Clinical Commentary Review

Addressing the Challenges of Penicillin Allergy Delabeling With Electronic Health Records and Mobile Applications

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Allergy labels are common, often incorrect, and potentially harmful. There are many opportunities for clinical decision support (CDS) tools integrated in the electronic health record (EHR) and mobile apps to address the challenges with drug allergy management, including penicillin allergy delabeling (PADL). Effective delabeling solutions must consider multidisciplinary clinical workflow and multistep processes, including documentation, assessment, plan (eg, allergy testing and referral), record update, drug allergy alert management, and allergy reconciliation over time. Developing a systematic infrastructure to manage allergies across the EHR is critical to improve the accuracy and completeness of a patient's allergy and avoid inadvertently relabeling. Improving the appropriateness and relevancy of drug allergy alerts is important to reduce alert fatigue. Using alerts to guide clinicians on appropriate antibiotic use may reduce unnecessary β-lactam avoidance. To date, EHR CDS tools have facilitated non-allergists to provide PADL at the point of care. A mobile app was shown to support PADL and provide specialist support and education. Future research is needed to standardize, integrate, and evaluate innovative CDS tools in the EHR to demonstrate patient safety and clinical utility and facilitate wider adoption. © 2022 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2023;11:414-21)

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INTRODUCTION

Drug allergies documented in the electronic health record (EHR), including penicillin allergies, are common and often incorrect.[1] Up to 15% of hospitalized patients[2,3] 6% to 10% of the general population[4,5] report a penicillin allergy. Of these individuals, 94% can tolerate penicillin after formal allergy testing, and many of the intolerances during testing are not representative of serious allergic responses.[6] Incorrect penicillin allergy labels are recognized as both a public health concern and a medication safety issue because of the many associated harms, which include increased multidrug-resistant infections and increased mortality.[1,7] Allergy testing has traditionally been delivered by allergists, but the paucity of allergy specialists worldwide[8,9] and traditional resource-intensive testing methods have limited wider deployment of penicillin allergy delabeling (PADL).[10] Less resource-intensive delabeling methods, such as delabeling according to history alone or after a drug challenge without prior skin testing, make PADL more assessable to non-allergists. The endorsement of non-allergists delivering PADL and the development of tool kits to support non-allergists create an opportunity for the wider adoption of PADL and safe delabeling on a broader scale.[1,11-14] This requires health care systems to incorporate new infrastructure and workflows and novel tools to facilitate allergy management, some of which can be integrated with the EHR.[15,16]

To design, develop, and implement effective delabeling solutions, it is important to recognize the broader clinical

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Abbreviations used
ADR- Adverse drug reaction
BPA- Best practice advisories
CDS- Clinical decision support
EHR- Electronic health record
HSR- Hypersensitivity reaction
NLP- Natural language processing
PADL- Penicillin allergy delabeling

multidisciplinary workflow and how delabeling fits within these pathways. Elements of allergy management that lend themselves to EHR solutions include the major components and processes of (1) documentation, (2) assessment, (3) plan (eg, allergy testing strategy/referral ordering), (4) record updates, (5) drug allergy alert management, and (6) allergy reconciliation. Each step is important to maintain quality care with minimal adverse drug events, reduced health care costs, and better health outcomes.[1,17]

In defining the workflow for allergy record maintenance and outlining the associated EHR functions, it is evident that there are multiple opportunities for EHR and decision support to guide allergy management and PADL effectively (Figure 1). Computerized clinical decision support (CDS) in the EHR is a key potential component of tool kits that have been developed to support non-allergist delivery of PADL.[1] Incorporating PADL decision support at the point of care would likely enhance the identification, assessment, and selection of the most appropriate testing strategy for patients while providing education for both health care workers and patients. Point of care antimicrobial stewardship decision support tools have been successfully incorporated into mobile phone apps.[18] The many identified challenges with PADL, from diagnosis to updating records, could be addressed by information technology.

In this article, we explore the role of EHR and applications in allergy management and PADL. We acknowledge that the term allergy here is used incorrectly because most patient allergy entries in the EHR are not true immune-mediated reactions but are incorrectly labeled as an allergy. For each major step in the process (as shown in Figure 1), we discuss the current status, unmet needs, and possible innovative solutions.

ELECTRONIC HEALTH RECORD TECHNOLOGY AND INNOVATION

Allergy documentation

Accurate and complete allergy documentation in the EHR is essential to guide clinical decision-making. The EHR allergy section (or allergy list) determines how health care professionals document allergies by providing defined data entry fields that characterize the allergy.[16,19] Allergy information can be entered through structured (drop-down lists or checkboxes) fields or as free text.[19] Structured fields support CDS that notify the physician of allergy risks before prescribing a potentially unsafe medication.

There are currently no consensus guidelines on documentation of allergies in EHR systems, and previously published recommendations from informatics societies and allergy specialists have not been widely adopted.[20-23] A work group within the Adverse Reactions to Drugs, Biologicals, and Latex Committee of the American Academy of Allergy, Asthma & Immunology was formed to publish guidelines for allergy documentation in the EHR; this document is in press.[24] Core elements of the drug allergy history include details related to the patient (eg, symptoms, date of reaction, duration of exposure), medication (eg, specific generic drug name, route of administration, timing of reaction), and treatment (eg, management and time to resolution).[25] To date, the allergy sections in most EHRs contain fields for documenting allergens, reaction(s), reaction type (intolerance vs allergy), and reaction severity, and thus do not meet the suggested core elements of a drug allergy history.[19] In addition, many allergy entries are incomplete, inaccurate, or blank.[19,26] When examining entries for β-lactam allergies, only 40% stated the specific β-lactam antibiotic and only 23% described the reaction.[27] In another study, less than half of documented reactions contained a reaction description and only 18% described the severity.[28] Incomplete documentation influences future prescribing behavior; providers were more likely to adopt a cautious approach and prescribe alternative antibiotics when vague or minimally descriptive allergy entries were provided.[27] Empowering prescribers with validated EHR functions that facilitate accurate structured allergy history taking and, when appropriate, PADL, will reduce the current practice of unnecessarily avoiding penicillins.

Although standardized training on how to document allergies in the EHR is necessary, this will not be sufficient alone because there are numerous EHR vendors across the United States, Europe, and other countries using a broad array of terminology and definitions. This lack of standardization results in frequent free-text entries, which cannot be used in algorithmic CDS. Standard definitions are essential to support both provider training and information technology across EHR vendors. Although this review focuses specifically on penicillin allergy, the definitions in Table I could be used for all medication reactions.

Although a variety of advances may prove to be helpful to enhance the EHR allergy field, including natural language processing (NLP) algorithms discussed subsequently, a new fine-tuned approach is necessary. The introduction of standardized data elements (eg, coded value sets mapped to a standard medical terminology) for critical information will minimize variability in documentation among providers and support better prescribing practices.[27] A study by Goss et al[29,30] used an NLP tool called Medical Text Extraction, Reasoning, and Mapping System to develop a comprehensive set of allergy reactions for the reaction field. The researchers identified over 700 reactions from free text in allergy entries with 98.0% precision and 95.6% recall, demonstrating the rich variety of reactions and the importance of comprehensive value sets to capture reaction details while coding information. Wang et al[31] continued this line of study by building a dynamic picklist that auto-populates appropriate reactions. This simplifies data entry by facilitating efficient, partly automated reaction documentation and can be broadly incorporated into EHR systems.

Improving documentation of the detail and the type of reaction is important because improper classification of intolerances as allergies is common.[32] In most records, intolerances were miscategorized as an allergy,[33] and although penicillin is often safe in patients who report an intolerance, physicians are more likely to avoid prescribing penicillin if the intolerance is recorded as an allergy. Redesigning the binary allergy or intolerance label in EHRs may be a valuable intervention. One suggestion is to redefine the entire allergy module in the EHR as adverse reactions to minimize erroneous entries classified as an allergy.[24] A general improvement may be to place greater emphasis on detailed

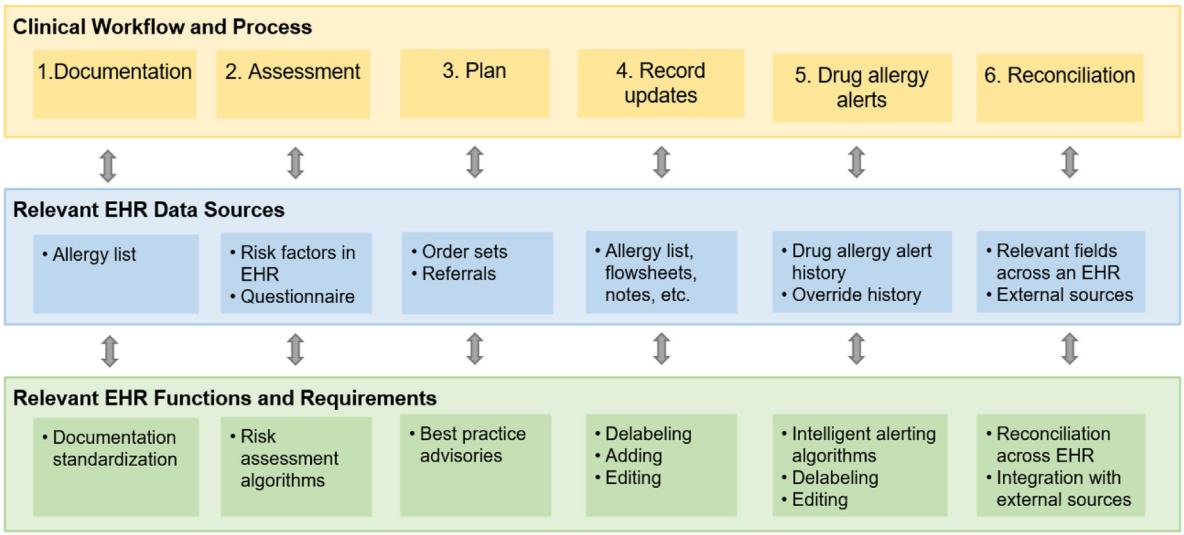

FIGURE 1. Drug allergy documentation and management process with relevant electronic health record (EHR) functions.

TABLE I. Standard drug reaction definitions

Drug reaction	Definition
ADR	Any unintended effect of a drug. They include all reactions to drugs such as nonimmune-mediated intolerances, immune-mediated HSRs, drug allergy, and contraindications, as discussed subsequently.[20]
Drug intolerances	Drugs that are not tolerated by specific individuals. These are ADRs that do not carry the same predictability and risk as immune-mediated reactions.[20] Intolerances include reactions such as nausea, headache, and fatigue.[21] If entered in the EHR allergy section, patient aversions or preferences for avoiding specific drugs and other agents should be coded as intolerances.[24]
Drug HSRs	Immune-mediated ADRs that can be immediate or delayed in onset. Prior studies identified hives, itching, and angioedema as the most common symptoms of immediate HSRs. Delayed HSRs were most frequently documented as causing rash, but delayed HSRs include severe cutaneous adverse reactions such as Stevens–Johnson syndrome, toxic epidermal necrolysis, and drug reaction eosinophilia and systemic symptoms.[23]
Drug allergy	Historically reserved for HSRs with an IgE-mediated mechanism (eg, anaphylaxis to penicillin).[22] Currently, drug allergy is considered synonymous with drug HSRs and includes all immune-mediated drug reactions.
Contraindication	A specific situation in which a drug should not be used because it may be harmful (eg, abacavir if patient has HLA-B*57:01, or angiotensin-converting enzyme inhibitors in angiotensin-converting enzyme inhibitor–induced angioedema)
Unknown	This should be used when the reaction type cannot be specified given the information known, such as when a reaction occurs that may be an intolerance or HSR. Unknown can also be used when the person entering the allergy is uncomfortable with choosing a reaction type, although overuse of this reaction type will lead to missing data and will not improve EHR allergy module quality. Unknown is also appropriate when patients are unaware of historical details related to the adverse drug effect.

ADR, adverse drug reaction; *HSR*, hypersensitivity reaction.

reaction documentation that can be used to classify allergy or intolerance by trained providers or after allergy validation. Ultimately, the EHR design influences allergy labeling and should be augmented to label only true penicillin allergies as such.

Assessment

Drug allergy diagnosis and evaluation result in more appropriate antibiotic prescribing and increased patient safety. Implementing CDS tools in the context of drug allergy management would support non-allergists in diagnosing drug allergy correctly and prescribing appropriate antibiotics to improve antimicrobial stewardship and reduce health care–associated expenditures.[34-37] Such tools also have the potential to serve as an efficient triaging platform that appropriately streamlines and prioritizes patient referrals for allergist assessment and testing.[38]

There have been many successful attempts to establish risk stratification pathways,[5,35,39-42] including pathways intended for nonspecialist PADL in hospitals,[43,44] which uses decision support tools such as the Drug Allergy App, a diagnostic algorithm designed to be used on mobile platforms.[38] The risk stratification criteria and testing methods have varied, with some patients delabeled according to history alone and others after the result of a direct oral challenge test or skin testing followed by an oral challenge test.[43-45] The literature to date demonstrates the safety and efficacy of nonspecialist PADL, and it is supported by many national and global organizations.[1,11,14,45] The outcomes have been positive overall, with few adverse reactions, all of which were mild.[44] Approximately 25% to 30% of patients with penicillin allergy were able to be delabeled using the clinical history alone.[8]

Digital tools such as the Drug Allergy App have the potential to improve and extend the functionality and usefulness of

EHRs.[8,37,38] When designed appropriately, particularly when they are codesigned with experts in drug allergy, algorithms built into the EHR may encourage and allow clinicians to engage with PADL that is embedded into the clinical workflow. Implementing these algorithms will require thoughtful attention to allergy history taking questions, clinician acceptability and confidence in the algorithm recommendations, and the validation of the algorithms and CDS tools.

Plan

The penicillin allergy assessment plan is determined by the outcome of the allergy risk assessment, based on the allergy history, coupled with patient factors, to determine the most appropriate allergy testing method. Algorithms have proven helpful in assessing patients to identify who would benefit from allergy testing[43] and who would be most appropriate for skin testing with challenge testing[11] or a direct drug provocation test.[46] An EHR-based algorithm was developed to screen patients admitted to the hospital automatically and identify those with a documented penicillin allergy who were prescribed high-value broad-spectrum antibiotics and were eligible for testing, leading to targeted testing by pharmacists.[43] Multidisciplinary interventions that integrate clinical expertise with informatics technology were reported to improve allergy evaluation; 80% to 96% of patients who tested negative led to removal of the penicillin allergy label.[11,43,46] The studies used algorithms that promoted appropriate allergy testing that led to reduced second-line antibiotic use. In the United States alone, most penicillin allergies are unverified. Only approximately 15,000 penicillin allergy tests are performed each year.[47] Staffing shortages, scarce testing resources, and a lack of education contribute to the underuse of allergy testing.

The use of algorithms and CDS provides non-allergists with access to allergist expertise at the point of care, addressing some unmet needs for the allergist delivery of PADL and for training non-allergists.

In addition to identifying patients who are eligible for allergy testing, placing referral orders and updating allergy records with test results are equally important steps that EHR functionalities can support. Low referral rates and infrequent allergy testing are partly attributable to limited time and a lack of familiarity with the testing and referral process.[48] To encourage referrals for formal allergy evaluation by specialists, best practice advisories (BPA), another CDS tool used in EHRs, can be designed to assist clinicians with referral orders. One BPA was dedicated to filling out the referral order automatically for patients with a penicillin allergy and providing patient instructions for allergy testing.[49] The BPA paired with educational programming increased the referral rate from 2% to 20% at Rady's Children Hospital in a 9-month period.

Even when an antibiotic challenge test was completed, over half of the records (55%) were not appropriately updated (also see subsequent discussion).[50] An alert was created to appear on the order entry screen 24 hours after the test was administered for the Partners Healthcare System and would cease either after 72 hours or when the provider overrode the alert. With this alert, allergy records were updated more promptly, and allergy updates increased from 51.3% to 66.7% across the health care system. These forms of CDS alerting tools facilitated allergy evaluation and allergy record editing by automatically filling out the referral order and bringing attention to test results that needed to be updated.

Record updates

Electronic health record features can be developed to identify allergy discrepancies readily and assist clinicians in updating allergy records in a timely fashion. Ortega et al[51] and Lo et al[52] demonstrated the unique capabilities of NLP for analyzing clinical notes and providing data-driven clinical recommendations. With an NLP tool, Ortega et al were able to identify over 260,000 allergy records effectively (~16% of total allergy records) with discrepancies that included free-text reactions that were not encoded, duplicate entries, and entries associated with three or more alert overrides. Greater study of the discrepancies also revealed that 36 penicillin allergies were not updated despite negative challenge test results. Lo et al further examined the application of NLP to identify challenge test discrepancies in patients' allergy records. With 96.1% precision, the NLP algorithm analyzed clinical notes and identified a greater number of allergy entries that did not correspond to the challenge test result compared with flow sheets alone (5.0% vs 2.0%).[52] They developed a pilot reconciliation module that employed this NLP algorithm to showcase the potential discrepancy and suggest an action to the provider. Pilot-tested with real-time EHR data, over 90% of recommendations suggested that allergy entries should be deleted based on the challenge test results, 59% of which were related to penicillin allergies. In this case, the EHR was far from a static platform used to document allergies; it can and should be reimagined as dynamic tool that can reinforce robust allergy documentation, facilitate PADL, and prevent relabeling.

Drug allergy alerts

Delabeling penicillin allergies safely and effectively will reduce excessive alerting and thus alert fatigue. Clinicians have described how allergy alerts often lack clinical relevance and are insufficiently targeted.[15] As a result, over 80% of inpatient alerts and 77% of outpatient alerts are overridden.[53] Based on 10 years of data at an integrated health care system, documented penicillin allergies accounted for approximately 7% of all drug allergy alerts (n = 66,215).[54] One study found that nearly seven alerts per encounter occurred for patients with a documented penicillin allergy, and of those patients, 49% had prior penicillin exposure.[55] These findings indicate that EHR technology must be better adapted for detailed allergy documentation and the administration of clinically relevant alerts.[56]

Several hospital systems are implementing interventions to reduce the number of nonspecific alerts. Alerts can be tiered based on severity such that only severe reactions such as anaphylaxis initiate alerts. Electronic health record systems that tier alerts have been shown to decrease alert overrides compared with those that do not tier alerts (100% acceptance vs 34% acceptance of alerts).[57] Buffone et al[28] retrospectively reviewed the impact of altering alerts so that they were displayed only when prescribing the medication in the allergy record or medications with similar side chains. The researchers found no reports of anaphylaxis, demonstrating that alerts might be dispensed with more discretion. Macy et al[58] studied the effects of removing cephalosporin alerts in a health system with over 4 million patients who received an antibiotic treatment. In a similar vein, their findings demonstrated that without frequent alerting, cephalosporin prescribing increased by 47% and did not

result in a significant difference in new adverse reactions, including anaphylaxis, and unsuccessful treatment regimens. Although general caution must be exercised before removing alerts, the study by Macy et al confirmed that many alerts are not clinically relevant and still alter clinician behavior.

Rather than removing alerts, a suggestion is to have CDS alerting systems factor in prior exposure to β-lactams and include such information in the alert itself.[55] Thus, providers might be more likely to consider patient history, change prescribing behaviors, and even consider updating the allergy record if needed. Some PADL interventions have added progress notes to describe the allergy testing and results before deleting the allergy record. Going further and attaching an alert that displays this information when providers incorrectly attempt to relabel patients might prevent incorrect relabeling of delabeled patients.[59,60]

Allergy information reconciliation

Allergy information is often documented in diverse sections of EHR, including the allergy list, medication discontinuation section, flow sheets, allergy test results, problem lists, and clinician notes. Systematically reconciling allergy information across the EHR is critical to improve the accuracy and completeness of a patient's allergy list. For instance, allergy entries can automatically be populated to the allergy section for patients predisposed to reactions owing to existing diagnoses or genetic markers.[16] An example includes screening for the HLA-B*1502 allele before initiating treatment with carbamazepine in patients with Asian ancestry because of the risk for Stevens–Johnson syndrome and toxic epidermal necrolysis.[61] For unverified allergy entries associated with high severity or reactions documented in other disparate EHR sections, intelligent EHR features can be developed to recommend allergy testing or specialist referral. A research team at Mass General Brigham has developed an allergy reconciliation tool able to detect allergy information discrepancies automatically documented across different EHR sections and provide actionable recommendations to clinicians to update allergy records via a user interface with the EHR.[51,52,62]

Allergy reconciliation and delabeling efforts are related to EHR interoperability. Health information exchange is a growing health care priority to support continuity of care and encourage strategic resource use.[3] Previous studies estimated the use of Care Everywhere, a record exchange tool for the Epic (Verona, WI) EHR, to be approximately 1.5% to 6.8%.[3] Clinicians reported that finding previous exposures to medication with Care Everywhere is time-consuming and often difficult to achieve without clear denotation of prior exposure and allergies.[55] Therefore, accurate allergy lists and standardized documentation are necessary to share important patient information successfully.[63] Delabeling allergies should be considered a joint initiative to promote safer prescribing practices across institutions. Because allergy testing resources, clinical time, and expertise are limited, sharing allergy test results and updated lists may guide prescribing practices in other institutions. Developing the infrastructure to reconcile allergies across institutions may improve identification of updated, reliable allergy list information when providing care.

BEYOND THE EHR: MOBILE AND WEB APPLICATIONS

Innovative interventions demonstrated that a well-constructed mobile CDS tool can support penicillin allergy delabeling, facilitating easy access to CDS in diverse clinical settings.[38] A decision support tool needs to be quick and easy to use at the point of care. This is ideally suited to a mobile device application with simple questions that practitioners can complete while they are with patients. Ideally, the questions should be clear and quick to answer with no ambiguity. The outcomes provided would similarly need to be clear, nonambiguous, and preferably aligned to national and international guidance, such as the National Institute for Health and Care Excellence drug allergy guidance.[4] User feedback during development of these tools is important to ensure usability of the final application.

Various mobile platforms support applications. In June 2021, iOS accounted for 53.66% and Android accounted for 46% of the market in North America.[64] Therefore, any mobile application should be developed for both the iOS and Android platforms to ensure equity of access to most mobile device users. Alternative options for mobile application development could include Web applications, which provide the advantage of being able to run on any Internet-connected device with a Web browser. A Web application is also more likely to be able to be integrated into hospital systems and therefore be accessible on hospital computers and possibly within the EHR. Hospitals may

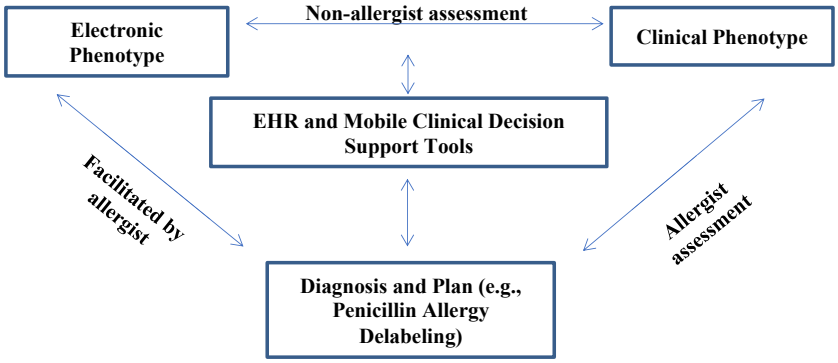

FIGURE 2. Roles of allergists and non-allergists in designing, assessing, and facilitating accurate drug allergy classifications and penicillin allergy delabeling when appropriate through clinical decision support. *EHR*, electronic health record.

have a poor or limited mobile signal related to building construction. This may need to be considered when selecting the platform on which to develop an application.[65] There are clear advantages to having access to the same decision support tool on users' mobile devices and computers and within the EHR, for consistency.

Currently, although there are several validated CDS tools,[66-68] we are aware of only one validated mobile app-based tool.[38] In addition, a Web application-based approach demonstrated increased use of penicillin and cephalosporin antimicrobials in patients reporting penicillin allergy.[69] The validation of any decision support tool would need to reassure the end user that the tool was safe and the risk for missing a potentially life-threatening allergy history was low regardless of the platform on which it runs.

ALLERGY PHENOTYPE

An accurate description and documentation of a patient's clinical allergy phenotype in the EHR would facilitate the application of CDS and allow for appropriate use of necessary first-line medications, especially antibiotics such as β-lactams. Electronic phenotyping is the factual description of clinical characteristics that can facilitate accurate drug allergy classifications using logical algorithms. The electronic phenotype can then be analyzed electronically to classify the drug reaction appropriately. Also, electronic phenotyping refers to the identification of patients with defined clinical characteristics that can be searched for within a structured digital platform, usually an EHR, via logical expressions and operators.[70] Therefore, electronic phenotyping can facilitate accurate drug allergy classifications using logical algorithms. As an example, the drug allergy app uses electronic phenotyping to support the classification of previous drug reactions.[38] The interaction between clinical and electronic phenotypes would be led by allergists and immunologists (Figure 2).

CONCLUSION

There are many opportunities for EHR and mobile decision support tools to guide allergy management and facilitate PADL by non-allergist specialists. To optimize CDS use and patient outcomes, internationally agreed-upon guidelines on documentation of allergies in EHR systems and precise definitions for adverse drug reactions are required. This will enable the incorporation of CDS into EHR and augment clinical decision-making, further optimizing the delabeling process. Innovations and applications for improving drug allergy documentation and management would reduce the burden of incorrect penicillin allergy labels and decrease unnecessary referrals to allergy services, streamlining allergists' care for patients who require allergists' input. Together, they will enable the appropriate use of antibiotics for more patients.

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