Clinical Commentary Review

Innovations in Health Care Delivery: Drug Allergy

Allison Ramsey, MD[a], and Aziz Sheikh, MD, FRCP[b] *Rochester, NY; and Edinburgh, United Kingdom*

This review focuses on advances in health information technology in the detection, diagnosis, and management of drug allergy. The data regarding the use of electronic health records and social media for the detection of drug allergy are reviewed, along with predictive algorithms and clinical decision support systems for drug allergy diagnosis. Drug allergy pathways, algorithms, computerized decision support systems, and computerized physician order entry for patient management are discussed. The use of electronic consults (e-consults) and telehealth in this field is described, as are efforts to improve communication among patients and providers. Future directions for research are suggested. © **2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2143-50)**

Key words: *Drug allergy; Algorithms; Clinical decision support system; Computerized physician order entry; Telehealth; Electronic health record; Drug allergy diagnosis; Health information technology; Social media; Pathways; Pharmacovigilance; Drug allergy documentation*

INTRODUCTION

Advances in health information technology (HIT) offer considerable potential to advance the field of drug allergy, though the application of HIT to this field is relatively nascent. This review will focus on the state of HIT relating to detection of adverse drug reactions (ADRs), diagnosis of drug allergy, and its clinical management (Table I). Specifically, the application and limitations of electronic health record (EHR) use, social media platforms, clinical decision support systems (CDSSs), diagnostic algorithms, strategies for improving communication, electronic consults (e-consults), and telehealth in the field of drug allergy will be reviewed.

[a]Rochester Regional Health, Rochester, NY
[b]Usher Institute of Population Health Sciences and Informatics University of Edinburgh, Edinburgh, United Kingdom

Conflicts of interest: A. Ramsey is a speaker for Sanofi/Regeneron; has research grants from Takeda, CSL Behring, and Sanofi/Regeneron; and has served on multiple advisory boards, all outside the current work. A. Sheikh has no relevant conflicts of interest.
Received for publication March 5, 2019; revised April 18, 2019; accepted for publication April 23, 2019.
Available online May 17, 2019.
Corresponding author: Allison Ramsey, MD, University of Rochester School of Medicine, Rochester Regional Health, 222 Alexander St, Ste 3000, Rochester, NY 14607. E-mail: allison.ramsey@rochesterregional.org. Or: Aziz Sheikh, MD, FRCP, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Teviot Place, Edinburgh EH8 9DX, UK. E-mail: aziz.sheikh@ed.ac.uk.
2213-2198
© 2019 American Academy of Allergy, Asthma & Immunology
https://doi.org/10.1016/j.jaip.2019.04.050

DETECTION OF POSSIBLE DRUG ALLERGY

Developments in HIT offer a number of opportunities for identifying patients who may have experienced hypersensitivity reactions to drugs and who may need a subsequent detailed clinical evaluation to either confirm or exclude the diagnosis. HIT may also be helpful at a population level in describing the epidemiology of possible drug allergy and identifying risk factors. As will be clear from the summary below, this is however as yet a relatively underdeveloped field of inquiry in relation to drug allergy. There is however a somewhat more developed literature in relation to the broader field of adverse drug events (ADEs), reference to which will be made in instances when specific data on drug allergy could not be identified.

Pharmacovigilance studies using EHRs

Many health systems have or are in the process of transitioning from paper-based record systems to EHRs. As these EHRs mature, a substantial body of data will be collated, which can be used to investigate issues relating to drug safety. Studying ambulatory patients managed at Brigham and Women's Hospital in Boston, Massachusetts, using the home-grown Brigham Integrated Computer System, Honigman et al[1] found that computerized search programs could be used to efficiently detect an array of ADEs. They compared 4 different computerized approaches, namely, *International Classification of Diseases*, *Ninth Revision* classification, computer event monitoring, text searching, and allergy rules, and found that allergy rules performed best overall with high specificity (88%) and reasonable sensitivity (58%) when compared with the criterion standard of chart review undertaken by a physician trained in the detection of ADEs.[1] The allergy rules involved searching for exposure to a medication (or its ingredients) to which there was a known allergy. This approach had a negative predictive value of 99.2%, meaning that those who were not identified by this method were extremely unlikely to have an ADE. Subsequent work by the same team found that 11% of these ADEs were preventable.[2] This approach could therefore be used to initially screen patients who needed a subsequent more detailed assessment.

In a similar vein, Kim et al[3] interrogated data from Seoul National University Bundang Hospital, Korea's first hospital with a comprehensive EHR, to identify patients who may have experienced contrast media–induced hypersensitivity reactions. They found that electronic surveillance, using coded data for exposure to contrast media and a record of symptoms/signs suggesting a hypersensitivity reaction and/or prescriptions for epinephrine/antihistamines, had a sensitivity of 66.7% and a specificity of 99.6%, with a negative predictive value of 99.7% when compared with the criterion standard of manual chart review by board-certified clinicians supervised by a board-certified allergist.[3]

The Food and Drug Administration's Mini-Sentinel pilot program and its subsequent Sentinel program are among the

Abbreviations used
ADE- Adverse drug event
ADR- Adverse drug reaction
CDSS- Clinical decision support system
CPOE- Computerized physician order entry
EHR- Electronic health record
HIT- Health information technology

most sophisticated attempts to develop an EHR infrastructure to study drug safety signals.[4,5] As part of the development work for Mini-Sentinel, Schneider et al[6,7] undertook systematic reviews to identify validated methods for identifying anaphylaxis (including anaphylactic shock and angioedema) and other severe drug hypersensitivity reactions. These reviews identified a number of algorithms, with positive predictive values ranging between 7% and 95%. Positive predictive values were poor when both drug exposure and diagnostic outcome were broadly defined (eg, any drug-related possible or probable anaphylaxis), but was much better when drug exposure and disease outcome were more specifically defined (eg, angioedema in new users of angiotensin-converting enzyme inhibitors). Greater clinical agreement on case definitions, the translation of these into specific *International Classification of Diseases* codes for hypersensitivity reactions, and data mining—based approaches are likely to help increase positive predictive values for detecting drug allergy. Current work is ongoing on *International Classification of Diseases, Eleventh Revision* on a unifying "drug hypersensitivity" subsection to improve hypersensitivity data accuracy and to better inform epidemiologic studies.[8]

Walsh et al[9] subsequently used the Food and Drug Administration's Mini-Sentinel database to validate an algorithm for identifying anaphylaxis. Their algorithm had a positive predictive value of 63%, leading the authors to conclude that this approach was perhaps best used to initially identify a population who should subsequently be further investigated through more detailed chart review.

In summary, although at an early stage, the use of EHR analysis to quickly and efficiently identify patients who may have experienced a drug hypersensitivity warrants further investigation. However, reliance on routine EHR and claims data may miss milder reactions because these may not present to health care providers or may not be recorded or billed for by health care providers.

Analysis of social media data and online communities

With increasing numbers of people regularly posting health-related data online, analysis of these data has the potential to yield complementary data to those available from EHRs and claims data, thereby overcoming, at least in part, the surveillance bias referred to above.[10] Berrewaerts et al[11] recently reviewed this evidence and found that various channels are now being used by patients to report presumed ADRs. These include social media platforms such as Facebook and Twitter, and also patient safety incident reporting systems and online health platforms. They conclude that there will be a continuous proliferation of patient-generated reports catalyzed by the near ubiquitous availability of smartphones in economically developed countries and their increasing rapid penetration into low-resource environments.

In a study of data using the online health platform Medhelp.org, Liu et al[12] were able to automate the process of identifying ADRs using a combination of analyzing the text of posts and machine learning—based techniques to learn from a sample of data with reasonable accuracy, thereby demonstrating that such data sets can now efficiently be mined at scale. Related work in relation to public Internet searches has been undertaken for allergy using Google Trends.[13]

In summary, this body of work indicates that it is now possible to automate searches of various online platforms to increase the sensitivity of identifying possible drug-triggered adverse reactions. This approach may be particularly useful for identifying milder reactions that may not be detected using EHR-based algorithms and for identifying patients' concerns.

DIAGNOSIS OF DRUG ALLERGY

Predictive algorithms

Predictive algorithms are now being developed in a number of clinical areas, for example, risk of developing diabetes mellitus, cardiovascular disease, and chronic obstructive pulmonary disease, and these can be used to guide clinical decision making with a view to reducing the risk of developing these outcomes. These predictive models should ideally go through formal development, validation, and impact assessment before being deployed in routine clinical care. In the case of drug allergy, it may be possible to predict which individuals are at high risk of developing allergic reactions to particular classes of drugs. We however failed to find any algorithms that had been through this full evaluation cycle. This may reflect the fact that it is currently difficult to predict drug allergy. This was demonstrated in a study by Chiriac et al[14] in which 2 independent approaches using clinical history variables were both found to have poor sensitivity in predicting beta-lactam allergy in suspected patients. A variant of this approach is to identify classes of drugs that may induce allergic side effects. Using a machine learning—based approach, Hammann et al[15] interrogated the Swiss drug registry and were able to achieve high predictive values of between 79% and 90% for identifying drugs that are likely to be associated with reported allergic side effects.

Clinical decision support systems

An accurate drug allergy history is the most important aspect of the diagnosis of drug allergy.[16] Reliable *in vivo* and *in vitro* diagnostic tools are lacking for most drugs, aside from skin testing for IgE-mediated reactions to select medications, immunocap in limited cases,[17] and the "criterion standard" of drug challenge.[16] However, drug challenge is generally contraindicated in cases of severe hypersensitivity reactions. In theory, CDSSs have excellent potential to help fill the gaps in diagnosis of drug allergy and thus enhance the safety of drug prescribing. CDSSs could help to avert administration of drugs placing patients at risk for a hypersensitivity reaction and also reduce unnecessary avoidance of needed drugs. These possibilities are encouraging, but the success of CDSS algorithms relies on the input of accurate and complete drug allergy information.[18] Unfortunately, there is at present no standardized approach for the documentation of drug allergy history in the EHR,[19] and multiple studies have established that complete and accurate documentation in EHRs is deficient.[20-27] As a result, reliable CDSS for drug allergy

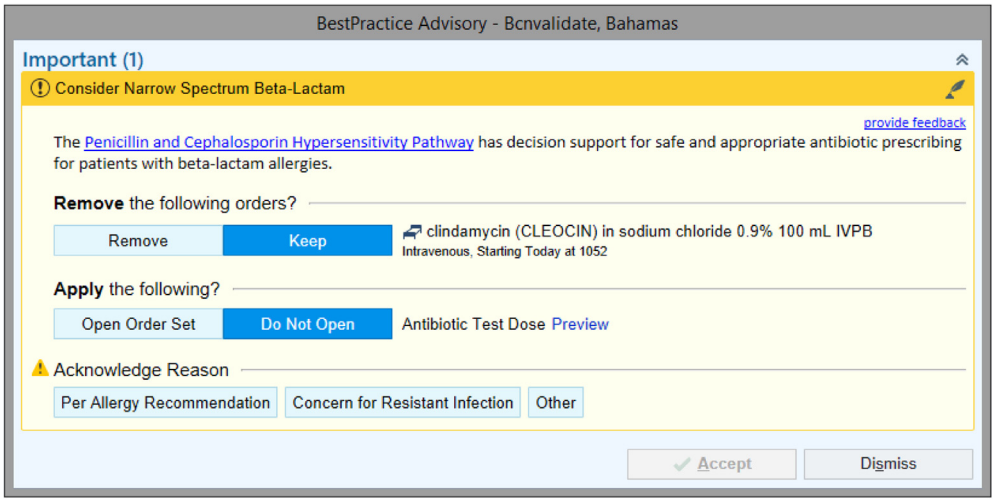

FIGURE 1. Example of a drug allergy alert from a CDSS incorporated into the EHR at Massachusetts General Hospital (K. Blumenthal, written personal communication, January 29, 2019). Reprinted with permission.

diagnosis is lacking, and there are no validated CDSSs for drug allergy diagnosis. There is a smartphone app, the ADR causality app, which was developed to assist clinicians with evaluating ADRs, but it also addresses other adverse effects based on the Liverpool causality assessment tool.[28] This app ranks ADRs as definite, probable, possible, or unlikely.[29] There is no published validation of this app to date.

CLINICAL MANAGEMENT OF DRUG ALLERGY

Improving documentation

As previously stated, multiple studies have illustrated that the documentation of drug allergy in the EHR is often inaccurate and/or incomplete, and different standardized approaches to improving EHR documentation have been published, including pharmacist-led approaches,[30-32] use of an allergist-developed structured questionnaire,[33] involvement of nursing staff, and use of a preoperative standardized drug allergy questionnaire.[34] Such standardized approaches could be useful to incorporate into EHR allergy fields; however, this incorporation into EHRs is complicated because of the need for appropriately coded information. There has been work regarding standardized terminologies for encoding drug allergy information,[35] and there is also work underway to understand the state of EHR allergy field documentation by the American Academy of Allergy, Asthma & Immunology Adverse Reactions to Drugs, Biologics, and Latex Committee (K. Blumenthal and A. Guyer, personal oral communication, January 29, 2019). There is also significant room to improve the "crosstalk" between different health system EHRs. A recent report on the Veterans Health Information Exchange demonstrated that exchange of Veterans Administration allergy information increased drug allergy documentation 8-fold, and reduced allergy field discrepancies between Veterans Administration and external health system EHRs.[36]

Drug allergy pathways/CDSSs/computerized physician order entry

The most extensive work on drug allergy pathways has been on beta-lactam allergy. CDSSs and drug allergy pathways for this important area of drug allergy were recently reviewed by Chiriac et al.[37] The authors direct readers to this thorough review regarding existing pathways for beta-lactam allergy. This review discusses the Massachusetts General Hospital approach, which has been adopted by a number of other institutions,[38] a UK clinical decision support tool, which identifies low-risk patients able to use penicillin without prior skin testing,[39] Australian therapeutic guidelines with a national standardized approach to beta-lactam allergy,[40] and other institutional multidisciplinary team approaches.[41-44] The pathway reported by Blumenthal et al[38] has been incorporated into a Web-based program and a smartphone app to support health care provider antibiotic choices for patients with a penicillin allergy label.

Some institutions have specifically focused on targeting the penicillin allergy label in inpatients receiving high-risk or expensive second-line antibiotics. A CDSS targeting penicillin-allergic inpatients was developed at the University of Texas Southwestern and incorporated into the EHR. Patients receiving aztreonam were identified to undergo pharmacist-led penicillin skin testing and challenge. The authors demonstrated a significant reduction in aztreonam use and a significant decrease in average antibiotic cost per patient.[45] Another approach targeting aztreonam did not incorporate penicillin skin testing, but used an institution-wide educational program, an electronic alert to pharmacists for all aztreonam orders, and pharmacist review of these orders.[46] This study demonstrated a significant decrease in aztreonam use and an estimated cost avoidance of $60,000 to $100,000 for the institution over a 6-month period. A recent study of an algorithm in the preoperative population involving a 3-step process of allergy consultation through a standardized questionnaire, penicillin skin testing, and challenge demonstrated that patients who avoided the use of vancomycin experienced an average of 22 minutes shorter operating room time due to decreased infusion times.[47]

Drug allergy management involves safely avoiding medications in patients who are truly allergic and reintroducing needed medications in patients previously labeled as allergic. Computerized physician order entry (CPOE) with CDSS has improved the safety of medication prescribing and has potential to be helpful in both aforementioned aspects of drug allergy management. However, as with drug allergy diagnosis and

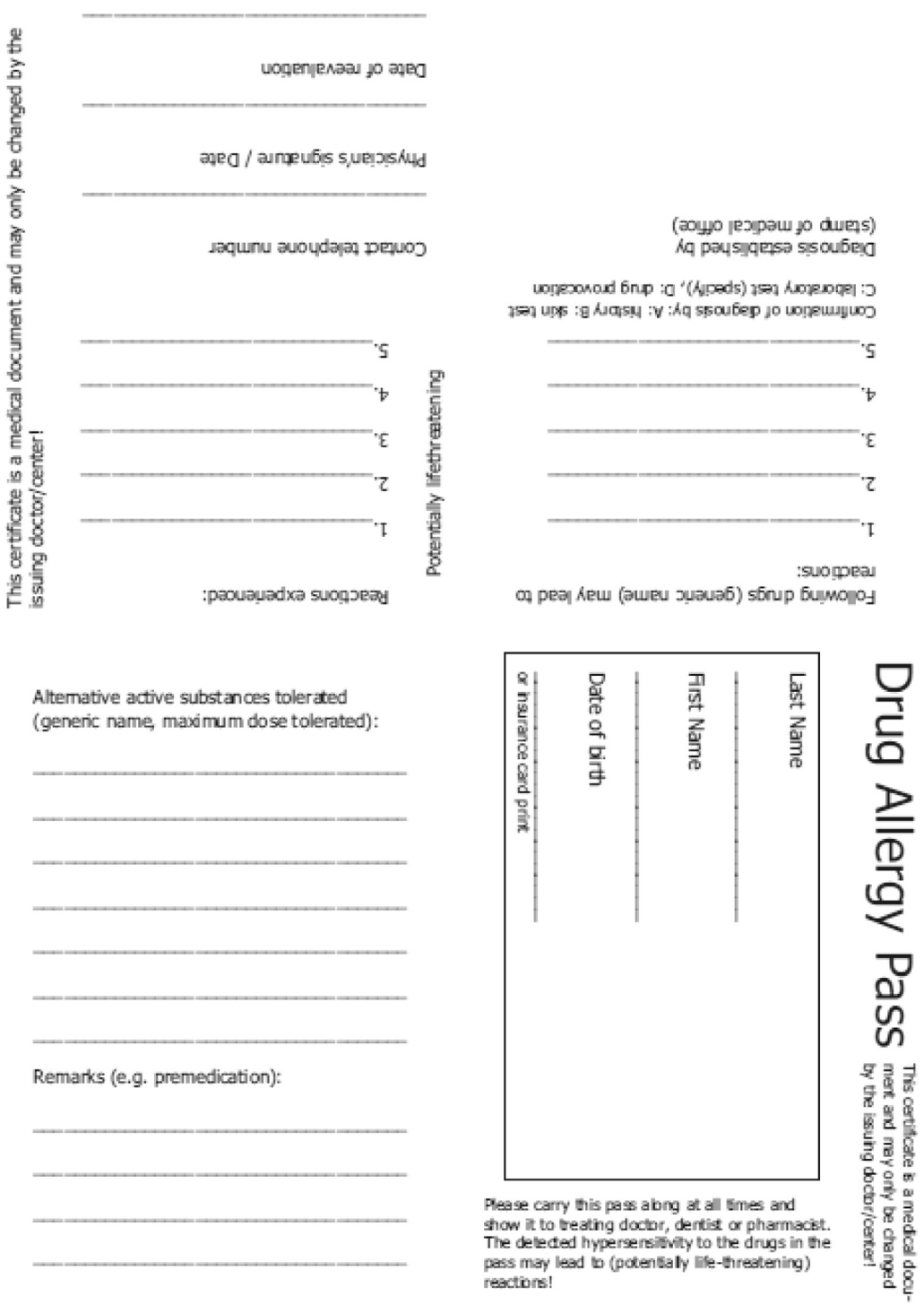

FIGURE 2. Drug allergy passport. This is an example of a paper drug allergy information sheet that is given to patients after drug allergy evaluations. Reprinted with permission from Brockow K, Aberer W, Atanaskovic-Markovic M, Bavbek S, Bircher A, Bilo B, et al. Drug allergy passport and other documentation for patients with drug hypersensitivity - An ENDA/EAACI Drug Allergy Interest Group Position Paper. Allergy 2016;71:1533-9.[57]

documentation, the usefulness of the EHR drug allergy field for CPOE with CDSS is limited by the quality of information inputted, as this has been demonstrated to be missing or incomplete in large data sets from health care networks.[48,49] Reliance on the "free-text" field has also hindered the accuracy of drug allergy CPOE with CDSS, because CDSSs rely on coded information to apply algorithms.[17] A UK study examining the effect of a CPOE/CDSS on the 78 most common prescribing errors reported a significant decrease in prescribing errors. However, administration of a penicillin-based antibiotic still

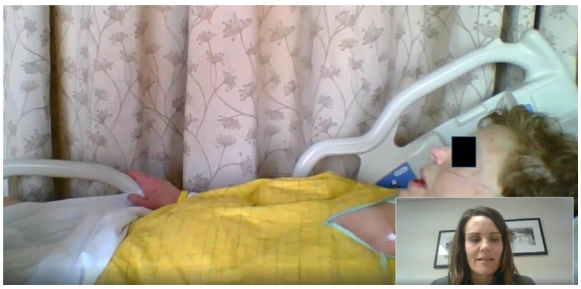

FIGURE 3. Picture of a telehealth encounter for penicillin allergy testing in the hospital, with the allergist in an outpatient setting. Written informed consent obtained from those included in the photograph.

occurred in patients labeled penicillin allergic despite the system because of lack of coded information.[50] The lack of quality standardization of drug allergy information has the ramification of "alert fatigue" in CPOE with embedded CDSS, where health care providers override both meaningful and meaningless alerts, with the assumption that all alerts will be the latter (Figure 1).[51] Multiple studies have shown that drug allergy override rates increase as the number of alerts increase,[52,53] with some reported rates approaching 90%.[53] The other side of alert fatigue is fear on the part of designers and vendors that they may be liable if removed CDSS alerts result in a dangerous drug exposure.[54] There is clear potential for benefit to reduce error from CPOE with CDSS, but significant improvement in the quality of drug allergy data input is needed, along with improved understanding of how health care providers interact with CDSS[5] and improved understanding of the liability associated with relaxed alerts. Improved quality of EHR drug allergy input could also lead to improvements in cross checking other potential drug sensitivities based on chemical structure.[52,55,56]

Improving communication between providers

Although there is vast opportunity to harness technology for the benefit of patients and medical providers, many of the published methods of improving communication between providers have resided with paper, rather than digital or electronic media. A European Network on Drug Allergy/European Academy of Allergy and Clinical Immunology position paper from 2016 supported the institution of a drug allergy passport (Figure 2) for drug-allergic patients throughout Europe. The goal of such a passport is to communicate the same drug allergy information to patients, health care providers, pharmacists, and dentists regarding drugs to avoid, alternative drug options, and risks of severe ADRs.[57] The authors also concurred that complementary information may accompany such a passport, including an alert card, bracelet, certificate, letter, or copy of the medication allergy record.[57] A wallet card has also been advocated to avoid relabeling penicillin allergic patients after negative evaluations.[58] The type of information conveyed by these paper documents has the prospect of incorporation into smartphone applications, but current data are limited to asthma and other disease states.[59-61]

Remote consultations/reviews

There is overall a paucity of literature regarding remote drug allergy consultations. There is no literature to date describing electronic consults (e-consults) specifically for drug allergy, though there is emerging data in multiple diverse specialties, including hospital medicine, cardiology, gastroenterology, hematology, and infectious disease.[62] However, an e-consult may be appropriate regarding questions of drug allergy cross-reactivity or other focused drug allergy questions that do not need specific patient interview information.

A step beyond an e-consult, telehealth, has emerged as a strategy to reach remote patient populations, particularly with an anticipated future shortage of allergy/immunology physicians. Teleheath is defined as the use of technology and its applications by health care providers to remotely evaluate, diagnose, and treat patients.[62,63] There is data regarding the use of telehealth in asthma,[64-66] food allergy,[67] and other allergic conditions.[68] The American College of Allergy, Asthma, and Immunology has published a position paper supporting the use of telehealth in the field of allergy/immunology,[69] and expansion of its use has been advocated in the field.[70] There is emerging data for telehealth in drug allergy. Waibel et al[68] recently published a retrospective report of 360 patients participating in 423 telehealth visits in the United States Military system, of which 16 patients were seen for drug allergy. In their telehealth model, patient presenters were not trained in skin testing or drug challenge, so these procedures required an in-person visit after the initial telehealth evaluation. The authors demonstrated high patient satisfaction scores, cost savings, reduction in missed work/school days, and travel savings among their patient cohort.[68] In addition, Staicu et al[71] studied telehealth for penicillin allergy skin testing. The authors demonstrated high patient satisfaction, a significant decrease in second-line antibiotic use, physician time savings, and cost savings through the use of this technology in 50 patients.[71] See Figure 3 for a picture of a telehealth encounter (A. Ramsey, unpublished data, March 2019).

Radiofrequency identification tags, bar-coding, and closed-loop prescribing systems

Bar-coding has been used in hospital medication tracking since being mandated by the Center for Medicare & Medicaid Services in 2012.[72] Another technology for drug tracking is radiofrequency identification,[72] which uses radio waves for collecting and transferring patient data. Closed-loop prescribing systems include automated dispensing of drugs, barcode scanning to confirm patient and ordered drug matching, and electronic medication administration records.[73] These technologies have been shown to reduce medication errors in total,[73-75] including drug allergy errors.[72,73] Despite their growing use,[72] studies linking these systems to improved patient outcomes are lacking,[74] and there are no current studies specifically addressing systems' impact on drug allergy. These systems are nuanced, expensive to implement, and require tailoring to specific settings,[74] but certainly have potential to improve the management of drug allergy.

Future directions

There are vast opportunities to continue to further the field of drug allergy through the use of HIT. A priority in this area should be the standardization of EHR entries for drug allergy and drug allergy outcomes, which should significantly improve the clinical management of drug allergy and research efforts in the field. Advances in natural language processing to identify and classify drug allergy and drug allergy—related outcomes are needed to avoid the need for strictly coded information. The

TABLE I. Outline of article sections.

Article section	Key discussion points
Detection of drug allergy	
Pharmacovigilance using EHRs	There are large bodies of EHR data to capture ADEs and contrast reactions and this is a developing area of pharmacovigilance The Food and Drug Administration's Mini-Sentinel and Sentinel databases have been used to create algorithms to identify anaphylaxis and severe drug hypersensitivity
Social media analysis	Patient reports ADE on social media and online health platforms are evolving as sources of data to study drug allergy
Patient-reported outcomes	Medical platforms are emerging as a way to study ADEs
Diagnosis of drug allergy	
Predictive algorithms	Large data sets may be used to predict the risk of ADEs in this nascent area of drug allergy
CPOE/CPSS	Development of CDSSs in EHRs is limited by quality of information in the drug allergy field There are no validated CDSSs for drug allergy diagnosis
Clinical management of drug allergy	
Improving documentation	Standardized and appropriately coded information is needed for the drug allergy field in EHR
CPOE/CDSS	CPOE/CDSS utilization in the management of drug allergy depends on appropriately coded information Health care providers face "alert fatigue" with CDSSs Better understanding is needed regarding how providers interact with CPOE/CDSS
Improving communication between providers	Most communication tools are paper-based, but opportunity exists to incorporate into EHR and smartphone apps
Remote consultations	There is little data on e-consults and emerging data on telehealth consultations for drug allergy
Radiofrequency identification tags, bar-coding, closed-loop prescribing	Technology exists to decrease medication administration errors. There are no studies specifically demonstrating improved patient outcomes or addressing drug allergy

algorithms for management of beta-lactam allergy have excellent potential for incorporation into CDSS within EHRs. Efforts should be focused on converting patient drug allergy information currently contained in paper forms (wallet cards/passports) into digital forms for patient smartphones that may interface with EHRs. The emerging fields of drug allergy genotyping and phenotyping may eventually be used in CDSSs for increased safety in drug prescribing.

CONCLUSIONS

Drug allergy continues to result in considerable morbidity, mortality, and health care expenditure, much of which has the potential to be avoided through careful development and deployment of HIT. HIT should not however be seen as a panacea; rather, it needs to be used as a means to support the redesign of care processes and pathways. We have in this article provided a synopsis of the state-of-the-art in relation to HIT and drug allergy, and identified key priority areas for further research.

REFERENCES

1. Honigman B, Lee J, Rothschild J, Light P, Pulling RM, Yu T, et al. Using computerized data to identify adverse drug events in outpatients. J Am Med Inform Assoc 2001;8:254-66.
2. Gandhi TK, Seger AC, Overhage JM, Murray MD, Hope C, Fiskio J, et al. Outpatient adverse drug events identified by screening electronic health records. J Patient Saf 2010;6:91-6.
3. Kim MH, Park CH, Kim DI, Kim KM, Kim HK, Lim KH, et al. Surveillance of contrast-media-induced hypersensitivity reactions using signals from an electronic medical recording system. Ann Allergy Asthma Immunol 2012;108:167-71.
4. Platt R, Wilson M, Chan KA, Benner JS, Marchibroda J, McClellan M. The new Sentinel Network–improving the evidence of medical-product safety. N Engl J Med 2009;361:645-7.
5. Platt R, Brown JS, Robb M, McClellan M, Ball R, Nguyen MD, et al. The FDA Sentinel Initiative—an evolving national resource. N Engl J Med 2018;379:2091-3.
6. Schneider G, Kachroo S, Jones N, Crean S, Rotella P, Avetisyan R, et al. A systematic review of validated methods for identifying anaphylaxis, including anaphylactic shock and angioneurotic edema, using administrative and claims data. Pharmacoepidemiol Drug Saf 2012;21:240-7.
7. Schneider G, Kachroo S, Jones N, Crean S, Rotella P, Avetisyan R, et al. A systematic review of validated methods for identifying hypersensitivity reactions other than anaphylaxis (fever, rash, and lymphadenopathy), using administrative and claims data. Pharmacoepidemiol Drug Saf 2012;21:248-55.
8. Tanno LK, Torres MJ, Castells M, Demoly P. What can we learn in drug allergy management from World Health Organization's international classifications? Allergy 2018;73:987-92.
9. Walsh KE, Cutrona SL, Foy S, Baker MA, Forrow S, Shoaibi A, et al. Validation of anaphylaxis in the Food and Drug Administration's Mini-Sentinel. Pharmacoepidemiol Drug Saf 2013;22:1205-13.
10. Gesualdo F, Stilo G, D'Ambrosio A, Carloni E, Pandolfi E, Velardi P, et al. Can Twitter be a source of information on allergy? Correlation of pollen counts with tweets reporting symptoms of allergic rhinoconjunctivitis and names of antihistamine drugs. PLoS One 2015;10:e0133706.
11. Berrewaerts J, Delbecque L, Orban P, Desseilles M. Patient participation and the use of Ehealth tools for pharmacoviligance. Front Pharmacol 2016;7:90.
12. Liu J, Zhang P, Lu Y. Automatic identification of messages related to adverse drug reactions from online user reviews using feature-based classification. Iran J Public Health 2014;43:1519-27.
13. Bousquet J, Agache I, Anto JM, Bergmann KC, Bachert C, Annesi-Maesano I, et al. Google Trends terms reporting rhinitis and related topics differ in European countries. Allergy 2017;72:1261-6.
14. Chiriac AM, Wang Y, Schrijvers R, Bousquet PJ, Mura T, Molinari N, et al. Designing predictive models for beta-lactam allergy using the drug allergy and hypersensitivity database. J Allergy Clin Immunol Pract 2018;6:139-148.e2.
15. Hammann F, Gutmann H, Vogt N, Helma C, Drewe J. Prediction of adverse drug reactions using decision tree modeling. Clin Pharmacol Ther 2010;88:52-9.
16. Solensky R, Khan DA. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol 2010;105:259-73.
17. Mayorga C, Celik G, Rouzaire P, Whitaker P, Bonadonna P, Rodrigues-Cernadas J, et al. In vitro tests for drug hypersensitivity reactions: an ENDA/EAACI Drug Allergy Interest Group position paper. Allergy 2016;71:1103-34.

18. Simpson CR, Anandan C, Fischbacher C, Lefevre K, Sheikh A. Will systematized nomenclature of medicine-clinical terms improve our understanding of disease burden posed by allergic disorders? Clin Exp Allergy 2007;37:1586-93.
19. Fernando B, Morrison Z, Kalra D, Cresswell K, Sheikh A. Approaches to recording drug allergies in electronic health records: qualitative study. PLoS One 2014;9:302-7.
20. Naude C, Fletcher P. Audit and re-audit of the completion of drug chart allergy boxes at St Mary's Hospital imperial college healthcare NHS trust. Arch Dis Child 2012;97:e12.
21. Gay K, Hill G, Bell T. Accuracy of drug-allergy recording in a district general hospital. IJPP 2009;17:253.
22. Ganguly A, Jayasekara N, Qureshi A, Sibly F. Recording allergies, avoiding disaster: an audit of drug charts of trauma and orthopaedic patients. Clin Gov Bull 2007;6:15.
23. Lyons N, Rankin S, Sarangarm P, Washington C 3rd, Weiss SJ, Ernst AA. Disparity in patients' self-reported and charted medication allergy information. South Med J 2015;108:332-6.
24. Lutomski D, Lafollette J, Biaglow M, Haglund L. Antibiotic allergies in the medical record: effect on drug selection and assessment of validity. Pharmacotherapy 2008;28:1348.
25. Khalil H, Leversha A, Khalil V. Drug allergy documentation—time for a change? Int J Clin Pharm 2001;33:610.
26. Farooq M, Kirke C, Foley K. Documentation of drug allergy on drug chart in patients presenting for surgery. Ir J Med Sci 2008;177:243.
27. Staicu M, Plakosh M, Ramsey A. Prospective evaluation of electronic medical record penicillin allergy documentation at a tertiary community teaching hospital. Ann Allergy Asthma Immunol 2017;119:94-5.
28. Gallagher RM, Kirkham JJ, Mason JR, Bird KA, Williamson PR, Nunn AJ, et al. Development and inter-rater reliability of the Liverpool adverse drug reaction causality assessment tool. PLoS One 2011;6:e28096.
29. Ithnin M, Mohd Rani MD, Abd Latif Z, Kani P, Syaiful A, NorAripin KN, et al. Mobile app design, development, and publication for adverse drug reaction assessments of causality, severity, and preventability. JMIR Mhealth Uhealth 2017;5:e78.
30. Burrell C, Tsourounis C, Quan D, Bcps, Jue V, Tam E, et al. Impact of a pharmacist-driven protocol to improve drug allergy documentation at a university hospital. Hosp Pharm 2013;48:302-7.
31. Kathawala M. Improving drug allergy documentation using a pharmacist-led campaign. Br J Clin Pharmacol 2010;2:244-6.
32. Bouwmeester MC, Laberge N, Bussières JF, Lebel D, Bailey B, Harel F. Program to remove incorrect allergy documentation in pediatrics medical records. Am J Health Syst Pharm 2001;58:1722-7.
33. Confino-Cohen R, Leader A, Klein N, Pereg D, Khoury S, Perl L, et al. Drug allergy in hospitalized patients: the contribution of allergy consultation and a structured questionnaire. Int Arch Allergy Immunol 2012;158:307-12.
34. Radford A, Undre S, Alkhamesi NA, Darzi SA. Recording of drug allergies: are we doing enough? J Eval Clin Pract 2007;13:130-7.
35. Goss FR, Zhou L, Plasek JM, Broverman C, Robinson G, Middleton B, et al. Evaluating standard terminologies for encoding allergy information. J Am Med Inform Assoc 2013;20:969-79.
36. Pan E, Botts N, Jordan H, Olinger L, Donahue M, Hsing N. Assessments of the Veteran Medication Allergy Knowledge Gap and Potential Safety Improvements with the Veteran Health Information Exchange (VHIE). AMIA Annu Symp Proc 2016;2016:1004-9.
37. Chiriac AM, Banerji A, Gruchalla RS, Thong BYH, Wickner P, Mertes PM, et al. Controversies in drug allergy: drug allergy pathways. J Allergy Clin Immunol Pract 2019;7:46-60.e4.
38. Blumenthal KG, Wickner PG, Hurwitz S, Pricco N, Nee AE, Laskowski K, et al. Tackling inpatient penicillin allergies: assessing tools for antimicrobial stewardship. J Allergy Clin Immunol 2017;140:154-61.
39. Krishna MT, Huissoon AP, Li M, Richter A, Pillay DG, Sambanthan D, et al. Enhancing antibiotic stewardship by tackling "spurious" penicillin allergy. Clin Exp Allergy 2017;47:1362-73.
40. Antimicrobial hypersensitivity. Australian Therapeutic Guidelines: Antibiotic, Version 15. Melbourne: Therapeutic Guidelines Limited. Available from: www.clinicalguidelines.gov.au/portal/2406/therapeutic-guidelines-antibiotic-version15. Accessed January 26, 2019.
41. Rimawi RH, Cook PP, Gooch M, Kabchi B, Ashraf MS, Rimawi BH, et al. The impact of penicillin skin testing on clinical practice and antimicrobial stewardship. J Hosp Med 2013;8:341-5.
42. Chen JR, Tarver SA, Alvarez KS, Tran T, Khan DA. A proactive approach to penicillin allergy testing in hospitalized patients. J Allergy Clin Immunol Pract 2017;5:686-93.
43. Ramsey A, Staicu ML. Use of a penicillin allergy screening algorithm and penicillin skin testing for transitioning hospitalized patients to first-line antibiotic therapy. J Allergy Clin Immunol Pract 2018;6:1349-55.
44. Trubiano JA, Thursky KA, Stewardson AJ, Urbancic K, Worth LJ, Jackson C, et al. Impact of an integrated antibiotic allergy testing program on antimicrobial stewardship: a multicenter evaluation. Clin Infect Dis 2017;65:166-74.
45. Chen JR, Tarver SA, Alvarez KS, Wei W, Khan DA. Improving aztreonam stewardship and cost through a penicillin allergy testing clinical guideline. Open Forum Infect Dis 2018;5:ofy106.
46. Staicu ML, Brundidge ML, Ramsey A, Brown J, Yamshchikov A, Peterson DR, et al. Implementation of a penicillin allergy screening tool to optimize aztreonam use. Am J Health Syst Pharm 2016;73:298-306.
47. Moussa Y, Shuster J, Matte G, Sullivan A, Goldstein RH, Cunningham D, et al. De-labeling of β-lactam allergy reduces intraoperative time and optimizes choice in antibiotic prophylaxis. Surgery 2018;164:117-23.
48. Moskow JM, Cook N, Champion-Lippmann C, Amofah SA, Garcia AS. Identifying opportunities in EHR to improve the quality of antibiotic allergy data. J Am Med Inform Assoc 2016;23:e108-12.
49. González-Gregori R, Dolores Hernández Fernandez De Rojas M, López-Salgueiro R, Díaz-Palacios M, García AN. Allergy alerts in electronic health records for hospitalized patients. Ann Allergy Asthma Immunol 2012;109:137-40.
50. Pontefract SK, Hodson J, Slee A, Shah S, Girling AJ, Williams R, et al. Impact of a commercial order entry system on prescribing errors amenable to computerised decision support in the hospital setting: a prospective pre-post study. BMJ Qual Saf 2018;27:725-36.
51. EHR Alert. Hyperspace, Epic Systems Corporation; 2019. Verona, WI. Accessed via Rochester Regional Health EMR, March 3.
52. Lin CP, Payne TH, Nichol WP, Hoey PJ, Anderson CL, Gennari JH. Evaluating clinical decision support systems: monitoring CPOE order check override rates in the Department of Veterans Affairs' computerized patient record system. J Am Med Inform Assoc 2008;15:620-6.
53. Topaz M, Seger DL, Slight SP, Goss F, Lai K, Wickner PG, et al. Rising drug allergy alert overrides in electronic health records: an observational retrospective study of a decade of experience. J Am Med Inform Assoc 2016;23:601-8.
54. Kesselheim AS, Cresswell K, Phansalkar S, Bates DW, Sheikh A. Clinical decision support systems could be modified to reduce 'alert fatigue' while still minimizing the risk of litigation. Health Aff 2011;30:2310-7.
55. Tolley CL, Slight SP, Husband AK, Watson N, Bates DW. Improving medication-related clinical decision support. Am J Health Syst Pharm 2018;75:239-46.
56. Brown CL, Mulcaster HL, Triffitt KL, Sittig DF, Ash JF, Reygate K, et al. A systematic review of the types and causes of prescribing errors generated from using computerized provider order entry systems in primary and secondary care. J Am Med Inform Assoc 2017;24:432-40.
57. Brockow K, Aberer W, Atanaskovic-Markovi M, Bavbek S, Bircher A, Bilo B, et al. Drug allergy passport and other documentation for patients with drug hypersensitivity — an ENDA/EAACI drug allergy interest group position paper. Allergy 2016;71:1533-9.
58. Patel S, Tarver S, Alvarez K, Lutek K, Schlebus D, Khan D. Effectiveness of inteventions to maintain penicillin allergy label removal as part of an inpatient penicillin allergy testing protocol. 2017 AAAAI Annual Meeting Oral Abstract, Orlando, FL. J Allergy Clin Immunol 2017;139:Ab183.
59. Anderson WC. Incorporating technology to advance asthma controller adherence. Curr Opin Allergy Clin Immunol 2017;17:153-9.
60. Dzubur E, Li M, Kawabata K, Sun Y, McConnell R, Intille S, et al. Design of a smartphone application to monitor stress, asthma symptoms, and asthma inhaler use. Ann Allergy Asthma Immunol 2015;114:341-342.e2.
61. Mosnaim G, Li H, Martin M, Richardson D, Belice PJ, Avery E, et al. A tailored mobile health intervention to improve adherence and asthma control in minority adolescents. J Allergy Clin Immunol Pract 2015;3:288-90.
62. Vimalananda VG, Gupte G, Seraj SM, Orlander J, Berlowitz D, Fincke BG, et al. Electronic consultations (e-consults) to improve access to specialty care: a systematic review and narrative synthesis. J Telemed Telecare 2015;21:323-30.
63. Bashshur RL. Telemedicine and health care. Telemed J E Health 2002;8:5.
64. Halterman JS, Fagnano M, Tajon RS, Tremblay P, Wang H, Butz A, et al. Effect of the school-based telemedicine enhanced asthma management (SB-TEAM) program on asthma morbidity: a randomized clinical trial. JAMA Pediatr 2018;172:e174938.
65. Portnoy JM, Waller M, De Lurgio S, Dinakar C. Telemedicine is as effective as in-person visits for patients with asthma. Ann Allergy Asthma Immunol 2016;117:241.

66. McLean S, Chandler D, Nurmatov U, Liu J, Pagliari C, Car J, et al. Telehealthcare for asthma. Cochrane Database Syst Rev 2010;6:CD007717.
67. Kelleher MM, Dunngalvin A, Sheikh A, Cullinane C, Fitzsimons J, Hourihane JO. Twenty four-hour helpline access to expert management advice for food-allergy-triggered anaphylaxis in infants, children and young people: a pragmatic, randomized controlled trial. Allergy 2013;68:1598-604.
68. Waibel KH, Bickel RA, Brown T. Outcomes from a regional synchronous telealergy service. J Allergy Clin Immunol Pract 2019;7:1017-21.
69. Elliott T, Shih J, Dinakar C, Portnoy J, Fineman S. American College of Allergy, Asthma & Immunology position paper on the use of telemedicine for allergists. Ann Allergy Asthma Immunol 2017;119:512.
70. Portnoy JM, Elliott T. Tele-allergy: here today and rapidly advancing. J Allergy Clin Immunol Pract 2019;7:1022-3.
71. Staicu ML, Holly AM, Conn KM, Ramsey A. The use of telemedicine for penicillin allergy skin testing. J Allergy Clin Immunol Pract 2018;6:2033-40.
72. Uy RC, Kury FP, Fontelo PA. The state and trends of barcode, RFID, biometric and pharmacy automation technologies in US hospitals. AMIA Annu Symp Proc 2015;2015:1242-51.
73. Franklin BD, O'Grady K, Donyai P, Jacklin A, Barber N. The impact of a closed-loop electronic prescribing and administration system on prescribing errors, administration errors and staff time: a before-and-after study. Qual Saf Health Care 2007;16:279-84.
74. Cresswell K, Coleman J, Smith P, Swainson C, Slee A, Sheikh A. Qualitative analysis of multi-disciplinary round-table discussions on the acceleration of benefits and data analytics through hospital electronic prescribing (ePrescribing) systems. J Innov Health Inform 2016;23:178.
75. Hwang Y, Yoon D, Ahn EK, Hwanh H, Park RW. Provider risk factors for medication administration error alerts: analyses of a large-scale closed-loop medication administration system using RFID and barcode. Pharmacoepidemiol Drug Saf 2016;25:1387-96.