

Use of Clinical Decision Support to Increase Premedication Regimen Homogeneity

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Abstract

Purpose: Patients with prior allergic reactions to iodinated contrast require premedication. This study aimed to increase the homogeneity of premedication orders in such patients.

Methods: A point-of-care (POC) clinical decision support (CDS) alert accompanied by an order set was implemented in the electronic health record (EHR) to notify providers of a prior allergic reaction upon ordering an examination involving iodinated contrast. Premedication regimens were retrospectively compared 11 months pre- and 11 months post-alert implementation, with the different regimens being classified as follows: (1) “preferred” (per ACR recommendations), (2) “nonpreferred” (corticosteroid administered <24 hours before examination, but not per ACR recommendations), or (3) “no premedication.”

Results: Over 22 months, 22,023 iodinated contrast examinations were performed, 200 (186 intravascular, 12 gastrointestinal/genitourinary, 1 intraarticular, 1 intrathecal) being in patients with a documented iodinated contrast allergy (106 pre-, 94 post-alert deployment). Prealert, 41 of 106 patients (38.7%) received a preferred regimen, 47 (44.3%) received nonpreferred regimens, and 18 (17.0%) received no premedication. Postalert, 58 of 94 patients (61.7%) received a preferred regimen, 21 (22.3%) nonpreferred regimens, and 15 (16.0%) no premedication. After alert initiation, the patients prescribed a preferred regimen significantly increased (Z -score = 3.25, P = .001), but there was no significant difference in the proportion of patients with no premedication (Z -score = -0.02, P = .85). In 2 of 200 patients (1.0%), an allergic reaction occurred, both after POC-CDS alert implementation with a preferred regimen administered.

Conclusions: The homogeneity of premedication regimens significantly increased after the alert’s launch. However, the proportion of patients with no premedication did not significantly change.

Key Words: Clinical decision support, premedication, allergy, iodinated contrast

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INTRODUCTION

Over the past decades, the number of CT scans using iodinated contrast performed annually in the United States has significantly increased [1-3]. The proportion of patients who have an acute allergic reaction to nonionic

intravenous (IV) contrast is relatively low; one large-scale study noted a reaction rate of 3.13%, whereas more recent studies report more conservative rates of 0.2% to 0.7% [2-7]. Nevertheless, acute allergic reactions continue to pose a risk to patients, with symptoms ranging from mild urticaria to anaphylaxis [6,7].

The ACR Manual on Contrast Media (2013 version) recommended that patients with a documented iodinated contrast allergy be premedicated by corticosteroids, with or without the addition of antihistamines [7]. However, the timing of premedication is crucial; the prophylactic effects significantly lessen without a 4- to 6-hour delay before contrast administration [7]. As such, ensuring provider compliance in ordering nationally recognized premedication regimens is critical to ensure treatment efficacy.

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Prior studies have demonstrated that physicians can prevent up to 28% of adverse drug events with optimized computerized provider order entry (CPOE), and that clinical decision support (CDS) alerts can positively impact providers' future treatment decisions [8-14]. At the participating institution, a point-of-care (POC) CDS alert with an accompanying premedication regimen order set was designed into the electronic health record (EHR) to assist providers in ordering pretreatment regimens. This study compared the administered premedication regimens before and after the alert's implementation. The purpose of this study was to determine if the alert improved the homogeneity of premedication regimens ordered for iodinated contrast-based radiologic examinations. The hypothesis was that an alert that is appropriately triggered by POC-CDS with an accompanying ACR recommendations-based order set would lead to greater homogeneity of iodinated contrast premedication in those with a history of allergies.

METHODS

Background and Design

Institutional review board approval was obtained for the purposes of this study. This study was performed at a county safety-net hospital and level 1 trauma center (455 beds, with a radiology department internally within the emergency department). Before the implementation of the POC-CDS alert into the hospital's EHR (Epic Systems Corporation, Verona, WI), clinicians could only choose a standardized, preexisting order set based on ACR recommendations for patients with contrast allergies. At that time, in patients with a documented history of iodinated contrast allergy, there was no "hard stop" type of alert in the EHR that would direct workflow toward the standardized order set; providers were expected to search for the order set after noting a patient's documented allergy.

An interdisciplinary team composed of clinicians (including radiologists), pharmacists, clinical informaticists, and EHR analysts designed a POC-CDS alert that accounted for all uses of iodinated contrast at the participating institution; the type and route (eg, intravenous, intraarterial, oral, intrathecal, rectal) were specified. The POC-CDS alert (1) informed providers of a documented allergy to contrast media when ordering examinations that utilized intravenous iodinated contrast and (2) offered providers an order set to select an ACR-recommended premedication regimen. The implementation of the POC-CDS alert in tandem with the

order set created a maximum of four extra "clicks" to order premedication, when necessary (alert/confirmation → order set choosing → confirmation of order → signing premedication order). The alert intervention was initiated within the EHR in April 2014. This retrospective study consisted of a 22-month period from May 2013 to March 2015. At the times of implementation and analysis, the EHR versions were Epic 2012 and Epic 2014, respectively.

Radiology Examination Selection

A set of radiologic examinations that utilized any iodinated contrast was manually constructed from the EHR by two clinical informaticist physicians: a staff radiologist (A.M.M.) and a hospital-based informaticist (Z.J.M.). The list of examinations was thereafter grouped according to one of three possible "modalities" and one of four possible "routes." The three modalities were CT or PET/CT, fluoroscopic, and interventional; these modalities are commonly known to potentially utilize iodinated contrast. MRI was excluded, as it does not utilize iodinated contrast. The four routes were intravascular (IV; including both intraarterial and intravenous), gastrointestinal/genitourinary, intraarticular, and intrathecal.

Alert Design and Triggering

The POC-CDS alert was triggered at the time of order entry if two inclusion criteria were met: (1) the patient's electronic orders contained a radiologic examination with a modality that utilized iodinated contrast, and (2) the patient had an EHR-documented iodinated contrast allergy. The alert was designed to *not* trigger if one of the four specified "preferred" premedication regimens had already been ordered for the patients, ie, if prescriptions already existed that matched the correct medication and frequency for each medication recommended in a particular regimen (Fig. 1). Patients' documented allergies exist in the EHR as "Allergies/Contraindications," which is composed of six fields that allow a provider to specify the "agent," "reactions," "reaction type," "severity," "date reaction noted," and "comments." Of these, the only two fields that triggered the alert were the agent being iodinated contrast, along with the reaction type being specified as an allergy (as opposed to another type of adverse drug event or contraindication, such as intolerance, nausea/vomiting, headache, etc.); the other four fields were not considered for the purposes of triggering the alert.

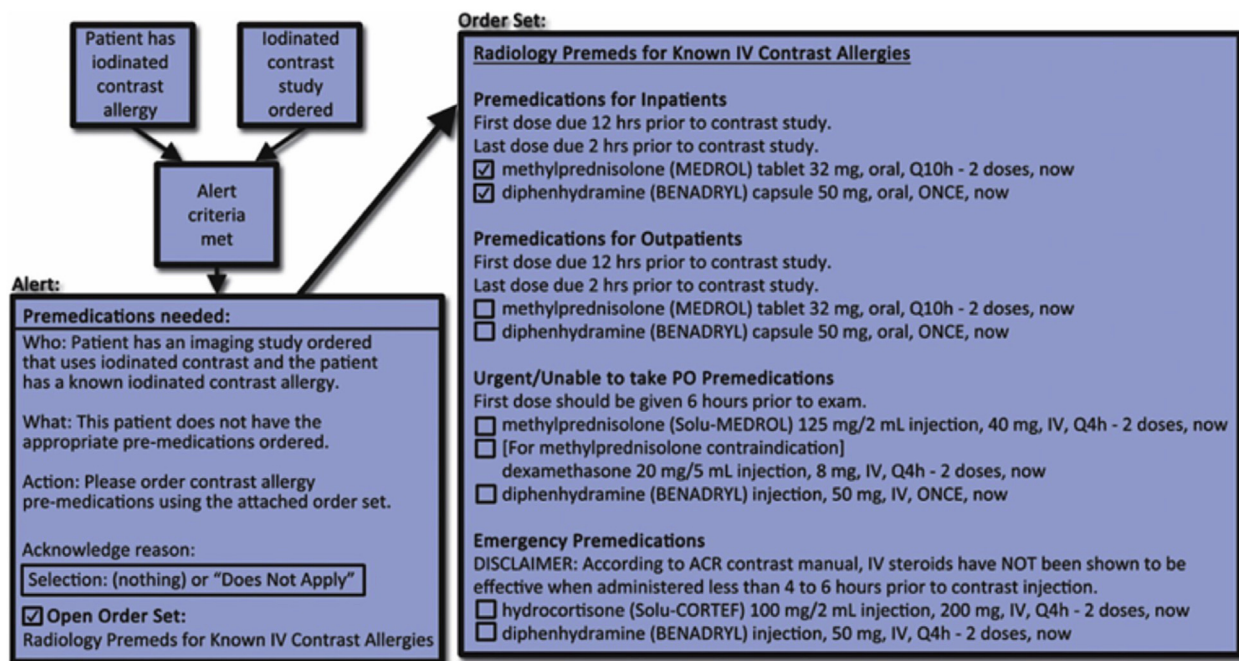


Fig 1. Alert logic and order set content. An alert programmed into the electronic health record warned providers of a patient's history of an allergy to iodinated contrast if an examination utilizing contrast was ordered. The alert automatically offered providers an option to use an order set of prescribed ACR-recommended premedication regimens (ie, a "preferred" regimen).

Data Collection and Analysis

The datasets were constructed retrospectively via standard query language queries that extract data from an EHR's relational database (Epic Clarity; Epic Systems Corporation, Verona, WI), upon completion of the post-alert period (April, 2014). Three datasets were formed: (1) all completed iodinated contrast examinations ordered between May 2013 and March 2015 in patients with a known contrast allergy, (2) all patients for whom the alert was triggered, and (3) an institution-wide order set monthly usage dataset that encompassed the study period. Contrast-based examinations in which a patient's initial allergic contrast reaction occurred on or after the date of the examination order were excluded, as a premedication order would not be expected if an allergy were unknown before the occurrence of the radiologic examination order.

Three types of data were recorded: examination-specific, alert-specific, and order set usage data. Examination-specific data included the name of the examination, when it was ordered and performed, the date of entry of a patient's allergy into the EHR, whether the alert triggered upon ordering the contrast examination, and whether either a "preferred" or "nonpreferred" corticosteroid premedication regimen was ordered. Alert-specific data included the name of the

examination that triggered the alert, whether the order set was opened or ordered, the date and time an action was taken from the alert, and which action originated from the alert. Order set usage data included the number of times the order set was used, number of orders generated by the order set's usage, and the number of users who used the order set.

Premedication Analysis Criteria

Examination-specific data were analyzed retrospectively for relevant premedication orders based on whether or not the medications matched a "preferred" regimen (Table 1), and on the timing of the medication orders. "Preferred" premedications matched one of the recommended sets of medications from the ACR criteria (Version 9, 2013). "Nonpreferred" regimens included any oral or IV corticosteroid medication ordered in the EHR that did not meet the criteria of a preferred regimen. Patients that did not have any corticosteroid ordered were considered as "no premedication," regardless of whether antihistamines were ordered, as the sole use of antihistamines is not recommended for contrast prophylaxis [7].

As the premedications were analyzed retrospectively, a temporal component of the regimen was defined for the premedication order relative to the examination being

Table 1. Criteria for types of premedication regimens: “preferred” (based on ACR recommendations), “nonpreferred,” and “no premedication”

Preferred premedication regimen	Prednisone: 50 mg PO at 13 hours, 7 hours, and 1 hour before examination OR Methylprednisolone: 32 mg PO at 12 hours and 2 hours before examination OR Hydrocortisone IV every 4 hours until the procedure is complete Optional: Diphenhydramine 50 mg IV, IM, or PO 1 hour before examination
Nonpreferred premedication regimen	IV or oral corticosteroid less than 24 hours before contrast administration, but not meeting the criteria of a preferred procedure
No premedication	No corticosteroids within 24 hours of contrast administration

Note: IM = intramuscular; IV = intravenous; PO = per os.

ordered and performed. For the premedication analysis, a medication ordered within 7 days before the examination's order, or less than 6 hours after the examination was performed, was included in the dataset. The inclusion of orders placed after the examination was performed was for the purpose of detecting potential false negatives in the alert criteria (examination orders where the alert did not trigger but should have), for example, when a premedication was given emergently at the time of the examination and the electronic order was placed retrospectively.

Statistical Analysis

Data were analyzed, and charts and graphs created, in Microsoft Excel (Version 15.0; Microsoft Corporation, Redmond, Washington). Statistical significance testing was performed via comparisons of proportions or means by Z test and *t* test analyses, respectively, which were used to test for a significant difference in the number of patients who received a type of regimen (preferred, nonpreferred, no premedication) pre- as compared with post-alert implementation, as well as to compare order set usage in the pre- to postalert periods. The threshold for statistical significance was set to $P < .05$. Alert sensitivity and specificity were calculated assuming positive or negative as whether or not the alert triggered, and true or false positives/negatives as whether or not the alert should have triggered.

RESULTS

Patient Population and Alert Triggering

The organizational chart in Figure 2 summarizes the patient population of this study. During the study period between June 1, 2013 and April 1, 2015 (669-day period), 22,023 imaging examinations using iodinated contrast were performed. Of these, 200 were performed on patients with a documented contrast allergy within the EHR (0.9%): 106 were performed in the 11 months before and 94 were performed in the 11 months after the alert was implemented (on April 29, 2014). Figure 3 depicts the composition of the pre- and postalert cohort for this study that necessitated premedication; this is shown by both *modality* and *route*. As demonstrated in Figure 3, the most common modality for which premedication was needed was CT or PET/CT examinations ($n = 122$), followed by interventional radiology ($n = 63$); the most common route was IV ($n = 186$).

Examination-Specific Data Regarding Triggering of the Alert

The alert did not trigger in 18 of 94 examinations ordered (19.1%) in patients with documented allergies in the postalert period. In 16 of these 18, the lack of triggering was considered appropriate; of these 16, 14 already had an order for premedication in place at the time the clinician ordered the examination, whereas 2 had a contrast allergy added to their chart after the examination was ordered (ie, the alert did not trigger because a history of an allergic reaction was not present within the EHR at the time that the examination was ordered). The remaining 2 of the 18 examinations met the criteria for the alert to trigger, but it failed to trigger (deemed a “false negative” for triggering). These two examinations that inappropriately failed to trigger likely met the alert exclusion criteria (ie, the patients were prescribed a preferred premedication regimen with the correct frequency), but not the analysis criteria (ie, the preferred regimen was not ordered within 7 days before and up to 6 hours after the examination), thus comprising the false negatives. Overall, the alert appropriately triggered in 92 of 94 patients (alert sensitivity = 97.9%), whereas the alert was never triggered when it should not have, according to the specified criteria (alert specificity = 100%).

Examination-Specific Data Regarding the Type of Premedication Regimen Triggered

Before the implementation of the CDS alert (prealert period May 2013 to April 2014), 41 of 106 patients

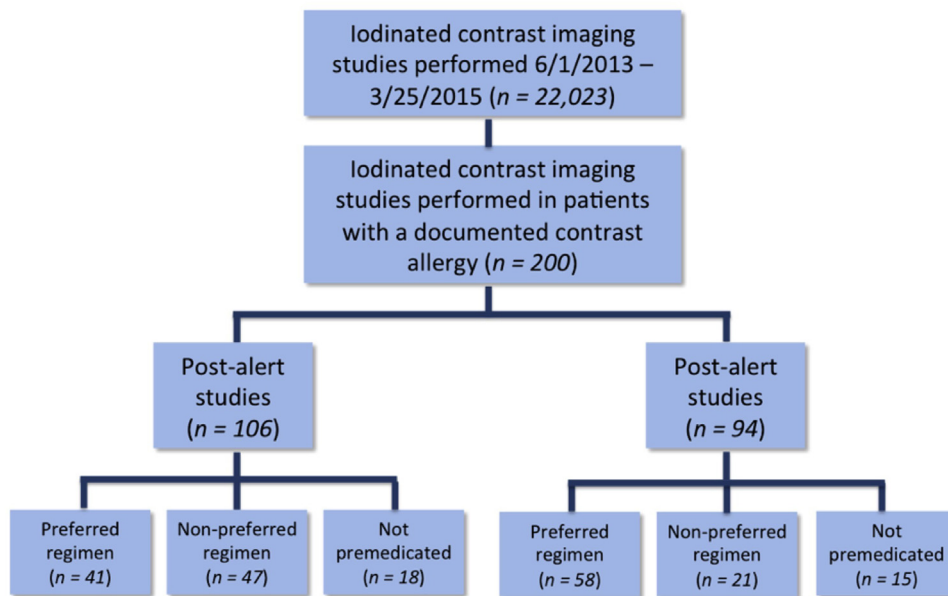


Fig 2. Patient population by study period and premedication criteria.

(38.7%) were given a preferred regimen (either oral or intravenous), 47 (44.3%) received a nonpreferred regimen, and 18 (17.0%) were not premedicated at all with a corticosteroid medication. Subsequent to the POC-CDS alert implementation (postalert period from April 2014 to March 2015), 58 of 94 patients (61.7%) were premedicated with a preferred regimen (oral or IV) and 21 (22.3%) with a nonpreferred regimen, and 15 (16.0%) were not premedicated with a corticosteroid (Fig. 2).

There was a statistically significant increase in the proportion of examinations that met the preferred premedication criteria in the postalert period versus the prealert period (Z-score = 3.25, $P = .001$); the proportion who received a nonpreferred corticosteroid regimen concurrently decreased (Z-score = -3.28, $P = .001$). In the pre- and postalert periods, no significant difference was noted in the proportion of patients who received no premedication (17.0% prealert, 16.0% postalert; Z-score = -0.20, $P = .85$) (Fig. 4).

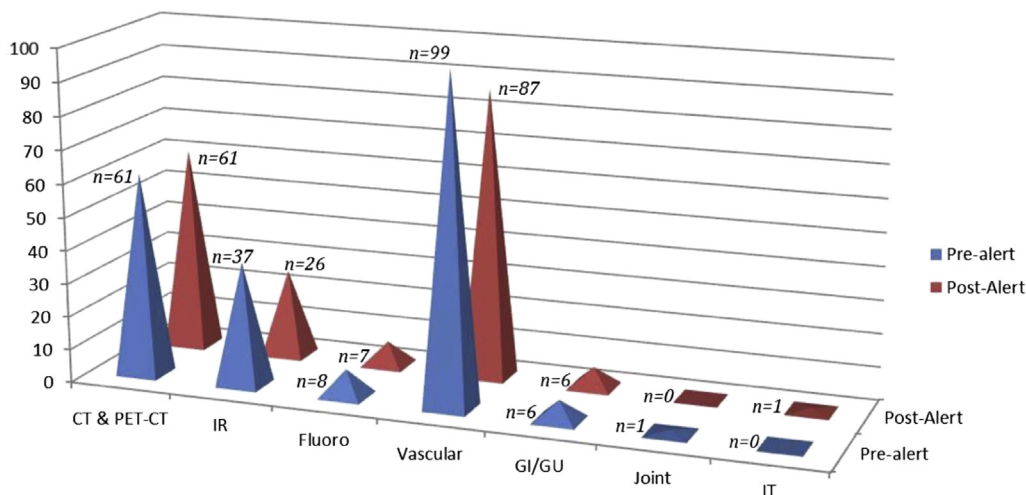


Fig 3. Types of premedications received before undergoing an iodinated contrast-enhanced imaging examination. The proportion of patients administered a “preferred” premedication regimen increased after the implementation of a clinical decision support alert into the electronic health record, whereas the proportion of patients who received a “nonpreferred” regimen of corticosteroids within 24 hours of the examination decreased. No significant change was noted in the proportion of patients that were not premedicated. GI/GU = gastrointestinal/genitourinary; IR = interventional radiology; IT=intrathecal.

Of all 200 patients with a prior history of an acute allergic reaction to iodinated contrast that subsequently received it, 2 (1.0%) suffered an allergic reaction to the contrast. Both occurred in the postalert implementation period in patients who received intravenous contrast after being given a preferred premedication regimen, and both allergic reactions were deemed “mild.” In one patient, the document reaction was hives locally, and the other had hives with dizziness (the latter considered a physiologic reaction).

Order Set Usage Data

The order set for premedication was utilized in 60 of 94 examinations in the postalert period (63.8%). Of those 60, 51 (85.0%) triggered the POC-CDS alert. Of the 58 examinations in which patients received a preferred regimen, the order set was utilized in 55 examinations (94.8%); in 47 of these 55 (85.5%), the alert had been triggered. Of the 21 examinations in the postalert period in which a nonpreferred premedication regimen was given, the order set was utilized in only 5 (23.8%), 4 of which (80.0%) triggered the alert. In these four instances, the order set was used, but the preferred regimen had been modified, ultimately resulting in the order being classified as a nonpreferred regimen. Those receiving a preferred regimen during the postalert period were significantly more likely to have their regimen prescribed via the order set and to have triggered the alert, as

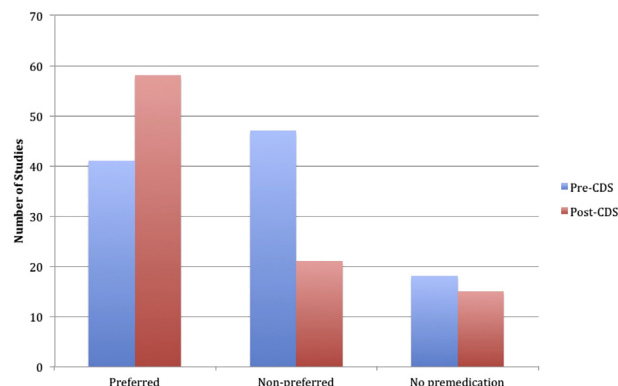


Fig 4. Types of premedications received before contrast-enhanced imaging examination. The proportion of patients administered a “preferred” premedication regimen significantly increased after the implementation of a clinical decision support alert into the electronic health record ($P = .001$), whereas the proportion of patients who received a “non-preferred” regimen of corticosteroids within 24 hours before the examination significantly decreased ($P = .001$). No significant change was noted.

compared with those administered a nonpreferred regimen (Z -score = 6.52, $P < .001$). Institution-wide usage of the order set significantly increased from 9.4 times per month during the prealert period to 16.0 times per month during the postalert period (T -score = -4.48, $P < .001$).

DISCUSSION

This study sought to describe the effects of the implementation of a CDS alert designed to (1) inform providers of a history of an allergic reaction when ordering an examination utilizing contrast media and (2) assist in ordering an ACR-recommended premedication regimen. The results indicate that the homogeneity of premedication regimens ordered significantly improved after the initiation of the alert. Also, the alert had a positive impact on optimizing CPOE; after the alert’s launch, patients prescribed a preferred regimen were significantly more likely to have their medications prescribed via the order set and for the alert to trigger, versus those prescribed a nonpreferred regimen.

Theoretically, the ramifications of implementing this alert and accompanying order set would be to increase standardization so that more at-risk patients are premedicated. However, the latter did not seem to occur, as the frequency of “no premedication” did not change after implementation of the alert and accompanying order set. Such noncompliance with CDS is usually attributed to “alert fatigue” (a provider deems an alert to be either inconsequential or disruptive), poor triggering, or out-of-date knowledge [15,16].

The administration of corticosteroids before iodinated contrast in patients with previously documented allergic reactions has been shown to decrease the incidence of recurrent reactions [17,18]. Nevertheless, acute allergic reactions may still occur after administration of a preferred premedication regimen; such “breakthrough” reactions occur at reported rates ranging from 2.1% to 10% [19-21]. In the current study, none of the patients in the prealert group suffered a breakthrough reaction, whereas 2 of 94 patients (2.1%) suffered a breakthrough reaction in the postalert group. However, because the expected rate of breakthrough reactions is relatively small, this study’s sample size ($n = 200$) limits its conclusions to those based on the homogeneity of premedications. Similarly, severe allergic reactions to iodinated contrast are quite rare, with rates reported to ranging from 0 to 2% [3,4,20,22,23]. Consequently, the sample size of this

study was not large enough to assess whether the CDS alert affected patient safety.

To our knowledge, only one prior study has assessed the efficacy of using CDS to improve premedication administration. Bae et al [24] implemented an alert that recommended premedication (via CDS) based on the severity of the patient's index reaction; they reported a similar rate of premedication before and after the CDS implementation (91% and 95%, respectively), but found a significantly higher rate of premedication administration. The current study similarly found a relatively unchanged overall rate of premedication (83.0% and 84.0%) but noted an improved adherence to preferred premedication regimens.

There are several limitations of the current study. First, as the data were collected retrospectively from the EHR, the number of breakthrough allergic reactions to contrast media may have been underrepresented. Additionally, because premedication adherence was presumed based on the EHR order rather than documentation of administered medications, the actual compliance with premedication may have differed from the prescription. Also, because of the timing criteria used, it is possible that false negatives occurred if medications met the alert exclusion criteria by being ordered >7 days before the examination being performed. However, it is the opinion of this study's authors that these limitations likely did not have a consequential effect on the study's overall conclusions. Finally, as previously described, a greater number of patients would be required to show a statistical difference in the occurrence of acute allergic reactions or outcomes; future studies may explore whether the implementation of this CDS alert impacts patient safety. Despite potential limitations, we opine that it is critical for radiologists to improve premedication regimen homogeneity, as (1) a repeat reaction in those with a documented allergy may be preventable, and (2) there is increasing governmental and public emphasis on quality, auditability, and practice improvement, and specifically regarding potential contrast-related events [25].

CONCLUSIONS

This study describes the implementation of a POC-CDS alert to inform providers of patients' iodinated contrast allergies and to recommend a preferred premedication regimen based on the ACR's suggestions, upon ordering examinations that utilize iodinated contrast. After alert implementation, the homogeneity of premedication regimens significantly increased, but the number of patients

who received no premedication was relatively unchanged. Future studies may be useful to assess whether the implemented change in the EHR will affect either the proportion of breakthrough allergic reactions or the outcome.

TAKE-HOME POINTS

- A CDS alert implemented into the EHR led to significantly increased prescription of preferred premedication regimens for patients with allergies to iodinated contrast.
- The alert helped to optimize CPOE by directing providers to the premedication order set within the EHR.
- No change was observed in the proportion of patients that received no premedication.

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