Improving Drug Allergy Information and Alerts: Health IT Interventions
Executive Summary

Accurate capture and use of drug allergy information is vital for delivery of safe, high-quality patient care. However, drug allergy information is often incomplete or inaccurate, leading to overuse of alternative antibiotics and potentially inappropriate firing of drug allergy alerts. More than 90% of drug allergy alerts are overridden, suggesting that many lack clinical utility and likely contribute to alert fatigue and slow clinical workflow.¹

In 2013, ECRI Institute convened the Partnership for Health IT Patient Safety, and its component, single-topic-focused workgroups followed. The Clinical Decision Support for Drug-Allergy Interactions (DAI) workgroup is a multi-stakeholder workgroup including providers, vendors/developers, healthcare leaders, and experts in the field from various healthcare settings. The group began with a proffered set of recommendations and focused on how technology could be used to implement those recommendations. To inform workgroup efforts, we performed this systematic literature review to identify how health information technology might enable these recommendations and determine to what extent interventions based on these recommendations have been assessed in the medical literature. Specifically, we asked the following Key Questions:

1. What is the efficiency of interventions to improve the accuracy of drug allergy documentation in electronic medical records?
2. What is the efficacy of health information technology (IT) interventions to improve the context and frequency of drug allergy alerts?
3. What is the efficacy of changes to institutional policies to improve management of drug allergy alerts?
4. What is the efficacy of monitoring allergy alerting and override rates for improving clinical care and efficiency?

We performed a comprehensive literature search to identify all relevant articles published from January 2003 through April 2018. We excluded non-English studies, narrative reviews, and studies not assessing an intervention. Overall, we identified 62 studies and focused on 7 for inclusion in this report.

Although drug allergy alerts have the potential to significantly improve the safety and quality of clinical care, in practice, these alerts often fire inappropriately (e.g., for inconsequential reactions) or may be overridden by busy practitioners despite serious safety concerns (e.g., angioedema).²

Our report found low-quality evidence from three studies to suggest that risk stratification tools can improve the accuracy and management of reported beta-lactam drug allergies. However, despite the potential for other health IT interventions—such as patient portals and active monitoring of drug allergy override rates—to improve this process, we found a paucity of evidence. Future work is needed to describe the development, implementation, and efficacy of such interventions. Insights gained will hopefully enable computerized provider order entry systems to improve the information available to enhance patient safety while minimizing unnecessary alerts and alert fatigue.
Background

Understanding a patient's allergy status is important to ensure safe, high-quality patient care. Although electronic tools have facilitated electronic prescribing, verifying accurate capture, confirmation, and exchange of drug allergy information within this electronic environment remains a challenge. Many factors may contribute to this problem. One significant problem is inaccurate, incomplete, and fragmented documentation of drug allergy information within the electronic health record (EHR). Adverse sensitivity information is often still recorded as unstructured free text, particularly if users are uncertain of how and where information should be captured. Subsequently, allergy information may be fragmented throughout the record in numerous free-text entries. This format is clearly suboptimal for recognizing, verifying, and tracking prior reactions, determining resolutions, or enabling systems to provide drug allergy alerts or drug-drug interactions.

Inaccurate or incomplete drug allergy information can result in inappropriate alerts. However, even when drug allergy information is captured accurately in the correct format, drug allergy alerts are often nonspecific, uninformative, or related to inactive ingredients or compounds. Perhaps not surprisingly, drug allergy alerts have extremely high override rates, with some estimates of more than 90%. Thus, many drug allergy alerts may fail to prevent adverse reactions, and simply contribute to alert fatigue and inefficiencies in clinical workflow.

Many recommendations for improving communication of drug allergy information exist. These include improving allergy documentation, enabling patient engagement, addressing alerting mechanisms and providing continuous alert monitoring and improvement, and addressing policies and guidelines. A subset of the Partnership for Health IT Patient Safety convened by ECRI Institute formed the Clinical Decision Support for Drug-Allergy Interactions (DAI) workgroup. This multi-stakeholder workgroup includes providers, vendor/developers, healthcare leaders, and experts.

The group began with a proffered set of recommendations and considered how technology could be used to implement those recommendations. To inform the workgroup’s efforts, we performed a systematic literature review to identify how health information technology (IT) might facilitate these recommendations and to what extent interventions based on these recommendations have been assessed in the medical literature. Specifically, we asked the following Key Questions:

1. What is the efficiency of interventions to improve the accuracy of drug allergy documentation in electronic medical records?
2. What is the efficacy of health IT interventions to improve the context and frequency of drug allergy alerts?
3. What is the efficacy of changes to institutional policies to improve management of drug allergy alerts?
4. What is the efficacy of monitoring allergy alerting and override rates for improving clinical care and efficiency?

Methods

We conducted a systematic literature search of the PubMed, MEDLINE, EMBASE, CINAHL, and Scopus databases, using a search strategy developed by a medical librarian. The search strategy identified studies published from January 2003 through April 2018 and used a combination of medical subject headings and keywords for allergy, clinical decision support, and electronic medical records. Several websites, including AHIMA, AHRQ, AMIA, HIMSS, and HL7 were searched for further references. The search strategy is available in Appendix A.

A physician analyst screened all studies using prespecified inclusion criteria (Figure 1).

For Key Question 1, we included all studies assessing interventions for more accurate documentation of drug allergies, including interventions aimed at increasing patient engagement (e.g., patient portals).

For Key Question 2, we included studies assessing interventions with information about reaction severity, patient history, and likelihood of adverse reaction to decide whether an alert fires (e.g., tiered alerts) or comparing informative (no action needed to override) versus interruptive (reason required to override) alerts.

For inclusion, all studies were required to report one of the following outcomes:
Improving Drug Allergy Information and Alerts: Health IT Interventions

- Improved accuracy of drug allergy documentation for individual patients
- More appropriate firing of drug allergy alerts
- Improved efficiency of clinical care
- Change in the rate of prescriptions for drugs (to which the patient is allergic)

We excluded non-English studies and studies addressing food or other non-drug allergies.

Study data was extracted by a physician analyst. For randomized controlled trials (RCTs), nonrandomized controlled trials, observational cohort studies, or case control studies, we used the U.S. Preventive Services Task Force (USPSTF) criteria for grading study quality. For pre/post or interrupted time-series study designs, study quality was assessed using Study Quality Assessment Tools from the National Heart, Lung, and Blood Institute. Quality assessments are available in Appendix C.

Figure 1. Flow Diagram

Results

We identified seven studies for inclusion. Six studies addressed Key Question 1 (interventions to improve allergy documentation) and one study addressed Key Question 2 (health IT interventions to improve context and frequency of allergy alerts). One study addressed both Key Questions 1 and 3, with another addressing both Key Questions 2 and 4.

An overview of all included studies is provided in Table 1. In addition, we highlight four studies that did not meet formal criteria for inclusion, but described tools potentially of interest to developers of clinical decision support focused in this area; these studies are listed in Table 2. Further details regarding all included studies are available in Appendix B.

Table 1. Overview of Interventions

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<thead>
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<th>Interventions</th>
<th>Number of Studies</th>
<th>Effect</th>
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<tr>
<td><em>KQ 1: Interventions for improving accuracy of drug allergy documentation in the electronic medical record</em></td>
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<td>Interventions</td>
<td>Number of Studies</td>
<td>Effect</td>
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<tr>
<td>Pharmacist protocol to clarify unclear allergy documentation</td>
<td>1 Pre/post study</td>
<td>Modest statistically significant improvement in proportion of complete allergy documentation and reaction fields (7% increase for adults, 12% for pediatric services [sic], p = 0.03 for both).</td>
<td>Burrell et al. 201310</td>
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</table>
Improving Drug Allergy Information and Alerts: Health IT Interventions

<table>
<thead>
<tr>
<th>Interventions</th>
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<th>Effect</th>
<th>References</th>
</tr>
</thead>
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<tr>
<td>Risk stratification tool</td>
<td>2 Pre/post studies</td>
<td>Significantly decreased inappropriate aztreonam use (9.5 to 4.4 days of therapy per 1,000 patient-days, p &lt;0.001).</td>
<td>Staicu et al. 2016</td>
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<tr>
<td></td>
<td>Descriptive</td>
<td>Significant decrease in monthly initiation of anti-pseudomonal carbapenem (7.01 to 6.14 per 1,000 patient days, p = 0.03).</td>
<td>Caplinger et al. 2016</td>
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<tr>
<td>Creation of database to standardize and improve coding of allergy information</td>
<td>Descriptive</td>
<td>21 of 32 patients (66%) with allergy documented received beta-lactam therapy. None had adverse reactions.</td>
<td>Sigona et al. 2016</td>
</tr>
<tr>
<td>Creation of a patient portal to allow patients to verify medication and allergy information</td>
<td>Lessons learned with descriptive data</td>
<td>94% of free-text allergens converted to coded terms. Low data transfer time from central data repository (CDR) to CareLink.</td>
<td>Zimmerman et al. 2009</td>
</tr>
</tbody>
</table>

**KQ2: Efficacy of health IT interventions to improve context and frequency of drug allergy alerts**

Restrict data entry to pharmacists, physicians, and nurses + Eliminate drug alert firing for inactive ingredients

Lessons learned with pre/post data

Decrease in override rates from 0.14 to 0.09 alerts per order (or 900 fewer alerts per day).

Brodowy et al. 2016

**KQ 3: Efficacy of changes to institutional policies to improve management of drug allergy alerts**

Creation of a database to standardize and improve coding of allergy information across health system

Descriptive

Only 1% of all hard-stop alerts assessed as inappropriate.

Zimmerman et al. 2009 (also appears in KQ 1)

**KQ 4: Efficacy of monitoring allergy alerting and override rates for improving clinical care and efficiency**

Restrict data entry to pharmacists, physicians, and nurses + Eliminate drug alert firing for inactive ingredients

Lessons Learned with pre/post data

Decrease in override rates from 0.14 to 0.09 alerts per order (or 900 fewer alerts per day).

Brodowy et al. 2016 (also appears in KQ 2)

**Table 2. Other Studies of Interest**

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Reference</th>
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<tr>
<td>Validated natural language processing intervention’s (Medical Text Extraction, Reasoning and Mapping System’s (MTERMS)) ability to identify true positive allergies from emergency department notes from Brigham and Women’s hospital (compared with assessments from 2 clinicians).</td>
<td>Goss et al. 2014</td>
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<tr>
<td>Validation study of algorithm in structured query language (SQL), Transact-SQL to categorize allergy information from free-text field of perioperative information management system for anesthetics at Vanderbilt University.</td>
<td>Epstein et al. 2013</td>
</tr>
<tr>
<td>Compared ability of 4 common adverse sensitivity information models (Health Level 7 Allergy and Intolerance Domain Analysis Model (HL-7 DAM), Fast Healthcare Interoperability Resources (FHIR), Consolidated Continuity of Care Document (C-CDA), and OpenEHR to capture attributes relevant for clinical decision-making from emergency department documents from Tufts Medical Center and Partners Healthcare.</td>
<td>Topaz et al. 2016</td>
</tr>
<tr>
<td>Assessed impact of incorporating human factors design (usability and satisfaction) with a variety of alerts (including drug allergy alerts) tested in a laboratory setting (Veterans Affairs Health Services Research and Development Human Computer Interaction and Simulation Laboratory).</td>
<td>Russ et al. 2014</td>
</tr>
</tbody>
</table>
Interventions for Improving Accuracy of Drug Allergy Documentation in the EHR

We identified six studies assessing interventions for improving accuracy of allergy documentation. One study evaluated a pharmacist-review protocol,\(^{10}\) three studies described risk stratification tools for beta-lactam allergies,\(^{13-15}\) one study described creation of a central data repository for allergy information across a healthcare system,\(^{11}\) and one study described a medication/allergy module within a patient portal.\(^{12}\)

**Pharmacist Review**

A pre/post study by Burrell et al. 2013\(^ {10}\) assessed impact of a new protocol on quality of allergy documentation at Upstate University Hospital (University of California at San Francisco [UCSF]). Pharmacists reviewed drug allergy information in the pharmacy order entry database (WORx) at two points: (1) at admission, all pre-existing or newly documented allergies without corresponding reaction information would be clarified through review of the record or (2) daily order clarification for any admitted patient with incomplete drug allergy information.

Allergy information was defined as complete if the reaction field contained sufficient information to allow clinical decision regarding re-administering drug to patient or blank if no information was entered. Allergy information for admitted patients was sampled at eight time points (four pre-intervention, four post-intervention, consisting of three consecutive day periods).

Overall, 770 allergies (pre-intervention) and 916 (post-intervention) were included. The proportion of complete allergy documentation significantly improved for both adult and pediatric services. For adults, completed documentation increased 7\% (from 57\% to 64\%, \(p=0.003\)); for pediatric services, documentation increased by 12\% (67\% to 79\%, \(p = 0.03\)). Completed reaction fields for all patients significantly increased from 59\% to 67\% (\(p = 0.001\)) and blank reaction fields decreased from 40\% to 32\% (\(p = 0.001\)).

**Risk Stratification Tools**

Three studies (Staicu et al.,\(^ {13}\) Caplinger et al.,\(^ {14}\) and Sigona et al.\(^ {15}\)) described risk stratification tools. Staicu et al. 2016\(^ {13}\) performed a retrospective interrupted time-series analysis to describe efficacy of a multi-faceted intervention to reduce inappropriate aztreonam use at Rochester General Hospital. Aztreonam is often used as an alternative antibiotic for patients with a beta-lactam allergy. The study intervention consisted of an educational campaign along with development and dissemination of the Penicillin Allergy Screening Tool (PAST), a decision algorithm.

Azmethronam orders were considered inappropriate for patients (1) without documented beta-lactam allergy or history of multi-drug resistant infection, (2) without severe or life-threatening penicillin (PCN) allergy, or (3) with reported PCN allergy but evidence of tolerating a beta-lactam antibiotic subsequent to date of the reported allergy reaction. Tolerance of beta-lactam drugs was verified by patient or family intervention and historical antibiotic administrative data from the electronic medical record (EMR). Aztreonam orders from infectious disease specialists were considered appropriate.

The emergency department’s sepsis order set was modified to include assessment of PCN allergy severity. Clinical reactions in patients switched from aztreonam to beta-lactam therapy were assessed using the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events.

Pharmacists screened all weekday aztreonam orders over six months before and after implementation. Overall, 496 aztreonam orders (for 459 patients) were reviewed (303 orders pre-intervention, 193 orders post-intervention). The intervention was associated with a significant decrease in aztreonam use: the total number of days of aztreonam therapy per 1,000 patient days decreased from 9.5 to 4.4 days (\(p <0.0001\)). Also, the overall rate of aztreonam use significantly decreased from 4.0 to 0.8 days of therapy per 1,000 patient days (\(p <0.001\)). Of 88 patients with an inappropriate aztreonam order, 56 (64\%) were rechallenged with a beta-lactam antibiotic. No patients had grade 3 or 4 reactions; however, one patient developed a grade 2 rash in the right arm 10 days into cefepime therapy.

A second study, by Caplinger et al. 2016,\(^ {14}\) also performed an interrupted time-series analysis in a small Veterans Affairs hospital. Hospital staff noted that anti-pseudomonal carbapenem (APC) was frequently used in patients with a beta-lactam allergy. This study assessed efficacy of a risk stratification tool to reduce APC use. The tool consisted of an
electronic ordering prompt directing providers to risk-stratify potential for PCN cross-reactivity and assess indications for appropriate APC therapy. No further details regarding the intervention were provided.

A retrospective assessment of APC orders in the 13 months before implementation and 15 months after was performed. Study authors found that aggregate monthly APC initiations decreased from 7.01 to 6.14 per 1,000 patient days ($p = 0.03$) after the intervention. The proportion of patients judged to be "low risk" but receiving APC decreased from 92% to 83% post-intervention, although this reduction was not statistically significant.

A third study, by Sigona et al. 2016,15 retrospectively evaluated the impact of implementing a protocol to review PCN allergy information. All adult patients with documented beta-lactam allergy in the EHR and receiving non-PCN antibiotics over a six-month period were included. Patients were interviewed by a pharmacy resident or infectious diseases clinical pharmacist using an eight-question, standardized questionnaire to assess validity of allergy and likelihood of tolerating beta-lactam. Afterwards, treatment recommendations were made to the provider.

Overall, 32 patients with were included: 24 had a documented PCN allergy, 5 had an amoxicillin or amoxicillin/clavulanate allergy, and 3 had a cephalosporin allergy. After review, transition to beta-lactam therapy was recommended for 24 patients; 21 of 24 were successfully transitioned without any adverse reactions. Thus, of the 32 patients included, 66% (21 of 32) successfully received beta-lactam therapy.

Central Data Repository for Allergy Information with Ongoing Conversion to Coded Data

Zimmerman et al. 200911 described efforts to standardize and code allergy information from 150 regional outpatient facilities and clinics across southeastern Michigan and a tertiary teaching facility in Ann Arbor. A one-time conversion of free-text allergy information into coded allergens/reactions was performed. CareWeb, the University of Michigan’s Web-based system for outpatient visits, encounters, and inpatient progress notes and discharge summaries did not support entry of coded allergen and reaction information.

At the outset, 52% of existing allergy information (272,519 of 519,986 records) were uncoded. A variety of techniques were used to convert this information, including matching, trimming, and modifying free-text strings and modification of the CareWeb interface. Ultimately, the proportion of uncoded allergen records in the central data repository was reduced to only 2.6% (19,904 of 756,340). Ongoing maintenance for gathering and converting uncoded allergens to coded allergens requires 15 hours per month. Study authors reported that when alerts from November 2006 through March 2008 were assessed, only 1% of hard stop alerts were inappropriate.

Patient Portal

Schnipper et al. 200812 describes implementation of a patient portal module for patients to review medication and allergy information in the Partners Healthcare Ambulatory Care Practices. The module was implemented between 2005 and 2007 at four primary care practices. Patients with active portal accounts and upcoming primary care visits were invited to participate. The patient portal allowed verification and updating of allergy information. If patients completed this verification, providers would be invited to verify and update the allergy section of the patient’s EMR with a few clicks.

In all, 1,457 patients consented to participate (64% of all eligible). Of these, 78% ($n = 1,131$) opened the medication journal, and 72% ($n = 1,053$) completed the review and update process. Of the completed medication journals, data were electronically reviewed in the EMR by providers for 77% ($n = 812$) of patients. No information regarding accuracy of changes requested to allergy information was reported.

Interventions to Improve the Context and Frequency of Drug Allergy Alerts

We identified one article7 describing adjustment of parameters to decrease inappropriate allergy alerts after implementation of a computerized order entry system. Brodowy et al. 20167 described the impact of steps taken to improve alert firing rates after deploying a computerized provider order entry (CPOE) system at the University of California at San Francisco (UCSF) medical center. Entry of allergy information in the EMR was restricted to pharmacists, physicians, and nurses. Roughly six months after the CPOE was implemented, all medication alerts firing for pharmacists and physicians over a three-month period were reviewed.
There were 0.14 drug allergy alerts per order fired, of which 94% were overridden. A more detailed review of the 120,669 inpatient drug allergy alerts found more than half were triggered by inactive drug ingredients. All allergies for which an active ingredient could not be identified (e.g., banana allergy) were categorized as having an inactive ingredient. The system was unable to interpret whether this inactive ingredient might interact with any medication, so it generated an alert for every medication order. After eliminating this alert, the number of alerts decreased by 67% (from 0.14 to 0.09 alerts per order), or 900 fewer alerts per day. The override rate also decreased, falling from 94% to 90%. With ongoing improvements, the authors note, as of December 2015, the override rate had fallen to 80%.

**Efficacy of Institutional Policy Changes and Monitoring Alert and Override Rates**

Two studies, described above, investigated institutional policy changes and monitoring override rates. Zimmerman et al. described an organization’s transition to a central data repository and encoding of free-text allergy information into a structured data format across a regional healthcare organization in southeastern Michigan. Authors reported that only 1% of hard stop alerts were found to be inappropriate. The other article, by Brodowy et al., described the process of monitoring alert override rates after organizational deployment of a CPOE and altering parameters for alert firing to decrease low-utility alerts.

**Strengths and Limitations of the Evidence Base**

We identified only a small literature base for inclusion, and the overall strength of this evidence was low: three studies provided only descriptive data, one study reported lessons learned along with pre/post data, and the remaining three studies used a pre/post study design. Although pre/post study designs are commonly used to assess quality improvement initiatives, such studies are problematic for inferring efficacy because they lack a parallel control group (with inability to account for secular trends) and are susceptible to the Hawthorne effect (in which behavior changes when people know they are being observed). Of the three pre/post studies, two failed to describe the intervention clearly, and one did not clearly describe the study outcome measure. More information regarding study quality characteristics is available in Appendix C.

**Discussion**

Despite widely acknowledged limitations of most drug allergy alert processes, our report identified only a small literature base assessing health information technology interventions for improving these systems. Six of the seven studies included in this report described interventions for reducing incomplete documentation or improving the clarity of allergy information provided.

In particular, three studies (one descriptive, and two pre/post studies) recounted efforts to risk stratify the severity and clinical implications for patients with reported beta-lactam allergies. In each study, patients with reported beta-lactam allergy or receiving an antibiotic frequently used for patients with beta-lactam allergies were identified, and pharmacists clarified details regarding the allergy. All three studies reported positive findings either from reductions in use of alternative antibiotics or successful use of a beta-lactam antibiotic without any adverse reactions.

Given how commonly beta-lactam allergies are reported and the importance of reducing overuse of beta-lactam antibiotic alternatives, these risk stratification interventions represent a promising strategy that is feasible for wider dissemination. Notably, these three studies followed patients over only a relatively short time period; thus, we lack evidence regarding whether changes or clarifications in the patient’s allergy status would be acknowledged by future providers (e.g., the patient no longer has a beta-lactam allergy or is able to tolerate cephalosporins), or whether the patient’s record might revert to their “old” pre-clarification status, particularly if rushed providers are aware of prior allergy documentation, but not the interval history of clarification.

Although patient portals represent an exciting strategy for engaging patients in their own healthcare, we identified only one study describing use of patient portals for patients to review their drug allergy history. While the study reported that 72% of patients completed the medication review and update process, no specific data regarding drug allergies was reported. Thus, at present, we lack evidence regarding how carefully patients are likely to review such information and to what degree information obtained through that medium might be accurate.
Finally, two studies described organization-level efforts to improve the drug allergy alert process in the context of transitioning to computerized order entry systems. Besides creating a central data repository for allergy information, Zimmerman et al. describe successfully reducing unstructured allergy information from 52.4% to 2.6% using a variety of techniques, including modifying the data entry screen for providers entering drug allergy information. Conversely, Brodowy et al. described monitoring drug allergy override rates and successfully adjusting firing parameters to reduce unnecessary alerts.

The experience of these two organizations demonstrates that with investment of resources in tracking and managing drug allergy information and alerts, improvement is possible. However, both of these organizations were large, with significant resources (UCSF and University of Michigan Hospitals and Health Care Centers). Thus, to what degree such interventions are feasible for organizations with fewer resources remains unclear.

In 2017, a multidisciplinary group spanning a wide range of expertise set out recommendations for improving the process drug allergy alerting. These recommendations included the following:

- Improving characterization of allergic information to improve alert accuracy
- Increasing patient engagement in review and update of allergy information
- Tailoring thresholds and criteria for alerts fired (to allow for more selective targeting)
- Continuously tracking alerts over time to allow for feedback
- Creating clear hospital/organizational guidelines for providers

Ultimately, aside from risk stratification algorithms for beta-lactam allergies, we found little evidence that interventions incorporating the principles articulated in these recommendations have been developed and assessed. As with many quality improvement initiatives, this may be a result of under-reporting such efforts in the medical literature. Nevertheless, future work with more rigorous studies is necessary to assess the efficacy of such interventions and inform considerations of generalizability.

**Conclusions**

Although drug allergy alerts have the potential to significantly improve the safety and quality of clinical care, in practice, these alerts often fire inappropriately (e.g., for inconsequential reactions), or may be overridden by busy practitioners despite serious safety concerns (e.g., angioedema). Our report found low-quality evidence to suggest that risk stratification algorithms can improve the accuracy and management of reported beta-lactam drug allergies. However, despite the potential for other health IT interventions—such as patient portals and active monitoring of drug allergy override rates—to improve this process, we found a paucity of evidence. Future work is needed to describe the development, implementation, and efficacy of such interventions. Insights gained will hopefully enable CPOE systems to improve patient safety while minimizing unnecessary alerts and alert fatigue.
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References


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Policy Statement
This Special Report presents a literature review and is designed to provide a snapshot of the status of this issue at the time literature searches and literature review were conducted. The information contained herein is derived primarily from the available, published, peer-reviewed scientific literature and searches of the World Wide Web. Publications referenced are limited to the English language. The conclusions and recommendations must be interpreted cautiously and judiciously. ECRI Institute implies no warranty and assumes no liability for the information, conclusions, and recommendations contained in this Special Report.

The conclusions and recommendations and the studies on which they are based are highly perishable and reflect the state of the issue at the time at which the report was compiled. The report was produced and updated by a multidisciplinary staff of scientists, clinicians, information specialists, medical writers, and other health professionals. For quality assurance, all reports are subject to review by experts within ECRI Institute and one or more selected external experts. Neither ECRI Institute nor its employees accept gifts, grants, or contributions from, or consult for medical device or pharmaceutical manufacturers.

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Appendix A. Search Strategies

We conducted a systematic literature search of the PubMed, MEDLINE, EMBASE, CINAHL, and Scopus databases, using a search strategy developed by a medical librarian. The search strategy identified studies published from January 2003 through April 2018 and used a combination of medical subject headings and keywords for allergy, clinical decision support and electronic medical records. Several websites, including AHIMA, AHRQ, AMIA, HIMSS, and HL7 were searched for further references. Detailed search strategies are available upon request.

Sources searched:

**Databases (5):** Medline; PubMed; EMBASE; CINAHL, Scopus

**Websites (5):** AHIMA, AHRQ, AMIA, HIMSS, HL7, Google

**Ovid Medline Strategy:**

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<td>1</td>
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<td>Combine sets</td>
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<td>4</td>
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**Website Search Strategy:**

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## Appendix B. Evidence Tables

### Table B-1. Evidence Tables: All Included Studies

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<thead>
<tr>
<th>Study Details</th>
<th>Patients/Interventions</th>
<th>Intervention/Treatment</th>
<th>Outcomes/Results</th>
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<tbody>
<tr>
<td><strong>Interventions to improve accuracy of drug allergy documentation in electronic medical records</strong></td>
<td></td>
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<tr>
<td><strong>Reference:</strong> Burrell et al. (2013)10</td>
<td><strong>Setting:</strong> Upstate University Hospital (University of California at San Francisco (UCSF))</td>
<td><strong>Intervention:</strong> Pharmacist driven protocol: 2 entry points for intervention 1) Time of admission (upon entry of new drug order by order entry pharmacist—all pre-existing or newly documented allergies without corresponding reaction information were to be clarified through review of record 2) Clinical pharmacist reviewed daily order clarification for any patient admitted, but incomplete drug allergy information</td>
<td><strong>1,686 allergies from 2,174 patient reviewed. (770 allergies pre-intervention, 916 post-intervention). Records included for analysis:</strong> Pre-intervention: 82% from adult services, 19% from pediatric Post-intervention: 83% adult, 17% pediatric</td>
</tr>
<tr>
<td><strong>Study Design:</strong> Pre/post study (prospective)</td>
<td><strong>Number of Patients:</strong> 1,686 allergies from 2,174 patients were reviewed; 770 allergies were reviewed from 1,016 patients</td>
<td><strong>Proportion of complete documentation</strong> for  • Adult services increased 7%: 57% (358 of 634) to 64% (488 of 759), p = 0.003  • Pediatric services increased 12%: 67% (97 of 144) to 79% (124 of 157), p = 0.032  • Complete reaction fields for all patients increased 8% (from 59%, 455 of 778) to 67% (612 of 916), p = 0.001  <strong>Blank reaction fields decreased from 40% (263 of 634) to 32% (245 of 759), p = 0.001</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Purpose:</strong> To assess impact of a pharmacist driving protocol on the quality of drug allergy and intolerance documentation</td>
<td><strong>Inclusion Criteria:</strong> Allergy information for all patients admitted 72 hours prior to and during assessment periods</td>
<td><strong>Exclusion Criteria:</strong> All non-drug allergies (e.g., food, adhesives or latex); also fields entered as no known allergy, or no known drug allergy</td>
<td></td>
</tr>
<tr>
<td><strong>Quality Rating:</strong> Poor</td>
<td><strong>Study Methods:</strong> 4 pre-intervention evaluations (3 consecutive days) every 2 weeks from Feb to April 2011. Included all patients admitted within prior 72 hours of sampling period. Allergy documentation defined as: (1) complete (if reaction field contained information that could enable provider to make clinical decision regarding re-administering drug to patient) (2) blank if no discernable information entered. Fields described as unknown were counted as neither complete nor blank. Post-intervention evaluation performed from August to October 2011, starting 1 week after initiation of intervention</td>
<td><strong>Outcome:</strong> • Proportion of complete documentation</td>
<td></td>
</tr>
<tr>
<td><strong>Reference:</strong> Sigona et al. 201615</td>
<td><strong>Setting:</strong> Upstate University Hospital in Syracuse, NY</td>
<td><strong>Intervention:</strong> Patients interviewed by pharmacy resident or infectious diseases clinical pharmacist about their penicillin (PCN) allergy using a standardized questionnaire (8 questions); alternative antimicrobial treatment recommendations were made to provider based on results of interview</td>
<td><strong>Documented allergies (n=32 total):</strong>  • 24 patients (75%) PCN allergy  • 5 patients (15.6%) amoxicillin or amoxicillin/clavulanate  • 3 patients (9.4%) cephalosporin  Most common reactions: Hives (n = 10), anaphylaxis (n = 8), rash (n = 7). &quot;None&quot; or &quot;Other&quot; in 3 and 4 patients respectively</td>
</tr>
<tr>
<td><strong>Study Design:</strong> Retrospective descriptive study</td>
<td><strong>Number of Patients:</strong> 32 patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Purpose:</strong> Determine impact of pharmacist driven beta-lactam allergy interview on antimicrobial therapy</td>
<td><strong>Mean age:</strong> 56.9 (SD 14.8), 56% male</td>
<td></td>
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</tr>
<tr>
<td><strong>Quality Rating:</strong> Poor</td>
<td><strong>Inclusion Criteria:</strong> Age ≥18, documented beta-lactam allergy in the EMR, and receiving non-penicillin antibiotics</td>
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<tr>
<td>Small number of patients</td>
<td><strong>Exclusion Criteria:</strong> Unable to participate in verbal interview of a reliable patient representative was not available</td>
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<td></td>
<td></td>
<td><strong>Outcome:</strong> Descriptive data including documentation of allergy, history of other</td>
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</tbody>
</table>
**Study Details**

<table>
<thead>
<tr>
<th>Study Methods</th>
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</table>
| Retrospective data collection over 6 months (Sep 1, 2014, to March 20, 2015). Patients identified Monday to Friday through EMR reports and interviewed by pharmacist using internally developed allergy questionnaire to assess validity of documented allergy and likelihood of tolerating a beta-lactam. If patients unable to give history, attempts were made to clarify allergies via outside hospital records and community pharmacies. Information was then confirmed with patient. | beta-lactams tolerated, pharmacist recommended antimicrobial, acceptance of pharmacist’s recommendation and tolerance of recommended beta-lactam | Recommendations after interview:  
- Beta-lactam recommended: 24  
  - Transitioned to beta-lactam (n = 21)  
    - Received pharmacist recommended beta-lactam (n = 19)  
    - Received other beta-lactam (n = 2)  
  - Continued on current therapy (n = 3)  
- Beta-lactam not recommended: 8  
  No patients transitioned to beta-lactam (n = 21) had an adverse reaction.  
66% (21 of 32) were recommended to have beta-lactam and no patients had adverse reactions.  
Of 20 patients with reported allergy to PCN or amoxicillin, 8 (26%) were found to have tolerated PCN or amoxicillin previously |

**Reference:** Zimmerman et al. 2009

**Study Design:** Descriptive  
**Purpose:** To describe design and implementation of Enterprise Allergy Project (EAP) at the University of Michigan Hospitals and Health Care Centers (UMHHC) to standardize and code allergy information across the health system  
**Setting:** 150 regional outpatient facilities and clinics across southeastern Michigan and 865 bed tertiary care teaching facility in Ann Arbor  
**Number of Patients:** N/A  
**Inclusion Criteria:** N/A  
**Exclusion Criteria:** N/A  
**Study Methods:** Phase I of EAP (CDR to WORx) implemented Nov 15, 2005; Phase 2 activated October 16, 2006.  
CareWeb: internally build enterprise-wide Web-based system for outpatient visits, encounter information, results, discharge information, pharmacy orders, and inpatient progress notes  
WORx version 2.8 (Medware Corp, Lenexa, KS) inpatient medication order-entry system used by the pharmacy department  
CDR : enterprise clinical data repository  
**Intervention:**  
EAP Stage 1: One-time conversion of existing free-text allergy information into coded allergens and reactions; (CDR contained 272,519 uncoded allergen records out of 519,986 total records); Modification of graphical user interface to support entry and selection of coded allergens and core elements  
**Outcome:** Allergens converted to coded allergens  
Conversion process resulted in conversion rate of 58% of free text to coded allergens.  
An initial process of allergy matching reduced the list of uncoded allergens from 272,519 to 29,500 by using terms that indicated no allergies were present and trimming and modifying free-text strings that closely matched or easily translated to coded allergen counterpart.  
Number of free-text allergens converted during Phase 1 resulted in a significant reduction (94%) in number of uncoded terms. The amount of uncoded allergens has remained low (2.6%) through ongoing allergen conversion.  
Data transfer time (from CDR to UM-CareLink for allergen information) was a mean 5.6 ± 2.2 seconds. The number of inappropriate hard-stop alerts from Nov 2006 to March 2008 (1.5 years post phase 2 activation) was: Of mean 826.1 ± 395 alerts, the number of inappropriate alerts was mean 10.4 ± 8.2 (representing 1% of all hard stop alerts).
Health IT Interventions

Improving Drug Allergy Information and Alerts: Preliminary Usage Data

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<tr>
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<th>Outcomes/Results</th>
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</thead>
<tbody>
<tr>
<td><strong>Reference:</strong> Schnipper et al. 2008&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Setting: Partners Healthcare Ambulatory Care practices (Boston)</td>
<td><strong>Intervention:</strong> Patient portal medications module: this included allowing verification of allergy information (patients interact with their coded allergy information and can verify update information as needed and submit). Providers can then communicate with patients, verify new information, and update allergy section in EMR with a few clicks</td>
<td>1,457 (64%) had forthcoming scheduled primary care visit and consented for participation. 1,131 patients (78%) opened medication journal. 1,053 (72%) completed review and updated process. Data were reviewed electronically within EMR for 812 (77%) of these patients.</td>
</tr>
<tr>
<td><strong>Study Design:</strong> Descriptive</td>
<td><strong>Number of Patients:</strong> 1,457 patients with upcoming primary care visit</td>
<td><strong>Exclusion Criteria:</strong> NR</td>
<td><strong>Quality Rating:</strong> N/A</td>
</tr>
<tr>
<td><strong>Purpose:</strong> To describe Patient Gateway (PG) medications module (patient portal) and preliminary usage data</td>
<td><strong>Inclusion Criteria:</strong> All patients with active patient gateway account and forthcoming scheduled visit with primary care physician were invited to complete a medication journal.</td>
<td><strong>Outcome:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Quality Rating:</strong> N/A</td>
<td><strong>Study Methods:</strong> Medications Module implemented between September 2005 and March 2007 at 4 primary care practices. 12,278 were invited to participate; 2,273 (19%) completed the consent process. 1,457 (64%) had forthcoming scheduled primary care visit. 1,131 patients (78%) opened medication journal, 1,053 (72%) completed review and updated process, and data were reviewed electronically within EMR for 812 (77%) of these patients.</td>
<td><strong>Primary Outcomes:</strong></td>
<td></td>
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</table>

**KQ2: Efficacy of health IT interventions to improve in what context and how often allergy alerts appear**

| Reference: Staicu et al. 2016<sup>13</sup> | Setting: Rochester General hospital (tertiary care, community hospital) | **Intervention:** Education + PCN allergy screening tool (PAST) | 303 orders (for 281 patients) pre-intervention; 193 orders (for 178 patients) post-intervention. Total number aztreonam days of therapy per 1,000 patient-days: Significantly decreased from 9.5 to 4.4 (p <0.0001) |
| Setting: Rochester General hospital (tertiary care, community hospital) | **Number of Patients:** 496 aztreonam orders (for 459 patients) | **Outcome:** | |
| **Study Design:** Pre/post | **Inclusion Criteria:** All patients prescribed aztreonam at any time during presentation to the hospital | **Primary Outcomes:** | |
| **Purpose:** To decrease use of aztreonam an assess a risk-stratification algorithm for allergic reactions to beta-lactams | **Exclusion Criteria:** All patients prescribed aztreonam by infectious disease physician, age <18 | **Inappropriate aztreonam order:** Aztreonam ordered for (1) Patient without severe of life-threatening PCN allergy or (2) PCN allergy of any severity, but prior tolerance of a beta-lactam antibiotic prescribed after date of reported reaction | |
| **Quality Rating:** Fair | **Study Methods:** All aztreonam orders during a pre-intervention (Jan 1 to Jun 30, 2013, and post-intervention (Sep 1, 2013, to Feb 28, 2014) period were identified. In July and August 2013 education regarding PCN allergy screening tool (PAST) was implemented. Pharmacists were required to pass a mandatory education module with a score of ≥80%. The emergency department’s sepsis order set modified to include assessment of severity of PCN allergy, stratified as either life threatening or not life-threatening. | **Outcomes:** | |
| Patient population and outcomes clearly described; details regarding intervention are provided. However, all patients prescribed aztreonam by infectious disease specialist were excluded | | **Total aztreonam usage (days of therapy per 1,000 patient days):** | |
| **Number of Patients:** 496 aztreonam orders (for 459 patients) | | Numbers of inappropriate days of therapy and doses per patient were significant reduced in the post-intervention period (p <0.0001). | |
| **Inclusion Criteria:** All patients prescribed aztreonam by infectious disease physician, age <18 | | However, the percentage of inappropriate orders in each group was similar before and after the intervention (49% pre, 46% post, p = 0.52). | |
| **Exclusion Criteria:** All patients prescribed aztreonam by infectious disease physician, age <18 | | No significant differences in antibiotic indication (pneumonia most common indication). | |
### Improving Drug Allergy Information and Alerts: Health IT Interventions

#### Study Details

<table>
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<tr>
<td>Tolerance of beta-lactam was verified via patient or family interview, historical antibiotic administration data with no adverse reactions documented in EMR. Pharmacists or the intervention team reviewed all aztreonam orders and communicated recommendations with the clinical team. Clinical reactions in patients switched from aztreonam to beta-lactam therapy were assessed using the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events.</td>
<td></td>
<td>The overall hospital rate of aztreonam use declined pre-post intervention. The mean rate of inappropriate aztreonam utilization significantly decreased from 4 days of therapy per 1,000 patient days to 0.8 (p&lt;0.001). Of 88 patients inappropriately receiving aztreonam (post-intervention), 56 (64%) were subsequently rechallenged with beta-lactam antibiotic. No grade 3 or 4 reactions were documented in EMR. However, 1 patient developed a grade 2 rash in the right upper extremity 10 days into antibiotic therapy with cefepime.</td>
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#### Reference:

Caplinger et al. 2016

#### Study Design:

Interrupted time-series analysis (retrospective)

#### Purpose:

To investigate implementing electronic ordering prompt to direct providers to risk-stratify PCN cross-reactivity potential and assess indications for appropriate anti-pseudomonal carbapenems (APC) therapy prior to ordering anti-microbials

#### Setting:

Small Veterans Affairs Teaching hospital, Boise

#### Number of Patients:

127 APC prescriptions

#### Inclusion Criteria:

Inpatient receiving at least 1 APC dose during hospitalization

#### Exclusion Criteria:

NR

#### Study Methods:

Assessment 13 months pre-implementation, and 15 months post-implementation (from July 2012 to October 2014). Intervention introduced between July and October 2013.

#### Intervention:

Computerized Decision support system (CDSS) to direct selection of APC therapy at order entry

#### Outcome:

APC initiations per 1,000 patient days

127 APC over study period:

68 (pre-implementation)

59 (post-implementation)

No significant differences in patient characteristics or indications for APC use pre/post intervention.

56.7% had documentation of prior beta-lactam allergy, of which 93% had documentation of low risk beta-lactam allergy.

Authors report the slope of the line prior to implementation and after intervention was negative: "The change in slope post-intervention was negative: -0.60, 95% CI -1.12 to -0.08, p=0.03)."

Aggregate monthly APC initiations decreased from 7.01 to 6.14 per 1,000 patient days after implementation (p = 0.03)

While post-intervention APC initiation for patients with low-risk beta lactam histories decreased from 92% to 83% (p = 0.17), this was not statistically significant.
### Improving Drug Allergy Information and Alerts: Health IT Interventions

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<tr>
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<th>Intervention/Treatment</th>
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<tbody>
<tr>
<td><strong>Reference:</strong> Brodowy et al. 2016</td>
<td>Setting: University of California San Francisco (UCSF) Medical Center</td>
<td><strong>Intervention:</strong> Restriction of entry and modification of allergy medication to pharmacists, physicians, and nurses, elimination of firing of inactive ingredient alerts for pharmacists and providers in April 2013.</td>
<td>Volume of drug allergy alerts per inpatient order dropped by 67% from 0.14 alerts per order to 0.09 alerts per order. This reduced the number of drug allergy alerts by end users by 900 per day. Close review of 120,669 inpatient drug allergy alerts firing in a 3 month period revealed over half of drug allergy alerts were attributable to inactive ingredients. <strong>Re-evaluation from May 1 to July 30, 2013:</strong> A higher percentage of drug allergy alerts were being acted on by all healthcare providers after the change. Override rate for allergy alerts dropped from 94% to 90% in post-evaluation period. As of December 2015 override rate has continued to improve and is currently 80%.</td>
</tr>
<tr>
<td><strong>Study Design:</strong> Descriptive with some Pre/Post data (Descriptive)</td>
<td><strong>Number of Patients:</strong> N/A</td>
<td><strong>Outcome:</strong> Drug alert overrides</td>
<td></td>
</tr>
<tr>
<td><strong>Purpose:</strong> To describe experience with implementation of CPOE and tweaking of drug firing alerts</td>
<td><strong>Inclusion Criteria:</strong> All alerts</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quality Rating:</strong> N/A</td>
<td><strong>Exclusion Criteria:</strong> NR</td>
<td></td>
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</tr>
<tr>
<td><strong>Study Methods:</strong> 6 months after CPOE went live a review of every medication alert that fired for pharmacists and physicians from Jan 1 through March 31, 2013. After second intervention (eliminating firing of inactive ingredient alerts), reevaluation of drug alerts</td>
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</table>

APC: anti-pseudomonal carbapenems; CDR: central data repository; CDSS: computerized decision support system; CPOE: computerized provider order entry; EAP: Enterprise Allergy Project; EMR: electronic medical record; N/A: not applicable; NR: not reported; PAST: penicillin allergy screening tool; PCN: penicillin.
Appendix C. Study Quality Assessment

Pre/Post Studies were assessed using items from the National Heart, Lung and Blood Institute (NHLBI).  

<table>
<thead>
<tr>
<th>References</th>
<th>Objective clearly stated</th>
<th>Participant eligibility criteria described</th>
<th>Participants representative of those in population of interest</th>
<th>All eligible participants enrolled</th>
<th>Sufficient sample size</th>
<th>Interventions clearly described, delivered across all participants</th>
<th>Valid, clearly described outcome measures assessed consistently</th>
<th>Blinded outcome assessors</th>
<th>Loss to f/u &lt;20%</th>
<th>Statistical methods for change before/after</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burrell et al. 2013</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Only 32 patients; “Before” is recorded allergy status; “After” is recommendations for antibiotic therapy and reactions</td>
</tr>
<tr>
<td>Sigona et al. 2016</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>N/A</td>
<td>N/A</td>
<td>No</td>
<td>Patients prescribed aztreonam by ID physician were excluded</td>
</tr>
<tr>
<td>Staicu et al. 2016</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Caplinger et al. 2016</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>NR</td>
<td>NR</td>
<td>Yes (although method NR)</td>
<td>Few details regarding intervention provided: Described as antimicrobial ordering menu changes which provided guidance on patients with history of -lactam allergy. Change in slope of line, statistical methods not reported</td>
</tr>
</tbody>
</table>

* A retrospective descriptive study (not true pre/post study design)  
f/u: Follow-up; ID: infectious disease; N/A: not applicable; NR: not reported.