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What, if all alerts were specific – Estimating the potential impact on drug interaction alert burden

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ABSTRACT

Purpose: Clinical decision support systems (CDSS) may potentially improve prescribing quality, but are subject to poor user acceptance. Reasons for alert overriding have been identified and counterstrategies have been suggested; however, poor alert specificity, a prominent reason of alert overriding, has not been well addressed. This paper aims at structuring modulators that determine alert specificity and estimating their quantitative impact on alert burden.

Methods: We developed and summarized optimizing strategies to guarantee the specificity of alerts and applied them to a set of 100 critical and frequent drug interaction (DDI) alerts. Hence, DDI alerts were classified as dynamic, i.e. potentially sensitive to prescription-, co-medication-, or patient-related factors that would change alert severity or render the alert inappropriate compared to static, i.e. always applicable alerts not modulated by cofactors.

Results: Within the subset of 100 critical DDI alerts, only 10 alerts were considered as static and for 7 alerts, relevant factors are not generally available in today's patient charts or their consideration would not impact alert severity. The vast majority, i.e. 83 alerts, might require a decrease in alert severity due to factors related to the prescription ($N = 13$), the co-medication ($N = 11$), individual patient data ($N = 36$), or combinations of them ($N = 23$). Patient-related factors consisted mainly of three lab values, i.e. renal function, potassium, and therapeutic drug monitoring results.

Conclusion: This paper outlines how promising the refinement of knowledge bases is in order to increase specificity and decrease alert burden and suggests how to structure knowledge bases to refine DDI alerting.

1. Introduction

Everybody was terrified when it became evident in the late nineties of the last century how hazardous drug treatment really can be [1]. Indeed, many of the mistakes that occurred during drug treatment were related to an erroneous prescription [2] and often, missing information or lacking knowledge contributed to the nascence of errors [3]. Therefore, electronic prescribing systems (computerized physician order entry, CPOE) were introduced and later, as

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their limitations became obvious, they were equipped with clinical decision support systems (CDSS). CDSS should guide physicians during prescription and warn them against the potential risks jeopardizing the ordering process and consequently patient safety. About 60% of all medication errors were supposedly preventable by implementation of CPOE/CDSS [4].

However, after setting these systems in place their impact was often only modest and left the high expectations unsatisfied. About 90% of all warnings were simply ignored because they were judged as irrelevant, not timely, had already been considered, or simply because the estimated benefit of the therapy outweighed the reported risks [5,6]. Additionally, some warnings likely had no impact because they were hidden somewhere on the screen and the user did not even have a chance to see them [7]. Similarly, also unissued alerts cannot impact care and therefore overridden, unrecognized, or missing warnings will neither impact clinical outcome. This may be deleterious if the warning was appropriate and may be favorable if not. Hence, increasing alert acceptance must be intertwined with measures increasing alert quality.

Today, a myriad of different CDSS and related databases have been developed but their performance varies largely and even when the same system is implemented in different settings the same clinical situation may trigger a warning only in some institutions [8]. Approaches to foster the impact of CDSS include refinement of implemented knowledge bases by consultation of an expert team. This partially improved alerting, e.g. by eliminating drug–drug interaction (DDI) warnings between systemically and topically administered drugs [9], or by implementing [10] or refining [11] a severity grading. Moreover, the importance of the characteristics of the machine–user interaction has been recognized [12] and recently a set of so-called human factors principles that may influence the user's handling of warnings was defined (e.g. color or textual information) [13]. Finally, also excessive numbers of alerts might reduce user acceptance and hence alerts should be prioritized according to the setting, the patient, and the warning itself [14].

This paper aims at suggesting strategies to increase alert specificity and assess their potential impact on alert burden within a pertinent sample of both frequent and critical DDI alerts. Because published evidence mostly refers to DDI systems, we did revert to DDI warnings. We do, however, believe that their characteristics are likely applicable to other CDSS as well.

2. Methods

Strategies to optimize specificity of DDI alerts were assessed in a two-step process: first, distinct factors influencing DDI alert specificity as identified in the literature ([15–22,9,23–26], search terms included "Decision Support Systems, Clinical" [MeSH Term]. "drug safety alert", "Drug Interactions" [Mesh Term], specificity (lastly performed on June 21st, 2013)) were structured and complemented by an expert team consisting of physicians, pharmacists, and health-IT specialists. As commonly done, we assumed that a DDI warning generally referred to two systemically available drugs that are concurrently given and, if several routes of administration are applicable, orally administered to an adult patient without co-morbidities [27,28]. An alert would be considered specific, if it was appropriately issued, i.e. warning against a hazardous situation that was indeed present. Conversely an alert would be considered non-specific if the particular risk was absent or if the situation of risk had changed and adaptation of alert severity was needed. Impact of distinct modulators for DDI alerts were classified as follows:

Category 1: The DDI alert is not susceptible to specificity modulators and applies under all conditions to all patients in the same manner (e.g. an additive risk of malignant neuroleptic syndrome under lithium and clozapine).
Category 2: The DDI alert might be susceptible to specificity modulators, however external conditions and relevant information are not conveniently available yet (e.g. continuous measuring of blood glucose).
Category 3: The DDI alert is susceptible to specificity modulators, however, the severity of the DDI alert will still be critical (e.g. a critical drug combination that requires monitoring or action, however, even if that is done, the risk is still imminent. In that case, the severity grade will not change while the textual information should reward the user for his actions).
Category 4: The DDI alert is susceptible to specificity modulators in a way that either makes the DDI alert obsolete (e.g. time-shifted administration of bivalent cations and fluoroquinolones avoids their DDI) or changes the severity of the alert (e.g. if the dosage of simvastatin in a simvastatin-amiodarone combination remains low, the pharmacokinetic DDI might be appropriately compensated for, however, additive pharmacodynamic effects of toxicity will remain and the patient should still be monitored for myopathy). Hence, the DDI is not obsolete, but should be graded less severe than for a regular (=high) dose combination.

Secondly, we applied these theoretical considerations to a set of critical DDI alerts to assess prevalent options for alert modification. Therefore we selected the top 100 critical DDI alerts that were triggered within 100 000 issued electronic prescriptions in the University Hospital Heidelberg through the hospital's electronic prescribing system for ambulatory patients and patients at discharge in 2011. The electronic prescribing system has several CDSS functionalities including a DDI database that covers about 16 000 drug pairs. Alerts are tiered into five severity categories (none, minor, moderate, critical, and contraindicated). An alert was considered critical if (1) the combination was contraindicated or (2) if the concurrent use was associated with a potential for serious adverse drug events and required clinical management for its prevention. For each DDI, the potential applicability of the modulators of specificity was checked.