Implementing Clinical Decision Support Systems In Pharmacy Practice For Drug Interaction Checks

Turki Abdulkarim Alharbi[1*], Abdullah Abed Abdullah Algethami[2], Wael Muslih Alsufyani[3], Mazen Saleh Alshehri[4], Saad Nasser Saad Al-Otaibi[5], Sami Nasser Saad Al-Otaibi[6], Meshari Eida Alharthi[7], Azhar Abdull Wahid Aljishi[8], Maria Merza Alghanim[8]

[1*]Pharmacy Department, Al-Rass General Hospital, Al-Rass, Saudi Arabia
[2] Medical Supply Department, Directorate of Health Affairs, Taif, Saudi Arabia
[3] Pharmacy Department, King Abdulaziz Specialist Hospital, Taif, Saudi Arabia
[4] Pharmaceutical Care Department, Al Noor Specialist Hospital, Mecca, Saudi Arabia
[5] Pharmacy Department, Prince Mohammed bin Abdulaziz Hospital, Riyadh, Saudi Arabia
[6] Pharmacy Department, Al Yamamah Hospital, Riyadh, Saudi Arabia
[7] Psychiatric Department, Eradah Mental Health Complex, Taif, Saudi Arabia
[8] Pharmacy Department, Maternity and Children Hospital, Dammam, Saudi Arabia

[*]**Corresponding Author:** Turki Abdulkarim Alharbi,
[*]Pharmacy Department, Al-Rass General Hospital, Al-Rass, Saudi Arabia. Email: mag.ws2020@hotmail.com

ABSTRACT
Clinical Decision Support Systems (CDSS) have become indispensable tools in healthcare, offering clinicians vital guidance and information to aid in patient care. Integrating CDSS into Computerized Physician Order Entry (CPOE) systems holds the promise of transforming healthcare by improving safety, quality, and efficiency. A key aspect of CDSS is its role in identifying and managing drug-drug interactions (DDIs), a critical concern in today's complex medication landscape. DDIs can lead to adverse drug events (ADEs), which have far-reaching consequences, including increased hospitalization rates, extended hospital stays, and patient morbidity and mortality. CDSS can play a pivotal role in early DDI detection, potentially mitigating these risks. However, the effectiveness of CDSS-generated DDI alerts varies, and many go unheeded due to various factors, including alert fatigue and shortcomings in design.
Efforts to enhance DDI alerts focus on standardizing their presentation, content, and resolution procedures. Elements such as clear drug pair identification, severity indication, clinical consequences, and risk mitigation guidance are deemed essential. Ensuring consistency in terminology, symbols, and symbols is crucial, as is incorporating patient-specific data and contextual information into alerting logic. A team-oriented approach to DDI management, involving various healthcare professionals, is advocated to ensure optimal patient care. Assessing the effectiveness of DDI alerts should consider both measurable and perceived value, recognizing that clinicians' perceptions may vary based on their expertise and roles. Additionally, it is essential to avoid over-reliance on override rates as the sole metric for evaluating alert efficacy. Overall, CDSS and DDI alerting systems have the potential to greatly improve patient safety and healthcare outcomes. However, continuous research, standardization, and user-centric design are necessary to fully realize their benefits and mitigate associated challenges.

Keywords: Clinical Decision Support Systems (CDSS), Drug-Drug Interactions (DDIs), Alert Fatigue, Patient Safety, Medication Management, Healthcare Optimization

INTRODUCTION

Clinical Decision Support Systems (CDSS) have emerged as indispensable tools within computerized physician order entry (CPOE) systems, aimed at augmenting healthcare decision-making processes. CDSS, as defined, refers to "computer software employing a knowledgebase designed for use by a clinician involved in patient care, as a direct aid to clinical decision making" (1). The integration of CDSS into CPOE systems has shown the potential to revolutionize patient care by enhancing safety, quality, and efficiency (2).
One pivotal facet of CDSS integration is its role in guiding prescribers regarding proper dosing and alerting them to potential drug-drug interactions (DDIs), duplicate therapies, and drug allergies(3). Traditionally, physicians and pharmacists have relied on their clinical expertise to assess and manage DDIs, a practice that may not be entirely foolproof given the increasing complexity and volume of medications in today's healthcare landscape. This situation beckons us to explore innovative approaches to enhance DDI identification, with the implementation of technology, particularly CDSS, as a prominent solution. DDIs can lead to adverse drug events (ADEs), which are not only predictable but also preventable in many instances(4).
ADEs contribute to higher hospitalization rates, prolonged lengths of stay, and ultimately, patient morbidity and mortality(5). Hence, the timely identification of DDIs becomes paramount in ensuring the safety and efficacy of pharmacotherapy. CDSS has demonstrated its ability to facilitate the early detection of DDIs, which can be a game-

changer (5).The effectiveness of CDSS in generating DDI alerts has shown variability, with percentages ranging from 7% to 36% of medication orders (6-9).

Prescribers' acceptance of these alerts, defined by their decision to cancel or modify the initial order, hovers between 9% and 12% (10). While these figures may appear modest, they do not capture the full scope of prescribers' actions that can further contribute to preventing adverse drug reactions, such as increased patient monitoring or adjustments in laboratory or drug levels (10). However, the precise impact of CDSS on patient outcomes remains to be fully understood. Despite the evident advantages, CDSS also faces certain limitations (11). A significant portion of DDI alerts generated by CDSS systems goes unheeded by physicians(12, 13). This could be attributed to various factors, including prescribers underestimating the significance of the DDI or the CDSS system overemphasizing its importance. Moreover, the oversight of human factors during alert system implementation and shortcomings in alert design have been associated with the bypassing of alerts(14, 15).

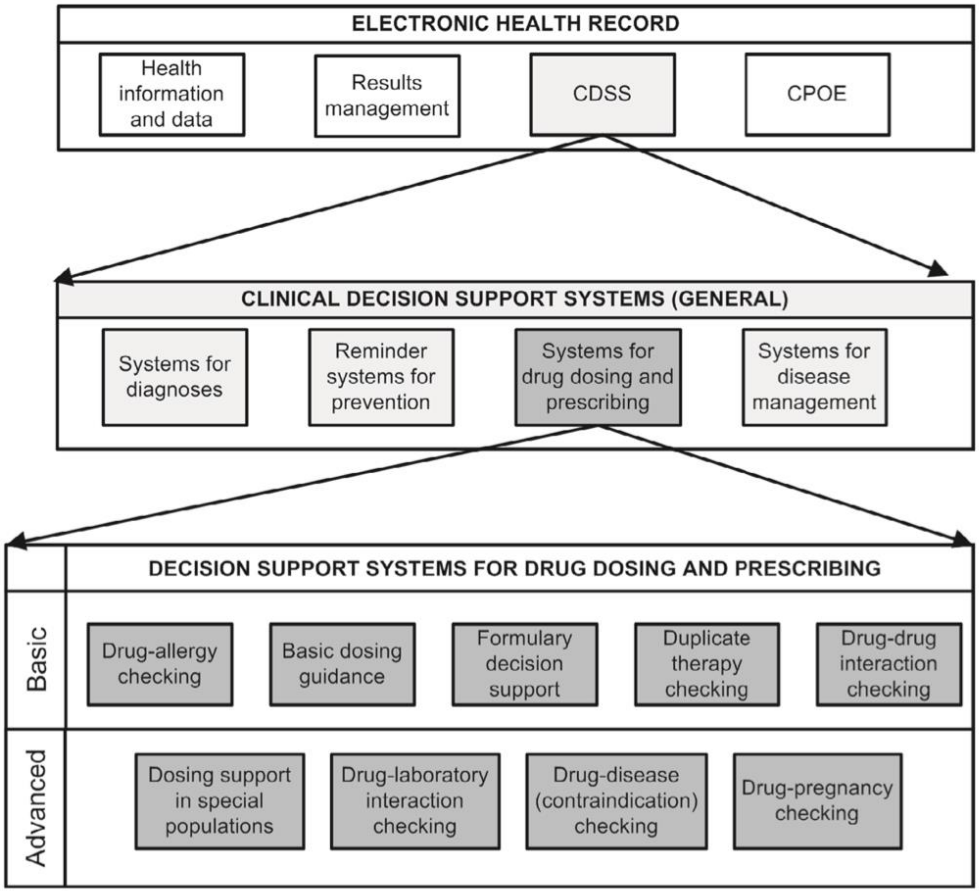

Figure 1. The spectrum of decision support (16).

Regulatory bodies worldwide advocate for the inclusion of CDSS within CPOE systems, making it a crucial component of modern healthcare practice(17, 18). Therefore, institutions must not only acknowledge the potential of CDSS but also strive to optimize its benefits while addressing its challenges. In this review, we will examine the implementation of CDSS in pharmacy practice for drug interaction checks. Through an analysis of existing research, we aim to provide insights into the efficacy, constraints, and prospective applications of this technology in elevating patient safety and optimizing healthcare outcomes.

METHODOLOGY

This study conducted a comprehensive literature search on January 30, 2023, in Medline and Cochrane databases, employing medical subject headings (MeSH) and relevant terms. To ensure thoroughness, a manual search was also carried out on Google Scholar using reference lists from identified papers as a starting point. No restrictions were placed on publication date, language, participant age, or publication type. The focus was on papers discussing Clinical Decision Support System implementation in pharmacy practice for drug interaction checks.

DISCUSSION

Implementing standardized procedures for the presentation, content, and resolution of DDI alerts has the potential to significantly enhance their effectiveness in clinical settings, fostering advancements in patient safety and healthcare productivity. Human factors engineering research underscores the significant impact of color, visibility, and prioritization on clinicians' responses to safety warnings(19). While this body of research offers valuable insights into designing

warnings for various safety hazards, its application to drug-related warnings remains limited(20). Notably, the inconsistent presentation of alert information to clinicians, especially when dealing with multiple systems, may lead to cognitive overload and confusion. There is a strong recommendation to enhance the consistency and uniformity of DDI alert presentations across various systems. Concerning the content of DDI alerts, existing safety literature proposes four essential elements: a signal word indicating the severity of the DDI, hazard information specifying the potentially harmful drug combination, guidance on risk mitigation, and an account of potential clinical consequences if the hazard goes unaddressed(19, 21). Recent research also emphasizes the value of integrating contextual information and patient-specific data into algorithm logic to improve DDI alerts (22, 23). As a result, DDI alerting systems are advised to incorporate seven essential elements including identification of the drugs involved, classification of severity, description of clinical consequences (including frequency), elucidation of the interaction's mechanism, integration of contextual information and modifiable factors, provision of recommended actions, and presentation of supporting evidence. To prevent confusion, initial DDI alerts should precisely identify the interacting drug pair or individual drugs(24). Research has shown that prescribers encounter challenges in understanding why alerts are triggered, emphasizing the importance of clear drug pair identification (23). To achieve this, it is recommended to use both the prescribed medication name and generic ingredient names, particularly when dealing with combination products(5).

Consistency in indicating the potential severity of DDIs using standardized terms and definitions across all CDSSs is crucial (14, 25). However, determining the most appropriate terminology requires further research. Additionally, DDI alerts should provide detailed descriptions of potential adverse clinical outcomes associated with the interaction, allowing clinicians to weigh the risks and benefits efficiently(26). If available, information regarding the frequency or incidence of adverse events linked to a specific DDI and predisposing risk factors should be included to assess individual patient risk. Clinicians must possess a comprehensive understanding of the underlying mechanism of a DDI to make informed decisions regarding suitable therapeutic alternatives(26). In addition, the incorporation of contextual details, such as concurrent medical conditions and laboratory findings, expedites alert processing and improves relevance. Patient-specific factors like age, pharmacogenomic phenotype, and specific drug regimens should be incorporated into alerting logic or displayed in the alert interface(27).

When presenting a DDI alert, guidance should be provided on strategies to mitigate potential harm, such as dose modification, order cancellation, alternative medication selection, and monitoring/surveillance measures(25, 27, 28). Since numerous DDIs may warrant multiple responses, CDS systems should offer customizable lists of recommendations that consider organizational and formulary factors. Alerts should convey information regarding the quality and source of the evidence supporting DDIs(5, 23). For instance, they could reference case reports or clinical trials. Using clear symbols, letters, or numbers to convey the evidence, along with detailed explanations of the grading framework, is advisable(25). Additionally, systematic assessment of DDI evidence should be part of alerting systems.

To ensure optimal usability, alert presentation should be consistent across and within EHR systems, allowing clinicians to identify and respond to alerts, even when transitioning between different environments quickly and accurately. Semantic clarity and visual cue processing can be improved by consistently using color and symbols, employing clear terminology, presenting information concisely, and minimizing textual content(5, 22). While interruptive alerts are recommended for the most severe DDIs, enhancing safety and efficiency can be achieved through proactive guidance to safer alternative options, eliminating the need for interruptive alerts. However, it is crucial for patient safety that institutions exercise prudence to prevent indiscriminate suppression of clinically relevant alerts(29).

Essential details should be displayed prominently in the alert, with supplementary information and secondary considerations accessible through hyperlinks(30). Balancing succinct communication with sufficient information for informed decision-making should be addressed through iterative alert prototyping and usability testing (19). Further research is needed to determine essential components for primary and secondary dialog boxes in DDI alerts.

To avoid the need for alerts, DDI alert information should be presented at the point of decision-making, guiding prescribers toward lower-risk drug selections during the initial stages of medication selection(31). To streamline alert resolution, clinicians should be presented with a list of actionable options, including discontinuing medications, adjusting doses, providing patient education, or ordering laboratory tests. Additionally, a system should facilitate clinicians in providing override reasons, aiding in the identification of false positives and false negatives in alerts. This feedback can be shared with other clinicians to ensure accountability and contribute to quality improvement initiatives. Investigating complex alert resolution options, such as delegating alerts to multiple clinicians or postponing alerts, should be done cautiously, with appropriate audit trails and workflows to guarantee patient safety (29).

Ensuring optimal patient care within a secure medication management process hinges on effective collaboration and interdisciplinary coordination. DDI decision support is relevant to all members of the healthcare team, encompassing patients, prescribers, pharmacists, and nurses. For clinicians without prescribing authority, DDI alerts serve as an additional layer of verification, guarding against inadequate monitoring or assessment of patients on interacting drug regimens. Full awareness of each team member's actions promotes superior patient care and safety(32). Thus, we advocate for a team-centric approach to DDI management, while suggesting that the core content of alerts remains consistent across different clinician categories. However, the presentation of this information should be flexible to align with the contexts, roles, functions, responsibilities, and privileges of diverse healthcare professionals. For instance, prescriber recommendations may focus on specifying monitoring parameters, while pharmacists could receive notifications to confirm monitoring orders and review results.

Another essential aspect to consider is how the alert display should evolve if a clinician encounters the same alert repeatedly without observable behavior changes. Likewise, there is a debate regarding whether alerts related to DDIs

managed routinely by specialists with specialized training or roles (e.g., warfarin clinic pharmacists receiving alerts for warfarin interactions with patients under their care) should be subjected to deactivation. Currently, there is no empirical evidence supporting the complete deactivation of DDI alerts for specialists. Nevertheless, implementing more discerning institutional practices for DDI alerts could alleviate a significant portion of the alert burden. EHR system architecture should facilitate institutions in making these adjustments based on clinician attributes. In addition to their critical role in DDI risk management, patients should actively participate in monitoring for signs of drug toxicity or reduced efficacy(33, 34). It is advisable to adhere to evidence-based best practices when providing printed patient information.

Evaluating the effectiveness of DDI decision support requires a comprehensive assessment that encompasses multiple dimensions. The assessment of Clinical Decision Support (CDS) value involves comparing outcomes to the costs associated with interactions, which encompass factors such as cognitive load and time commitment(35). Effectiveness in clinical decision support (CDS) can be defined as the result of both measurable and perceived value. Perceived value encompasses various aspects such as the cost associated with Adverse Drug Events (ADEs), heuristics, evidence quality, and clinician satisfaction. For instance, when considering a drug interaction between amiodarone and warfarin, evaluating value could entail monitoring increased rates of appropriately ordered International Normalized Ratio (INR) tests, adjusting the warfarin dosage, providing patient counseling, and conducting follow-up at anticoagulation clinics. Nevertheless, it is essential to recognize that clinicians' perceptions of the value of alerts may vary based on their professional settings and level of expertise. For example, the utility of an alert may differ among practicing cardiologists; medical residents, for instance, may find it exceptionally valuable if it merely serves as a reminder to request an INR test. Relying solely on alert override rates to assess effectiveness may fail to consider these value-added actions, unless they are explicitly documented in conjunction with the alert. Conversely, alerts that fail to provide value, whether quantified or perceived, should be precisely blocked to improve precision while maintaining sensitivity. Generally, an improvement in the effectiveness of an alert results in an increase in its value, which may potentially alleviate alert fatigue. It is advisable for alert logic to consider mitigating factors associated with a low occurrence of negative outcomes. Neglecting to account for these factors could lead to a diminished positive predictive value and, consequently, a reduced perceived value(6).

It is crucial to acknowledge that override rates alone cannot be used as the sole criterion for evaluating the efficacy of alerts(6, 36). A notable constraint is that existing systems fail to fully capture the cognitive processes and subsequent behaviors of clinicians. The rate of overrides provides a rudimentary indication of alert compliance. Override rates can be utilized as an initial step to identify alerts that require a more comprehensive evaluation process, including the incorporation of clinician feedback, in the short term. The comprehensive assessment should consider various elements, including clinician consensus on the perceived value of the alert, factors that alter its relevance, and actions performed in response to the alert (e.g., ordering additional monitoring). These aspects can be difficult to record using the alert system. There are ample opportunities for institutions to augment alerts and enhance their value; however, prior to implementing any modifications, they should undertake thorough evaluations. It may be rational to consider implementing a more selective alerting approach as a potential strategy to reduce alert fatigue without compromising clinical efficacy.

In the current realm of CDS, an overwhelming influx of DDI notifications has led to critical clinical alerts being overshadowed by a deluge of poorly presented and inconsequential messages. The findings of our research are poised to provide valuable guidance for optimizing and standardizing DDI alert procedures, ultimately aiming to alleviate alert fatigue and minimize patient harm. Prominent recommendations emphasize the importance of maintaining consistency in terminology, icons, symbols, color usage, minimizing textual content, employing appropriate formatting, and adhering to reporting and content standards to enhance usability. Many of these suggestions are applicable to various other facets of drug safety alerts and decision support, encompassing alerts for duplicate therapies and drug allergies.

Enhancing the usability of DDI decision support is of paramount importance as it places patient safety in jeopardy when clinicians dismiss DDI alerts due to their perceived lack of relevance or inadequate presentation. Clinicians tend to prioritize matters they perceive as having greater value when confronted with a multitude of concurrent requests and decisions. Striking an optimal balance between the time, attention, and cognitive resources allocated to DDI alerts and other critical responsibilities, such as patient interaction and diagnostic deliberations, is of utmost importance (37, 38).

Nevertheless, the implementation of the recommendations outlined in the existing literature encounters significant obstacles. The proprietary nature of commercial CDS software presents a substantial barrier, as obtaining vendor cooperation to relinquish control over specific design elements is no trivial task. Successful adoption of current recommendations necessitates a willingness on the part of institutions and vendors to embrace novel alert algorithms and design standards. This may entail, for instance, enabling laboratory monitoring directly from the DDI alert screen. Furthermore, there may be resistance to mandating the submission of standardized, de-identified data, citing increased labor and time requirements, along with concerns about potential risks associated with comparisons to alternative software systems. In the realm of DDI alerts, prioritizing safety concerns over vendor incentives is paramount, with the goal being the comprehension and mitigation of risks associated with patient harm.

While the existing recommendations hold promise in enhancing the consistency and comprehensibility of alerts, they may not significantly alleviate alert fatigue without substantial modifications to the knowledgebase content and alert logic. The efficacy of these suggestions is intrinsically tied to the reduction of interruptive DDI alerts, which are exclusively issued for the most critical DDIs requiring immediate clinician attention. Additionally, the establishment of a nationwide repository for alert data is a multifaceted and resource-intensive undertaking, and the implementation of further recommendations concerning the assessment of DDI alerting systems will prove challenging without access to population data.

To assess the impact of the DDI alert recommendations and the subsequent iteration of DDI decision support systems,

additional research is imperative. Rather than solely relying on DDI override rates, it is crucial to evaluate the most effective content and design of DDI alerts and prioritize outcomes, including the actual occurrence or prevention of ADEs. Further investigation is necessary to ascertain the most effective strategies for mitigating alert fatigue and, ultimately, enhancing patient safety. Although initially tailored for DDI alerts, these recommendations possess the potential to serve as a foundational framework for improving a wide array of drug safety alerts. For instance, clinicians frequently encounter multiple medication safety alerts concurrently, and the design considerations for DDI alerts and drug-allergy alerts exhibit considerable overlap. Consequently, most of the technical components are equally applicable to other medication-related alerts.

Table 1. Problems with detecting DDIs and developing alerts

Problem	**Description**
Healthcare Professionals' Knowledge	Limited pharmacological training for physicians can result in a lack of awareness regarding the dangers of various drug interactions, contributing to adverse reactions from clinically significant DDIs. (39, 40)
Clinical Significance of DDIs	Lack of standardization in ratings and classifications of DDIs due to different knowledgebases and severity rankings in CDSS, leading to inconsistencies in determining clinical significance. (14)
Alert Fatigue	Excessive alerts from CDSS can lead to alert fatigue, where important alerts may be ignored due to the overwhelming number of alerts received. (6)
Alert Information Complexity	Complex or lengthy drug interaction information can be challenging for clinicians to interpret, potentially leading to alert overrides. Clear communication of clinical consequences is essential. (6)
Justified vs. Unjustified Overrides	Overrides may be justified when benefits outweigh risks, but unjustified overrides, such as ignoring alerts, can compromise patient safety. (6)
Pharmacy Order Processing	Pharmacy systems involving support staff in order processing may result in pharmacists not seeing overridden or bypassed alerts, impacting medication safety. (41)

CONCLUSION

In summary, CDSS hold great potential to enhance healthcare decision-making and improve patient safety. The effectiveness of CDSS in generating DDI alerts can significantly impact patient outcomes. Standardization and improvements in alert presentation and content are essential to optimize CDSS performance. A team-oriented approach involving various healthcare professionals is crucial for comprehensive DDI management. Continuous research and refinement are needed to maximize the benefits of CDSS in evolving healthcare environments.

REFERENCES

1. Braden B, Corritore C, McNees P, editors. Computerized decision support systems: implications for practice. Nursing Informatics; 1997: IOS Press.
2. Teich JM, Osheroff JA, Pifer EA, Sittig DF, Jenders RA. Clinical decision support in electronic prescribing: recommendations and an action plan: report of the joint clinical decision support workgroup. Journal of the American Medical Informatics Association. 2005;12(4):365-76.
3. Kuperman GJ, Bobb A, Payne TH, Avery AJ, Gandhi TK, Burns G, et al. Medication-related clinical decision support in computerized provider order entry systems: a review. Journal of the American Medical Informatics Association. 2007;14(1):29-40.
4. Bertsche T, Pfaff J, Schiller P, Kaltschmidt J, Pruszydlo MG, Stremmel W, et al. Prevention of adverse drug reactions in intensive care patients by personal intervention based on an electronic clinical decision support system. Intensive care medicine. 2010;36:665-72.
5. van Roon EN, Flikweert S, le Comte M, Langendijk PN, Kwee-Zuiderwijk WJ, Smits P, et al. Clinical relevance of drug-drug interactions: a structured assessment procedure. Drug safety. 2005;28:1131-9.
6. Van Der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. Journal of the American Medical Informatics Association. 2006;13(2):138-47.
7. Kalmeijer MD, Holtzer W, van Dongen R, Guchelaar H-J. Implementation of a computerized physician medication order entry system at the Academic Medical Centre in Amsterdam. Pharmacy World and Science. 2003;25:88-93.
8. Oppenheim MI, Vidal C, Velasco FT, Boyer AG, Cooper MR, Hayes JG, et al., editors. Impact of a computerized alert during physician order entry on medication dosing in patients with renal impairment. Proceedings of the AMIA Symposium; 2002: American Medical Informatics Association.
9. Payne TH, Nichol WP, Hoey P, Savarino J, editors. Characteristics and override rates of order checks in a practitioner order entry system. Proceedings of the AMIA Symposium; 2002: American Medical Informatics Association.
10. van der Sijs H, Mulder A, van Gelder T, Aarts J, Berg M, Vulto A. Drug safety alert generation and overriding in a large Dutch university medical centre. Pharmacoepidemiology and drug safety. 2009;18(10):941-7.
11. Seidling HM, Storch CH, Bertsche T, Senger C, Kaltschmidt J, Walter-Sack I, et al. Successful strategy to improve the specificity of electronic statin–drug interaction alerts. European journal of clinical pharmacology. 2009;65:1149-57.

12. Lapane KL, Waring ME, Schneider KL, Dubé C, Quilliam BJ. A mixed method study of the merits of e-prescribing drug alerts in primary care. Journal of General Internal Medicine. 2008;23:442-6.
13. Feldstein AC, Smith DH, Perrin N, Yang X, Simon SR, Krall M, et al. Reducing warfarin medication interactions: an interrupted time series evaluation. Archives of Internal Medicine. 2006;166(9):1009-15.
14. Smithburger PL, Kane-Gill SL, Seybert AL. Drug-drug interactions in cardiac and cardiothoracic intensive care units: an analysis of patients in an academic medical centre in the US. Drug safety. 2010;33:879-88.
15. Shah NR, Seger AC, Seger DL, Fiskio JM, Kuperman GJ, Blumenfeld B, et al. Improving acceptance of computerized prescribing alerts in ambulatory care. Journal of the American Medical Informatics Association. 2006;13(1):5-11.
16. Helmons P. Medication safety through information technology: a focus on medication prescribing and administration. 2014.
17. Magro L, Moretti U, Leone R. Epidemiology and characteristics of adverse drug reactions caused by drug–drug interactions. Expert opinion on drug safety. 2012;11(1):83-94.
18. Hines LE, Murphy JE. Potentially harmful drug–drug interactions in the elderly: a review. The American journal of geriatric pharmacotherapy. 2011;9(6):364-77.
19. Wogalter MS, Silver NC, Leonard SD, Zaikina H. Warning symbols. Handbook of warnings. 2006;1.
20. Russ AL, Zillich AJ, Melton BL, Russell SA, Chen S, Spina JR, et al. Applying human factors principles to alert design increases efficiency and reduces prescribing errors in a scenario-based simulation. Journal of the American Medical Informatics Association. 2014;21(e2):e287-e96.
21. Phansalkar S, Edworthy J, Hellier E, Seger DL, Schedlbauer A, Avery AJ, et al. A review of human factors principles for the design and implementation of medication safety alerts in clinical information systems. Journal of the American Medical Informatics Association. 2010;17(5):493-501.
22. Horsky J, Phansalkar S, Desai A, Bell D, Middleton B. Design of decision support interventions for medication prescribing. International journal of medical informatics. 2013;82(6):492-503.
23. Russ AL, Zillich AJ, McManus MS, Doebbeling BN, Saleem JJ. Prescribers' interactions with medication alerts at the point of prescribing: a multi-method, in situ investigation of the human–computer interaction. International journal of medical informatics. 2012;81(4):232-43.
24. Zachariah M, Phansalkar S, Seidling HM, Neri PM, Cresswell KM, Duke J, et al. Development and preliminary evidence for the validity of an instrument assessing implementation of human-factors principles in medication-related decision-support systems—I-MeDeSA. Journal of the American Medical Informatics Association. 2011;18(Supplement_1):i62-i72.
25. Floor-Schreudering A, Geerts AF, Aronson JK, Bouvy ML, Ferner RE, De Smet PA. Checklist for standardized reporting of drug–drug interaction management guidelines. European journal of clinical pharmacology. 2014;70:313-8.
26. Ashworth M. Re: GPs' views on computerized drug interaction alerts. Journal of clinical pharmacy and therapeutics. 2002;27(5):311-2.
27. Hansten PD, Horn JR, Hazlet TK. ORCA: OpeRational ClassificAtion of drug interactions. Journal of the American Pharmaceutical Association (1996). 2001;41(2):161-5.
28. Murphy JE, Malone DC, Olson BM, Grizzle AJ, Armstrong EP, Skrepnek GH. Development of computerized alerts with management strategies for 25 serious drug–drug interactions. American Journal of Health-System Pharmacy. 2009;66(1):38-44.
29. Russ AL, Saleem JJ, McManus MS, Frankel RM, Zillich AJ, editors. The workflow of computerized medication ordering in primary care is not prescriptive. Proceedings of the Human Factors and Ergonomics Society Annual Meeting; 2010: SAGE Publications Sage CA: Los Angeles, CA.
30. Kuilboer MM, van der Lei J, Bohnen AM, van Bemmel JH, editors. The availability of unavailable information. Proceedings of the AMIA Annual Fall Symposium; 1997: American Medical Informatics Association.
31. Coleman JJ, van der Sijs H, Haefeli WE, Slight SP, McDowell SE, Seidling HM, et al. On the alert: future priorities for alerts in clinical decision support for computerized physician order entry identified from a European workshop. BMC medical informatics and decision making. 2013;13(1):1-8.
32. Baker DP, Gustafson S, Beaubien J, Salas E, Barach P. Medical teamwork and patient safety: the evidence-based relation. AHRQ publication. 2005;5(53):1-64.
33. Ryan RE, Santesso N, Lowe D, Hill S, Grimshaw JM, Prictor M, et al. Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. Cochrane Database of Systematic Reviews. 2014(4).
34. Mutebi A, Warholak TL, Hines LE, Plummer R, Malone DC. Assessing patients' information needs regarding drug–drug interactions. Journal of the American Pharmacists Association. 2013;53(1):39-45.
35. Porter ME. What is value in health care. N Engl J Med. 2010;363(26):2477-81.
36. McCoy AB, Waitman LR, Lewis JB, Wright JA, Choma DP, Miller RA, et al. A framework for evaluating the appropriateness of clinical decision support alerts and responses. Journal of the American Medical Informatics Association. 2012;19(3):346-52.
37. Chaiken S, Ledgerwood A. A theory of heuristic and systematic information processing. Handbook of theories of social psychology. 2012;1:246-66.
38. Maheswaran D, Chaiken S. Promoting systematic processing in low-motivation settings: Effect of incongruent information on processing and judgment. Journal of personality and social psychology. 1991;61(1):13.

39. Classen DC. Clinical decision support systems to improve clinical practice and quality of care. Jama. 1998;280(15):1360-1.
40. Raschke RA, Gollihare B, Wunderlich TA, Guidry JR, Leibowitz AI, Peirce JC, et al. A computer alert system to prevent injury from adverse drug events: development and evaluation in a community teaching hospital. Jama. 1998;280(15):1317-20.
41. Practices. IfSM. Heed this warning! Don’t miss important computer alerts. 2016.