





With funding from GORDON AND BETTY MOORE FOUNDATION



### Acknowledgments

We would like to thank the workgroup chairs and all of those that contributed to the workgroup and the development of safe practices. Thank you to the workgroup co-chairs John D. McGreevey III, MD (Penn Medicine) and Adam Wright, PhD (Vanderbilt University Medical Center) as well as to Christina Michalek, BSc Pharm, RPh (ISMP), and Robert Giannini (ECRI).

We thank those who presented to the workgroup throughout the various meetings sharing valuable information and techniques with the workgroup members, in particular we would like to again thank the workgroup chairs, John D. McGreevey III, MD, and Adam Wright, PhD, for their presentations; vendor/developers James Doyle (Epic), Gordon Mann (Epic), Joan Kapusnik-Uner, PharmD, FASHP, FCSHP (First Databank, Inc.), and Trisha Flanagan, RN, MSN, CPPS (athenahealth); clinical experts Craig Norquist, MD, FACEP (Honor Health), Naveen Muthu, MD (Children's Hospital of Philadelphia), Evan Orenstein, MD (Children's Healthcare of Atlanta/Emory University), and Raymond Chan, PharmD (Sentara Healthcare) for their information and presentations and to the ISMP fellows and student interns Allison Hanson, Manju Anthony, Benedicta Asamoah, Yashar Rafi, and Nistha Shah for their contributions.

Finally, a thank you to all the participants listed below who volunteered and gave freely of their time contributing valuable information throughout the workgroup process. The ability to collaborate and to share this information contributed to the workgroup meetings and to the development of this publication.

#### **Co-chairs**

John D. McGreevey III, MD, Penn Medicine Adam Wright, PhD, Vanderbilt University Christina Michalek, BSc Pharm, RPh, FASH, Medication Safety Specialist, Institute for Safe Medication Practices Robert Giannini, NHA, CHTS-IM/CP, patient safety analyst and consultant, ECRI

#### **Workgroup Participants**

Kristi Atkins, BSN, RN, Walden University Henry Bayuzick, Flatiron Health Anthony Blackford, PharmD, Honor Health

Jennifer Brothers, RN, Williamson Medical Center

Raymond Chan, PharmD, Sentara Healthcare Marilyn Costache, Moffitt Cancer Center

James Doyle, Epic Brian (Alex) Dummett, MD, CPPS, Kaiser Permanente

Sharon Fiveash, Baptist Memorial Health Care Trisha Flanagan, RN, MSN, CPPS, athenahealth

Tejal Gandhi, MD, MPH, CPPS, Press Ganey Michael J. Gaunt, PharmD, medication

safety specialist, Institute for Safe Medication Practices

**Cheryl A. Hager,** MSN, RN-BC, NEA-BC, ONP-C, Franciscan Health

**Dwayne Hoelscher,** DNP, RN-BC, CPHIMS, UMC Health System

Stephanie H. Hoelscher, DNP, RN-BC, CPHIMS, CHISP, FHIMSS, Texas Tech University Health Sciences Center - School of Nursing

**David Hunt, MD, FACS,** Office of the National Coordinator for Health IT

Joan Kapusnik-Uner, PharmD, FASHP, FCSHP, First Databank, Inc.

**Dean Karavite,** Children's Hospital of Philadelphia

Shannon Kearney Lyons, Medhost Amina Khan, Children's Hospital of Philadelphia Christoph Lehmann, MD, UT Southwestern Sheralyn Long, MHI, BSN, RN, Franciscan Missionaries of Our Lady Health System Gordon Mann, Epic

Jessica Moss, Hospital Sisters Health System Naveen Muthu, MD, Children's Hospital of Philadelphia

Craig Norquist, MD, FACEP, Honor Health Evan Orenstein, MD, Children's Healthcare of Atlanta/Emory University

Randa M. Perkins, MD, FAMIA, Moffitt Cancer Center

Marc Perkins-Carrillo, MSN, RN, NE-BC, HACP, Moffitt Cancer Center

**Richard Schreiber,** MD, FACP, FAMIA, ABPM-CI, Geisinger Holy Spirit

Jeanie Scott, MS, VHA Office of Informatics and Analytics Health Informatics

Dean Sittig, PhD, The University of Texas Health Science Center At Houston, School of Biomedical Informatics

Brent Stevens, Veterans Administration Kevin Taylor, American Medical Association

Georgia Thomas, BSN, MBA, RN, HACP,

Memorial Hermann Hospital System

Marc Tobias, MD, Phrase Health

Nate Wade, PharmD, MSBA, BCOP, Flatiron Health

#### ECRI Internal Partnership Contributors

Asa Adadey, MS, data scientist Julia Barndt, MA, editor Carol Beckman, MSI, MSE, senior research librarian

**Patricia Giuffrida,** MSN, RN, CPHIMS, senior patient safety and health IT safety analyst

Ramya Krishnan, MS, senior project officer Jeffery Miszczak, PharmD, data engineer

Ben Pauldine, MBA, art manager

Lorraine Possanza, DPM, JD, MBE, FACFOAM, FAPWCA, program director, *Partnership for Health It Patient Safety*  Priyanka Shah, MS, senior project officer Amy Stone, MLS, library director Diana Winters, copyeditor Andrea Zavod, managing editor

#### **Expert Advisory Panel**

David Bates, MD, MSc, Brigham and Women's Hospital Kathleen Blake, MD, MPH, American Medical Association

**Pascale Carayon,** PhD, University of Wisconsin-Madison College of Engineering

Christoph Lehmann, MD, UT Southwestern Peter J. Pronovost. MD. PhD.

University Hospitals

Daniel J. Ross, MD, DDS, Department of Defense, Defense Health Agency

Jeannie Scott, MS, VHA Office of Informatics and Analytics Health Informatics

Patricia P. Sengstack, DNP, RN-BC, CPHIMS, Vanderbilt University Medical Center

Hardeep Singh, MD, MPH, Michael E. DeBakey VA Medical Center and Baylor College of Medicine

Dean Sittig, PhD, The University of Texas Health Science Center At Houston, School of Biomedical Informatics

Paul Tang, MD, MS, IBM Watson Health

#### Gordon and Betty Moore Foundation

We offer special thanks to the Gordon and Betty Moore Foundation for their generous support in building a sustainable private sector infrastructure for effective health IT patient safety practices.





### Partnership Collaborating Organizations\*



\* Healthcare providers and provider organizations participate in the *Partnership*. However, they are not listed here as they submit event information confidentially under the protections of ECRI and the Institute for Safe Medication Practices Patient Safety Organization.



### Contents

Executive Summary	.5
Introduction	
Background	.6
Methods	.7
Workgroup Survey	.8
Findings	.9
Literature Review	13
Recommendations	14
Discussion	14
Conclusion	19
References	
Appendix A. Safe Practice Recommendations	22
Appendix B. Literature Review	26
Appendix C. Tools	37
Appendix D. Additional Resources	38



### **Executive Summary**

Technology and its associated tools, in particular clinical decision support (CDS) alerts, have produced both benefits and unanticipated consequences. While alerts can facilitate patient safety, they may also contribute to alert fatigue and clinician burden. Burden is associated with overalerting and with inappropriate, ineffective, and nonspecific alerts.<sup>1</sup> With the increase in patient parameters to monitor, informational reminders, and alerts associated with outside data, the need increases to identify effective mechanisms to monitor, analyze, optimize, and govern alerts. The rationale for addressing this issue is to ensure that the persons most impacted—the end users of the technology—receive correct and timely information at the right point in the patient's care while minimizing the interruption and volume of alerts.

In order to evaluate and supply effective recommendations, a subgroup of the *Partnership for Health IT Patient Safety*'s stakeholders and other interested experts volunteered their time to participate in a virtual workgroup conducted from April through September 2020. Stakeholders actively engaged in the workgroup focused on finding ways to reduce alert fatigue associated with computerized provider order entry (CPOE) through monitoring, analysis, and optimization.

Through a series of web-based interactive meetings, the group shared data, evaluated evidence from the literature, presented exemplars, weighed solutions and options, and queried what held the most value for improving safety both now and in the future. The group focused their efforts by looking at CPOE workflow alerts, given their frequency and the increasingly substantial number of overrides.<sup>2</sup> The group developed recommendations that not only are applicable to CPOE workflow alerts but also might be extrapolated to apply to other forms of CDS, and their associated components (e.g., knowledge bases, clinical guidelines, patient-specific data). The group proffered four safe practice recommendations, related to the following areas:

- 1. **Governance:** Identify, develop, and execute a CDS and knowledge base governance plan.
- 2. Monitoring: Gather data and information using CDS-specific metrics and other tools to identify real-time and/or near real-time CDS alert functioning and impact.
- 3. **Analysis:** Regularly assess, evaluate, and interpret metrics, functionalities, usability, and impact to determine effectiveness and value while balancing and minimizing burden.
- 4. **Optimization:** Maximize the use of technology and various tools to create and promote effective, targeted, relevant, and routinely updated alerts.

The four safe practice recommendations offered in this report are interwoven and do not follow a linear progression. Rather, the steps involved in monitoring, analysis, and optimization are cyclical and often overlapping. But in order to execute each of the steps and processes associated with monitoring, analysis, and optimization, a comprehensive governance plan is important. The group identified elements for a successful governance strategy and then looked at how the strategy can be applied to CPOE alerts.

Committee-led systematic governance approaches to alert monitoring have met with multiple successes.<sup>3-5</sup> Governance is an important foundational step in conducting and executing these safe practice recommendations. The safe practices can be applied not only to CPOE alerts but also to other CDS alerts (e.g., immediate alerts, event-driven alerts, reminders). Good governance functions also apply to knowledge base management and guideline governance. Detailed recommendations, strategies to implement them, and a preview of recommended future actions are contained herein.



### Introduction

### Background

Clinical decision support (CDS) is available in various technologies, including electronic health records (EHRs). CDS is a group of tools designed to promote patient safety by providing information to enhance care and facilitate decision-making.<sup>6</sup> CDS functionalities include order sets; care plans and protocols; smart documentation forms; data summaries; monitors and dashboards; predictive analytics; and reference information.<sup>5,7</sup> These tools are sometimes informed by patient-specific information, knowledge base information, quality measures,<sup>8</sup> and clinical guidelines.<sup>9</sup> CDS tools are designed to enhance clinical decision-making at the needed point of care (see The "5 **Rights" of CDS**.<sup>7</sup>

Clinical decision support (CDS) provides clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care.<sup>6</sup> CDS encompasses a variety of tools to enhance decision-making in the clinical workflow.<sup>6</sup> These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information, among other tools.<sup>6</sup>

Alerts are often the first type of CDS that comes to mind.<sup>10</sup> "CDS primarily takes the form of alert windows notifying clinicians of drug-drug interactions, drug-allergy interactions, dosing ranges, and other warnings."<sup>11</sup> Alerts related to CPOE have been the focus of studies because of their low acceptance rates, which can range from 4% to 11%.<sup>2</sup> The reduced response to alerts and the increasing emphasis on clinician well-being have focused the spotlight on needed improvements to this safety tool.

Although CDS is designed to promote efficient, informed, and relevant decision-making, the tools are frequently ineffective. Problems include overrides, missed notifications, failure to return to interrupted tasks,<sup>2</sup> and a lack of related action (e.g., clinician did not see or react to an alert).<sup>3</sup> These reactions to CDS alerts are often attributed to alert fatigue. Peterson and Bates<sup>12</sup> define alert fatigue as a "condition in which too many alerts consume time and mental energy to the point that both important warnings and clinically unimportant ones can be ignored."<sup>4</sup> However, alert fatigue has proven difficult to

### The "5 Rights" of CDS

The "5 Rights" model of clinical decision support (CDS) states that CDS-supported improvements resulting in desired healthcare outcomes can be achieved if the following are communicated:

- 1. The right information: evidence-based, suitable to guide action, pertinent to the circumstance
- 2. To the right person: considering all members of the care team, including clinicians, patients, and their caregivers
- 3. In the right CDS intervention format: such as an alert, order set, or reference information to answer a clinical question
- 4. Through the right channel: for example, a clinical information system such as an electronic medical record, personal health record, or a more general channel such as the internet or a mobile device
- 5. At the right time in workflow: for example, at time of decision, action, or need

**Source:** Osheroff JA, Teich JM, Levick D, Saldana L, Velasco F, Sittig D, Rogers K, Jenders R. Improving outcomes with clinical decision support: an implementer's guide. 2nd ed. Chicago (IL): Healthcare Information and Management Systems Society; 2012.

measure. There is no established metric for alert burden; it is not simply a measure of the number of alerts, but also reflects the usefulness of alerts to the end-user.<sup>2</sup> As explained in the Department of Health and Human Services's (HHS) strategy to reduce administrative and regulatory burden relating to the use of health information technology (IT) and EHRs,<sup>11</sup> alert fatigue and its impact on clinician burden are increasingly seen as tightly coupled.

Recognizing the importance of safety improvements, the *Partnership for Health IT Patient Safety* sought to identify safe practices to improve the effectiveness of alerts while minimizing the burden placed on clinicians. Taking a multi-stakeholder approach, the group focused on the foundation to achieving identified safe practice recommendations, namely governance. With that framework in mind, the group examined three elements: monitoring, analysis, and optimization.



In order to narrow the scope of the project, the group looked at alerts associated with computerized provider order entry (CPOE). The alerts generated by this tool, using a CDS knowledge base and patient information, involve drug indications, drug dosing, and medication contraindications (e.g., drugallergy, drug-drug, drug-disease, drug duplication), diagnostic and treatment alerts, and alerts based on disease (e.g., renal impairment) or condition (e.g., pregnancy). Events associated with CPOE alerts are frequently reported as safety events, providing additional insight into their function. CPOE alerts are designed to facilitate clinical decision-making, serve as prompts or reminders, and aid in ensuring safe action by the clinician in the care of the patient. The purpose of CPOE alerts, regardless of the mechanism by which they are delivered, is to support clinicians in making optimal clinical decisions.

### **Methods**

A multi-stakeholder workgroup was assembled consisting of volunteer *Partnership* members including clinicians, pharmacists, healthcare organizations, EHR vendor/developers, knowledge base developer/vendors, researchers, IT professionals, and experts in patient safety, human factors, and regulations. The workgroup chairs (identified above) set forth a plan to look at the three key steps in evaluating the use of technology to safely provide CDS information while minimizing burden. These steps were identified as monitoring, analysis, and optimization. Workgroup meetings focused on each of these areas. It also became apparent that a fourth area of focus, governance, was an important foundational component on which to structure these activities. The group obtained information from data submitted to patient safety organizations (PSOs) between January 2019 and February 2020. These data were curated, evaluated, analyzed, and presented to the group, noting any limitations in the type and content of the data.

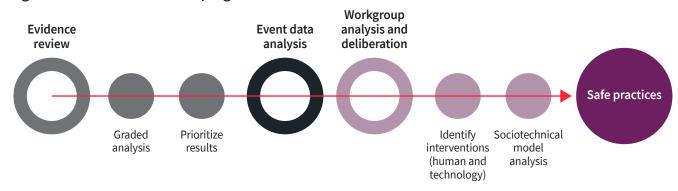
In addition, evidence from a review of the literature between January 2015 and July 2020 was provided to the group to facilitate the evaluation of various strategies that were both successfully and unsuccessfully used to address monitoring, analysis, optimization, and governance of CPOE alerts (see **Appendix B**).

The workgroup followed the established *Partnership*developed workgroup process for issue evaluation (see **Figure 1**).

Workgroup sessions provided the opportunity for various subject matter experts and IT developers to contribute their exemplars and learnings for group evaluation. These resources served as the structure for further development of ideas, strategies, and implementations for the safe practices. Workgroup activities conducted included the following:

- Identifying topic and workgroup chairs
- Gathering volunteer participants
- Identifying focus areas (monitoring, analysis, optimization)
- Performing data searches
- Developing a taxonomy
- Analyzing data
- Performing a literature search and review
- Surveying workgroup participants
- Making presentations to the workgroup

(Continued on page 8)



#### Figure 1 . Process for Developing Health IT Safe Practice Recommendations

Table of Contents | e hitsafety@ecri.org | 7 ©2021 ECRI. All Rights Reserved.



(Cont. from page 7)

- Gathering findings
- Evaluating various metrics and measures
- Identifying and refining key areas of focus
- Developing and drafting safe practice recommendations
- Vetting recommendations with workgroup
- Developing implementation strategies
- Expanding review
- Gathering and publishing information
- Disseminating safe practices
- Facilitating implementation across stakeholder groups
- Reevaluating and assessing for needed change

### Workgroup Survey

Before identifying specific information that would inform safe practices for monitoring, analysis, and optimization, workgroup participants shared their own perspectives on what CDS alerts they evaluate. Nineteen of 30 individuals participating in the workgroup completed a four-question informational survey. The survey questions gathered information on the following topics:

- What CDS alerts and reminders were available in their current systems
- What categories of CDS alerts and reminders they tracked and monitored
- How often the specific CDS alerts and reminders are monitored
- What measures are currently in use for evaluating what is being monitored

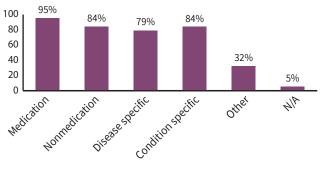
**Workgroup survey results.** Workgroup participants identified medication alerts as the largest category of their CDS alerts, with nonmedication, condition-specific, and disease-specific alerts accounting for a large percentage of the reported available alerts (see Figure 2). Respondents most frequently reported monitoring the functioning of medication-related alerts, including drug-drug interactions, drug-allergy interactions, drug-dose, drug-disease, and duplicate therapy alerts (see Table 1).

The workgroup survey respondents reported that of the CDS alerts they identified, alerts were most frequently monitored on an "as needed" basis (see **Table 2**). The results from the work-group survey provided a baseline for the workgroup discussions of the identified focus areas.

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

#### Figure 2. Workgroup Survey Results— Available Alerts and Reminders (N = 19)

What alerts and reminders are available within your electronic health record?



## Table 1. Workgroup Survey Results: Categories for Monitoring (N = 18\*)

What categories of alerts and reminders do you track/include/monitor?

Drug-drug interactions	17 (94.44%)
Drug–allergy interactions	15 (83.33%)
Drug dose	13 (72.22%)
Drug–disease	11 (61.11%)
Drug-lactation	7 (38.89%)
Drug-pregnancy	9 (50.00%)
Drug-food	6 (33.33%)
Drug–duplicate therapeutic class	11 (61.11%)
Drug–duplicate medication	11 (61.11%)
Drug-age/gender	7 (38.89%)
Other alerts and reminders	9 (50.00%)

\*Responses could include more than one answer.

**Note:** Other alerts and reminders included billing related, overrides, transgender, medication administration, custom alerts (best practice advisories), infectious diseases, admission alerts, preventive alerts and reminders, and formulary restrictions.

#### Table 2. Workgroup Survey Results: Frequency of Monitoring Alerts and Reminders (N = 19)

How often does your organization monitor these alerts and reminders?

	Continuous	Periodic	As needed	Do not monitor
Medication (16 respondents)	4 (25.00%)	3 (18.75%)	7 (43.75%)	2 (12.50%)
Nonmedication (14 respondents)	2 (14.29%)	4 (28.57%)	5 (35.71%)	3 (21.43%)
Disease specific (15 respondents)	3 (20.00%)	4 (26.67%)	6 (40.00%)	2 (13.33%)
Condition specific (15 respondents)	3 (20.00%)	4 (26.67%)	5 (33.33%)	3 (20.00%)
Other (11 respondents)	3 (27.27%)	1 (9.09%)	5 (45.45%)	2 (18.18%)



**Metrics.** After reviewing the survey findings, the analysis of the safety event data, and the literature review, the workgroup focused on suggesting metrics that would address furthering information for monitoring, analysis, and optimization. Four categories of potential metrics were identified (see Figure 3).

These four categories were further refined to reflect associated tasks needed to evaluate the metric. The metric categories include descriptive, performance, response, and burden (or impact) metrics.

- 1. **Descriptive.** Descriptive metrics focus on measures that determine how many alerts are received and who receives them.
- 2. **Performance.** Performance (functionality) metrics look at whether the alert fired appropriately as well as at the design of the alert (designed for a particular problem, e.g., serum potassium level, or targeted to a particular condition).
- 3. **Response.** Response metrics are about how the alert recipient responded to the alert (e.g., moving beyond override, accept, cancel), and whether the alert provided actionable content. It is important to recognize that the alert may have triggered an action that was not recorded or visible in such a metric.
- 4. Burden. The final category, burden metrics, address how the alert recipient was impacted or burdened. Did the alert interrupt workflow, was the interruption valuable (e.g., having positive predictive value [PPV]) or was it excessive, and was the alert targeted to the correct user?

Metrics were identified by their role in monitoring, in analysis, and for the ability to contribute to alert optimization. The workgroup discussed various strategies including how measures can potentially impact effective interventions.

### **Findings**

#### Data

Data used for this evaluation were received under the protections of ECRI and the ISMP PSO, which is recognized by the Agency for Healthcare Research and Quality (AHRQ) and authorized under the Patient Safety and Quality Improvement Act of 2005. The events include safety events that were submitted voluntarily between January 2019 and February 2020.

The information from the events and the text containing event descriptions were gathered and analyzed. The data reviewed from safety events included order-related (CPOE) events (e.g., medication, diagnostics, treatment, disease, condition) and events involving alerts that were available for safer care (e.g., patient monitoring devices, laboratory results, and reminders). An example of an event description follows:

Tylenol ordered q4hrs. Went to give 0400 Tylenol dose after skipping 0000 dose. Max Tylenol limit warning fired. Per patient weight, patient can receive only five doses in a 24-hour period; six doses were scheduled to be given. Medication held and pharmacy notified.

A machine learning (ML) classifier was trained on a set of validated events to predict whether an event was CDS related. The search yielded 3,665 events. A statistical sample was then

How many alerts fired and who received them?	Did the alert fire appropriately or not?	How did the alert recipient interact with the alert?	What was the impact of alerts on recipients?
Descriptive	Performance	Clinician interaction/response	Burden
<ul> <li>Alerts per 100 orders</li> <li>Alerts per encounter</li> <li>Firing rate (by department, provider, specialty, etc.) or firing rate/day</li> <li>User data (emergency department nurses, surgical residents, respiratory technicians at location X)</li> </ul>	<ul> <li>Sensitivity</li> <li>Specificity</li> <li>Positive predictive value</li> <li>Negative predictive value</li> </ul>	<ul> <li>Dwell time/think time</li> <li>Acceptance rate</li> <li>Override rate</li> <li>Override reasons</li> <li>Clinician comments</li> </ul>	<ul> <li>Burden index</li> <li>Number needed to alert</li> <li>Effectiveness</li> <li>Efficiency</li> <li>Some combination of metrics in preceding categories</li> </ul>

#### **Figure 3. Identifying Alert Metrics**



identified for analysis. A total of 610 events were selected for review. Of these events, 460 were deemed relevant, with 37% (n = 227) related to CPOE alerts and 38% (n = 233) related to other alerts. Application of the "safeguard taxonomy" identified how the alert (e.g., safeguard) functioned.

Table 3 summarizes these findings. The taxonomy indicates whether the alert, which was acting as a safeguard, functioned; whether the alert was available; whether the alert was overlooked or was bypassed; and whether the alert was functioning as it was expected to function.

Taxonomy Classification	CPOE*	<b>Other</b> <sup>†</sup>
Safeguard/alert did not function as expected	97 (43%)	87 (37%)
Safeguard/alert was not available	34 (15%)	33 (14%)
Safeguard/alert overlooked/bypassed	65 (29%)	52 (22%)
Safeguard/alert working as expected	28 (12%)	60 (26%)
Safeguard/alert not activated/discontinued	2 (1%)	1 (<1%)
Other	1 (<1%)	_

#### Table 3. Taxonomy Classification

\*Percentage of 227 reported events.

<sup>†</sup>Percentage of 233 reported events.

The CPOE-related safety events were most frequently reported. These safety events involved duplicate therapy, dosing issues, and drug allergies. Figure 4 shows events reported by CPOE alert type. Here, duplicate drug therapy events were most frequently reported (n = 65), followed by drug-dose alerts (n = 52) and alerts for drug-allergy interactions (n = 38). Less commonly reported were events that involved drug-disease alerts (n = 24) and drug-drug interaction alerts (n = 17).

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

Table 4 depicts the relationship between the type of CPOE alert and how the alert functioned, for instance whether the alert functioned as anticipated, was bypassed, or was unavailable (either because the alert was not turned on or because it was not included in the system that was in use).

In the following event, involving a patient for whom multiple anticoagulants had been prescribed, an alert did not function as it was expected to function:

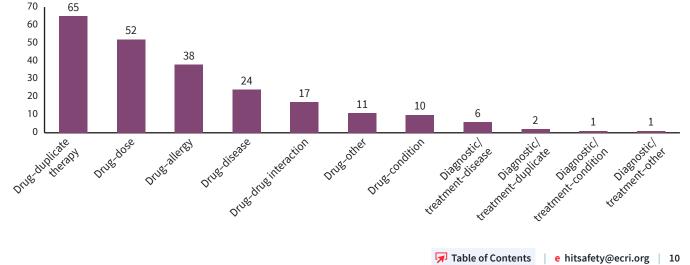
No alert was provided to the prescriber. A patient was presently on an anticoagulant. Prescriber wrote for an anticoagulant. Expecting that there would be an alert when prescribing additional medications of the same class.

Table 5 details the non-CPOE alerts and their functions. The numbers reflect whether these alerts were not functioning, not functioning as expected, not available, bypassed, or were working as expected to work.

#### DATA LIMITATIONS

The PSO event database does not contain reports for administrative alerts or reminders. Administrative alerts include items such as in-box notifications and reminders about data entry or missing data. These alerts are often associated with clinician burden and burnout.<sup>1</sup> Obtaining information about these alerts will require additional data sources. Events are reported to the PSO voluntarily.

The data obtained informed the development of the safe practice recommendations. See **Data Summary Findings from ECRI and the ISMP PSO**.



#### Figure 4. Events Reported by CPOE Alert Type (N = 227)

©2021 ECRI. All Rights Reserved.



#### **Table 4. Function of Identified CPOE Alerts**

CPOE Alerts	Safeguard did not function as expected	Safeguard not acknowledged/ bypassed	Safeguard not available	Safeguard functioned as expected	Safeguard not activated/ discontinued	Other	Total
Drug–duplicate therapy	24	33	2	6			65
Drug-dose	29	11	7	5			52
Drug-allergy	15	12	2	9			38
Drug-disease	12	3	7	1	1		24
Drug–drug interaction	7	2	2	5	1		17
Drug-other	1	1	8			1	11
Drug-condition	5	1	4				10
Diagnostic/treatment-disease	4	1		1			6
Diagnostic/treatment-duplicate			1	1			2
Diagnostic/treatment-condition			1				1
Diagnostic/treatment-other		1					1
Total	97 (43%)	65 (29%)	34 (15%)	28 (12%)	2 (1%)	1 (<1%)	227

### Data Summary Findings from ECRI and the ISMP PSO

Information that was gleaned from the presented data includes:

- Additional information and metrics are needed for other types Event data does not provide information on the effectiveness of alerts
- Event reports are one source to identify when alerts are unavailable but are desired
- of existing alerts
- Reporting on effective alerts (those working as expected) is infrequent



#### Table 5. Function of Identified Non-CPOE Alerts

Non-CPOE Alerts	Safeguard did not function as expected	Safeguard functioned as expected	Safeguard not acknowledged/ bypassed	Safeguard not available	Safeguard not activated/ discontinued	Total
Barcode medication administration	30	19	29	3		81
Automated dispensing cabinet	13	8	6	7		34
Electronic medication administration record	13	6	6	6		31
Laboratory results	7	9	1	4	1	22
Pump	6	3	1	2		12
Patient weight	4	2		2		8
Blood	3	1		1		5
Glucometer			3	1		4
Infection			4			4
Laboratory testing	2	2				4
Medication preparation		2	1			3
Physiologic monitors	1	1	1			3
Document scanning				2		2
Lab collection	1	1				2
Patient height	1	1				2
Dispensing	1			1		2
Medication reconciliation		2				2
Drug diversion		1				1
Paging	1					1
Expiration	1					1
Computer downtime	1					1
Diagnostic testing	1					1
Diet				1		1
Patient identification	1					1
Medical device		1				1
Reports		1				1
Imaging results				1		1
E-prescribing				1		1
Gender				1		1
Total	87 (37%)	60 (26%)	52 (22%)	33 (14%)	1 (<1%)	233



### **Literature Review**

A systematic search of the literature was conducted by master'slevel medical librarians. A search of English-language studies published between January 2015 and April 2020 using a key word search was conducted of the Medline/PubMed, Embase, CINAHL, and Scopus databases (see **Appendix B**). The focus questions for the literature review included the following:

- 1. What fields are important to monitor in order to analyze alerts?
- 2. How can analysis and prioritization of alerts determine focus for optimizations?
- 3. How can alerts be effectively optimized to maintain safety and minimize user burden?

A clinical analyst screened 177 titles and abstracts and identified 77 initially relevant texts for full-text review by a single clinical reviewer. Studies older than 2015 (n = 9) and studies conducted in non-US settings (n = 5) were excluded, leaving 63 studies for review.

The materials were first distinguished by whether they provided information related to the key questions. Initial evaluation looked at monitoring (n = 52), analysis (n = 7), and optimization (n = 4). Articles addressing monitoring were then identified for joint characterizations, namely monitoring and analysis (n = 24); monitoring and optimization (n = 1); and monitoring, analysis, and optimization (n = 25). (Two articles addressed monitoring alone; n = 2.) Upon final evaluation, 12 studies identified were included to directly inform the workgroup's efforts (see **Appendix B**).

Researchers have sought to identify mechanisms to reduce burden and determine why CDS alerts go perceptively unnoticed. Much of this focus is on the alerts themselves. Investigations have focused on the volume of alerts received, their timing (e.g., mismatch with CPOE workflow),<sup>5</sup> their repetitiveness,<sup>13</sup> clinician desensitization to alerts,<sup>13</sup> and the PPV of CDS alerts.<sup>14</sup> Actions that alert recipients take based on the content of the alerts they receive have also been investigated, but this area remains a difficult area to examine retrospectively when the alert display does not include this information.<sup>15,16</sup> Researchers have also looked at CDS alert function and usability,<sup>17</sup> noting when the tools work or do not work as designed.<sup>18</sup> These studies make clear there is no consensus as to how to manage CDS alerts without some level of burden.<sup>1</sup> The consequences of alert fatigue include lost efficiency, overdependence on the technology, decreased satisfaction with the EHR, and desensitization to alerts, resulting in patient harm.<sup>3</sup>

Most studies agree that "it is essential to refine alerting systems to highlight clinically significant alerts and eliminate inconsequential alerts thereby preventing alert fatigue and maintaining patient safety."<sup>16</sup> While recommendations have been made to improve alert functionality to prioritize critical information and to minimize alert fatigue,<sup>11</sup> additional strategies are still needed. These strategies can be used to address the multiple contributors to clinician alert burden.<sup>11</sup>

As such, there is a need to localize CDS alerts, balancing the patient information available with the level of burden created so that clinicians receive relevant information to inform their clinical decision-making in order to provide safe effective care. See **Key Findings from the Literature Review**.

#### Key Findings from the Literature Review

- More research is needed on the efficacy of interventions, but also on the tradeoffs associated with implementation
- Workarounds present ongoing barriers to improvement
- User feedback is important and should be automated
- Sustained improvement likely requires smart design and technology, but also cultural acceptance
- Standardization plays a role



### Recommendations

The workgroup identified four safe practice recommendations, strategies to address these recommendations, and actions for their implementation (see **Appendix A**). The safe practices include the following:

#### Governance

Identify, develop, and execute a CDS and knowledge base governance plan.

#### Monitoring

Gather data and information using CDS-specific metrics and other tools to identify real-time or near real-time CDS alert functioning and impact.

#### Analysis

Regularly assess, evaluate, and interpret metrics, functionalities, usability, and impact to determine effectiveness and value while balancing and minimizing burden.

#### Optimization

Maximize the use of technology and various tools to create and promote effective, targeted, relevant, and routinely updated alerts.

### Discussion

The workgroup set out to fulfill two goals: first, to promote patient safety by optimizing necessary, clinically important alerts, increasing clinician response to these alerts, and second, to promote clinician wellness and health IT safety and thus patient safety. In executing these goals, the workgroup was cognizant of how strategies and implementation actions would impact burden. With a focus on monitoring, analysis, and optimization, the group identified these four safe practices. While the strategies developed focus on CPOE alerts, they can be generalized to non-CPOE alerts, other CDS tools, and to the information on which CDS tools draw, including patient information, knowledge base materials, and guidelines. By implementing safe practices to monitor, analyze, and optimize CDS tools, the results will not only drive improvements in the tools themselves but will achieve burden reduction for stakeholders.

As the workgroup soon discovered, a solid foundational structure was essential before focusing on monitoring, analysis, and optimization. The structure can be achieved by setting in place a governance plan that addresses not only CPOE alerts but also the knowledge base and the guidelines that inform CDS tools. Governance does not depend on technology management alone but resides in leadership and in safety culture. Once those are in place, the foundation exists for the development of tools and strategies to identify issues, set priorities, and use the evaluations conducted to execute needed interventions (see **Appendix A**). While in theory EHR alerts can help clinicians deliver higher quality care, in practice clinicians are often inundated with popup alerts ranging from very minor interactions to truly critical risks. <sup>11</sup> This can lead to "alert fatigue"— a phenomenon where the user, faced with many lower level alerts, starts to ignore all alerts and thereby misses critical alerts that can impact patient health and safety . . . Thus, a potentially life-saving tool, when implemented without considering usability, can become an additional source of burden to EHR end users.<sup>11</sup>

## Governance: Identify, develop, and execute a CDS and knowledge base governance plan

Governance was deemed foundational to a focus on the identified elements for monitoring, analysis, and optimization. The group set forth guidance on developing a governance plan; gathering and monitoring data about the functions informing safety, in particular CPOE alert function; identifying strategies for assessing the data gathered; and then using that information, seeking strategies to identify available tools and find innovative options for CPOE alerts (see **Strategies for Alerts Governance**).

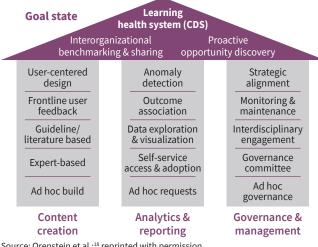
Leadership must be on board to ensure the success of a governance plan. Demonstrating a return on investment is the most challenging task in engaging leadership. Good governance creates the structure and a process to identify improvements through prioritization, decision-making, evaluation, and optimization. It provides opportunities to assess practices and identify improvements. Additionally, looking at workflow, monitoring



tools, and pathways and protocols is an essential step. Setting a governance plan in place provides the opportunity to evaluate the actions and the results of the actions taken so that any approaches that are not achieving the intended results can be modified.

A "maturity model" for clinical decision support operations is shown in Figure 5. The model demonstrates one stepwise approach that has been taken to aid organizations looking to "maximize the impact of their operational investment in CDS."19 This model provides one example of how a framework can be created to enable organizations to "use CDS more effectively to drive better outcomes."19 Governance forms a foundational pillar in this model.

#### Figure 5. Clinical Decision Support: **Operations Maturity Model**



Source: Orenstein et al.;<sup>18</sup> reprinted with permission.

Evaluating software and identifying where technology can be used to create safer care (e.g., standards, interoperability, use of application programming interfaces [APIs], CDS hooks), while minimizing burden, are considerations that should be incorporated into a governance structure.

Technology considerations. The ability to enact good governance depends on identifying standards that can be included within the technology. Considerations include items such as the following:

- Providing consistent alert formatting and response options across systems<sup>20</sup> (nomenclature, interruptive versus noninterruptive)
- Enabling the reporting of standard alert metrics

#### Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

- Developing tools to monitor CDS inventory and interventions<sup>5</sup>
- Employing tools for monitoring and tracking that permit analysts to examine CDS alerts without the need for additional technical support
- Facilitating adoption of anomaly-detection tools

Healthcare organizations, clinicians, and researchers are better positioned to identify a return on investment and outcomes assessment with standards in place. Recommendations do currently exist for "the development and adoption of technical standards; tools to measure efficacy of CDS; collaboration surrounding a common repository for CDS tools; a legal framework for CDS; and research into the safety, quality, productivity, and outcomes of successful CDS implementation that will help drive the business case for future CDS adoption."11 However, these recommendations have not been widely implemented.

Until the time that recommendations for technical standards, tools to measure CDS efficacy, identification of necessary alerts, and uniform implementation are in place, organizations will continue along their own adoption paths. Organizations will individually inventory, monitor, implement, observe, and analyze their CDS tools. What is clear is that consistent content review and evaluation, revisions and retirements of alerts, and the implementation of new CDS could be more efficient. While projects such as CDS Connect (AHRQ)<sup>11</sup> move forward, researchers must continue to seek ways to share their findings within and across various organizations and vendors to improve these processes.

Today, organizations are in various stages of CDS implementation and use. As CDS continues to mature, a governance plan will aid in driving that maturity. "A strong governance process adheres to a defined strategy and sets metrics and specific goals."4 The Partnership workgroup's safe practice recommendation and implementation actions for governance are outlined in Appendix A (also see Strategies for Alerts Governance).

With safe practice recommendations for governance established, it was then possible to focus on the pillars the workgroup set forth-monitoring, analysis, and optimization. These often-overlapping areas demonstrate that executing these functions is not a linear process. Rather, the pattern is recurrent and cyclical, with overlapping actions in each of these three areas. See Key Actions for Optimizing Strategies for CDS Adoption and Use.



#### Strategies for Alerts Governance

- Engage leadership by providing an understanding of the value and organizational impact of alerts governance
- Identify a multi-stakeholder oversight team and assign ongoing accountability
- Conduct an inventory of all CDS
- Perform a content review of the knowledge base that feeds into the CDS
- Evaluate findings to identify and update actions
- Disseminate best practices

In 2017, the National Academy of Medicine took a closer look at CDS and reported, in *Optimizing Strategies for Clinical Decision Support*, that CDS measurement practices and standards were lacking;<sup>6</sup> this remains true today. It is difficult to identify every instance of where and what CDS is deployed, let alone to identify its function, value, and impact. It remains difficult to fulfill the recommendation from the [NAM] report<sup>21</sup> that "evaluation of current and future CDS should assess whether it measurably improves quality, health outcomes, safety, cost, and physician productivity."<sup>6</sup> Identifying safe practices for monitoring, analysis, and optimization combined with a governance structure takes stakeholders one step closer to achieving these goals.

To address these considerations, along with improving CDS and minimizing burden, the workgroup first focused on monitoring, in particular monitoring of CPOE alerts. It is important to use the inventory of CDS to assess metrics revealing information about the frequency of alerts, how alerts are functioning (e.g., whether they are firing, when they are firing, whether they are firing when expected), how clinicians are interacting with the alerts, and the impact the alerts are having (e.g., improving safety).

#### Monitoring: Gather data and information using CDS-specific metrics and other tools to identify real-time and/or near real-time CDS alert functioning and impact

As the National Academy's report notes,<sup>6</sup> it is difficult to obtain sufficient data to determine whether a CDS intervention is being used, whether it is working consistently and correctly, and whether the recommendations provided are initiating action.<sup>6</sup> Moreover, it is often difficult to determine which CDS is effective.<sup>6</sup>

## Key Actions for Optimizing Strategies for CDS Adoption and Use

Develop, test, establish, validate, and apply CDS standards:

- 1. Establish CDS technical standards
- 2. Engage federal leadership for CDS standards development and maturation
- 3. Create CDS technical information resources

Encourage CDS adoption, use, and assessment at the delivery system level:

- 4. Disseminate best practices
- 5. Create a national CDS repository network
- 6. Measure CDS usage
- 7. Develop tools to assess CDS efficacy
- 8. Publish performance evaluations
- 9. Market CDS to stakeholders
- 10. Promote financing and measurement to accelerate CDS adoption

Establish a national CDS infrastructure:

- 11. Create a CDS legal framework
- 12. Develop a multi-stakeholder CDS learning community to inform usability
- 13. Establish an investment program in CDS research

**Source:** Tcheng et al.; <sup>20</sup> reprinted with permission.

**Technology considerations.** Data must be readily accessible without the need for specialized actions in order to understand the functioning of CDS:

- Employing tools for monitoring and tracking that permit users to analyze CDS alerts without the need for additional technical support
- Incorporate metrics that reflect function and use of CDS
- Enable reporting of standard alert metrics
- Provide tools for near real-time monitoring<sup>18</sup>
- $-\,$  Automate tools that ensure that systems are working in concert^{\sc 18}



Metrics that determine how many alerts are being received and who receives them in order to identify trends are not yet universal. Determinations about the descriptive nature of CPOE alerts include such parameters as the number of alerts per order, the firing rate of the alert, and the number of alerts per encounter.<sup>5</sup>

More difficult is monitoring the performance of an alert. Here questions as to the sensitivity, specificity, and the positive or negative predictive value of an alert can provide an indication of its value, but such an assessment is difficult and potentially subjective. When looking at metrics that reflect clinicians' interactions with alerts, variables such as dwell time,<sup>4</sup> acceptance rate, the number of overrides, and the reasons for overrides have been considered.<sup>4,5</sup>

Metric information can provide insight not only about alert function but also about the impact of the alert on the user. To date, information about ideal and optimal override rates and the best metrics for evaluating effectiveness and appropriateness remains elusive.<sup>4</sup> In one study, looking at "repeat reminders" specific alerts or reminders that were sent to the same individual multiple times for the same patient—"the clinician's acceptance rate decreased by about 30% with each additional alert received per patient encounter and by 10% for every five percentage point increment in percent of repeated alerts."<sup>13</sup> Creating awareness and ownership are key to executing these safe practices for monitoring (see **Strategies for Alerts Monitoring**).

With a handle on what is being monitored, it is then possible to use that information for improvement. Having structures in place to assess risk, function, value, and impact will be useful in considering the gathered metrics.

#### Analysis: Regularly assess, evaluate, and interpret metrics, functionalities, usability, and impact to determine effectiveness and value while balancing and minimizing burden

When beginning an analysis, the terminology is not always clear. For example, how is an override defined? If the alert is ignored, is that an override? If the alert is not applicable (e.g., the patient is not pregnant or does not have that allergy), is that an override? And if the clinician indicates that the dose was changed or that the patient will be monitored, is that an override?<sup>22</sup> To answer these questions the information must be readily available. Using live monitoring, obtaining feedback, and visualizing information through the use of dashboards are ways to focus and bring attention while balancing the often limited resources needed to begin to understand alert function.<sup>2</sup>

#### Strategies for Alerts Monitoring

- Use technology to assemble information needed to monitor CDS alerts:
  - Descriptive
  - Performance
  - Response
- Burden
- Expand resources for CDS alert monitoring to include information obtained from safety events, help desk tickets, walkrounds, trends, and reports
- Measure alert performance by accessing information about specific volumes, clinical users, triggers

**Technology considerations.** Technology considerations for analysis include the following:

- Automate assessments of CDS function (e.g., whether alerts are firing appropriately)
- Evaluate information to suggest other designs and tools for communicating and bringing attention to critical information
- Examine technology's impact (including design, configuration)<sup>6</sup> on workflow

The safe practice considerations and actions appear below (see Strategies for Alerts Analysis).

#### Strategies for Alerts Analysis

- Analyze (interpret data) information about CDS alerts to evaluate frequency, function, impact, value, and burden on a regular and on an "as needed" basis
- Conduct proactive and reactive risk assessments as part of ongoing analysis and evaluation

When evaluating CDS and planning changes to CDS tools, the impact of these tools on the user must be taken into consideration. Optimization should consider the alerts, their content, their location in the workflow, as well as how the end user interacts with them. For an alert to be accepted by the clinician, there are several important considerations:

For there to be optimal clinician buy-in, a CDS system must foster the clinician's belief that a worthwhile problem is being addressed, that CDS can solve the problem (patient outcomes), that it is targeting the correct patients (sensitivity and specificity, trust), that the alerts are relevant (PPV and



alert burden), and that workflow interruptions are worth the benefits, all while using language that lifts up instead of denigrating the clinician.<sup>1</sup>

These considerations are often difficult to implement on an individual basis. The challenge lies in the fact that there are "no standard/repeatable implementations across institutions" or "easily-accessed store of good exemplars of CDS design,"<sup>6</sup> and no widely exchanged operational components (triggers, notifications, standard sets and templates).<sup>6</sup> Systems vary considerably as to where to place CDS trigger points or with vendor-imposed trigger-point limitations.

#### Optimization: Maximize the use of technology and various tools to create and promote effective, targeted, relevant, and routinely updated alerts

Multiple parameters can be observed when looking at optimization. For example, information about alert volume or alert type (interruptive versus noninterruptive alerts), the targeted users for an alert, or the location or department where the alert occurs (e.g., emergency department, clinic, inpatient) can provide valuable information about alerts' role in the workflow and how they are being received. End-user feedback is another tool to identify targets for optimization. Reviewing feedback from users is one way to identify why an alert is not helpful or is not applicable.<sup>2</sup> Today, tools such as natural language processing (NLP) allow analysis of various types of free-text feedback from end users. This creates a dialogue for improvement.

In initiating optimization efforts, it is important to ask the following questions:

- What problem is the alert going to solve?<sup>4</sup>
- Is the alert in line with the goals and policies of the practice or organization?
- How will the alert impact the clinician's workflow?<sup>4</sup>
- Is the alert beneficial (e.g., does it reduce adverse events, increase screening, or increase referrals)?<sup>4</sup>
- Is an alert the appropriate tool (i.e., is there another alternative to accomplish the same goal)?

Attention has focused recently on human factor considerations. Human factors affect interface features, such as the following: Is the presentation simple? Does it use consistent terminology?<sup>23</sup> Is the information readable? How is the information displayed? Is consideration given to the position of the alert, its placement, and the use of space?<sup>24</sup> Considerations must also be given to evaluation of the information that is contained within the alert, and how the user interacts with the alert. Identifying which providers receive high volumes of alerts for which patients, as well as what types of alerts are less frequent, may provide additional insights and in some instances point to build errors or issues.<sup>2</sup> Flexibility in identifying the areas of focus is especially important as new CDS tools and new uses of existing tools take form. Optimizing for safety then encompasses all of these areas.

**Technology considerations.** Technology considerations for optimization encompass the following:

- Have a comprehensive strategy<sup>25</sup>
- Consider adaptive design (e.g., CDS that addresses user behavior and can filter alerts with previous responses)<sup>4</sup>
- Deactivate or redesign alerts of low quality or minimal effectiveness<sup>4</sup>
- Incorporate underlying data and rationale for CDS recommendation<sup>6</sup>
- Transition alert and reminder content to other areas of the EHR<sup>5</sup>
- Incorporate human factor design (e.g., presentation, display)<sup>24</sup>
- Work to minimize cognitive load<sup>24</sup>
- Consider and involve patients

Considerations for optimization appear below (see **Strategies** for Alerts Optimization).

#### Strategies for Alerts Optimization

- Consider both patient safety and clinician burden when choosing to incorporate CDS alerts, or when modifying or optimizing alerts
- Determine the appropriate tool or intervention to convey the intended information while balancing the burden created by the intervention
- Collaborate across departments, systems, and vendors to maximize the usefulness of the current technologies, to modify current functions, and to innovate for additional improvements assessed through measures, functions, usability, impact, and burden

While the safe practice recommendations focus on actions that may not be readily executed today, there are several things that can be done. See a summary of suggestions for areas that can be addressed in **What You Can Do Today**.



#### What You Can Do Today\*

- Recognize that alerts are an effective and straightforward way to communicate and initiate change
- Acknowledge, however, that too many alerts may lead to frustration and anticipation, then ignoring
- Commit to the recognition that if it is not working, it needs to be removed
- Use a committee structure to obtain buy-in and vet new alerts
- Use defaults when possible
- Iterate and improve what you have
- Get rid of stupid stuff
- Anticipate issues and give plenty of choices

\*Modified from Honor Health (workgroup participant).

Moving forward, it is important to identify mechanisms to capture and share feedback. This is important within an organization and across organizations and systems. The ability of organizations to exchange information regarding recommended strategies, implementations, and modifications will facilitate new avenues for improving patient safety.

### Conclusion

CPOE alerts hold promise to improve patient safety but may also endanger it. Finding the balance between effectiveness, efficiency, safety, burden, and clinician concerns such as loss of autonomy will remain a challenge when executing safe practice recommendations for governance, monitoring, analysis, and optimization of CDS alerts. Health IT and content developers, clinicians, pharmacists, hospital administrators, IT professionals, researchers, regulators, and other subject matter experts must work collaboratively to fulfill the goals—both short and long term—surrounding CDS interventions. With effective use and expansion of the safe practice recommendations, it will be possible to optimize alerting within clinical workflows and share knowledge and strategies across organizations to improve safety without contributing to alert burden for clinicians.



### References

- 1. Jankovic I, Chen JH. Clinical decision support and implications for the clinician burnout crisis. Yearb Med Inform. 2020 Aug;29(1):145-54. Also available: <u>http://dx.doi.org/10.1055/s-0040-1701986</u>. PMID: 32823308.
- Chaparro JD, Hussain C, Lee JA, Hehmeyer J, Nguyen M, Hoffman J. Reducing interruptive alert burden using quality improvement methodology. Appl Clin Inform. 2020 Jan;11(1):46-58. Also available: <u>https://dx.doi.org/10.1055/s-0039-3402757</u>. PMID: 31940671.
- 3. Bhakta SB, Colavecchia AC, Haines L, Varkey D, Garey KW. A systematic approach to optimize electronic health record medication alerts in a health system. Am J Health Syst Pharm. 2019 Apr 8;76(8):530-6. Also available: <a href="https://dx.doi.org/10.1093/ajhp/zxz012">https://dx.doi.org/10.1093/ajhp/zxz012</a>. PMID: 31361861.
- McGreevey JD 3rd, Mallozzi CP, Perkins RM, Shelov E, Schreiber R. Reducing alert burden in electronic health records: state of the art recommendations from four health systems. Appl Clin Inform. 2020 Jan;11(1):1-12. Also available: <u>https://dx.doi.org/10.1055/s-0039-3402715</u>. PMID: 31893559.
- Kawamanto K, Flynn MC, Kukhareva P, ElHalta D, Hess R, Gregory T, Walls C, Wigren AM, Borbolla D, Bray BE, Parsons MH, Clayson BL, Briley MS, Stipelman CH, Taylor D, King CS, Del Fiol G, Reese TJ, Weir CR, Taft T, Strong MB. A pragmatic guide to establishing clinical decision support governance and addressing decision support fatigue: a case study. AMIA Annu Symp Proc. 2018 Dec 5;2018:624-33. PMID: 30815104.
- 6. Tcheng JE, Bakken S, Bates DW, Bonner III H, Gandhi TK, Josephs M, Kawamoto K, Lomotan EA, Mackay E, Middleton B, Teich JM, Weingarten S, Lopez MH, editor(s). Optimizing strategies for clinical decision support: summary of a meeting series. Washington (DC): National Academy of Medicine; 2017. 77 p. Also available: <u>https://www.healthit.gov/sites/default/files/page/2018-04/Optimizing\_Strategies\_508.pdf</u>.
- Osheroff JA, editor(s). Improving medication use and outcomes with clinical decision support: a step-by-step guide. Chicago (IL): Health Information Management Systems Society; 2009. Chapter 1: Approaching clinical decision support in medication management. Section 2: Overview of CDS five rights. Also available: <u>https://digital.ahrq.gov/ahrq-funded-projects/current-health-it-priorities/clinical-decision-support-cds/ chapter-1-approaching-clinical-decision/section-2-overview-cds-five-rights.
  </u>
- 8. Quality measures. [Web site]. Baltimore (MD): Centers for Medicare & Medicaid Services; 2020 Feb 11 [accessed 2020 Oct 26]. [6 p]. Available: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityMeasures.
- 9. Clinical practice guidelines. [Web site]. Bethesda (MD): National Institutes of Health, National Center for Complementary and Integrative Health; [accessed 2020 Oct 26]. [6 p]. Available: <u>https://www.nccih.nih.gov/health/providers/clinicalpractice</u>.
- 10. Clinical decision support: more than just 'alerts' tipsheet. Baltimore (MD): Centers for Medicare & Medicaid Services; 2014 Oct. 5 p. Also available: https://www.cms.gov/eHealth/downloads/ClinicalDecisionSupport\_AlertsTipsheet.pdf.
- Strategy on reducing regulatory and administrative burden relating to the use of health IT and EHRs [draft for public comment]. Washington (DC): Office of the National Coordinator for Health Information Technology (ONC); 2018 Nov. 74 p. Also available: <u>https://www.healthit.gov/topic/usability-and-provider-burden/strategy-reducing-burden-relating-use-health-it-and-ehrs</u>.
- 12. Peterson JF, Bates DW. Preventable medication errors: identifying and eliminating serious drug interactions. J Am Pharm Assoc (Wash). 2001 Mar-Apr;41(2):159-60. Also available: <u>http://dx.doi.org/10.1016/s1086-5802(16)31243-8</u>. PMID: 11297326.
- Ancker JS, Edwards A, Nosal S, Hauser D, Mauer E, Kaushal R, with the HITEC Investigators. Effects of workload, work complexity, and repeated alerts on alert fatigue in a clinical decision support system. BMC Med Inform Decis Mak. 2017 Apr 10;17:36. Also available: <u>https://dx.doi.org/10.1186/s12911-017-0430-8</u>. PMID: 28395667.
- Carli D, Fahrni G, Bonnabry P, Lovis C. Quality of decision support in computerized provider order entry: systematic literature review. JMIR Med Inform. 2018 Jan 24;6(1):e3. Also available: <u>https://dx.doi.org/10.2196/medinform.7170</u>. PMID: 29367187.
- 15. Rehr CA, Wong A, Seger DL, Bates DW. Determining inappropriate medication alerts from "inaccurate warning" overrides in the intensive care unit. Appl Clin Inform. 2018 Apr;9(2):268-74. Epub 2018 Apr 25. Also available: <u>http://dx.doi.org/10.1055/s-0038-1642608</u>. PMID: 29695013.
- Genco EK, Forster JE, Flaten H, Goss F, Heard KJ, Hoppe J, Monte AA. Clinically inconsequential alerts: the characteristics of opioid drug alerts and their utility in preventing adverse drug events in the emergency department. Ann Emerg Med. 2016 Feb;67(2):240-248.e3. Also available: <u>http:// dx.doi.org/10.1016/j.annemergmed.2015.09.020</u>. PMID: 26553282.
- Bubp JL, Park MA, Kapusnik-Uner J, Dang T, Matuszewski K, Ly D, Chiang K, Shia S, Hoberman B. Successful deployment of drug-disease interaction clinical decision support across multiple Kaiser Permanente regions. J Am Med Inform Assoc. 2019 Oct;26(10):905-10. Also available: <u>https://dx.doi.org/10.1093/jamia/ocz020</u>. PMID: 30986823.
- Wright A, Ai A, Ash J, Wiesen JF, Hickman TT, Aaron S, McEvoy D, Borkowsky S, Dissanayake PI, Embi P, Galanter W, Harper J, Kassakian SZ, Ramoni R, Schreiber R, Sirajuddin A, Bates DW, Sittig DF. Clinical decision support alert malfunctions: analysis and empirically derived taxonomy. J Am Med Inform Assoc. 2018 May;25(5):496-506. Also available: <u>https://dx.doi.org/10.1093/jamia/ocx106</u>. PMID: 29045651.
- Orenstein EW, Muthu N, Weitkamp AO, Ferro DF, Zeidlhack MD, Slagle J, Shelov E, Tobias MC. Towards a maturity model for clinical decision support operations. Appl Clin Inform. 2019 Oct;10(5):810-9. Also available: <u>http://dx.doi.org/10.1055/s-0039-1697905</u>. PMID: 31667818.
- McEvoy DS, Sittig DF, Hickman TT, Aaron S, Ai A, Amato M, Bauer DW, Fraser GM, Harper J, Kennemer A, Krall MA, Lehmann CU, Malhotra S, Murphy DR, O'Kelley B, Samal L, Schreiber R, Singh H, Thomas EJ, Vartian CV, Westmorland J, McCoy AB, Wright A. Variation in high-priority drug-drug interaction alerts across institutions and electronic health records. J Am Med Inform Assoc. 2017 Mar 1;24(2):331-8. Also available: <a href="http://dx.doi.org/10.1093/jamia/ocw114">http://dx.doi.org/10.1093/jamia/ocw114</a>. PMID: 27570216.
- 21. Giordano TP. The HIV treatment cascade–a new tool in HIV prevention. JAMA Intern Med. 2015 Apr;175(4):596-7. Also available: <u>http://dx.doi.org/10.1001/jamainternmed.2014.8199</u>. PMID: 25706538.



- Wright A, McEvoy DS, Aaron S, McCoy AB, Amato MG, Kim H, Ai A, Cimino JJ, Desai BR, El-Kareh R, Galanter W, Longhurst CA, Malhotra S, Radecki RP, Samal L, Schreiber R, Shelov E, Sirajuddin AM, Sittig DF. Structured override reasons for drug-drug interaction alerts in electronic health records. J Am Med Inform Assoc. 2019 Oct;26(10):934-42. Also available: <u>https://dx.doi.org/10.1093/jamia/ocz033</u>. PMID: 31329891.
- Payne TH, Hines LE, Chan RC, Hartman S, Kapusnik-Uner J, Russ AL, Chaffee BW, Hartman C, Tamis V, Galbreth B, Glassman PA, Phansalkar S, van der Sijs H, Gephart SM, Mann G, Strasberg HR, Grizzle AJ, Brown M, Kuperman GJ, Steiner C, Sullins A, Ryan H, Wittie MA, Malone DC. Recommendations to improve the usability of drug-drug interaction clinical decision support alerts. J Am Med Inform Assoc. 2015 Nov;22(6):1243-50. Also available: <a href="http://dx.doi.org/10.1093/jamia/ocv011">http://dx.doi.org/10.1093/jamia/ocv011</a>. PMID: 25829460.
- 24. Miller K, Mosby D, Capan M, Kowalski R, Ratwani R, Noaiseh Y, Kraft R, Schwartz S, Weintraub WS, Arnold R. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc. 2018 May;25(5):585-92. Also available: <a href="https://dx.doi.org/10.1093/jamia/ocx118">https://dx.doi.org/10.1093/jamia/ocx118</a>. PMID: 29126196.
- 25. Saiyed SM, Davis KR, Kaelber DC. Differences, opportunities, and strategies in drug alert optimization-experiences of two different integrated health care systems. Appl Clin Inform. 2019 Dec;10(5):777-82. Also available: <a href="https://dx.doi.org/10.1055/s-0039-1697596">https://dx.doi.org/10.1055/s-0039-1697596</a>. PMID: 31618781.



### Appendix A. Safe Practice Recommendations

Safe Practice Recommendations				Stakeh	olders	*
Governance	Strategies	Implementation Actions	нсо	V/D	REG	RES
Identify, develop, and execute a CDS and knowl- edge base governance plan	Engage leadership by providing an understanding of value and organizational impact	Provide information to senior leadership regarding the importance of regular and routine management of CDS (e.g., alerts) and knowledge base software	x			
Rationale: Good governance		Provide leadership with use cases demonstrating return on investment and outcomes assessment <sup>1</sup>				
does not reside in the technology alone, rather good governance creates	Identify a multi-stakeholder oversight team and assign ongoing accountability	Convene team members from multiple disciplines. Include subject matter experts who have roles at each phase in the process	х			
the structure and a process, for leadership and for those assigned to identify improvements through prioritization, deci- sion-making, evaluation,		Focus the team's activities on monitoring, analyzing, and optimizing CDS functions to make the most of information obtained from the EHR, knowledge base, and guidelines to improve safety and usability (see The "5 Rights" of CDS <sup>1</sup> ) <sup>2</sup>	x			Х
and optimization		Identify and obtain resources; delegate, assign resources	x			
	Conduct a CDS inventory	Track CDS tools (e.g., alert implementation, use, actions taken, and updates) to identify modifications that may be needed	x	х		Х
		<ul> <li>Identify and evaluate CDS tools (e.g., alerts) regardless of origin:</li> <li>EHR-provided CDS and alert configuration options</li> <li>Customized by HCO—both organization specific and vendor provided</li> </ul>	x	x		
		<ul> <li>Vendor/developer knowledge bases</li> </ul>		х		
	Perform knowledge base content review	<ul> <li>Perform ongoing and periodic evaluations of knowledge base, guidelines, and CDS triggers to adjust content and actions</li> <li>Reassess customizations against new knowledge</li> <li>Review knowledge base and incorporated guidelines for agreement with current standards of practice, accuracy, strength of evidence</li> <li>Retire/remove and adjust alerts or change alert thresholds as appropriate</li> <li>Reevaluate and update as appropriate based on local outcomes or population evidence</li> </ul>	x	x		
	Evaluate findings to identify and update actions	<ul> <li>Identify modification or actions that are required or desired</li> <li>Determine whether other tools would achieve the desired results</li> <li>Prepare for processes for routine monitoring, analysis, and optimization</li> </ul>	x	х		
	Disseminate best practices	<ul> <li>Enable functions that provide the ability to improve healthcare safety by:</li> <li>Sharing alert logic, metrics, benchmarks, and other information</li> <li>Sharing learnings and best practices within and across systems</li> </ul>	x	x	х	Х



Safe Practice Recommendations			9	Stakeh	olders	*
Monitoring	Strategies	Implementation Actions	нсо	V/D	REG	RES
Gather data and information using CDS-specific metrics and other tools to identify	Use technology to assemble information needed to monitor CDS alerts:	Continually monitor alerts in order to identify trends (e.g., is the alert commonly overridden?)	х	х		х
real-time and/or near real- time CDS alert functioning	<ul> <li>Descriptive</li> <li>Performance</li> </ul>	Incorporate mechanisms (reports/dashboards) to facilitate analysis	х	х		
and impact	— Response — Burden	Assign accountability/ownership for ongoing monitoring and reports of those findings	х			
	Expand resources for CDS alert monitoring to include information obtained from safety events, help desk tickets, walkrounds, trends, and reports	<ul> <li>Enable patient safety/risk/quality, informatics/IT, and staff to:</li> <li>Identify and report events related to CDS alerts:</li> <li>Create issue awareness</li> <li>Use a variety of reporting tools (event reporting, help desk tickets, walkrounds)</li> <li>Incorporate a safety reporting culture</li> <li>Receive feedback:</li> <li>About CDS alert function</li> <li>Changes requested</li> <li>Tools available to provide the requested information</li> </ul>	x	x		х
	Measure alert performance by accessing information about specific volumes, clinical users, triggers	<ul> <li>Create consensus around a set of alert metrics to assess the following aspects of alerts:</li> <li>Descriptive: measures and frequency—what were the volume and targets of CDS alerts, what actions were taken?</li> <li>Performance: functionality—did the alert fire, and did it fire as expected?</li> <li>Response: clinician interaction/usability—how did the alert recipient interact with the alert?</li> <li>Burden: harm index/impact—what was the impact of alerts on recipients?</li> </ul>	Х	Х		х

Safe Practice Recommendations				Stakeh	olders	*
Analysis	Strategies	Implementation Actions	нсо	V/D	REG	RES
Regularly assess, evaluate, and interpret metrics, functionalities, usability, and	Analyze CDS alert data to evaluate findings on frequency, function, impact, value, and	Identify opportunities for improvement by looking at trends, patterns, and anomalies identified when moni- toring frequency, function, impact, value, and burden	х	х		
impact to determine effec- tiveness while balancing and minimizing burden	burden on a regular and on an "as needed" basis	Evaluate alerts using the "5 rights" of $CDS^{12}$	Х	Х		
	Conduct proactive and reactive risk assessments as part of ongoing analysis and evaluation	Develop risk assessment scoring process (e.g., FMEA risk scoring process) to prioritize work on alerts and the actions to be taken	х	х		
		Develop triage mechanism to evaluate and prioritize changes and evaluate the impact of CDS alerts on patient safety/clinician burden	х	х		
		Provide feedback mechanisms	Х	Х		



Safe Practice Recommendations			9	Stakeh	olders	*
Optimization	Strategies	Implementation Actions	нсо	V/D	REG	RES
Maximize the use of technology and	Consider both safety and burden when choosing to	Engage oversight team and processes for decision-making on optimization actions	x	х		
various tools to create and promote effective, targeted, relevant, and routinely updated alerts	incorporate CDS alerts, or when modifying or optimizing alerts	<ul> <li>Modify alerts based on data obtained through monitoring and analysis to:</li> <li>Modify CDS alerts to maximize or enhance recognition of the alert</li> <li>Provide valued, relevant, timely information to the user</li> <li>Direct CDS alert to the specific user</li> <li>Direct CDS alert to a particular patient or condition</li> </ul>	x	x		
		Use a risk-priority scoring mechanism, when applicable, to identify priorities for alert changes or modifications	х	Х		
	Determine the appropriate	Optimize CDS alerts considering the "5 rights" of $CDS^{\dagger_2}$	X	Х		
	tool or intervention to convey the intended information while balancing the burden	Determine whether the intervention should be displayed as a CDS alert or if there are other non-alert alternatives	х	х		
	created by the intervention	<ul> <li>When considering optimization actions:</li> <li>Assess CDS alert justification, evidence analysis</li> <li>Balance priorities</li> <li>Consider appropriate CDS alert type (interruptive versus noninterruptive)</li> </ul>	x	x		
	Collaborate across depart- ments, systems, vendors to maximize the current technologies, modify current functions, and innovate for additional improvements assessed through measures, functions, usability, impact, and burden	<ul> <li>Identify workflow interventions:</li> <li>Work with frontline users to establish appropriate timing of alerts and in which workflow</li> <li>Take actions to achieve the identified goals of CDS alert incorporation: <ul> <li>Ensure the information is noticed</li> <li>Allow for customization options</li> <li>Provide relevant information as part of the alert display</li> <li>Facilitate appropriate actions based on the information</li> <li>Provide value at the point of care</li> <li>Allow for informed decision-making</li> <li>Minimize user interruptions</li> <li>Communicate updates</li> </ul> </li> <li>Work with developers to maximize CDS alert functions within the workflow</li> </ul>	x	x		х
		<ul> <li>Incorporate a feedback loop to include all stakeholders (e.g., vendors, leadership, clinicians, informatics, IT):</li> <li>Allow for real-time or near real-time feedback within the workflow from end user</li> <li>Where appropriate, communicate changes and updates to alerts</li> <li>Develop a triage mechanism to evaluate and prioritize changes, and evaluate the impact of CDS alerts on patient safety and clinician burden</li> <li>Provide feedback mechanisms</li> </ul>	x	x	x	X
		<ul> <li>Share alert logic, metrics, benchmarks, and other information within and across systems to improve healthcare safety</li> </ul>	х	х	х	Х

\* Stakeholder key: HCO, healthcare organization (includes clinicians, providers, and internal IT personnel); V/D, vendor/developer (includes EHR, knowledge base and third-party vendors); REG, regulatory (includes government, regulatory agencies, and accreditation agencies); RES, researchers

† 5 rights of CDS: 1. Right information 2. Right person 3. Right CDS intervention format 4. Right channel 5. Right time in workflow<sup>2</sup>

CDS, clinical decision support; EHR, electronic health record; FMEA, failure mode and effects analysis; IT, information technology



### References

- Tcheng JE, Bakken S, Bates DW, Bonner III H, Gandhi TK, Josephs M, Kawamoto K, Lomotan EA, Mackay E, Middleton B, Teich JM, Weingarten S, Lopez MH, editor(s). Optimizing strategies for clinical decision support: summary of a meeting series. Washington (DC): National Academy of Medicine; 2017. 77 p. Also available: <u>https://www.healthit.gov/sites/default/files/ page/2018-04/Optimizing\_Strategies\_508.pdf</u>.
- Osheroff JA, editor(s). Improving medication use and outcomes with clinical decision support: a step-by-step guide. Chicago (IL): Health Information Management Systems Society; 2009. Chapter 1: Approaching clinical decision support in medication management. Section 2: Overview of CDS five rights. Also available: <u>https://digital.ahrq.gov/ ahrq-funded-projects/current-health-it-priorities/clinical-decision-support-cds/chapter-1-approaching-clinical-decision/ section-2-overview-cds-five-rights.
  </u>



### **Appendix B. Literature Review**

### **Executive Summary**

Clinical decision support (CDS) tools, in particular computerized provider order entry (CPOE) alerts, are designed to facilitate both decision-making and safer care.<sup>1</sup> However, the integration of CPOE alerts creates changes in workflow and communication that sometimes have unexpected consequences, including incorrect or untimely alerts that impact patient safety and increase clinician burden. ECRI's *Partnership for Health IT Patient Safety*, recognizing that technology has the potential to improve alerting and to minimize burden, brought together a group of experts to evaluate CPOE alerts. The group focused on monitoring, analysis, and optimization of CPOE alerts. This literature review is part of that analysis.

### Background

Clinical decision support (CDS) encompasses a number of different tools, but alerts are often the first CDS tool that comes to mind.<sup>2</sup> However, while CDS alerts are focused on providing information to promote patient safety, recently attention has focused on the role alerts play in increasing clinician burden and the role they may play in clinician burnout.<sup>3</sup> As a contributor to clinician burden, alerts are often tagged as having low specificity (lack of clinical relevance for an individual patient); providing poor content; and contributing to systems with high sensitivity but low specificity.4 "Low acceptance rates of alerts are concerning because when alerts are identified as inappropriate, clinicians have shown reduced responsiveness to future alerts."5 Clinician burden attributed to alerts has also been identified as resulting from interruptions, numerous required actions (e.g., mouse clicks),<sup>2</sup> and increased time spent interacting with the technology. "Alert fatigue in medicine has primarily focused on alerts related to computerized physician order entry (CPOE)."5

A number of investigations and pilot studies have been conducted to determine how to best evaluate and address issues surrounding the use of alerts and clinician burden, in particular how to improve alerts and minimize burden. As part of the work conducted by the *Partnership for Health IT Patient Safety*, collaborators sought to advance strategies to minimize alert fatigue and decrease burden. This evidence review was conducted as part of the *Partnership*'s process. This literature review looks at three questions, focusing on what can be done to improve alert monitoring, analysis, and optimization:

- What fields are important to monitor in order to analyze alerts?
- How can analysis and prioritization of alerts determine focus for optimizations?
- How can alerts be effectively optimized to maintain safety and minimize user burden?

While the *Partnership* workgroup was investigating the areas of monitoring, analysis, and optimization, an additional theme emerged: It became evident that a discussion of governance processes would shed light on these three areas. The *Partnership*'s recommendations to improve alert recognition and minimize burden thus include governance, monitoring, analysis, and optimization, with considerations for design, implementation, and use.<sup>6</sup>

### **Methods**

A systematic search of the literature was conducted by master'slevel medical librarians. A search of English-language studies published between January 2015 and April 2020 using a key word search was conducted of the Medline/PubMed, Embase, CINAHL, and Scopus databases. The initial key word search focused on the following terms: computerized provider order entry, CPOE, clinical decision support, CDS, alert, alerting, alert fatigue, system improvement, safety, governance, health information technology, health IT, and electronic prescribing. This search yielded approximately 15,000 results. The search was refined to focus on order entry, drug-drug interactions (DDIs), fatigue, optimization, overrides, and scoring tools. This reduced the results to 700 records. From here, further refinement using the key questions identified above resulted in 177 abstracts.

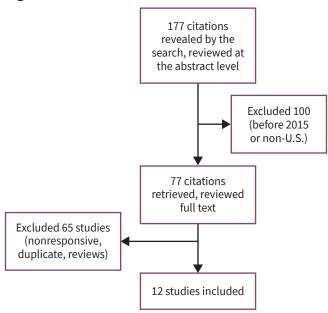
All 177 titles and abstracts were screened by a clinical analyst and 77 initially relevant texts were identified for full-text review by a single clinical reviewer. Studies older than 2015 (n = 9) and studies conducted in non-US settings (n = 5) were excluded. The resulting 63 articles were reviewed by a combination of clinical analysts, pharmacy fellows, and pharmacy students. Each reviewer was tasked with full-text review and evaluation, determining the type of study (e.g., before-and-after, pilot),



identifying unique study design (alert type, population, location), and assessing whether an article met the inclusion criteria and addressed the three questions for CPOE alerts. Any conflict in determinations were resolved by the reviewer who had examined all of the materials.

The materials that were part of the review were distinguished by whether they provided information regarding the key questions. Initial evaluation looked at monitoring (n = 52), analysis (n = 7), and optimization (n = 4). Articles addressing monitoring were then identified for joint characterizations, namely monitoring and analysis (n = 24), monitoring and optimization (n = 1), monitoring, analysis, and optimization (n = 25), and monitoring (n = 2). Upon final evaluation, 12 studies identified were included, with three studies highlighting monitoring, four studies highlighting analysis, and five studies focused on considerations for optimization.

#### Figure. Literature Review



### Results

Researchers have sought to identify mechanisms to reduce burden and determine why some CDS alerts go unnoticed. Much work focuses on the alerts themselves. Investigations have focused on the volume of alerts received, their timing (e.g., mismatch with CPOE workflow),<sup>7</sup> the repetitiveness of alerts,<sup>8</sup> clinician desensitization to alerts,<sup>8</sup> and the value of alerts, such as their positive predictive value (PPV).<sup>9</sup>

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

The actions taken based on alert content have also been investigated, but this remains a difficult area to examine retrospectively.<sup>10,11</sup> Other studies have looked at CDS alert function and usability,<sup>12</sup> noting when the tools work as designed and when they do not.<sup>13</sup> No consensus exists as to how to manage CDS alerts without some level of burden.<sup>14</sup> The consequences of burden, and in particular alert fatigue, include lost efficiency, overdependence on the technology, decreased satisfaction with the electronic health record (EHR), and desensitization to alerts, resulting in patient harm.<sup>15</sup>

Most studies agree that "it is essential to refine alerting systems to highlight clinically significant alerts and eliminate inconsequential alerts thereby preventing alert fatigue and maintaining patient safety."<sup>11</sup> While recommendations have been made to improve alert functionality to prioritize critical information and minimize alert fatigue,<sup>2</sup> additional strategies are still needed. These strategies should take into account the multiple contributors to clinician alert burden.<sup>2</sup>

Prioritizing what to monitor to improve alerts and to lessen burden is complex. Determining what to monitor and who should be responsible remains an issue. The processes and determinations of what to monitor are challenging, especially when the content is obtained through a number of vendors. Wright et al. provide some insight into what tools to use and how to monitor CDS to mitigate error.<sup>13</sup>

#### 1. Fields to Monitor

Three of the studies included addressed fields for monitoring, focusing on features such as timing and appearance of alerts; their content (accurate, actionable); interactions with the alerts (alerts unopened, low adherence to recommendations provided, overrides); and governance of current and new alerts with attention to customization and evidence. Measures remain a challenge as there "[]is no agreed upon measure to assess alert effectiveness and burden."<sup>3</sup>

Wright et al. looked at reasons for alert overrides, in particular overrides for DDI alerts.<sup>16</sup> Monitoring override reasons provides insight into a provider's rationale for overriding an alert, highlights clinician understanding surrounding alerts (awareness of harm, awareness of potential interaction), may be capable of influencing clinician behavior, and provides data that can be used to support improvements.<sup>16</sup>

Methods to monitor override reasons can include free-text (not used in Wright's study) and coded options for overrides (with the



number of available choices varying); length and detail provided for override reasons vary, with some sites able to tailor reasons to the type of the alert and some not.<sup>16</sup> The quality of override reasons varied and did not always provide actionable items for improvement. <sup>16</sup> Given that monitoring and improvement actions are resource intensive, the researchers suggested prioritizing alerts by first looking at those most commonly firing, those most frequently overridden, and the most risky interactions for the treatments.<sup>16</sup>

Yoshida et al.<sup>17</sup> noted that monitoring CDS provides opportunities to identify malfunctions and opportunities for improvement, for instance by detecting when alerts stop firing. These authors focused on monitoring CDS firing rates and patterns, monitoring 248 CDS interventions over a two-year period looking at the "whens" and "whys" of alert firing.<sup>17</sup> The group identified all point-of-care alerts and reminders that were targeted to users providing care, regardless of care setting but focusing on alerts that interrupted workflow.<sup>17</sup> Monitoring was divided into four areas: preactivation monitoring, ad hoc monitoring (occurring as needed), and continuous automated monitoring (occurring indefinitely after postactivation monitoring).<sup>17</sup>

The data elements that were monitored included:

- Alert instance identification number
- Date and time of alert
- Name and identification of CDS intervention
- Type of CDS intervention: interruptive, noninterruptive, or CDS that is not seen by providers
- CDS monitoring status
- Patient and provider identification
- Location of service
- Provider interaction with an interruptive alert (follow-up action)<sup>17</sup>

Plotting daily alerted patient counts against days and daily alert counts against days was used in this instance as a method to assess burden of a particular intervention.<sup>17</sup> The information the authors obtained could then be tailored to users and show subsets of CDS interventions, time periods, and locations.<sup>17</sup> Continuous automated monitoring was achieved by an algorithm that processed the alert data of individual CDS interventions for a given time frame.<sup>17</sup> Monitoring these elements informed the investigation and led to improvements.

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

Wright et al.<sup>13</sup> took monitoring a bit further, focusing on the role CDS can play in causing error. Recognizing that CDS may not always work as designed or expected, attention turned to log data analysis. Data were obtained for the number of times an alert fired each day for a period of at least one year, noting spikes and dips in firing; additionally, case report survey information was gathered, and override comments were aggregated and analyzed.<sup>13</sup> User reports (e.g., help desk tickets, safety reports, contacts with the chief medical information officer or knowledge engineers) were identified as the most common source of information about CDS malfunctions (reporting false positives rather than an alert that should have fired but did not).<sup>13</sup> This examination shed light on how CDS can malfunction.<sup>13</sup>

The malfunctions' causes resided in build errors, conceptualization errors (rule not designed correctly), release of new codes, defects in EHR software (which may have required a patch or resulted from a system upgrade), environment migration and logic corruption (e.g., migrating between development, test, production), failures in external computing services (e.g., medication classification service), mismatches between alert logic and alert display, and inadvertent changes in a rule or modification of a component of a rule that causes an inadvertent change in other rules.13 The authors suggested that robust pre- and postgo-live testing and monitoring would improve CDS and decrease its potential for malfunction. EHR vendors and content suppliers, they suggested, should supply tools for monitoring CDS in real time or near real time, and enhance tools for content authoring and knowledge management (e.g., automated dependency checking tools to mitigate errors related to code changes).<sup>13</sup>

As Yoshida et al.<sup>17</sup> suggested that, ongoing, continuous, and automated monitoring is essential to implementing and maintaining CDS.

#### 2. Analysis and Prioritization for Optimization

Four studies were included in response to the analysis question. How information from alert monitoring is evaluated and used to identify issues and prioritize improvements is reflected in these studies.

Bhakta et al.<sup>15</sup> evaluated interventions made in optimizing DDI alerts. The study demonstrated a decrease in the total number of weekly inpatient alerts and an increase in acknowledged alerts. By using a risk-based systematic and coordinated strategy for alerts, the team focused on improving alert performance by decreasing the number of alerts and increasing the alert responsiveness. The analytic team comprised physicians,



pharmacists, medication safety officers, bioinformaticists, and other healthcare professionals across the health system involved in the medication-use process along with representatives from the eight entity hospitals.<sup>15</sup> Those supporting the analytic team included the chief quality officer, chief medical informatics officer, EHR analysts, and the system medication safety officer.

Data on alert and warning frequencies, severity, and response type were analyzed before and after interventions. Following reclassification of DDIs, weekly alert override rates and alert acceptance rates were assessed. The actions taken included turning off 802 of 875 moderate DDI alerts that were deemed unnecessary and reclassifying the remaining 73 alerts. Prescribers saw an increase in the number of alerts, but pharmacists saw a decrease during the order-verification stage. This resulted in a total of 1,265 DDI alerts, 446 (35%) contraindicated and 819 (65%) severe. The study emphasized the importance of a multidisciplinary analytic team to facilitate decisions on optimization. Importantly, this study was conducted at a university-affiliated medical center with strong leadership, the ability to make system-wide changes, and dedicated information technology (IT) support, resources that may not be readily available to those seeking to conduct similar analyses.

Chaparro et al.<sup>5</sup> used a quality improvement methodology to focus on reducing the number of interruptive alerts received by providers. An additional focus of their work included "increasing physician feedback on alert utility and usability." Their study focused on non-CPOE alerts (alerts created outside of CPOE, such as reminders of overdue vaccinations, the need to complete documentation, creating awareness of high-risk conditions that may impact decision-making). Recall that such alerts are triggered by patient and/or provider characteristics at various times within the workflow.<sup>5</sup>

The study identified key drivers: appropriate display of alerts, clear alert content, alert governance, user feedback regarding overrides, and respect for user knowledge and intent, with regard to 11 interventions.<sup>5</sup> For example, when seeking to identify the "right person," the drivers consisted of appropriate display of alerts and respect for user knowledge and intent. While multiple drivers were identified, the focus was on five key drivers: review of clinical content; use of more workflow-specific triggers; targeting the "right" person; reviewing rules and criteria to target "right" patients, and analyzing override comments, as well as standardizing text display and standardizing intake processes.<sup>5</sup>

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

The study addressed the top 25 of the 170 interruptive alerts with a goal of reducing the total volume of weekly interruptive alerts shown to providers by 35% (from 7,250 to 4,700 per week).<sup>5</sup> The group exceeded their goal and continued to achieve decreases from baseline. They concluded that by using a quality improvement approach and using tools such as Pareto charts and live monitoring dashboards, they were "able to better focus [their] limited resources toward changing alerts that would provide the most return."<sup>5</sup>

McGreevey et al.<sup>3</sup> noted that alerts are not without cost. These costs impact the clinician, the organization, and the patient. They include opportunity costs, time, lost productivity, fatigue, and safety costs. These authors focused on governance and management, noting that management is often difficult because of "regulatory mandates, public reporting initiatives, liability concerns, [and] other external pressures that may incline institutions to advocate for more rather than fewer alerts to avoid preventable harm."<sup>3</sup> Also contributing to governance and management issues were variations in clinicians' drug knowledge and experience; system inertia where alerts, once created and deployed, may accumulate over time and compete for ongoing attention; and other priorities in the health system.<sup>3</sup> The researchers noted that organizations should conduct ongoing analysis and review of alerts, emphasizing that governance is complex but essential infrastructure for effective alert management.<sup>3</sup>

McEvoy et al.<sup>18</sup> recognized the benefits and the challenges of CDS alerts, noting that while alerts have high override rates, clinicians recognize that alerts are beneficial in preventing prescription of "never" combinations of drugs.<sup>18</sup> The authors studied 15 drug pairs that should "always be alerted on" from a list developed by Phansalkar et al.<sup>19</sup> with sponsorship of the Office of the National Coordinator for Health Information Technology, and evaluated the implementation of these alerts.<sup>18</sup> The authors assessed whether there was a standard of care regarding DDI alert implementation, and analyzed and evaluated the impact of EHR vendors and of healthcare organizations on DDI alert implementation and display.<sup>18</sup>

The authors concluded that a standard should be developed for DDI alerts across institutions; however, to be optimally effective clinical workflows, user interfaces, and data quality—in particular the accuracy and currency of medication lists—require improvement.<sup>18</sup> Endorsing the recommendations set forth by Payne et al. (discussed in Section 3),<sup>20</sup> the authors offered two additional recommendations. First, they suggest that DDI



knowledge bases be assessed to evaluate clinical significance and to look at DDI alerts to determine whether the proper interactions generate alerts. Determining and assessing tiering approaches looking at display (interruptive, passive, on request) and when and how override reasons are needed are part of that evaluation. Second, the authors recommend development of an officially approved, standardized DDI knowledge base, and consideration for a possible "safe harbor" or other legal protections for those implementing that knowledge base.<sup>18</sup>

#### 3. Optimizing Alerts to Maintain Safety and Minimize Burden/Burnout

Five studies were included in response to the optimization question. Wright et al.<sup>16</sup> have suggested improvements that could be made collaboratively with healthcare organizations, EHR vendors, and knowledge base vendors in order to create more specific actionable alerts. These suggestions included tiering alerts by severity; identifying and displaying relevant data; creating the ability to take action directly from the alert window; allowing action from the alert (e.g., cancellation of new medications and discontinuation of existing medications that are indicated); creating only a small number of override reasons, and allowing users to document their reasoning with a coded override that includes the ability to communicate the reasoning to others; and allowing users to provide feedback for improvement.<sup>16</sup>

Payne et al.<sup>20</sup> focused on improving the usability of DDI alerts with a focus on streamlining and standardizing DDI alert processes with consistent terminology, symbols and icons, color, minimal text, formatting, content, and reporting standards. The key areas of focus included the what, how, where, and when to display DDI decision support; whether the presentation of DDI decision support should vary by clinician; and how effectiveness of DDI decision support should be measured.

In improving alerts it is imperative to consider the contributing factors to excessive DDI alerts, which Payne et al. noted include inconsistent evaluation and classification of interactions, lack of specificity in alert logic, and perceived risk of legal liability. Noting that design presentation lacked clear recommendations and best practices, the researchers recommended "the consistent use of terminology, visual cues, minimal text, formatting, content, and reporting standards."<sup>20</sup> They also identified as means of optimization the use of signal words indicating the seriousness of the DDI, hazard information, instructions or actions on how to reduce risk of injury, and specific clinical

consequences that may ensue if the hazard is not averted.<sup>20</sup>

The study identified seven core elements that should be included in DDI decision support, suggesting that DDI information should be presented to all clinicians.<sup>20</sup> These core elements include drugs involved, seriousness, clinical consequences, mechanism of the interaction, contextual information and modifying factors, recommended actions, and evidence.<sup>20</sup> In alert presentation, they recommend consistent use of color and visual clues, consistent terminology, brevity, and minimizing the impact on workflow.<sup>20</sup> They also point to the importance of the "where" and "how" of information presentation. They note that alert display should be at the point of decision-making and that taking actions should be possible directly from the alert (with the clinician selecting from a list of actionable choices).<sup>20</sup> Importantly, this study noted that "in their current form, override rates have limited capability to evaluate alert effectiveness" as the information is often not granular enough to identify needed modifications or determine the underlying reason for the override.<sup>20</sup> Payne et al. concluded that having standard DDI alert data collection and analysis would lead to greater collaboration, help identify value and clinical relevance, and allow collective outcome measures.<sup>20</sup>

Jankovic and Chen<sup>14</sup> conducted a survey assessment to identify ways to optimize CDS to reduce clinician burnout. They define burnout as "a syndrome of emotional exhaustion, depersonalization, and a low sense of personal accomplishment." The authors identify multiple factors as causes of burnout, including workload, inefficiencies, and moral distress<sup>14</sup> and note that burnout can result in depression, substance abuse, occupational injury, suicide, and increases in medical errors, patient dissatisfaction, and patient mortality.<sup>14</sup>

Jankovic and Chen stress consideration of the "5 rights" of CDS (right information at the right time, given to the right people, in the right format, via the right channel).<sup>14</sup> They recommend including stakeholders in the design, implementation, and optimization of alerts.<sup>14</sup> To reduce burden, they suggest minimizing within-patient identical alerts to reduce cognitive load; considering sensitivity and specificity of alerts; considering tiering of alerts to improve acceptance; considering human factors in CDS design; and including role-tailored alerts, for instance to pharmacists instead of physicians as appropriate. "Incorporating as much specific patient data as possible to improve positive predictive value," they note, is "more important than using a large database of knowledge that may generate false positives,"<sup>14</sup> as is reviewing CDS at regular intervals after



implementation to ensure that rules are up to date.<sup>14</sup> Improving CDS interfaces, limiting mouse clicks, and not having pop-up windows block access to the chart were seen as ways to improve how clinicians interact with CDS within the EHR. Using CDS to limit excessive documentation, addressing how CDS is incorporated into workflows, and integrating CDS into the existing EHR are other optimization strategies the authors propose.<sup>14</sup>

Saiyed et at.<sup>21</sup> looked at two sites and evaluated medication alert rates with the aim of reducing these alerts. The authors recommend that healthcare systems develop a strategy that involves all categories of drug alerts. Using silent alerting as part of this strategy allows data gathering about the frequency, the type, and the possible clinical significance of alert overrides.<sup>21</sup> They recommend encouraging vendors to produce standard reports on drug alerts by category to allow for comparisons within and across institutions.<sup>21</sup> The process for review of drug CDS should be continuous and should focus on improvement. The authors offer eight recommendations, including instituting an integrated team with a leader to design and maintain drug alerting; using a trusted drug-information reference source that is updated regularly and automatically; developing a comprehensive strategy; balancing the risks and benefits of alerts; using silent alerting to evaluate alerts before showing them to users; implementing standard reporting; focusing on systemic approaches; and using continual refinement with ongoing analysis, user feedback, and continuous improvement.<sup>21</sup>

Kawamanto et al.<sup>7</sup> focused on the governance of CDS, noting that "If the right solution is not implemented, a vicious cycle may ensue where new CDS—however how accurate and valuable as it may be—leads to further CDS fatigue, reduced overall CDS effectiveness, and provider dissatisfaction." The governance plan included an enterprise CDS committee that met monthly, reviewed requests for new CDS, and reviewed existing CDS for optimization or retirement.<sup>7</sup> "Bug fixes" could be changed by IT without additional review.<sup>7</sup> Safety issues were addressed without review by the entire committee.<sup>7</sup> Core principles included requiring new CDS to be added only if actually desired by the intended recipients; using the most appropriate and least disruptive workflow integration approach; and requiring that the benefits from CDS outweigh the costs.<sup>7</sup> Emphasis was also placed on communicating change.

Reliance on active solicitation of feedback was important for optimizing content, as was data analytics (frequency, user response—override versus acceptance) and the transition of alert

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

and reminder content to more appropriate areas of the EHR.<sup>7</sup> To evaluate CDS burden, metrics consisted of "the average number of clinician-facing medication alerts per visit; the average number of clinician-facing [best practice advisories] per visit, and the combined per-visit average of both CDS types."<sup>7</sup> Three years after implementation of the governance plan, "overall alert and reminder volume was reduced by 53.8%, with medication alerts being reduced by 19.8% and [best practice advisories] reduced by 66.9%."<sup>22</sup> The study had several limitations: it focused on clinicians, defined as excluding pharmacists, nurses, and medical assistants; it did not include review of CDS for health maintenance; it investigated CDS recommendations that occur in a voluntarily accessed section of the EHR; the approach used does not have wide adoption; and the study did not look at the impact of CDS governance on clinical outcomes.<sup>7</sup>

Miller et al.<sup>23</sup> looked at design criteria by conducting a narrative review for the period 2000 to 2016, including 14 papers. Beginning with the belief that "lack of knowledge regarding alert presentation to provider has impeded optimization," recommendations were aimed at optimizing "design, organization, management presentation and utilization of information through presentation content and function." A total of 42 recommendations included those for the interface (11), the information (10), and the interaction (21) with CDS system. These categories were additionally broken into presentation, placement positioning and provision of multiple presentation layers, clean and concise, content guidance and consistency, and "fast, fit, feedback, forgiveness, and flexible" design.<sup>23</sup>

Optimizing alerts is a difficult process. The challenge lies in the fact that there are "no standard/repeatable implementations across institutions, no easily-accessed store of good exemplars of CDS design,"<sup>24</sup> and no widely exchanged operational components (triggers, notifications, standard sets and templates).<sup>24</sup>

### Conclusion

The research focused on gathering information. User feedback was identified as a valuable source of information. Alert metrics while not standard, and often difficult to interpret, will play a role in analysis and optimization. In order to sustain improvements, smart design, technology use, human factor considerations, and cultural acceptance will all play a role. More research is needed. And we will need the results of that research and resulting improvements to be readily shareable across organizations and systems in order to improve alerting and minimize burden.



### **Evidence Tables**

Study Details	Study Goals	Design and Context	Results	Conclusions
Monitoring				
<b>Reference:</b> Wright et al. (2018) <sup>13</sup>	Develop an empirically derived taxonomy for clinical decision support (CDS) alert malfunctions	<ul> <li>Identified CDS alert malfunctions using a mix of qualitative and quantitative methods:</li> <li>Site visits with interviews of chief medical officers, CDS developers, clinical leaders, and CDS end users</li> <li>Survey of chief medical informatics officers</li> <li>Analysis of: <ul> <li>Firing rates</li> <li>Override CDS</li> </ul> </li> </ul>	<ul> <li>68 CDS alert malfunction cases from 14 sites with different elec- tronic health records (EHRs) were examined. User feedback was the predominated mode of discovery. Four primary axes emerged: <ol> <li>The cause of the malfunction,</li> <li>Its mode of discovery,</li> <li>When it began, and</li> <li>How it affected rule firing.</li> </ol> </li> <li>Most frequent cause of errors identified: <ol> <li>Build errors</li> <li>Conceptualization errors</li> <li>Introduction of new concepts or terms</li> </ol> </li> </ul>	Used a taxonomy to: – Identify CDS alert malfunctions – Look at common recurring issues that cause the malfunctions – Prevent the malfunctions – Detect and resolve them
<b>Reference:</b> Wright et al. (2019) <sup>16</sup>	Determine availability and use of structured override reasons for drug-drug interaction (DDI) alerts in EHRs	Collected data on DDI alerts and override reasons from 10 clinical sites using a multistage iterative card sort method to categorize the override reasons form all sites and identified best practices	<ul> <li>177 unique override reasons across the 10 sites were identified, with coded override reasons at each site ranging from 3 to 100:</li> <li>Some sites had override reasons that were not relevant to DDIs</li> <li>Three categories accounted for 78% of all overrides: "will monitor or take precautions," "not clinically significant," and "benefit outweighs risk."</li> </ul>	Providers should have options to choose when indicating reasons for overriding DDI alerts. DDI alerts should be actionable and tailored to the patient and drug pairs
Reference: Yoshida et al. (2018) <sup>17</sup>	Implementation of a program to create and maintain properly functioning CDS by systemat- ically monitoring CDS firing rates and patterns	<ul> <li>Before-and-after study</li> <li>Four types of CDS monitoring activities were implemented as part of the CDS lifecycle: <ul> <li>One type of monitoring occurs prior to releasing active CDS</li> <li>The other 3 types occur at different points after CDS activation</li> </ul> </li> </ul>	<ul> <li>248 CDS interventions were monitored over a 2-year period:</li> <li>The rate of detecting a malfunction or opportunity for improvement was:</li> <li>37% during preactivation</li> <li>18% during immediate postactivation</li> <li>Monitoring also informed the process of user feedback</li> <li>An automated alert detection tool identified 128 instances of alert pattern changes</li> </ul>	<ul> <li>The study recommended ongoing, continuous, and automated monitoring to detect malfunctions in real time, before problems are reported:</li> <li>CDS monitoring can identify malfunctions and improvement opportunities</li> <li>CDS monitoring provides information when responding to user feedback</li> </ul>



#### PARTNERSHIP for HEALTH IT PATIENT SAFETY a national collaborative

## Safe Practices to Reduce CPOE Alert Fatigue through Monitoring, Analysis, and Optimization

Study Details	Study Goals	Design and Context	Results	Conclusions
Analysis				
Reference: Bhakta et al. (2019) <sup>15</sup>	Evaluate the impact of a risk-based systematic inter- vention designed to streamline medication-related alerts and warnings	<ul> <li>Before-and-after study</li> <li>A committee was formed to review alert data and categorize alerts based on severity and ability to guide decision-making while minimizing the potential for unanticipated negative outcome to improve appropriate acknowledgement rates while minimizing alert: <ul> <li>Modification of existing knowledge database alerts</li> <li>Intraorder set medication alert suppression</li> <li>DDI tiering and reclassifica- tion was employed fatigue</li> </ul> </li> </ul>	Total number of weekly inpatient alerts decreased: <ul> <li>Preintervention 68,900</li> <li>Postintervention 50,300</li> </ul> Alerts acknowledged weekly increased: <ul> <li>Preintervention 11.8%</li> <li>Post intervention 13.7%</li> </ul> Alerts that were modified increased: <ul> <li>Preintervention 5.0%</li> <li>Postintervention (IQR 4.9%–5.3%) to (post) 7.3%</li> </ul> Both increases were primarily seen with pharmacists versus other healthcare professionals	Optimizing DDI alerts, through a committee-led systematic approach, decreased the overall number of alerts and increased medication alert acknowledgment and modification rates
<b>Reference:</b> Chaparro et al. (2020) <sup>5</sup>	Utilize the Institute for Healthcare Improvement quality improve- ment (QI) methods to reduce the volume of interrup- tive alerts	<ul> <li>QI tools to evaluate selected interruptive alerts implemented an interactive dashboard for:</li> <li>Baseline alert data</li> <li>Monitor frequency and outcomes</li> <li>Prioritize interventions</li> </ul>	<ul> <li>Total volume of interruptive alert volume -</li> <li>Preinterventions:</li> <li>Alerts shown to providers per week-7,250</li> <li>The top 25 unique alerts accounted for 90%</li> <li>The top 65 firing alerts accounted for 99%</li> <li>Postintervention:</li> <li>Alert shown to providers per-4,400</li> </ul>	Systematic and structured improvements were used to reduce interruptive alerts QI methods helped to prioritize the interventions Further evaluation is recommended to reduce interruptive alerts and determine how the reductions will impact patient outcomes, usability, cognitive burden, and direct feedback mechanisms
Reference: McGreevey et al. (2020) <sup>3</sup>	Provide practical guidance to those considering creating an EHR manage- ment program	Review and synthesis of several approaches and recom- mendations for better alert management derived from the experience of four healthcare institutions	<ul> <li>Successful alert management programs must include:</li> <li>Governance is complex but an essential infrastructure</li> <li>Ongoing analysis and review of alerts</li> <li>Optimal agreed upon metric for analyzing</li> <li>Looking at organizations that have reported successful implementation</li> <li>Consider: <ul> <li>New design paradigm</li> <li>Data and alert visualization displays</li> <li>Emerging technologies</li> </ul> </li> </ul>	Alert management programs must strive to meet common goals of improving patient care, while at the same time decreasing the alert burden on clinicians
Reference: McEvoy et al. (2017) <sup>18</sup>	Assess the adoption of the Office of the National Coordinator for Health IT Technology's "high-priority" list of DDIs and alerting practices	<ul> <li>Evaluation of 19 systems conducted at 13 sites using 14 different EHRs looked at:</li> <li>Alert implementation (presence or absence of an alert)</li> <li>Display (alert appearance as interruptive or passive)</li> </ul>	<ul> <li>Across systems 69% of the high-priority DDI pairs produced alerts</li> <li>Implementation and display of the DDI alerts tested varied between systems (even with the same EHR vendor)</li> <li>Across drug pairs implementa- tion and display ranged from 27% (4/15) to 93% (14/15)</li> </ul>	<ul> <li>DDI alerting is clinically important but not standardized</li> <li>Focus on evidence-based DDIs will allow for improvement</li> </ul>



Study Details	Study Goals	Design and Context	Results	Conclusions
Optimization				
Reference: Jankovic and Chen (2020) <sup>14</sup>	Review aspects of CDS that contribute to burnout and identify key themes for improving the acceptability of CDS and decreasing burnout	Conducted a survey of relevant articles to identify ways to optimize CDS to reduce clinician burnout; 89 articles met the inclusion criteria	<ul> <li>Studies found that:</li> <li>Alarm fatigue from both a high volume of alerts and alerts of poor relevance, such as low PPV, were commonly described problems leading to high rates of alert overrides or avoidance of CDS</li> <li>Generally poor performance of many CDS tools has been reported</li> <li>Overrides, avoidance, and workarounds decrease effectiveness of CDS</li> <li>Few studies directly evaluated the effectiveness of CDS on changing health-related patient outcomes</li> <li>CDS tools need to have clinician buy-in</li> </ul>	The survey of the literature points to the key factors for CDS tool to be accepted and used by healthcare professionals they must be: - Relevant - Solicit feedback - Customizable - Measure outcomes - Iterative
Reference: Kawamanto et al. (2018) <sup>7</sup>	Describe how CDS governance and improving CDS effectiveness was accomplished in a resource efficient manner	Case study addressing decision support fatigue How the University of Utah Health established an enterprises CDS governance leveraging existing resources	<ul> <li>The governance committee included multi-stakeholder participation to:</li> <li>Look at new CDS requests and review current CDS</li> <li>Require that what is proposed is actually desired by intended recipients</li> <li>Coordinate with other governance bodies</li> <li>Analysis to identify: <ul> <li>High-frequency, low-value CDS</li> <li>Monitor progress</li> <li>Obtain info from user issues</li> <li>Transition alert and reminder content to more appropriate areas in the EHR</li> <li>Use experimental designs to guide decision-making regarding CDS effectiveness</li> </ul> </li> </ul>	A significant infusion of new resources is not a prerequisite for implementing formal CDS gover- nance to reduce CDS volume and CDS fatigue and achieve meaningful reductions in CDS burden
Reference: Miller et al. (2018) <sup>23</sup>	Recommendations for alert optimiza- tion and workflow focused on identifying human factor presentations for CDS	Literature/systematic review was conducted from 2000 to 2016 with aggregated human factor suggestions for optimization	Recommendations for human factors include presentation content and functions include - Interface (presentation): – Presentation – Placement and positioning – Provision of multiple presenta- tion layers Information (content): – Clean and concise – Content guidance – Consistency Interaction (function): – Fast – Fit – Feedback – Forgiveness – Flexible design	Recommendations for human factor improvements to CDS alerts



Study Details	Study Goals	Design and Context	Results	Conclusions
Reference: Payne et al. (2015) <sup>20</sup>	Describe recom- mendations from the DDI Clinical Decision Support Conference Series usability workgoup for preferred DDI alerting strategies within CDS systems	<ul> <li>A workgroup consisting of 24 individuals from diverse back- ground and areas of expertise meet to address three key questions to improve usability and increase consistency of:</li> <li>1. What, how, where, and when do we display DDI decision support?</li> <li>2. Should presentation of DDI decision support vary by clinicians?</li> <li>3. How should effectiveness of DDI decision support be measured?</li> </ul>	Information: Seven core elements should be included in DDI decision support: 1. Drug involved 2. Seriousness 3. Clinical consequences 4. Mechanism of the interaction 5. Contextual information/ modifying factor 6. Recommended actions 7. Evidence Presentation: 1. General alert content should be consistent among various types of clinicians 2. Presentation to various professionals may be based on context or functions Effectiveness: 1. Measure by the achievement of outcomes relative to the interaction cost (e.g., cognitive burden, time)	The recommendations focus on improving the usability of DDI alerts, particularly on streamlining and standardizing DDI alert processes (consistent terminology, symbols/ icons, color, minimal text, formatting, content and reporting standards)
Reference: Saiyed et at. (2019) <sup>21</sup>	Report on comprehensive drug alerting rates and develops strategies to reduce drug alerts across two different health care systems	Standardized reports compared drug alert rates between the two systems, among 13 categories of drug alerts. Both health care systems made modifications to the out-of-box alerts available from their EHR and drug information vendors	<ul> <li>Drug alerting rates even after initial optimization were 38 and 51 alerts per 100 drug orders, respectively, in the 2 systems</li> <li>Eight strategies were identified for the optimization of drug alerts:</li> <li>Integrated team</li> <li>Drug information vendor</li> <li>Comprehensive strategy for all drug CDS categories</li> <li>Balance risk/benefit of alerts</li> <li>Silent alerting</li> <li>Utilize standard reporting</li> <li>Systemic and drug-specific tactics</li> <li>Continual refinement</li> </ul>	A team-based, systematic approach to optimizing drug alerting strategies can reduce the number of drug alerts. Strategic principles, guidelines, and recommendations need to be developed to enhance drug CDS alerts

#### References

- 1. Hussain MI, Reynolds TL, Zheng K. Medication safety alert fatigue may be reduced via interaction design and clinical role tailoring: a systematic review. J Am Med Inform Assoc. 2019 Oct 1;26(10):1141-9. Also available: <a href="https://dx.doi.org/10.1093/jamia/ocz095">https://dx.doi.org/10.1093/jamia/ocz095</a>. PMID: 31206159.
- Strategy on reducing regulatory and administrative burden relating to the use of health IT and EHRs [draft for public comment]. Washington (DC): Office of the National Coordinator for Health Information Technology (ONC); 2018 Nov. 74 p. Also available: <u>https://www.healthit.gov/topic/usability-and-provider-burden/strategy-reducing-burden-relating-use-health-it-and-ehrs</u>.
- McGreevey JD 3rd, Mallozzi CP, Perkins RM, Shelov E, Schreiber R. Reducing alert burden in electronic health records: state of the art recommendations from four health systems. Appl Clin Inform. 2020 Jan;11(1):1-12. Also available: <u>https://dx.doi.org/10.1055/s-0039-3402715</u>. PMID: 31893559.
- Tolley CL, Slight SP, Husband AK, Watson N, Bates DW. Improving medication-related clinical decision support. Am J Health Syst Pharm. 2018 Feb 15;75(4):239-46. Also available: <u>https://dx.doi.org/10.2146/ajhp160830</u>. PMID: 29436470.
- 5. Chaparro JD, Hussain C, Lee JA, Hehmeyer J, Nguyen M, Hoffman J. Reducing interruptive alert burden using quality improvement methodology. Appl Clin Inform. 2020 Jan;11(1):46-58. Also available: <u>https://dx.doi.org/10.1055/s-0039-3402757</u>. PMID: 31940671.



- 6. Slight SP, Eguale T, Amato MG, Seger AC, Whitney DL, Bates DW, Schiff GD. The vulnerabilities of computerized physician order entry systems: a qualitative study. J Am Med Inform Assoc. 2016 Mar;23(2):311-6. Also available: <a href="https://dx.doi.org/10.1093/jamia/ocv135">https://dx.doi.org/10.1093/jamia/ocv135</a>. PMID: 26568606.
- Kawamanto K, Flynn MC, Kukhareva P, ElHalta D, Hess R, Gregory T, Walls C, Wigren AM, Borbolla D, Bray BE, Parsons MH, Clayson BL, Briley MS, Stipelman CH, Taylor D, King CS, Del Fiol G, Reese TJ, Weir CR, Taft T, Strong MB. A pragmatic guide to establishing clinical decision support governance and addressing decision support fatigue: a case study. AMIA Annu Symp Proc. 2018 Dec 5;2018:624-33. PMID: 30815104.
- Ancker JS, Edwards A, Nosal S, Hauser D, Mauer E, Kaushal R, with the HITEC Investigators. Effects of workload, work complexity, and repeated alerts on alert fatigue in a clinical decision support system. BMC Med Inform Decis Mak. 2017 Apr 10;17:36. Also available: <u>https://dx.doi.org/10.1186/s12911-017-0430-8</u>. PMID: 28395667.
- 9. Carli D, Fahrni G, Bonnabry P, Lovis C. Quality of decision support in computerized provider order entry: systematic literature review. JMIR Med Inform. 2018 Jan 24;6(1):e3. Also available: <u>https://dx.doi.org/10.2196/medinform.7170</u>. PMID: 29367187.
- 10. Rehr CA, Wong A, Seger DL, Bates DW. Determining inappropriate medication alerts from "inaccurate warning" overrides in the intensive care unit. Appl Clin Inform. 2018 Apr;9(2):268-74. Epub 2018 Apr 25. Also available: <u>http://dx.doi.org/10.1055/s-0038-1642608</u>. PMID: 29695013.
- Genco EK, Forster JE, Flaten H, Goss F, Heard KJ, Hoppe J, Monte AA. Clinically inconsequential alerts: the characteristics of opioid drug alerts and their utility in preventing adverse drug events in the emergency department. Ann Emerg Med. 2016 Feb;67(2):240-248.e3. Also available: <u>http:// dx.doi.org/10.1016/j.annemergmed.2015.09.020</u>. PMID: 26553282.
- Bubp JL, Park MA, Kapusnik-Uner J, Dang T, Matuszewski K, Ly D, Chiang K, Shia S, Hoberman B. Successful deployment of drug-disease interaction clinical decision support across multiple Kaiser Permanente regions. J Am Med Inform Assoc. 2019 Oct;26(10):905-10. Also available: <u>https://dx.doi.org/10.1093/jamia/ocz020</u>. PMID: 30986823.
- Wright A, Ai A, Ash J, Wiesen JF, Hickman TT, Aaron S, McEvoy D, Borkowsky S, Dissanayake PI, Embi P, Galanter W, Harper J, Kassakian SZ, Ramoni R, Schreiber R, Sirajuddin A, Bates DW, Sittig DF. Clinical decision support alert malfunctions: analysis and empirically derived taxonomy. J Am Med Inform Assoc. 2018 May;25(5):496-506. Also available: <u>https://dx.doi.org/10.1093/jamia/ocx106</u>. PMID: 29045651.
- 14. Jankovic I, Chen JH. Clinical decision support and implications for the clinician burnout crisis. Yearb Med Inform. 2020 Aug;29(1):145-54. Also available: <a href="http://dx.doi.org/10.1055/s-0040-1701986">http://dx.doi.org/10.1055/s-0040-1701986</a>. PMID: 32823308.
- 15. Bhakta SB, Colavecchia AC, Haines L, Varkey D, Garey KW. A systematic approach to optimize electronic health record medication alerts in a health system. Am J Health Syst Pharm. 2019 Apr 8;76(8):530-6. Also available: <a href="https://dx.doi.org/10.1093/ajhp/zxz012">https://dx.doi.org/10.1093/ajhp/zxz012</a>. PMID: 31361861.
- Wright A, McEvoy DS, Aaron S, McCoy AB, Amato MG, Kim H, Ai A, Cimino JJ, Desai BR, El-Kareh R, Galanter W, Longhurst CA, Malhotra S, Radecki RP, Samal L, Schreiber R, Shelov E, Sirajuddin AM, Sittig DF. Structured override reasons for drug-drug interaction alerts in electronic health records. J Am Med Inform Assoc. 2019 Oct;26(10):934-42. Also available: <u>https://dx.doi.org/10.1093/jamia/ocz033</u>. PMID: 31329891.
- 17. Yoshida E, Fei S, Bavuso K, Lagor C, Maviglia S. The value of monitoring clinical decision support interventions. Appl Clin Inform. 2018 Jan;9(1):163-73. Also available: <u>https://dx.doi.org/10.1055/s-0038-1632397</u>. PMID: 29514353.
- McEvoy DS, Sittig DF, Hickman TT, Aaron S, Ai A, Amato M, Bauer DW, Fraser GM, Harper J, Kennemer A, Krall MA, Lehmann CU, Malhotra S, Murphy DR, O'Kelley B, Samal L, Schreiber R, Singh H, Thomas EJ, Vartian CV, Westmorland J, McCoy AB, Wright A. Variation in high-priority drug-drug interaction alerts across institutions and electronic health records. J Am Med Inform Assoc. 2017 Mar 1;24(2):331-8. Also available: <u>http://dx.doi.org/10.1093/jamia/ocw114</u>. PMID: 27570216.
- Phansalkar S, Desai AA, Bell D, et al. High-priority drug-drug interactions for use in electronic health records. J Am Med Inform Assoc. 2012 Sep-Oct;19(5):735-43. Also available: <u>http://dx.doi.org/10.1136/amiajnl-2011-000612</u>. PMID: 22539083.
- Payne TH, Hines LE, Chan RC, Hartman S, Kapusnik-Uner J, Russ AL, Chaffee BW, Hartman C, Tamis V, Galbreth B, Glassman PA, Phansalkar S, van der Sijs H, Gephart SM, Mann G, Strasberg HR, Grizzle AJ, Brown M, Kuperman GJ, Steiner C, Sullins A, Ryan H, Wittie MA, Malone DC. Recommendations to improve the usability of drug-drug interaction clinical decision support alerts. J Am Med Inform Assoc. 2015 Nov;22(6):1243-50. Also available: <u>http://dx.doi.org/10.1093/jamia/ocv011</u>. PMID: 25829460.
- 21. Saiyed SM, Davis KR, Kaelber DC. Differences, opportunities, and strategies in drug alert optimization-experiences of two different integrated health care systems. Appl Clin Inform. 2019 Dec;10(5):777-82. Also available: <u>https://dx.doi.org/10.1055/s-0039-1697596</u>. PMID: 31618781.
- Basit MA, Baldwin KL, Kannan V, Flahaven EL, Parks CJ, Ott JM, Willett DL. Agile acceptance test-driven development of clinical decision support advisories: feasibility of using open source software. JMIR Med Inform. 2018 Apr 13;6(2):e23. Also available: <u>https://dx.doi.org/10.2196/ medinform.9679</u>. PMID: 29653922.
- Miller K, Mosby D, Capan M, Kowalski R, Ratwani R, Noaiseh Y, Kraft R, Schwartz S, Weintraub WS, Arnold R. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc. 2018 May;25(5):585-92. Also available: <u>https://dx.doi.org/10.1093/jamia/ocx118</u>. PMID: 29126196.
- Tcheng JE, Bakken S, Bates DW, Bonner III H, Gandhi TK, Josephs M, Kawamoto K, Lomotan EA, Mackay E, Middleton B, Teich JM, Weingarten S, Lopez MH, editor(s). Optimizing strategies for clinical decision support: summary of a meeting series. Washington (DC): National Academy of Medicine; 2017. 77 p. Also available: <u>https://www.healthit.gov/sites/default/files/page/2018-04/Optimizing\_Strategies\_508.pdf</u>.



### Appendix C. Tools

### Health IT Issues Log—Conducting Risk Analysis and Documenting Findings

The Health IT Issues Log is used to gather information about electronic health record (EHR)-related issues, hazards, concerns, and unintended consequences. The log helps document and track health information technology (IT) issues, hazards, and events. Additionally, it provides a means to capture how the issue was identified, assessed, and reviewed. It helps identify what is needed to develop, deploy, and remediate the issue, hazard, or concern. Keeping this information in a central place allows users to track and communicate the action plan and to monitor successes or identify the need for additional activities. An Excel version of the tool can be accessed at <u>Health IT Issues Log</u>.

### **CDS Drug Allergy Dashboard**

The CDS Drug Allergy Dashboard helps users gather data and information about drug allergy clinical decision support (CDS) for tracking, trend analysis, and dissemination of data throughout the organization. It provides the opportunity to look at the CDS allergy process to ensure the right people get the right information at the right time. It also provides the ability to assess and track the patient safety risk level of CDS allergy issues in order to develop a mitigation plan. The dashboard can be <u>accessed online</u>.

### Algorithm: Review Process for CDS for Drug Allergies

Identify trends	Find meaning	Plan improvement	Execute change	Monitor & reassess
What clinically	Why are these	Who are the	Establish goals	<ul> <li>Collect data</li> </ul>
significant drug	trends occurring?	internal experts?	and objectives	Identify trends
allergy interactions are getting the most alerts?	<ul> <li>How would practices need to change to make</li> </ul>	What needs to be changed to decrease alerts?	<ul> <li>Identify steps to accomplish goals and objectives</li> </ul>	and compare
<ul> <li>Which clinicians are receiving the alerts?</li> </ul>	the alerts more meaningful?	What is safest for patients?	Create timeline	
<ul> <li>How did the clinicians respond</li> </ul>				

### **Additional Resources**

to the alerts?

- HealthIT.gov: Assemble a CDS Implementation Team
- Agency for Healthcare Research and Quality: <u>Risk Assessment Tools</u>
- SAFER guides (Safety Assurance Factors for EHR Resilience):
  - <u>Computerized Provider Order Entry with Decision Support</u>
  - <u>High Priority Practices</u>
  - <u>Organizational Responsibilities</u>
- Institute for Healthcare Improvement:
  - Patient Safety Leadership WalkRounds<sup>™</sup>
  - <u>Safety Briefings Tool</u>
- Joint Commission: Daily safety briefings



### **Appendix D. Additional Resources**

Amato MG, Salazar A, Hickman TT, Quist AJ, Volk LA, Wright A, McEvoy D, Galanter WL, Koppel R, Loudin B, Adelman J, McGreevey JD 3rd, Smith DH, Bates DW, Schiff GD. Computerized prescriber order entry-related patient safety reports: analysis of 2522 medication errors. J Am Med Inform Assoc. 2017 Mar;24(2):316-22. Also available: <u>https://dx.doi.org/10.1093/jamia/ocw125</u>. PMID: 27678459.

Backman R, Bayliss S, Moore D, Litchfield I. Clinical reminder alert fatigue in healthcare: a systematic literature review protocol using qualitative evidence. Syst Rev. 2017 Dec 13;6:255. Also available: <u>https://dx.doi. org/10.1186/s13643-017-0627-z</u>. PMID: 29237488.

Bagri H, Dahri K, Legal M. Hospital pharmacists' perceptions and decision-making related to drug-drug interactions. Can J Hosp Pharm. 2019 Jul-Aug;72(4):288-94. Also available: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6699872/</u>.

Bhakta SB, Colavecchia AC, Haines L, Varkey D, Garey KW. A systematic approach to optimize electronic health record medication alerts in a health system. Am J Health Syst Pharm. 2019 Apr 8;76(8):530-6. Also available: https://dx.doi.org/10.1093/ajhp/zxz012. PMID: 31361861.

Basit MA, Baldwin KL, Kannan V, Flahaven EL, Parks CJ, Ott JM, Willett DL. Agile acceptance test-driven development of clinical decision support advisories: feasibility of using open source software. JMIR Med Inform. 2018 Apr 13;6(2):e23. Also available: <u>https://dx.doi.org/10.2196/medinform.9679</u>. PMID: 29653922.

Baysari MT, Tariq A, Day RO, Westbrook JI. Alert override as a habitual behavior - a new perspective on a persistent problem. J Am Med Inform Assoc. 2017 Mar;24(2):409-12. Also available: <u>https://dx.doi.org/10.1093/jamia/ocw072</u>. PMID: 27274015.

Blecker S, Pandya R, Stork S, Mann D, Kuperman G, Shelley D, Austrian JS. Interruptive versus noninterruptive clinical decision support: usability study. JMIR Hum Factors. 2019 Apr 17;6(2):e12469. Also available: <u>https://dx.doi.org/10.2196/12469</u>. PMID: 30994460.

Kane-Gill SL, O'Connor MF, Rothschild JM, Selby NM, McLean B, Bonafide CP, Cvach MM, Hu X, Konkani A, Pelter MM, Winters BD. Technologic distractions (part 1): summary of approaches to manage alert quantity with intent to reduce alert fatigue and suggestions for alert fatigue metrics. Crit Care Med. 2017 Sep;45(9):1481-8. Also available: <a href="https://dx.doi.org/10.1097/CCM.0000000002580">https://dx.doi.org/10.1097/CCM.0000000002580</a>. PMID: 28682835.

Marcilly R, Ammenwerth E, Roehrer E, Nies J, Beuscart-Zephir MC. Evidence-based usability design principles for medication alerting systems. BMC Med Inform Decis Mak. 2018 Jul;18:69. Also available: https://dx.doi.org/10.1186/s12911-018-0615-9. PMID: 30041647.

Muhlenkamp R, Ash N, Ziegenbusch K, Rampe N, Bishop B, Adane E. Effect of modifying dose alerts in an electronic health record on frequency of alerts. Am J Health Syst Pharm. 2019 Feb 8;76(Supplement\_1):S1-S8. Also available: <u>https://dx.doi.org/10.1093/</u> <u>ajhp/zxy016</u>. PMID: 30753316.

Powers EM, Shiffman RN, Melnick ER, Hickner A, Sharifi M. Efficacy and unintended consequences of hard-stop alerts in electronic health record systems: a systematic review. J Am Med Inform Assoc. 2018 Nov;25(11):1556-66. Also available: <u>https://dx.doi.org/10.1093/jamia/ ocy112</u>. PMID: 30239810.

Ramirez M, Maranon R, Fu J, Chon JS, Chen K, Mangione CM, Moreno G, Bell DS. Primary care provider adherence to an alert for intensification of diabetes blood pressure medications before and after the addition of a "chart closure" hard stop. J Am Med Inform Assoc. 2018 Sep;25(9):1167-74. Also available: <u>https://dx.doi.org/10.1093/jamia/ocy073</u>. PMID: 30060013. Ray S, McEvoy DS, Aaron S, Hickman TT, Wright A. Using statistical anomaly detection models to find clinical decision support malfunctions. J Am Med Inform Assoc. 2018 Jul;25(7):862-71. Also available: <u>http:// dx.doi.org/10.1093/jamia/ocy041</u>. PMID: 29762678.

Rayo MF, Kowalczyk N, Liston BW, Sanders EB, White S, Patterson ES. Comparing the effectiveness of alerts and Dynamically Annotated Visualizations (DAVs) in improving clinical decision making. Hum Factors. 2015 Sep;57(6):1002-14. Also available: <u>https://dx.doi.org/10.1177/0018720815585666</u>. PMID: 25957043.

Richesson RL, Staes CJ, Douthit BJ, Thoureen T, Hatch DJ, Kawamoto K, Del Fiol G. Measuring implementation feasibility of clinical decision support alerts for clinical practice recommendations. J Am Med Inform Assoc. 2020 Apr;27(4):514-21. Also available: <u>https://dx.doi.org/10.1093/jamia/ocz225</u>. PMID: 32027357.

Saiyed SM, Greco PJ, Fernandes G, Kaelber DC. Optimizing drug-dose alerts using commercial software throughout an integrated health care system. J Am Med Inform Assoc. 2017 Nov;24(6):1149-54. Also available: https://dx.doi.org/10.1093/jamia/ocx031. PMID: 28444383.

Slight SP, Eguale T, Amato MG, Seger AC, Whitney DL, Bates DW, Schiff GD. The vulnerabilities of computerized physician order entry systems: a qualitative study. J Am Med Inform Assoc. 2016 Mar;23(2):311-6. Also available: <u>https://dx.doi.org/10.1093/jamia/ocv135</u>. PMID: 26568606.

Tilson H, Hines LE, McEvoy G, Weinstein DM, Hansten PD, Matuszewski K, le Comte M, Higby-Baker S, Hanlon JT, Pezzullo L, Vieson K, Helwig AL, Huang SM, Perre A, Bates DW, Poikonen J, Wittie MA, Grizzle AJ, Brown M, Malone DC. Recommendations for selecting drug-drug interactions for clinical decision support. Am J Health Syst Pharm. 2016 Apr 15;73(8):576-85. Also available: <u>https://dx.doi.org/10.2146/ajhp150565</u>. PMID: 27045070.

Tolley CL, Slight SP, Husband AK, Watson N, Bates DW. Improving medication-related clinical decision support. Am J Health Syst Pharm. 2018 Feb 15;75(4):239-46. Also available: <u>https://dx.doi.org/10.2146/ajhp160830</u>. PMID: 29436470.

Vélez-Díaz-Pallarés M, Perez-Menendez-Conde C, Bermejo-Vicedo T. Systematic review of computerized prescriber order entry and clinical decision support. Am J Health Syst Pharm. 2018 Dec 1;75(23):1909-21. Also available: <u>https://dx.doi.org/10.2146/ajhp170870</u>. PMID: 30463867.

Whitehead NS, Williams L, Meleth S, Kennedy S, Ubaka-Blackmoore N, Kanter M, O'Leary KJ, Classen D, Jackson B, Murphy DR, Nichols J, Stockwell D, Lorey T, Epner P, Taylor J, Graber ML. The effect of laboratory test-based clinical decision support tools on medication errors and adverse drug events: a laboratory medicine best practices systematic review. J Appl Lab Med. 2019 May;3(6):1035-48. Also available: <u>https://dx.doi.org/10.1373/jalm.2018.028019</u>. PMID: 31639695.

Yoshida E, Fei S, Bavuso K, Lagor C, Maviglia S. The value of monitoring clinical decision support interventions. Appl Clin Inform. 2018 Jan;9(1):163-73. Also available: <u>https://dx.doi.org/10.1055/s-0038-1632397</u>. PMID: 29514353.





