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## Automated/integrated real-time clinical decision support in acute kidney injury

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### Abstract

**Purpose of review**—Health information technology (HIT) advancements have resulted in recent increased sophistication of the electronic health record (EHR), whereby patient demographic, physiological and laboratory data can be extracted real-time and integrated into clinical decision support (CDS).

**Recent findings**—The implementation of HIT advancements into CDS in the renal realm have been focused mainly on assessment of kidney function, to guide medication dosing in the setting of reduced function, or to reactively detect acute kidney injury (AKI), heralded by an abrupt increase in serum creatinine. More recent work has combined risk stratification algorithms to guide proactive diagnostic or therapeutic intervention to prevent AKI or reduce its severity.

**Summary**—Early, real-time identification and notification to health care providers of patients at risk for, or with, acute or chronic kidney disease can drive simple interventions to reduce harm. Similarly, screening patients at risk for AKI with these platforms to alert research personnel will lead to improve study subject recruitment. However, sole reliance on EHR generated alerts without active health care team integration and assessment represents a major barrier to the realization of the potential of CDS to improve health care quality and outcomes.

### Keywords

electronic health record; acute kidney injury; clinical decision support

### Introduction

Since 2009, the United States federal government has set aside billions of dollars in incentives to encourage hospitals and physician practices to adopt electronic health records (EHRs). The incentives require demonstration of meaningful use of EHRs to measure and track clinical quality measures, many of which are driven by published clinical practice guidelines or recommendations. The common data domains in EHRs include demographic

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### Conflicts of interest

None

and laboratory parameters, which can be easily extracted and analyzed to track various these quality metrics.

Acute kidney injury (AKI) is currently defined by an abrupt rise in serum creatinine or decrease in urine output<sup>1</sup>. Each of this metrics is delimited by certain time ranges; serum creatinine increases should occur with 48 hours to 7 days depending on the metric and urine output decreases are measured in 6 hour increments. These data are easily abstracted from EHRs, as they are discrete elements, often in real-time or near real-time to alert clinicians as to the occurrence of AKI. In addition, clinical epidemiological studies have focused upon identifying patients at risk for AKI; EHRs can be used in this context to drive diagnostic interventions to perform systematic surveillance in patients who are at increased AKI risk. However, reliance solely on AKI alerts will not improve outcomes if the data are not integrated into a reliable clinical decision support (CDS) system. Fundamentally, a process needs to be put into place that directs clinicians as to how to use the information they receive regarding the risk of, or development of AKI.

## AKI Detection

As noted above, AKI can be detected and its severity staged by an abrupt rise in serum creatinine from a baseline value using standard, accepted criteria<sup>1</sup>. Selby and colleagues were among the first to implement a hospital wide AKI detection system, demonstrating very low false positive and false negative rates (1.7% and 0.2 %, respectively)<sup>2</sup>. They also observed that AKI was an independent risk factor for mortality and hospital length of stay. Perhaps most importantly, they discovered that the majority of patients with AKI in their hospital were cared for by non-nephrologists. Increasing awareness of the presence of, and poor outcomes associated with AKI in the non-nephrology community with readily available AKI detection is a first and essential step, to improving outcomes for these patients<sup>3</sup>. More recently, Porter<sup>4</sup> and Ahmed<sup>5</sup> also successfully implemented AKI EHR detection “sniffers” in their large health care systems. Porter identified that nearly 11% of their patients had AKI, and that AKI was independently associated with mortality. Ahmed noted that AKI detection was much more reliable than ICD-9 coding for AKI. We have also observed that systematic surveillance for AKI yields higher detection AKI detection rates than reliance on ICD-9 coding for hospitalized children exposed to nephrotoxic medications<sup>6</sup>.

While Porter speculated that their alert system was “likely to have improved detection and management of AKI”, management improvement cannot be confirmed without integration of the information into clinical practice and measuring a pre-determined outcome. It is likely that raising awareness in the absence of integrating the information via clinical decision support will not be enough to improve care. One logical use of EHR directed AKI detection includes providing a trigger to alert physicians and pharmacists when kidney function is at a level that warrants dosing adjustments for medications excreted by the renal route. While not specific to AKI, Chertow and colleagues assessed the implementation of a medication dosing algorithm integrated into the computerized physician order entry system (CPOE)<sup>7</sup>. This system used the latest serum creatinine to calculate an estimated glomerular filtration rate (eGFR), and then recommended a medication dose and frequency based on the results in the intervention period. In the control period, dose adjustment recommendations were not

given to providers. The CPOE application recommended a dose adjustment suggestion in 15% of cases. Rates of appropriate orders increased significantly in the intervention period, irrespective of whether the CPOE recommendation was for medication dose or frequency.

McCoy and colleagues created an EHR integrated alert when patients 1) had an active recurring order of at least one nephrotoxic or renally excreted medication from a list of 122 medications on their formulary and 2) developed AKI as defined by a 0.5 mg/dl increase in serum creatinine within 48 hours<sup>8</sup>. Their primary outcome was the discontinuation or dose adjustment of one of the medications of interest within 24 hours of the alert. Their CPOE alert was also innovative in that it presented the providers a visual cue of the medication of interest and the potential options to either adjust the dose, or discontinue or continue the medication(s). Compared to pre-intervention baseline rates, the post-intervention time period was characterized by an increased rate of response within 24 hours to either avoid or adjust medications with a decrease in response times to the action. The alerts in this study were relegated to the computerized provider entry interface and on printed rounding reports. However, with the exception of physician training during the study period, the alert was not integrated into a clinical decision support process or in team rounds. As a result, providers deferred more than ¾ of the initial interruptive alerts. In addition, no determination was made as to the medical appropriateness of the changes made by the provider. Nevertheless, presenting the providers with an interactive trigger that logged their responses did increase the rate and timeliness of response to the medications of interest.

Colpaert and colleagues assessed the effect of a real-time AKI alert sent to ICU physicians on targeted AKI interventions, which included a fluid bolus, initiation of vasopressor medications and prescription of diuretics<sup>9</sup>. In their study, an alert was triggered by an increase in serum creatinine or reduction in urine output to fulfill the RIFLE criteria<sup>10</sup>. The study was designed with a pre-intervention era, an intervention alert era, and a post-intervention (non-alert) era. Therapeutic intervention rates, whether characterized by a fluid bolus, vasopressor initiation or diuretic administration, were significantly increased in the alert period compared to either the pre- or post- alert eras. Furthermore, the time to intervention was decreased in the alert era, and a higher proportion of patients in the alert group demonstrated a return to baseline kidney function within 8 hours of AKI detection. A critical finding was that the improvement in care was not sustained in the post-alert group. Lack of sustainability of any quality improvement initiative has been identified as a barrier to widespread practice adoption of single center processes such as identified by Colpaert, even with these impressive results<sup>11</sup>. Furthermore, as with the McCoy study, the appropriateness of the interventions was not assessed, and the alert was not integrated into a clinical decision support algorithm; the response was left to the provider on call at the time.

Most recently, Wilson and colleagues reported on the results of a single randomized controlled trial to assess the effect of a real-time AKI alert on the progression of AKI in hospitalized adults<sup>12</sup>. The innovation of this study resides in the randomization of patients to providers (intern, resident or nurse practitioner) who received *vs.* did not receive a real time AKI alert. As with the studies mentioned above, the alerts were not integrated into a clinical decision support algorithm. Wilson observed no differences in outcomes (AKI progression, dialysis provision or death at 7, 14, or 30 days after randomization) between the two groups.

While the authors were guarded in their interpretation of their data, and they note some limitations, they did not acknowledge that a major limitation was that the providers were aware of the randomization of patients, and this led to the single-blind nature of the study. Since the same providers could care for patients in the control and intervention group, one cannot exclude the possibility that providers had heightened awareness of AKI for all patients under their care, irrespective of randomization. Finally, the editorial regarding Wilson's study notes that "in the future, more sophisticated decision-support systems might not only enable detection of acute kidney injury, but be extended to development of algorithm-based predictive, diagnostic, and risk-stratification instruments<sup>13</sup>." This comment is quite applicable to all of the studies mentioned so far and has led us to develop an upstream AKI alerting system.

## Use of the EHR to identify patients at risk for AKI and integration into Clinical Decision Support

Nephrotoxic medication (NTMx) exposure is one of the most common causes AKI in hospitalized children<sup>14, 15</sup>. Non-critically ill hospitalized children who develop AKI are more likely to be exposed to a nephrotoxin<sup>16</sup>, and AKI risk increases with exposure to 3 nephrotoxins<sup>16</sup>. Such children receiving an intravenous aminoglycoside (IV AG) for >5 days have nephrotoxin-AKI rates of 19–31%<sup>17</sup>. Kidney function monitoring with serum creatinine (SCr) is inexpensive and available in all hospital laboratories, SCr was measured at low frequency. Although many nephrotoxic medications are needed for successful treatment of disease, we observed in two different healthcare systems that only 50% of children receiving multiple nephrotoxic medications are adequately monitored for AKI<sup>16–18</sup>. Thus, a larger AKI cohort may be undetected because SCr is not monitored systematically in at-risk patients. We hypothesized an unrecognized iatrogenic epidemic of nephrotoxin-AKI may exist, which is a *potentially modifiable adverse safety event* if systematic SCr assessment detects AKI reliably.

Our goal was to ensure children receive only the nephrotoxic medications they need for the time they need them. We developed an automated daily electronic health record trigger to optimize clinical decision making via communication between pharmacists, nurses, physicians and patients/families rounding at the bedside<sup>14, 19</sup>. This project, entitled Nephrotoxic Injury Negated by Just-in-Time Action (NINJA), empowered pharmacists to recommend daily serum creatinine measurement, dose adjustment or less nephrotoxic regimens in nephrotoxic medication-exposed patients. We rejected the notion that nephrotoxic medication-AKI is a necessary evil of providing quaternary healthcare to hospitalized children and viewed nephrotoxic medications exposure and nephrotoxic -AKI as potentially avoidable adverse safety events. Since 10–49% of patients with AKI develop chronic, irreversible kidney damage, nephrotoxic -AKI prevention could reduce rates of chronic disease as well.

In its first year, NINJA implementation was associated with a 42% reduction in AKI days per 100 days of nephrotoxic medication exposure<sup>14</sup>. This reduction corresponds to >900 days of nephrotoxic- AKI avoided annually in our single center. In the subsequent three

years of NINJA, this reduction was sustained and we also observed a 38% reduction in nephrotoxic medication-exposure, and a 67% reduction in nephrotoxic-AKI rates (data being prepared for submission). Of great concern is that 77% of patients with nephrotoxic-AKI had evidence of chronic kidney disease 6 months later<sup>20</sup>, which is associated with hypertension, and the potential future need for dialysis or kidney transplant. By focusing on a discrete, measurable type of preventable adverse drug event, we targeted interventions to reduce rates of harm at our institution. The sustainability of NINJA associated improvements was realized by integrating the alerts with the pharmacy team to make recommendations regarding AKI surveillance. We did not rely on a passive EHR alert which could be overridden by the provider; we viewed the discussion on rounds as essential to perpetuating AKI awareness and forcing deliberate conversations regarding NTMx medication choices. We are currently disseminating the NINJA project to nine other US pediatric institutions to assess for the contextual factors that accelerate or retard implementation at these sites (1R18HS023763-01).

## Conclusion

The studies cited above demonstrate, for the most part, the potential of AKI detection alerts to improve care. The next step to realize these improvements will be to integrate the alerts into a systematic provider response based on best practices (Table 1). Low hanging fruit would include medication adjustment, nephrotoxic medication withdrawal, appropriate imaging, reassessment of volume status and blood pressure management. In the pediatric ICU, we have demonstrated the ability of a simple score, the Renal Angina Index<sup>21, 22</sup>, to predict which children will have persistent AKI 72 hours after admission. We are working on integrating the RAI into CDS, with an alert for both providers and research personnel to identify patients at risk for AKI, with a goal of guiding fluid administration, novel biomarker testing and enrollment in AKI therapeutic studies.

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**Key Points**

- Electronic health records can be programmed to identify patients with acute kidney injury
- Electronic health records can be designed to identify patients at risk for developing AKI in the ICU or nephrotoxic medication associated AKI
- Notification of AKI risk or development alone will not improve care—this information needs to be integrated into clinical decision support in a systematic fashion



**Table 1**

## Electronic Health Record and Acute Kidney Injury Clinical Decision Support Areas

<b>Temporal Relationship to AKI</b>	<b>Examples</b>	<b>Potential for Clinical Decision Support</b>
Risk Assessment Prior to AKI Development	Nephrotoxic Injury AKI Risk Renal Angina ICU AKI Risk	Standardize and guide functional and damage AKI biomarker assessment
AKI Detection	Serum creatinine change Urine output change	Adjust doses of medications with renal excretion Guide fluid administration

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