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RESEARCH ARTICLE
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USING CLINICAL DECISION SUPPORT SYSTEMS IN PRACTICE AND ITS EFFECT ON DRUG INTERACTION

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Abstract
Clinical Decision Support Systems (CDSS) are now essential tools in healthcare, providing clinicians with crucial guidance and information to assist in patient care. Their integration into Computerized Physician Order Entry (CPOE) systems has the potential to revolutionize healthcare by enhancing safety, quality, and efficiency. A key function of CDSS is identifying and managing drug-drug interactions (DDIs), which are a major concern in today's complex medication landscape. DDIs can lead to adverse drug events (ADEs), resulting in increased hospitalization rates, longer hospital stays, and patient morbidity and mortality. CDSS can play a crucial role in detecting DDIs early, potentially reducing these risks. However, the effectiveness of CDSS-generated DDI alerts varies, and many alerts are ignored due to factors like alert fatigue and design flaws. Efforts to improve DDI alerts focus on standardizing their presentation, content, and resolution processes. It is crucial to include clear identification of drug pairs, indication of severity, explanation of clinical consequences, and

guidance on risk mitigation. Consistency in terminology, symbols, and formats is essential, as is incorporating patient-specific data and context into alert logic. A team approach to DDI management, involving various healthcare professionals, is recommended for optimal patient care. Evaluating the effectiveness of DDI alerts should consider both measurable and perceived value, recognizing that clinicians' perceptions may differ based on their expertise and roles. Additionally, it is important not to rely solely on override rates as the metric for assessing alert efficacy. In conclusion, CDSS and DDI alerting systems have the potential to significantly enhance patient safety and healthcare outcomes. However, ongoing research, standardization, and user-centered design are essential to fully realize their benefits and address 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 become essential components of computerized physician order entry (CPOE) systems, enhancing healthcare decision-making. CDSS is defined as "computer software employing a knowledgebase designed for use by a clinician involved in patient care, as a direct aid to clinical decision making" (1). Their integration into CPOE systems holds the potential to transform patient care by improving safety, quality, and efficiency (2).

A key aspect of CDSS integration is its ability to assist prescribers with appropriate dosing and alert them to potential drug-drug interactions (DDIs), duplicate therapies, and drug allergies (3). Historically, healthcare professionals relied on their expertise to manage DDIs, a method that may not be foolproof given the growing complexity and volume of medications. This scenario underscores the need for innovative approaches to enhance DDI identification, with CDSS being a prominent solution. DDIs can lead to adverse drug events (ADEs), which are often predictable and preventable (4).

ADEs can result in increased hospitalization rates, longer stays, and higher patient morbidity and mortality (5). Therefore, timely DDI identification is crucial for the safety and efficacy of pharmacotherapy. CDSS has proven its worth in facilitating early DDI detection, which can be a game-changer (5). The effectiveness of CDSS in generating DDI alerts varies, with percentages ranging from 7% to 36% of medication orders (6-9).

The acceptance rate of these alerts by prescribers, measured by their decision to cancel or modify the initial order, ranges between 9% and 12% (10). Although these numbers may seem modest, they don't fully represent the extent of prescriber actions that can help prevent adverse drug reactions, such as increased patient monitoring or adjustments in laboratory or drug levels (10). However, the exact impact of CDSS on patient outcomes is still not completely clear. Despite its clear benefits, CDSS also faces certain limitations (11). A significant number of DDI alerts generated by CDSS systems are ignored by physicians (12, 13). This could be due to various reasons, including prescribers underestimating the significance of the DDI or the CDSS system overemphasizing its importance. Additionally, neglecting human factors during alert system implementation and flaws in alert design have been linked to the bypassing of alerts. Regulatory bodies worldwide advocate for the inclusion of CDSS within CPOE systems, making it a crucial component of modern healthcare practice. 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.

DISCUSSION

Standardizing the presentation, content, and resolution of drug-drug interaction (DDI) alerts could greatly improve their effectiveness in clinical settings, enhancing patient safety and healthcare

efficiency. Research in human factors engineering highlights the importance of color, visibility, and prioritization in influencing clinicians' responses to safety warnings (3). Although this research provides valuable insights for designing warnings for various safety hazards, its application to drug-related warnings is still limited (4). The inconsistent presentation of alert information, especially across multiple systems, can lead to cognitive overload and confusion among clinicians. Therefore, there is a strong call for improving the consistency and uniformity of DDI alert presentations across different systems.

Regarding the content of DDI alerts, the existing safety literature suggests four key elements: a signal word indicating the severity of the DDI, hazard information specifying the harmful drug combination, guidance on risk mitigation, and a description of potential clinical consequences if the hazard is not addressed (3, 5). Recent studies also highlight the importance of incorporating contextual information and patient-specific data into the algorithm logic to enhance DDI alerts (6, 7). Consequently, DDI alerting systems should include seven critical elements: identification of the involved drugs, classification of severity, description of clinical consequences (including frequency), explanation of the interaction mechanism, integration of contextual information and modifiable factors, provision of recommended actions, and presentation of supporting evidence.

To avoid confusion, initial DDI alerts should clearly identify the interacting drug pair or individual drugs (8). Research indicates that prescribers often struggle to understand why alerts are triggered, underscoring the need for clear identification of the drug pair (7). To achieve this, it is recommended to use both the prescribed medication name and generic ingredient names, especially for combination products (9).Consistency in indicating the potential severity of DDIs using standardized terms and definitions across all CDSSs is crucial (1, 2). 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(3). 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(3). 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(4).

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(2, 4, 5). 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(6, 7). 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(2). 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(7, 8). 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(9).

Essential details should be displayed prominently in the alert, with supplementary information and secondary considerations accessible through hyperlinks(10). Balancing succinct communication with sufficient information for informed decision-making should be addressed through iterative alert prototyping and usability testing (11). 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(12). 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 (9).

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(13). 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(14, 15). 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(16). 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(17).

It is crucial to acknowledge that override rates alone cannot be used as the sole criterion for evaluating the efficacy of alerts(17, 18). 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 (19, 20).

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.

CONCLUSION

Clinical Decision Support Systems (CDSS) have significant potential to improve healthcare decision-making and patient safety. The ability of CDSS to produce effective drug-drug interaction (DDI) alerts can have a substantial impact on patient outcomes. It is crucial to standardize and enhance the presentation and content of alerts to optimize the performance of CDSS. A collaborative approach involving different healthcare professionals is essential for thorough DDI management. Ongoing research and development are necessary to fully leverage the advantages of CDSS in the dynamic healthcare landscape.

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