Medical School
Professor of Health Policy and Management, Harvard T.H. Chan School of Public Health
Boston, MA

Sumant Ranji, M.D., SFHM
Professor of Clinical Medicine, University of California San Francisco
Division of Hospital Medicine, San Francisco General Hospital
San Francisco, CA

Disclaimers

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any

medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe. AHRQ recognizes that people are struggling with urgent questions on how to make healthcare safer. AHRQ is using this rapid format for the fourth edition of its Making Healthcare Safer series of reports, produced by the EPC Program and the General Patient Safety Program. To shorten timelines, reviewers make strategic choices about which processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

AHRQ expects that these rapid evidence products will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to AHRQ. If you have comments related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to MHS@ahrq.hhs.gov.

Robert Otto Valdez, Ph.D., M.H.S.A.
Director
Agency for Healthcare Research and Quality

Therese Miller, D.P.H.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Christine Chang, M.D., M.P.H.
Director
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

David W. Niebuhr, M.D., M.P.H., M.Sc.
Evidence-based Practice Center Program Liaison
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Craig A. Umscheid, M.D., M.S.
Director
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Margie Shofer, B.S.N., M.B.A.
Director, General Patient Safety Program
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Jennifer Eskandari
Task Order Officer
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Farzana Samad, Pharm.D., FISMP, CPPS
Health Scientist Administrator
Center for Quality Improvement and Patient Safety
Agency for Healthcare Research and Quality

Appendixes

Appendix A. Methods

Search Strategies for Published Literature

Database(s):

1. PubMed
2. Cochrane Library

Limits:

1. English
2. 2015 – 2023

Deliverables:

1. Word doc of search strategy
2. EndNote library of search results

Results:

Total # imported to EndNote Library: **1,044**
PubMed SRs only: **79**

Table A-1. PubMed search strategy

Set #	Search	# of Results
1	"decision support"[tiab] OR "CDSS*"[tiab] OR "computer assisted decision making"[tiab] OR "computer aided decision making"[tiab] OR "medication alert*"[tiab] OR "medication warning*"[tiab] OR "drug alert*"[tiab] OR "drug allergy alert*"[tiab] OR "alert system*"[tiab] OR "safety alert*"[tiab] OR "computerized alert*"[tiab] OR "computerised alert*"[tiab] OR "electronic alert*"[tiab] OR "computer alert*"[tiab] OR "automated alert*"[tiab] OR "automated system*"[tiab] OR "automatic alert*"[tiab] OR ADR[tiab] OR ADRs[tiab] OR "Decision Making, Computer-Assisted"[Mesh] OR "Decision Support Systems, Clinical"[Mesh] OR "Decision Making, Computer-Assisted"[Mesh] OR "Decision Support Systems, Clinical"[Mesh] OR "Reminder Systems"[Mesh]	181,156

Set #	Search	# of Results
2	"medical order entry"[tiab] OR "MOES"[tiab] OR "medication order*"[tiab] OR "electronic prescribing"[tiab] OR "e-prescribing"[tiab] OR "electronic ordering"[tiab] OR "computerized order*"[tiab] OR "computerised order*"[tiab] OR "computerized provider order entry"[tiab] OR "computerised provider order entry"[tiab] OR "computerized physician order entry"[tiab] OR "computerised physician order entry"[tiab] OR "computerized order entry"[tiab] OR "computerised order entry"[tiab] OR "CPOE*"[tiab] OR "electronic health record*"[tiab] OR "EHR"[tiab] OR "EHRs"[tiab] OR "electronic medical record*"[tiab] OR "EMR"[tiab] OR "EMRs"[tiab] OR "Electronic Health Records"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "Hospital Information Systems"[Mesh] OR "Clinical Pharmacy Information Systems"[Mesh] OR "Medication Systems, Hospital"[Mesh] OR "Pharmacy Service, Hospital"[Mesh] OR "Medical Order Entry Systems"[Mesh]	127,353
3	"medication error*"[tiab] OR "drug error*"[tiab] OR "medical error*"[tiab] OR "high alert drug error*"[tiab] OR "prescription error*"[tiab] OR "adverse drug event*"[tiab] OR "adverse reaction*"[tiab] OR "drug reaction*"[tiab] OR "pADE*"[tiab] OR "drug contraindicat*"[tiab] OR "drug interaction*"[tiab] OR "medication reconciliation"[tiab] OR "safety event*"[tiab] OR "patient harm"[tiab] OR "close call*"[tiab] OR "near miss*"[tiab] OR "critical incident*"[tiab] OR "medication safety"[tiab] OR "patient safety"[tiab] OR "alert fatigue"[tiab] OR "alarm fatigue"[tiab] OR ((alert*[tiab] OR alarm*[tiab] OR warn*[tiab]) AND (override*[tiab] OR overridden[tiab] OR over-rid*[tiab] OR ignor*[tiab])) OR ((alert*[tiab] OR alarm*[tiab] OR warn*[tiab]) AND (accept*[tiab] OR cooperat*[tiab] OR "co operate"[tiab] OR compliance[tiab] OR comply[tiab] OR recogniz*[tiab] OR recognis*[tiab])) OR "Alert Fatigue, Health Personnel"[Mesh] OR "Patient Safety"[MAJR] OR "Patient Harm"[MAJR] OR "Near Miss, Healthcare"[Mesh] OR "Medication Errors"[Mesh] OR "Medical Errors"[Mesh] OR "Alert Fatigue, Health Personnel"[Mesh] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Drug Interactions"[MAJR] OR "Drug Hypersensitivity"[MAJR] OR "Contraindications, Drug"[Mesh] OR "Medication Reconciliation"[Mesh]	402,491
4	#1 AND #2 AND #3	2,324
5	#4 AND ((2015/1/1:2023/12/31[pdat]) AND (english[Filter]))	**978**
6*	32371457 35981555 31206159 34990941 36287267 24894078 32706721 31390471 29742757 33691690	10
7	#5 AND #6	9**
8	("systematic review*"[tiab] OR "systematic literature review*"[tiab] OR "systematic overview*"[tiab] OR "systematic qualitative review*"[tiab] OR "systematic search*"[tiab] OR "systematic quantitative review*"[tiab] OR "systematic meta-review*"[tiab] OR "systematic critical review*"[tiab] OR "systematic evidence review*"[tiab] OR "Cochrane review*"[tiab] OR "systemic review*"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR "meta analysis"[tiab] OR meta-review[tiab] OR "meta synthesis"[tiab] OR metasynthesis[tiab] OR "quantitative review"[tiab] OR "quantitative synthesis"[tiab] OR "scoping review*"[tiab] OR "mapping review*"[tiab] OR (meta-analytic*[tiab] AND review[tiab]) OR meta-analysis[pt] OR "systematic review"[pt] OR (Cochrane Database Syst Rev[ta] AND review[pt])) NOT (comment[pt] OR protocol*[ti])	453,619
9	#5 AND #8	**79**

*Sentinel articles
**Nuckols, et al. (2014) not captured due to year limits.

Table A-2. Cochrane Library search strategy

Set #	Search	# of Results
1	(("decision support" OR "CDSS*" OR "computer assisted decision making" OR "computer aided decision making" OR "medication alert*" OR "medication warning*" OR "drug alert*" OR "drug allergy alert*" OR "alert system*" OR "safety alert*" OR "computerized alert*" OR "computerised alert*" OR "electronic alert*" OR "computer alert*" OR "automated alert*" OR "automated system*" OR "automatic alert*" OR ADR OR ADRs OR "reminder systems")):ti,ab,kw	7,968

Set #	Search	# of Results
2	(("medical order entry" OR "MOES" OR "medication order*" OR "electronic prescribing" OR "e-prescribing" OR "hospital medication system*" OR "electronic ordering" OR "computerized order*" OR "computerised order*" OR "computerized provider order entry" OR "computerised provider order entry" OR "computerized physician order entry" OR "computerised physician order entry" OR "computerized order entry" OR "computerised order entry" OR "CPOE*" OR "electronic health record*" OR "EHR" OR "EHRs" OR "electronic medical record*" OR "EMR" OR "EMRs" OR "computerized medical records system*" OR "pharmacy information system*")):ti,ab,kw	5,778
3	(("medication error*" OR "drug error*" OR "medical error*" OR "high alert drug error*" OR "prescription error*" OR "adverse drug event*" OR "adverse reaction*" OR "drug reaction*" OR "drug related side effect*" OR "pADE*" OR "drug contraindicat*" OR "drug interaction*" OR "drug hypersensitivity" OR "medication reconciliation" OR "safety event*" OR "patient harm" OR "close call*" OR "near miss*" OR "critical incident*" OR "medication safety" OR "patient safety" OR "alert fatigue" OR "alarm fatigue")):ti,ab,kw	78,622
4	((alert* OR alarm* OR warn*) AND (override* OR overridden OR over-rid* OR ignor*)):ti,ab,kw	108
5	((alert* OR alarm* OR warn*) AND (accept* OR cooperat* OR "co operate" OR compliance OR comply OR recogniz* OR recognis*)):ti,ab,kw	1,892
6	#1 AND #2 AND #3	92
7	#1 AND #2 AND #3 AND (#4 OR #5)	12
8	#7 2015 – 2023	67 1 Review; 1 CCA; 65 Trials

Appendix B. List of Excluded Studies Upon Full-Text Review

Excluded Studies

The reason for exclusion are noted at the end of the citation.

1. Actrn. The Effects of an Intervention to Optimise Quality Use Of Medicines In Older People in Hospital. https://trialsearch.who.int/Trial2.aspx?TrialID=ACTRN12622000374763. 2022. PMID: CN-02408023. *Study Design*

2. Agarwal S, Glenton C, Tamrat T, et al. Decision-support tools via mobile devices to improve quality of care in primary healthcare settings. Cochrane Database Syst Rev. 2021 Jul 27;7(7):Cd012944. doi: 10.1002/14651858.CD012944.pub2. PMID: 34314020. *Intervention*

3. Alagiakrishnan K, Ballermann M, Rolfson D, et al. Utilization of computerized clinical decision support for potentially inappropriate medications. Clin Interv Aging. 2019;14:753-62. doi: 10.2147/cia.S192927. PMID: 31118596. *Study Design*

4. Ali SM, Giordano R, Lakhani S, et al. A review of randomized controlled trials of medical record powered clinical decision support system to improve quality of diabetes care. Int J Med Inform. 2016 Mar;87:91-100. doi: 10.1016/j.ijmedinf.2015.12.017. PMID: 26806716. *Outcome*

5. Atia J, Evison F, Gallier S, et al. Does acute kidney injury alerting improve patient outcomes? BMC Nephrol. 2023 Jan 17;24(1):14. doi: 10.1186/s12882-022-03031-y. PMID: 36647011. *Intervention*

6. Awdishu L, Coates CR, Lyddane A, et al. The impact of real-time alerting on appropriate prescribing in kidney disease: a cluster randomized controlled trial. J Am Med Inform Assoc. 2016 May;23(3):609-16. doi: 10.1093/jamia/ocv159. PMID: 26615182. *Timing*

7. Aziz MT, Ur-Rehman T, Qureshi S, et al. Reduction in chemotherapy order errors with computerised physician order entry and clinical decision support systems. Health Inf Manag. 2015;44(3):13-22. doi: 10.1177/183335831504400303. PMID: 26464298. *Intervention*

8. Berge GT, Granmo OC, Tveit TO, et al. Machine learning-driven clinical decision support system for concept-based searching: a field trial in a Norwegian hospital. BMC Med Inform Decis Mak. 2023 Jan 10;23(1):5. doi: 10.1186/s12911-023-02101-x. PMID: 36627624. *Outcome*

9. Bittmann JA, Rein EK, Metzner M, et al. The Acceptance of Interruptive Medication Alerts in an Electronic Decision Support System Differs between Different Alert Types. Methods Inf Med. 2021 Dec;60(5-06):180-4. doi: 10.1055/s-0041-1735169. PMID: 34450669. *Study Design*

10. Blumenthal KG, Park MA, Macy EM. Redesigning the allergy module of the electronic health record. Ann Allergy Asthma Immunol. 2016 Aug;117(2):126-31. doi: 10.1016/j.anai.2016.05.017. PMID: 27315742. *Study Design*

11. Brenner SK, Kaushal R, Grinspan Z, et al. Effects of health information technology on patient outcomes: a systematic review. J Am Med Inform Assoc. 2016 Sep;23(5):1016-36. doi: 10.1093/jamia/ocv138. PMID: 26568607. *Intervention*

12. Brodowy B, Nguyen D. Optimization of clinical decision support through minimization of excessive drug allergy alerts. Am J Health Syst Pharm. 2016 Apr 15;73(8):526-8. doi: 10.2146/ajhp150252. PMID: 27045062. *Timing*

13. Brown T, Persell S, Lee JY, et al. Reducing high-risk geriatric polypharmacy via electronic health record nudges. Journal of general internal medicine. 2020;35(SUPPL 1):S253. doi: 10.1007/s11606-020-05890-3. PMID: CN-02257643. *Intervention*

14. Caraballo PJ, Parkulo M, Blair D, et al. Clinical Decision Support to Implement CYP2D6 Drug-Gene Interaction. Stud Health Technol Inform. 2015;216:946. PMID: 26262248. *Timing*

15. Chaparro JD, Hussain C, Lee JA, et al. Reducing Interruptive Alert Burden Using Quality Improvement Methodology. Appl Clin Inform. 2020 Jan;11(1):46-58. doi: 10.1055/s-0039-3402757. PMID: 31940671. *Population*

16. Chernoby K, Lucey MF, Hartner CL, et al. Impact of a clinical decision support tool targeting QT-prolonging medications. Am J Health Syst Pharm. 2020 Nov 16;77(Supplement_4):S111-s7. doi: 10.1093/ajhp/zxaa269. PMID: 32839818. *Study Design*

17. Ciapponi A, Fernandez Nievas SE, Seijo M, et al. Reducing medication errors for adults in hospital settings. Cochrane Database of Systematic Reviews. 2021(11). doi: 10.1002/14651858.CD009985.pub2. PMID: CD009985. *Duplicate*

18. Colombini N, Abbes M, Cherpin A, et al. Comprehensive evaluation of using computerised provider order-entry system for hospital discharge orders. Int J Med Inform. 2022 Apr;160:104703. doi: 10.1016/j.ijmedinf.2022.104703. PMID: 35124391. *Intervention*

19. Cornu P, Steurbaut S, Gentens K, et al. Pilot evaluation of an optimized context-specific drug-drug interaction alerting system: A controlled pre-post study. Int J Med Inform. 2015 Sep;84(9):617-29. doi: 10.1016/j.ijmedinf.2015.05.005. PMID: 26051616. *Timing*

20. Corny J, Rajkumar A, Martin O, et al. A machine learning-based clinical decision support system to identify prescriptions with a high risk of medication error. J Am Med Inform Assoc. 2020 Nov 1;27(11):1688-94. doi: 10.1093/jamia/ocaa154. PMID: 32984901. *Study Design*

21. Cossette B, Éthier JF, Joly-Mischlich T, et al. Reduction in targeted potentially inappropriate medication use in elderly inpatients: a pragmatic randomized controlled trial. Eur J Clin Pharmacol. 2017 Oct;73(10):1237-45. doi: 10.1007/s00228-017-2293-4. PMID: 28717929. *Population*

22. Curtis CE, Al Bahar F, Marriott JF. The effectiveness of computerised decision support on antibiotic use in hospitals: A systematic review. PLoS One. 2017;12(8):e0183062. doi: 10.1371/journal.pone.0183062. PMID: 28837665. *Intervention*

23. Czock D, Konias M, Seidling HM, et al. Tailoring of alerts substantially reduces the alert burden in computerized clinical decision support for drugs that should be avoided in patients with renal disease. J Am Med Inform Assoc. 2015 Jul;22(4):881-7. doi: 10.1093/jamia/ocv027. PMID: 25911673. *Timing*

24. Dekarske BM, Zimmerman CR, Chang R, et al. Increased appropriateness of customized alert acknowledgement reasons for overridden medication alerts in a computerized provider

order entry system. Int J Med Inform. 2015 Dec;84(12):1085-93. doi: 10.1016/j.ijmedinf.2015.09.001. PMID: 26428286. *Timing*

25. Dewan M, Wolfe H, Young C, et al. Payer Formulary Alerts as a Cause of Patient Harm and the Journey to Change Them. Hosp Pediatr. 2016 Sep;6(9):529-35. doi: 10.1542/hpeds.2015-0279. PMID: 27507118. *Population*

26. Elias P, Peterson E, Wachter B, et al. Evaluating the Impact of Interruptive Alerts within a Health System: Use, Response Time, and Cumulative Time Burden. Appl Clin Inform. 2019 Oct;10(5):909-17. doi: 10.1055/s-0039-1700869. PMID: 31777057. *Study Design*

27. Epstein RH, Dexter F, Patel N. Influencing Anesthesia Provider Behavior Using Anesthesia Information Management System Data for Near Real-Time Alerts and Post Hoc Reports. Anesth Analg. 2015 Sep;121(3):678-92. doi: 10.1213/ane.0000000000000677. PMID: 26262500. *Intervention*

28. Eschmann E, Beeler PE, Blaser J. Impact of Specific Alerts in Potassium-Increasing Drug-Drug Interactions. Stud Health Technol Inform. 2015;216:949. PMID: 26262251. *Timing*

29. Feather C, Appelbaum N, Darzi A, et al. Indication documentation and indication-based prescribing within electronic prescribing systems: a systematic review and narrative synthesis. BMJ Qual Saf. 2023 Feb 14. doi: 10.1136/bmjqs-2022-015452. PMID: 36788034. *Intervention*

30. Fraccaro P, Arguello Casteleiro M, Ainsworth J, et al. Adoption of clinical decision support in multimorbidity: a systematic review. JMIR Med Inform. 2015 Jan 7;3(1):e4. doi: 10.2196/medinform.3503. PMID: 25785897. *Intervention*

31. Fried TR, Niehoff KM, Street RL, et al. Effect of the Tool to Reduce Inappropriate Medications on Medication Communication and Deprescribing. J Am Geriatr Soc. 2017 Oct;65(10):2265-71. doi: 10.1111/jgs.15042. PMID: 28804870. *Intervention*

32. Fung KW, Kapusnik-Uner J, Cunningham J, et al. Comparison of three commercial knowledge bases for detection of drug-drug interactions in clinical decision support. J Am Med Inform Assoc. 2017 Jul 1;24(4):806-12. doi: 10.1093/jamia/ocx010. PMID: 28339701. *Outcome*

33. Gallagher J, O'Sullivan D, McCarthy S, et al. Structured Pharmacist Review of Medication in Older Hospitalised Patients: A Cost-Effectiveness Analysis. Drugs Aging. 2016 Apr;33(4):285-94. doi: 10.1007/s40266-016-0348-3. PMID: 26861468. *Timing*

34. George B, Gonzales S, Patel K, et al. Impact of a Clinical Decision-Support Tool on Venous Thromboembolism Prophylaxis in Acutely Ill Medical Patients. J Pharm Technol. 2020 Aug;36(4):141-7. doi: 10.1177/8755122520930288. PMID: 34752541. *Study Design*

35. Green RA, Hripcsak G, Salmasian H, et al. Intercepting wrong-patient orders in a computerized provider order entry system. Ann Emerg Med. 2015 Jun;65(6):679-86.e1. doi: 10.1016/j.annemergmed.2014.11.017. PMID: 25534652. *Timing*

36. Greene RA, Zullo AR, Mailloux CM, et al. Effect of Best Practice Advisories on Sedation Protocol Compliance and Drug-Related Hazardous Condition Mitigation Among Critical Care Patients. Crit Care Med. 2020 Feb;48(2):185-91. doi: 10.1097/ccm.0000000000004116. PMID: 31939786. *Intervention*

37. Guédon A, Rome A, Deville JL, et al. Computerized Provider Order Entry Using Two Prescription-Writing Software in Oncology. Am J Med Qual. 2017 Mar/Apr;32(2):220. doi: 10.1177/1062860616666164. PMID: 27565815. *Study Design*

38. Heck CC, Tichy EM, Vonderheyde R, et al. Optimizing pharmacist-driven protocols and documentation of interventions using clinical decision support systems. Am J Health Syst Pharm. 2020 May 19;77(11):830-4. doi: 10.1093/ajhp/zxaa061. PMID: 32426844. *Outcome*

39. Hinderer M, Boeker M, Wagner SA, et al. Integrating clinical decision support systems for pharmacogenomic testing into clinical routine - a scoping review of designs of user-system interactions in recent system development. BMC Med Inform Decis Mak. 2017 Jun 6;17(1):81. doi: 10.1186/s12911-017-0480-y. PMID: 28587608. *Outcome*

40. Jani YH, Franklin BD. Interruptive alerts: only one part of the solution for clinical decision support. BMJ Qual Saf. 2021 Dec;30(12):933-6. doi: 10.1136/bmjqs-2021-013391. PMID: 34385285. *Study Design*

41. Kang A, Thompson A, Rau J, et al. Effects of clinical decision support and pharmacist prescribing authority on a therapeutic interchange program. Am J Health Syst Pharm. 2018 Sep 1;75(17 Supplement 3):S77-s81. doi: 10.2146/ajhp170465. PMID: 30139727. *Study Design*

42. Koeck JA, Young NJ, Kontny U, et al. Interventions to Reduce Pediatric Prescribing Errors in Professional Healthcare Settings: A Systematic Review of the Last Decade. Paediatr Drugs. 2021 May;23(3):223-40. doi: 10.1007/s40272-021-00450-6. PMID: 33959936. *Population*

43. Kulenovic A, Lagumdzija-Kulenovic A. PM-TOM: A Method for Finding Personalized Polypharmacy Therapies with Minimal Adverse Drug-Drug, Drug-Gene and Drug-Condition Interactions. Stud Health Technol Inform. 2020 Jun 16;270:648-52. doi: 10.3233/shti200240. PMID: 32570463. *Outcome*

44. Kuper KM, Nagel JL, Kile JW, et al. The role of electronic health record and "add-on" clinical decision support systems to enhance antimicrobial stewardship programs. Infect Control Hosp Epidemiol. 2019 May;40(5):501-11. doi: 10.1017/ice.2019.51. PMID: 31020944. *Intervention*

45. Lee TC, Shah NU, Haack A, et al. Clinical Implementation of Predictive Models Embedded within Electronic Health Record Systems: A Systematic Review. Informatics (MDPI). 2020 Sep;7(3). doi: 10.3390/informatics7030025. PMID: 33274178. *Intervention*

46. Marasinghe KM. Computerised clinical decision support systems to improve medication safety in long-term care homes: a systematic review. BMJ Open. 2015 May 12;5(5):e006539. doi: 10.1136/bmjopen-2014-006539. PMID: 25967986. *Population*

47. McCourt E, Harper N, Butnoris M, et al. The effect of Computerised Physician Order Entry on prescribing errors: An interrupted time-series study at a secondary referral hospital in Australia. Int J Med Inform. 2022 Sep;165:104829. doi: 10.1016/j.ijmedinf.2022.104829. PMID: 35810657. *Population*

48. Moja L, Polo Friz H, Capobussi M, et al. Effectiveness of a Hospital-Based Computerized Decision Support System on Clinician Recommendations and Patient Outcomes: A Randomized

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Appendix C. Evidence Tables

Table C-1. QUADAS-2 risk of bias for individual studies

Author, Year	Patient Selection	Index Test	Reference Standard	Flow and Timing
Shah, 2021[83]	Unclear Risk	Low	Low	Low

Table C-2. SOE table for systematic reviews of CDSS effectiveness

Author, Year	Type of Evidence Synthesis	Number of Included Studies	Heterogeneity (Either Quantitative Estimate or Narrative From the Authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Austin, 2020[24]	Narrative	27 studies (3 RCTs, 20 pre/post studies, other observational studies)	Heterogeneity in outcome measures	"Majority of research is pre/post studies"; "potential exclusion of some relevant articles"; "outcome measures differed"	"…may be an effective method for optimizing…anticoagulation"	Low
Bassir, 2022[26]	Narrative	140 studies (Most were observational studies [difficult to know the percent])	Heterogeneity	"it is possible we did not include all relevant studies…" "we were not able to evaluate bias consistently…"	"allergy alerting mechanisms lack specificity and clinical relevance…"	Very Low

Author, Year	Type of Evidence Synthesis	Number of Included Studies	Heterogeneity (Either Quantitative Estimate or Narrative From the Authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Cerqueira, 2021[32]	Narrative	9 studies (3 RCTs and 6 observational studies)	None mentioned	"limited number of high-quality studies…"	"clear indication alerts are effective at changing provider behavior"; "limited evidence, not strong evidence that this contributes to patient safety"	Low
Ciapponi, 2021[35]	Meta-analytic	13 studies (6 RCTs and 7 observational studies)	Not applicable	Not applicable	"Moderate-certainty evidence shows that CPOE/CDSS probably reduce medication errors"; "Moderate-certainty evidence shows that, compared with standard CPOE/CDSS, improved CPOE/CDSS probably reduce medication errors"	We use their GRADE assessments

Author, Year	Type of Evidence Synthesis	Number of Included Studies	Heterogeneity (Either Quantitative Estimate or Narrative From the Authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Hajesmeel Gohari, 2021[41]	Narrative	11 studies (2 RCTs and 9 observational studies)	Heterogeneity	"some related studies were not found in our search result…"; "no homogeneity in the study design and outcome measures…"; "differences between home-grown and commercial systems were not considered…."	"Use of CPOE and CDSS can lower [adverse drug events]."	Very Low

Author, Year	Type of Evidence Synthesis	Number of Included Studies	Heterogeneity (Either Quantitative Estimate or Narrative From the Authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Poly, 2020[74]	Narrative	23 studies (all studies are observational)	Heterogeneity and methods issues	"We could not determine bias of the included studies…"; "…could not provide the percentage of [adverse drug events] when alerts were inappropriately overridden owing to data scarcity…"	In some cases, CDSSs "could diminish safety…"	Very Low for a specific estimate for overrides, Moderate for a conclusion that the override rate is clinically important
Prgomet, 2017[75]	Meta-analytic	20 studies (1 RCT and 19 observational studies)	I^2 on pooled analysis for medication errors is 100%	"…the quality of the included studies…"	"Current evidence suggests CDSS might be effective…"	Very Low

Author, Year	Type of Evidence Synthesis	Number of Included Studies	Heterogeneity (Either Quantitative Estimate or Narrative From the Authors)	Limitations Reported by Authors	Authors' Conclusions	Assigned Strength of Evidence
Rahimi, 2019[76]	Narrative	27 studies (all are observational)	Heterogeneity	"…only research published in English…"; "some [articles] may have escaped our attention…."; "…design and quality of the studies were variable…"	CDSSs "would generally be effective.."	Low
Roumeliotis, 2019[78]	Meta-analytic	38 studies (11 RCTs and 27 observational studies)	Not applicable	Not applicable	"Very low-quality evidence that current era electronic prescribing strategies reduced medication errors and adverse drug events"	We use their GRADE assessments
Whitehead, 2019[97]	Meta-analytic	10 studies (3 RCTs and 7 observational studies)	Not applicable	Not applicable	"The body of evidence that [clinical decision support] tools can reduce medication errors was rated as moderate and consistent."	We use their SoE assessments - not GRADE

Note: "Not applicable" means that these domains do not need our assessment as the systematic review authors performed a strength of evidence assessment themselves.