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Towards improved drug allergy alerts: Multidisciplinary expert recommendations

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Drug allergy alerts represent one of the key clinical decision support features of computerized provider order entry (CPOE) in electronic health record systems. These alerts can safeguard against prescription or administration of medications that could result in an adverse reaction by comparing ingredients and cross reactivity between prescribed medications and medications on the patient's allergy list.

While effective in theory, in practice, these alerts as currently used in most systems have serious limitations with over 90% of these alerts are now overridden [1–6]. Observations from the last 15 years show override rates increasing from 50% in the mid 1990s [1] to almost 90% in 2015 [2,3]. Many allergy alerts are inconsequential and rarely, if ever, result in an adverse reaction [4,7]. It is estimated that providers need to field more than 123 unnecessary alerts to prevent one adverse drug event [4]. This identifies a massive problem with drug allergy alert systems that demands multidisciplinary attention.

While most of the overrides may simply indicate low value alerts that are not providing useful decision support to providers, many alerts are overridden in situations that are not safe, for example, when patients have a history of severe or immune-mediated reactions. Though surprising, alert override rates for anaphylaxis or angioedema are often greater than 75% [2–6].

Several reasons can explain such high drug allergy alert override rates. First, inaccurate or outdated allergies abound in the patient records and are infrequently (or never) edited or removed by clinicians. In one recent study, we found that more than half of the drug allergy alerts were triggered for medications that patients have previously tolerated or had been deemed not allergic; however, these allergies were not removed from the patients' records, causing alerts to continuously fire and be overridden by clinicians [2,3]. Table 1 shows a real example of one patient's allergy list with 25 allergies. The patient was not allergic to most of these substances and yet no one had reconciled her allergies or referred her to an allergist. Second, some alerts are based on cross-reactivity or sensitivity inference that is overly inclusive. Alerts of this type account for 90% of all alerts, comprising many low value, clinically unimportant alerts [2]. One example is the cross sensitivity between penicillins and 3rd or 4th generation cephalosporins. Even in Type I, IgE-mediated reactions to

penicillin, there is minimal evidence of cross-reaction when patients are put on later generation of cephalosporins [8]. Thirdly, a significant portion of alerts are triggered by mild, non-immune mediated reactions (e.g., intolerances, typically gastrointestinal upset). Our prior data shows that only one-third of reactions are potentially immune-mediated and one-tenth of reactions are severe [2].

Clearly, new approaches to allergy alerting are critical. We assembled a multidisciplinary group of experts from allergy/immunology, emergency medicine, internal medicine, pharmacology, pharmacy, quality and safety, nursing, and clinical informatics to identify new approaches for drug allergy alerting systems. We present a set of conceptual and practical recommendations to improve drug allergy alerting and design a new generation of adverse event avoidance systems.

1. Improving allergy documentation: Improved characterization of allergic information to improve alert accuracy. It is crucial for allergy information to accurately characterize and distinguish adverse drug reactions as side effects, toxicities, intolerance, idiosyncrasy, or allergies. Clinicians recording these events may not know the distinctions; computerized clinical decision support could assist in these determinations, when possible. For example, when entering an allergic reaction of rash- a reaction that comprises nearly 30% of reaction entries- clinical decision support systems should help clinicians specify the types of rash patients have experienced by prompting a few questions about the timing and appearance of the rash. By distinguishing between types of hypersensitivity reactions, alerts can be tailored to fire only for likely IgE-mediated (e.g., drug-induced-urticaria) or severe reactions (e.g., Stevens-Johnson Syndrome). A more detailed characterization of the patient's allergy at the time of entry or reconciliation will ensure that alerts are triggered when they matter most, and avoid unnecessary alerts on mild intolerances or previously-tolerated medications.

2. Patient engagement: Patient engagement in the allergy reconciliation process is a key to creation and maintenance of meaningful allergy lists in electronic health record systems. Often, once an allergy is recorded, it is considered immutable, and rarely are allergies removed; at the same time, even when patients have a medication allergy, it may not appear on the list. Strategies to engage patients in reviewing and updating their allergy information should be further tested and implemented. For example, patients should be able to update their allergy information in their personal health portals, which will prompt the clinician to review the information with them on their next encounter.

3. Alerting mechanism: Allergy alerting systems should consider reaction severity and other contextual information (e.g., the type of match between the allergen and prescribed medication, reaction occurrence probabilities, information on whether this alert was fired or overridden in the past, etc.) into consideration when presenting alerts to clinicians. Un-targeted alerting approaches produce noisy alerts that are not clinically meaningful. Alert tiering is one potential solution that is common in drug–drug interaction alerts. Based on adverse drug

reaction severity, or the likelihood of an immune-mediated reactions, such as immediate, IgE-mediated allergic reaction that on repeat exposure could lead to severe outcomes, drug allergy alerts can be classified as either *informative* (providers will still see the alert information but would not need to take an action to override the alert) or *interruptive* (providers will be required to provide a reason for override or cancel the prescription). More work is needed to identify which alerts should be eliminated, and how alerts should be tiered as interruptive vs. informative.

4. Hospital Polices and Guidelines: To reduce the risks of liability associated with a more patient-centered allergy alerting system (e.g., turning off allergy alerts with no clear evidence of cross-reactivity – e.g., 3rd/4th generation cephalosporins and penicillins) [9], healthcare organizations should develop clear policies and guidelines for their providers. Using established best practices put forth by drug allergy experts can help mitigate those risks.

5. Continuous alert monitoring and improvement: organizations should track their allergy alerting and override rates over time. This will help identify changes in alerting patterns and turn-off alerts that are disruptive.

We believe that these steps can substantially improve allergy alerting. The rates at which clinicians are interrupted will be much lower, thereby refocusing attention on the alerts and patient safety will improve, because providers will be more likely to adhere to warnings that represent a serious concern.

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Table 1

An example of a patient's allergy list with 29 allergies. The patient said that she was not allergic to most of these substances and yet no one had reconciled her allergies or referred her to an allergist.

Allergies	Reaction	Severity
Aleve (Naproxen Sodium)	Anaphylaxis	High
Amoxicillin	Anaphylaxis	High
Augmentin (Amoxicillin-pot Clavulanate)	Anaphylaxis	High
Bactrim (Sulfamethoxazole and Trimethoprim)	Anaphylaxis	High
Compazine (Prochiorperazine)	Anaphylaxis, Swelling of face/tongue/nose	High
Doxycycline	Anaphylaxis	High
Floricet (Butalbital- Acetaminophen)	Anaphylaxis	High
Flagyl (Metronidazole HCl)	Anaphylaxis	High
Gentamicin	Anaphylaxis	High
Levaquin (Levofloxacin)	Anaphylaxis	High
Macrobid (Nitrofurantoin)	Anaphylaxis	High
NSAIDs (nonsteroidal anti-inflammatory drugs)	Anaphylaxis	High
Sulfa	Anaphylaxis	High
Tetracycline	Anaphylaxis	High
Zyvox (Linezolid)	Anaphylaxis	High
Ammonia	Hives	-
Azithromycin	Diarrhea, Nausea	-
Bleach (Sodium Hypochlorite)	Hives, Swelling	-
Ceftin	Itching, Swelling	-
Cigarette Smoke	Hives	-
Depakote (Divalproex)	Suicidal ideation	-
Inderal (Propranolol)	Hypotension	-
Lyrica (Pregabalin)	Suicidal ideation	-
Marcaine (Bupivacaine)	Hives, Facial swelling	-
Neurontin (Gabapentin)	Hypotension	-