Key Question 1: Should presentation of DDI decision support vary by clinicians?

A safe medication use process is built on interdisciplinary interactions and cooperation to assure that patients receive the best possible care. DDI decision support applies to all clinicians on the care team: prescriber, pharmacist, nurse, patient, and others (Figure 1). For non prescribing clinicians, DDI alerts may be deployed as a second check to help ensure that patients receiving interacting drug pairs are being monitored or assessed. Patient care and safety are best achieved when all members of the team have knowledge of what other members are doing. As such, we advocate a team approach to managing DDIs (Figure 1). We recommend that general alert content be consistent among various types of clinicians. What may differ, however, is how the information is presented to various professionals. The message may be changed based on the context or functions, recognizing that professionals in different settings have different roles, responsibilities, and privileges. For example, prescriber recommendations may focus on ordering specific monitoring parameters, while pharmacists may be notified to ensure monitoring orders were placed and results reviewed. Another important question we considered is how an alert display should change if an individual clinician has been exposed many times to an alert yet there is no detectable behavior change? Similarly, should specialists with unique training or roles be allowed to "turn off" alerts for DDIs that they routinely manage (e.g., warfarin clinic pharmacists receiving warfarin interaction alerts when the patient is currently being monitored)? We are not aware of evidence that demonstrates that it is safe to eliminate DDI alerts for specialists. However, establishing more selective institutional DDI alerting practices overall may relieve much of the alert burden. EHR system architecture should allow institutions to easily make these changes based on clinician characteristics. Patients play an important role managing risks associated with DDIs, and need to be engaged in monitoring for signs of toxicity or loss of efficacy. Although evidence-based best practices for printed patient information are recommended, the logistics and manner in how patients should be informed is beyond our Workgroup's scope of work. **Key Question 3: How should** effectiveness of DDI decision support be measured?

The value of CDS may be measured by the achievement of outcomes relative to the interaction cost (e.g., cognitive burden, time), and thus encompasses efficiency in using resources. Effectiveness of CDS can be defined as a product of both measured value as well as perceived value, since components of value include, but are not limited to, the following: clinical outcomes, process efficiency measures, clinician satisfaction, heuristics, evidence, usability, and cost of ADEs. Examples of measured value for the DDI between warfarin and amiodarone include increased rates of appropriate international normalized ratio (INR) ordering, warfarin dose adjustments, patient counselling, and anticoagulation clinic follow up. The perceived value of alerts likely differs by



ordering, warfarin dose adjustments, patient counselling, and anticoagulation clinic follow up. The perceived value of alerts likely differs by clinician type and experience. For example, practicing cardiologists may perceive little value, while medical residents may perceive high value if it reminds them to order an INR. Using solely alert override rates to determine effectiveness of alerts may not account for these value-added actions. unless the actions were discreetly captured with the alert (Supplementary Appendix C). Conversely, alerts that do not provide value (measured or perceived) should be suppressed with precision (i.e., increase specificity) without jeopardizing sensitivity. Generally speaking, as alert effectiveness increases, alert value increases, and thus alert fatigue may decrease. Alert logic that does not consider mitigating factors associated with a low prevalence of adverse outcomes (e.g., single-doses of precipitant drugs) may produce a low positive predictive value, and a corresponding lower perceived value. Although important, override rates alone cannot be used to assess the effectiveness of alerts. A primary reason is that the thought process of clinicians and subsequent actions are not fully captured by current systems.

For example, it is unclear if the override is due to disregard of the alert, careful consideration of the risks and benefits. or time constraints preventing a full evaluation. Therefore, override rates provide a crude estimate of alert adherence. In the near term, override rates should be used to identify alerts that require a detailed evaluation process, including the incorporation of clinician feedback. This detailed evaluation should include the presence of modifying factors (e.g., lab values, co-morbidities), actions taken as a result of the alert (e.g., monitoring ordered), and a consensus on perceived value by clinicians (which is difficult to record with the alert) (see Supplementary Appendix C for an explanation of how Bayesian methods can measure alert effectiveness). There are a myriad of opportunities for optimizing alerts and increasing their value.

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Recommendations to Improve the Usability of Drug-Drug Interaction **Clinical Decision Support Alerts**

Clinical decision support (CDS) has the potential to make patient care more efficient, safe, and effective. CDS encompasses a variety of tools presented in an electronic health record (EHR) based on relevant patient and care process information in order to improve clinical decision making. Though drug-drug interactions (DDIs) are known to cause harm, there is little information on how best to use CDS tools to improve patient outcomes. End-users of DDI decision support are clinicians (i.e., healthcare professionals such as physicians, pharmacists, and nurses) who encounter alerts and other forms of DDI decision support in the process of prescribing, reviewing, verifying, preparing, dispensing, and administering medications, and monitoring patients for adverse drug events. The most common form of DDI decision support is interruptive alerts, although other types of CDS tools are also used. It is widely recognized that clinicians are generally unsatisfied with the lack of patient specificity and inappropriate context of DDI alerts. These alerts are occurring with escalating frequency with the increased use of EHRs. Factors contributing to excessive DDI alerts may include inconsistent evaluation and classification of interactions, lack of specificity in alerting logic, and perceived risk of legal liability. Other drug safety alerts, such as drug-allergy, drug-disease, and duplicate therapy alerts are also problematic and contribute to clinician dissatisfaction



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These drug safety alerts are so common that it becomes difficult to distinguish important from less important ones, causing clinically relevant alerts to be ignored. Reports of override rates as high as 90% raise concern that DDI decision support needs fundamental revision. There is also wide variation across healthcare organizations and health information technology (IT) vendors in how DDI alerts are presented to clinicians, with no clear recommendations derived from studies or best practices to provide guidance. Thus, addressing the design of DDI decision support is a timely and important topic. Although the focus of this work is specific to DDI decision support, we recognize that other drug safety alerts, such as drug allergy alerts, pose similar decision support design challenges. We assembled a group of experts and conducted a series of meeting over 13 months to develop specific recommendations to improve the quality of DDI decision support. This paper describes recommendations from the Usability Workgroup for preferred DDI alerting strategies within CDS systems. These principles are intended to convey drug information effectively while reducing clinicians' cognitive effort in order to improve medication safety.