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Physician perspectives of CYP2C19 and clopidogrel drug-gene interaction active clinical decision support alerts

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ABSTRACT

Objective: To determine if physicians find clinical decision support alerts for pharmacogenomic drug-gene interactions useful and assess their perceptions of usability aspects that impact usefulness.
Materials and methods: 52 physicians participated in an online simulation and questionnaire involving a prototype alert for the clopidogrel and *CYP2C19* drug-gene interaction.
Results: Only 4% of participants stated they would override the alert. 92% agreed that the alerts were useful. 87% found the visual interface appropriate, 91% felt the timing of the alert was appropriate and 75% were unfamiliar with the specific drug-gene interaction. 80% of providers preferred the ability to order the recommended medication within the alert. Qualitative responses suggested that supplementary information is important, but should be provided as external links, and that the utility of pharmacogenomic alerts depends on the broader ecosystem of alerts.
Principal conclusions: Pharmacogenomic alerts would be welcomed by many physicians, can be built with minimalist design principles, and are appropriately placed at the end of the prescribing process. Since many physicians lack familiarity with pharmacogenomics but have limited time, information and educational resources within the alert should be carefully selected and presented in concise ways.

1. Introduction

As gene sequencing costs decrease and the body of literature supporting genomic-guided therapies grows, pharmacogenomic biomarkers are becoming more relevant to standard medical practice. The Food and Drug Administration (FDA) has identified over 43 pharmacogenomic biomarkers associated with a total of 139 medications commonly used in cardiac, oncological, surgical, and psychiatric care [1]. Black box warnings are included on the labels of several such drugs to alert providers to pharmacogenomic effects, yet disseminating this information for use at the point of care remains a formidable challenge.

EMR[1] systems and their CDS[2] features may prove crucial in the application of pharmacogenomics to patient care [2]. The increasing prevalence of EMR systems makes CDS a potentially ubiquitous tool. In addition, CDS can interact dynamically with patient-specific information in the EMR, allowing it to draw on genomic data stored in an individual's record [3–6]. Point of care alerts are one form of CDS that may be a convenient option for pharmacogenomics as they can be driven by rules engines already in use for drug–drug or drug-allergy interactions. Yet, while drug-genome alerts are a theoretically simple way to inform providers about their patients' pharmacogenomic test results, they should be implemented with caution.

Ill-conceived and poorly-designed alerts can distract health care providers from other important aspects of a patient's care [7]. Alert fatigue is a growing concern as providers are frequently inundated with low-priority and irrelevant alerts in day-to-day clinical activities [8]. Novel alerts should be considered useful by physicians and designed to quickly and accurately aid them in understanding the information and its implications [9,10]. The usefulness of alerts depends on their visual aesthetics, content composition, and timing within the clinical workflow [11,12]. Past research highlights

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[1] Electronic medical record.
[2] Clinical decision support.

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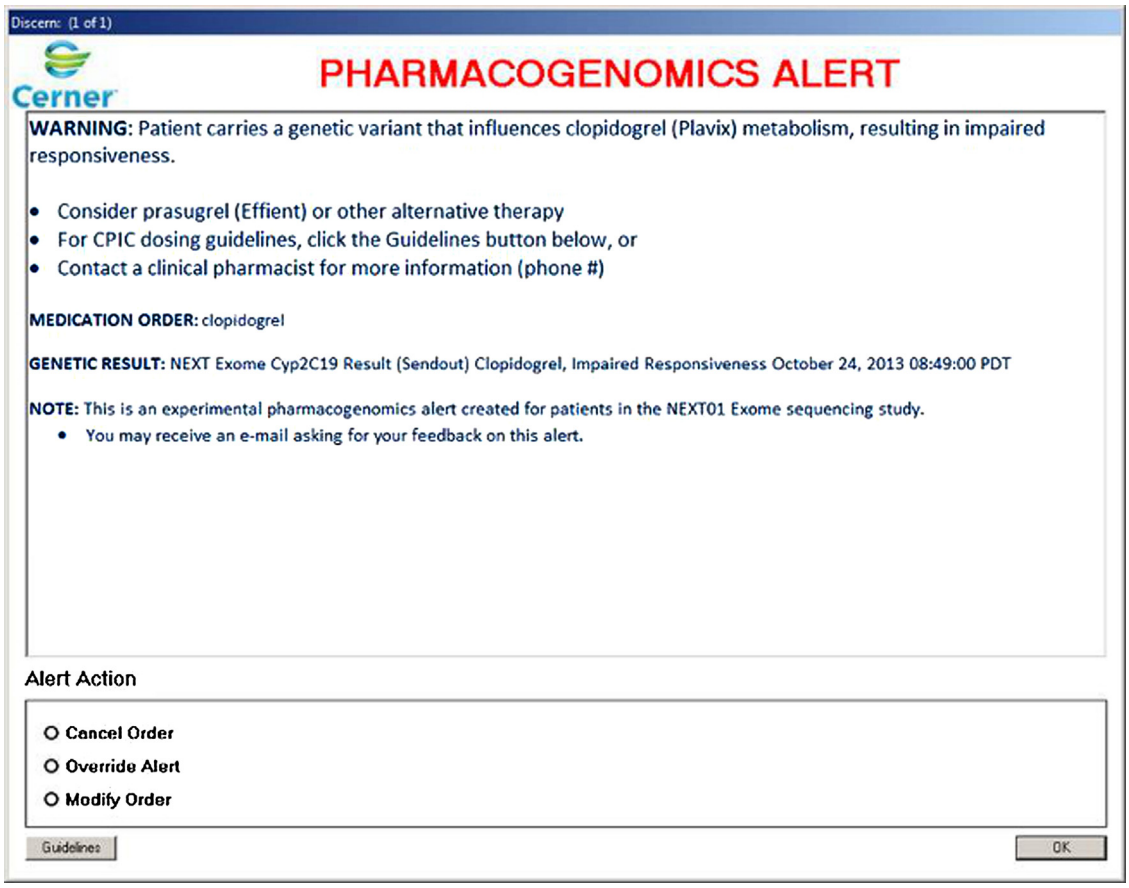

Fig. 1. Screenshot of prototype clopidogrel and *CYP2C19* alert. The prototype variant-drug alert was created in Cerner® with the Discern® rules engine. Concise information is provided explaining the variant-drug interaction and several possible actions. The "Guidelines" button loads the *CYP2C19* and clopidogrel Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines in a browser window.

the importance of these features for the success of drug–drug or drug-allergy alerts, but little has been studied specifically for pharmacogenomic alerts.

Early efforts to assess the usability of pharmacogenomic alerts have begun at the UW[3]. Devine and Overby performed a multi-methods study of pharmacogenomic alerts that were created in a simulation version of PowerChart® (Cerner Millenium®) and exposed to ten fellows in cardiology and oncology specialties [13]. Qualitative results aided in refinement of the alerts and survey results showed the participants found the alerts to be overall useful. In 2013, work began to create similar pharmacogenomic alerts in the university's live Cerner EMR system for colorectal cancer patients in a clinical trial comparing exome sequencing driven care to usual care. In the current study, our goal was to determine if this sample of physicians found the pharmacogenomic alert useful and to ascertain their perspectives on elements of usability including visual design, content choice and workflow placement. To address these goals, we created a simulation and questionnaire that could be performed online and was specific to a single drug-gene interaction between clopidogrel and *CYP2C19* variants.

2. Methods

2.1. Recruitment

Physicians were recruited from the UW's major medical centers, outpatient and specialty clinics, and emergency departments. Inclusion criteria required participants to be in the UW Physicians Network or residency training program with the credentials to prescribe medications. A recruitment e-mail was sent to a random sample of 457 attending physicians, fellows, and residents that linked them to an online consent form. Physicians that consented proceeded to the online simulation portion of the study. A reminder e-mail was sent to physicians who did not respond within one week. Recruitment occurred between April 28th 2014 and May 28th 2014. Internal Review Board approval was obtained from the UW Human Subjects Division (#46932).

2.2. Simulation

A case scenario was presented in which the participant was responsible for prescribing dual anti-platelet therapy to a patient recovering from a coronary stent placement procedure (Appendix A in Supplementary information). The participant was given a choice of therapies to select: aspirin and clopidogrel, aspirin and ticagrelor, aspirin and prasugral, or "other" drug. Medication choices were consistent with current American College of Cardiology Foundation and American Heart Association guidelines for management of myocardial infarction [14]. Regardless of the participant's therapy of choice, he or she was then directed to an image of a pharmacogenomic alert for clopidogrel and the *CYP2C19* variant. The image was created from an actual pharmacogenomic alert created in the UW Cerner® EMR for patients who were participating in the New EXome Technology (NEXT) CSER trial (Fig. 1).

Development of the alert has been described in detail elsewhere [15]. Briefly, the variant-drug alert was created with input from physicians, pharmacists and lab geneticists to function similarly to drug–drug interaction (DDI) alerts, triggering when a provider

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