Heterogeneity of Drug Allergies and Reaction Lists in Two U.S. Health Care Systems' Electronic Health Records

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Appl Clin Inform 2022;13:741–751.

Abstract

Background Health care institutions have their own "picklist" for clinicians to document adverse drug reactions (ADRs) into the electronic health record (EHR) allergy list. Whether the lack of a nationally standardized picklist impacts clinician data entries is unknown.

Objectives The objective of this study was to assess the impact of defined reaction picklists on clinical documentation and, therefore, downstream analytics and clinical research using these data at two institutions.

Methods ADR data were obtained from the EHRs of patients who visited the emergency department or outpatient clinics at Brigham and Women's Hospital (BWH) and University of Colorado Hospital (UCH) from 2013 to 2018. Reported drug class ADR prevalences were calculated. We investigated the reactions on each picklist and compared the top 40 reactions at each institution, as well as the top 10 reactions within each drug class.

Results Of 2,160,116 patients, 640,444 (30%) had 928,973 active drug allergies. The most commonly reported drug class allergens were similar between BWH and UCH.

Keywords
- clinical documentation
- quality of care
- interoperability
- electronic health records

received
December 8, 2021
accepted after revision
May 23, 2022

DOI https://doi.org/10.1055/a-1862-9425.
ISSN 1869-0327.

BWH's picklist had 48 reactions, and UCH's had 160 reactions; 29 reactions were shared by both picklists. While the top four reactions overall (rash, GI upset/nausea/vomiting, hives, itching) were identical between sites, reactions by drug class exhibited greater documentation diversity. For example, while the summed prevalence of swelling-related reactions to angiotensin-converting-enzyme inhibitors was comparable across sites, swelling was represented by two terms ("swelling," "angioedema") at BWH but 11 terms at UCH (e.g., "swelling," "edema," by body locality).

Conclusion The availability and granularity of reaction picklists impact ADR documentation in the EHR by health care providers; picklists may partially explain variations in reported ADRs across health care systems.

Background and Significance

Accurate documentation of adverse reactions to medications, foods, or other substances is important to patient safety and quality of care. Most electronic health record (EHR) systems have an allergy module where providers document patients' allergies and other adverse reactions (e.g., intolerances and contraindications). The EHR allergy module relies on underlying terminologies to represent and encode allergy and adverse drug reaction (ADR) information.[1] However, health care institutions in the United States utilize EHR systems supplied by hundreds of certified health information technology developers, each siloed in nature and often equipped with different features and clinical terminologies. Allergy reaction "picklists" (i.e., coded reaction options presented to the health care provider when entering the allergy) are often provided by third-party content vendors and/or are customized to institution-specific dictionaries; even health care institutions that use the same EHR vendor system can have different reaction picklists, ranging from a dozen to a hundred reactions.[2,3]

The standard terminologies and value sets (a list of codes and corresponding terms used to describe specific clinical information) within each EHR system serve as "building blocks" that enable data exchange and sharing.[4,5] While initiatives for interoperable EHR systems have made progress in some domains, such as medications, this has not held true in others, such as allergic reactions.[6] The lack of standardization and interoperability has downstream consequences on data exchange between different providers, organizations, and research studies that rely on the accuracy and consistency of coded data.[7–9] Standardization of allergy reaction picklists is fundamental to the utility of these data for patient care, clinical research, drug safety, and postmarketing pharmacovigilance.[10] For example, many EHR systems have functions for clinicians to reconcile allergy and ADR information from outside sources; however, different picklists and coding mechanisms for reactions pose challenges for exchanging this information. In addition, if data collection mechanisms vary by sites, the use of allergy and ADR EHR findings from one site may not be generalizable to other populations. However, it is currently unknown whether the lack of standardized reaction picklists impacts health care provider data entry.

Objective

In the present study, we investigated differences in ADRs documented in the EHR allergy list between two large U.S. health care delivery networks over a 5-year period. We hypothesized that the prevalence of reported drug reactions would be similar but that differences between sites could be influenced by differences between predefined reaction picklists.

Methods

Clinical Settings and Data Collection

We obtained ADR data from Brigham and Women's Hospital (BWH, Boston, MA, United States) and University of Colorado Hospital (UCH, Aurora, CO, United States). BWH and UCH are both large tertiary academic hospitals and members of the integrated health care delivery networks Mass General Brigham (formerly Partners HealthCare) and University of Colorado Health, respectively. BWH and UCH were considered ideal comparison sites given that they utilize the same commercial EHR system (e.g., Epic Systems, Verona, WI, United States) but have institution-specific reaction picklists. At both sites, patient ADR information can be documented by any health care team member via the EHR allergy module.

In this study, patients who visited the emergency department and/or outpatient clinics at BWH or UCH between 2013 and 2018 were included. We extracted patients' demographics (e.g., sex and racial/ethnic group) and ADR information, including allergen (e.g., culprit drug), allergy status (active, inactive, or deleted), date/time of entry/update, coded reaction(s), and role of the documenting health care team member (e.g., physician, nurse, and medical assistant) from the EHR data warehouses at each site.

Data Analysis

In EHRs, the documented drug allergen can be a specific drug or drug class. Using an approach similar to our previous work,[11] we classified drugs into corresponding drug classes using the American Hospital Formulary Service (AHFS)

Pharmacologic-Therapeutic Classification; we further classified some drug classes into broader classes (e.g., "cephalosporin antibiotics—first generation" and "cephalosporin antibiotics—second generation" were combined into "cephalosporins").[12] We included only the most common drug class allergens that comprised at least 0.5% of all reported drug allergies. *Note*: Within the EHR, the allergy module is where clinicians document both true allergies and other adverse reactions (i.e., ADRs). The reaction picklist for documenting allergies and ADRs is identical. While the field on the electronic form is called an "allergy field," this article focuses on specific ADRs rather than true allergies. Throughout this text, we focus on ADRs, and any use of the term "allergy" refers to the EHR module and common reaction picklist. Furthermore, the term "drug class allergen" refers to ADRs reported in reference to a particular drug agent.

We compared patient demographics of the overall population and those with allergies between BWH and UCH. We also examined the number of ADR records entered by health care provider role. Because BWH transitioned to a new EHR system during the study period, some ADR records were updated via a conversion process. We, therefore, used a subset of the records postconversion from August 1, 2018 to December 31, 2018 to estimate the proportions of reactions entered by different types of providers. Reported ADR prevalences were calculated as the number of patients with an active ADR to a drug class considering the total study population. We compared the proportions of the 40 most frequently reported reactions at both institutions. Reaction proportions were calculated out of the total number of reported reactions at each institution. We further examined and compared the top 10 reported coded reactions for each drug class at each institution. In all comparable analyses, we considered 1% a notable difference; thus 1% was used as the difference threshold. At each institution, because gastrointestinal (GI) reactions were documented using a group of specific reaction codes (e.g., BWH has "GI Upset," "Nausea Only," "Vomiting," "Nausea And Vomiting," and "Nausea and/or Vomiting" and UCH has "GI Reaction," "Nausea," and "Vomiting"), we merged GI reactions into a single group. We compared frequencies using a chi-square test. All reported p-values with type I error (α) of <0.05 were considered to be statistically significant. Statistical analyses were performed using Microsoft SQL Management Studio Version 18.4. This study was approved by the Mass General Brigham Human Research Committee and Colorado Multiple Institutional Review Board.

Results

General Description of the Patient Population

A total of 2,160,116 patients were included in this study, with 1,530,641 (71%) from BWH and 629,475 (29%) from UCH (►Table 1). Approximately, one-third of the populations at BWH (30%, $n = 454{,}011$) and UCH (30%, $n = 186{,}433$) had at least one EHR ADRs documented. In total, there were 705,413 active drug ADR records with 1,230,165 reactions at BWH and 223,560 ADR records with 586,750 reactions at UCH. Among patients with allergic reactions, the majority of patients at both institutions were White (76%) and female (60%).

ADR information was primarily documented by medical assistants and registered nurses with a higher proportion at UCH than at BWH (36 vs. 16% and 32 vs. 30%, respectively, $p < 0.0001$). In contrast, physicians and nurse practitioners documented allergies considerably more at BWH than at UCH (18 vs. 7% and 7 vs. 2%, respectively, $p < 0.0001$).

Most Commonly Reported Drug Class Allergens

Across both institutions, the most commonly reported drug class allergens were penicillins (14%), opioids (10%), sulfonamide antibiotics (9%), and nonsteroidal anti-inflammatory drugs (NSAIDs) (5%) (►Table 2). The frequency of the most commonly reported drug class allergens was similar at both institutions, with the exception of two classes that exhibited greater than 1% difference across sites: opioids (BWH: 10 vs. UCH: 12%) and angiotensin-converting-enzyme (ACE) inhibitors (BWH: 3 vs. UCH: 2%).

Diversity in Prevalences of Adverse Drug Reactions between Two Institutions

While BWH's reaction picklist had only 48 reactions, UCH's had 160. Of the 179 unique reactions, 29 (16%) were common to both picklists, 19 (11%) only on BWH's, and 131 (74%) only on UCH's (►Supplementary Table 1, available in the online version). ►Table 3 displays the top 40 coded reactions reported at both sites, including "other (see comments)," which indicates there was a free-text reaction documented, "unknown," and "null" (e.g., no coded reaction). The most commonly reported reactions at both institutions were similar, including "rash," "GI upset," "hives," "itching" and "anaphylaxis."

The naming and prevalences of the remaining reactions on the picklists are more diverse. For example, reactions related to "swelling" and "angioedema" were coded differently at both sites. "Swelling" was reported with a noticeable difference, 2.4% at BWH versus 3.5% at UCH. "Angioedema" was on BWH's picklist but not on UCH's, while UCH included "throat swelling," "swollen tongue," and "edema." Another example of the differences in the reactions was "myalgia," which appeared on both picklists, but "musculoskeletal pain," appeared only on BWH's.

Of the top 25 reactions, "mental status change," "musculoskeletal pain', "bronchospasm," "dystonia," "wheezing," and "renal toxicity" were only reported at BWH. In contrast, "abdominal cramping," "hallucination," "blistering," "itchy watery eyes," "confusion," and "congestion nose" were only reported at UCH. In addition, BWH's picklist included severe and rare hypersensitivity reactions, such as "acute generalized exanthematous pustulosis" and "rash with skin desquamation." Health care team members more frequently entered "other (see comments)" at BWH than at UCH (18 vs. 3%, respectively). On the contrary, UCH had considerably more "NULL" (e.g., left blank) reactions than BWH (29 vs. 12%, respectively).

Table 1 Demographics of overall patient population and patients with allergies at each institution and health care team members role who documented allergies in the EHR

		Institution		
	Total ***n*** **(%)**	**BWH** ***n*** **(%)**	**UCH** ***n*** **(%)**	
All patient demographics[e]	($n = 2,160,116$)	($n = 1,530,641$)	($n = 629,475$)	c^2
Sex				994.8
Female	1,299,274 (60)	930,421 (61)	368,853 (59)	
Male	857,389 (40)	596,878 (39)	260,511 (41)	
Race/Ethnic group				20,556.6
White	1,635,350 (76)	1,171,107 (77)	464,243 (74)	
Non-White	483,984 (24)	294,139 (23)	189,845 (26)	
Hispanic	189,582 (9)	116,990 (8)	72,592 (12)	
Black	138,460 (6)	99,460 (7)	39,000 (6)	
Asian	76,133 (4)	61,213 (4)	14,920 (2)	
Other[a,b]	79,809 (4)	16,476 (1)	63,333 (10)	
Patients with reported allergies demographics[e]	($n = 640,433$)	($n = 454,011$)	($n = 186,433$)	
Sex				3,787.1
Female	448,259 (70)	327,739 (72)	120,520 (65)	
Male	190,832 (30)	124,934 (28)	65,898 (35)	
Race/Ethnic group	0			6,798.1
White	530,420 (83)	380,545 (84)	149,875 (80)	
Non-White	99,799 (17)	58,549 (16)	41,250 (20)	
Hispanic	37,218 (6)	21,931 (5)	15,287 (8)	
Black	31,115 (5)	21,435 (5)	9,680 (5)	
Asian	14,589 (2)	11,220 (2)	3,369 (2)	
Other[a,b]	16,877 (3)	3,963 (1)	12,914	
Number reactions entered by provider role[c,e]	($n = 70,915$)	($n = 48,335$)	($n = 22,580$)	
Registered nurse	21,487 (30.3)	14,328 (29.6)	7,159 (31.7)	4,933.4
Medical assistant	16,042 (22.6)	7,828 (16.2)	8,214 (36.4)	
Physician	10,278 (14.5)	8,774 (18.2)	1,504 (6.7)	
Nurse practitioner	4,014 (5.7)	3,526 (7.3)	488 (2.2)	
Physician assistant pharmacist	1,418 (2.0) 825 (1.2)	1,148 (2.4) 436 (0.9)	270 (1.2) 389 (1.7)	
Others[d]	9,267 (13.1)	5,293 (11.0)	3,974 (17.6)	
Unknown	7,584 (10.7)	7,002 (14.5)	582 (2.6)	

Abbreviations: BWH, Brigham and Women's Hospital; EHR, electronic health record; UCH, University of Colorado Hospital.
[a]Other (BWH) includes Hawaiian, Mixed, Native American.
[b]Other (UCH) includes American Indian and Alaska Native, more than one race, Native Hawaiian and other Pacific Islander, and others.
[c]Because BWH transitioned to a new EHR system during the study period, some allergy records were updated via a conversion process. We, therefore, used a subset of the records postconversion from August 1, 2018 to December 31, 2018 to estimate the proportions of reactions entered by different types of providers.
[d]Other refers to provider roles not listed (i.e., pharmacist, pharmacy technician, resident, etc).
[e]*p*-Values comparing BWH and UCH by chi-square analysis were significant for all analyses (sex, race/ethnic group, number reactions entered by provider role, and $p < 0.001$).

Furthermore, if an institution does not have a structured entry option for a certain reaction within its picklist, the reaction must be entered as free text in the comments field. ►**Table 4** shows several examples of commonly found reactions that are available as a structured entry in one institution's picklist but not in that of the other institution's, thus requiring the use of free-text entry. Reactions that were already available as a structured entry option in an institution's picklist were recorded at a higher frequency in the EHR when compared with another institution whose picklist did

Table 2 Frequently reported drug class allergens among the total patient population at each institution

Allergen drug class[a,e]	Total patients ($n = 2,160,116$) n (%)	BWH ($n = 1,530,641$)		UCH ($n = 629,475$)		
		n (%)	Ranking	n (%)	Ranking	c^2
Penicillins	297,354 (13.8)	210,215 (13.7)	1	87,139 (13.8)	1	50,941.6
Opioids	225,116 (10.4)	147,783 (9.7)	2	77,333 (12.3)	2	22,047.3
Sulfonamides	192,994 (8.9)	135,026 (8.8)	3	57,968 (9.2)	3	30,767.5
NSAIDs[b]	102,574 (4.7)	73,596 (4.8)	4	28,978 (4.6)	4	19,408.1
Macrolides	65,792 (3.0)	49,475 (3.2)	5	16,317 (2.6)	6	16,711.0
ACE inhibitors[c]	60,734 (2.8)	48,963 (3.2)	6	11,771 (1.9)	8	22,775.5
Cephalosporins	59,875 (2.8)	43,130 (2.8)	7	16,745 (2.7)	5	11,627.0
Fluoroquinolones	49,268 (2.3)	35,338 (2.3)	8	13,930 (2.2)	7	9,302.2
Statins	42,115 (1.9)	33,448 (2.2)	9	8,667 (1.4)	10	14,581.5
Tetracyclines	34,150 (1.6)	25,115 (1.6)	10	9,035 (1.4)	9	7,571.5
Phenothiazines	18,816 (0.9)	12,680 (0.8)	11	6,136 (1.0)	11	2,275.9
Thiazide diuretics	13,406 (0.6)	10,846 (0.7)	12	2,560 (0.4)	13	5,121.4
Lincosamides	15,124 (0.7)	10,839 (0.7)	13	4,285 (0.7)	12	2,840.23
Other[d]	182,985 (8.5)	103,654 (6.8)	n/a	79,331 (12.6)	n/a	3,233.1

Abbreviations: ACE, angiotensin-converting-enzyme; BWH, Brigham and Women's Hospital; n/a, not available; NSAID, nonsteroidal anti-inflammatory drugs; UCH, University of Colorado Hospital.

[a]Reported drug allergy frequencies were calculated as the number of patients with an active allergy to the drug class considering the total study population.

[b]NSAIDs is an abbreviation for nonsteroidal anti-inflammatory drugs.

[c]ACE inhibitors is an abbreviation for angiotensin-converting enzyme inhibitors.

[d]"Other" aggregates patients with reported allergies to all other drug classes not presented.

[e]p-Values comparing BWH and UCH by chi-square analysis were significant for all allergen drug classes (penicillins, $p = 0.0341$; lincosamides, $p = 0.0281$; all other allergen drug classes, $p < 0.0001$). Note that as our dataset is very large, p-values are getting very small, even though the differences are not really significant clinically based on the percentages.

not contain a structured entry for the reaction, thus requiring free-text entry (►Table 4).

Diversity in Proportion of Adverse Drug Reactions by Drug Class between Two Institutions

Overall, the majority of reported reactions to antibiotic drug classes were potential hypersensitivity reactions (e.g., rash and hives) which appear on both institutions' picklists (►Fig. 1A). Penicillins, sulfonamides, cephalosporins, and lincosamides displayed similar reaction distribution across sites; however, rash was reported more at BWH than at UCH across all antibiotic drug classes. Musculoskeletal pain to fluoroquinolones at BWH was comparable in prevalence to myalgia to fluoroquinolones at UCH.

Reported reactions to nonantibiotics exhibited greater variability (►Fig. 1B). Rash to opioids, NSAIDs, and thiazide diuretics was reported considerably more at BWH than at UCH. While mental status change to opioids was reported at BWH, this term is not included on UCH's picklist. Instead, hallucinations to opioids were reported at UCH. The sum of "swelling" and "angioedema" reported reactions to ACE inhibitors at BWH is comparable to "swelling" at UCH, as angioedema does not exist on UCH's reaction picklist. For NSAIDs, bronchospasm and renal toxicity were among the top 10 reactions at only BWH as they do not appear on UCH's picklist, while bleeding was only reported at UCH as it is absent from BWH's picklist. For statins, both myalgia and musculoskeletal pain comprised the top 10 reactions at BWH, which were comparable in prevalence to myalgia at UCH, as their picklist does not include musculoskeletal pain. Dystonia to phenothiazines was reported considerably more at BWH than at UCH. Cough encompassed most of the reported reactions to ACE inhibitors at both BWH and UCH.

Discussion

This study presents an investigation of the diversity of drug allergies and reactions documented in the EHR across two large sites. Few previous studies have focused on reported drug allergies by patients and patient characteristics,[11] but no study to date has focused on reaction differences across institutions with the same commercial EHR vendor but different reaction picklists. We found that the top reported drug allergens were largely similar between BWH and UCH. Antibiotics, opiates, and sulfonamides continue to represent a large proportion of drug allergies across multiple institutions. On the contrary, we found greater variability in the commonly reported ADRs across the two institutions. This variation is, perhaps, a product of each institution having its own reaction picklist. Clinicians' reporting of drug allergen reactions is indeed picklist-driven and influenced by the available coded entries. The EHR design and what is available

Table 3 Top 40 reported drug allergen reactions institution wide and considering picklist reactions not shared by both institutions (bold)

Ranking	BWH ($n = 1{,}230{,}165$)		UCH ($n = 586{,}750$)	
	Reaction[a]	*n* (%)	Reaction[a]	*n* (%)[b]
1	Rash	169,288 (13.8)	Rash	77,689 (13.2)
2	Hives	108,233 (8.8)	Hives	50,434 (8.6)
3	GI upset	66,036 (5.4)	Nausea/vomiting	47,433 (8.1)
4	Nausea/vomiting	60,448 (4.9)	Itching	26,337 (4.5)
5	Itching	50,560 (4.1)	Swelling	20,345 (3.5)
6	Anaphylaxis	39,949 (3.2)	Anaphylaxis	18,435 (3.1)
7	Swelling	29,767 (2.4)	Shortness of breath	10,935 (1.9)
8	Cough	21,873 (1.8)	Diarrhea	7,540 (1.3)
9	**Angioedema**	18,816 (1.5)	Headache	6,929 (1.2)
10	**Mental status change**	17,492 (1.4)	GI reaction[c]	6,769 (1.2)
			Throat swelling	6,079 (1.0)
11	Shortness of breath	14,767 (1.2)	**Abdominal cramping**	5,972 (1.0)
12	Diarrhea	13,396 (1.1)	Cough	5,903 (1.0)
13	Headache	10,184 (0.8)	**Hallucination**	5,416 (0.9)
14	Myalgia	9,714 (0.8)	Sneezing	5,329 (0.9)
15	Sneezing	7,137 (0.6)	Dizziness	4,980 (0.8)
16	**Musculoskeletal pain**	6,262 (0.5)	**Blistering**	4,113 (0.7)
17	Palpitations	4,877 (0.4)	Anxiety	3,781 (0.6)
18	Flushing	4,812 (0.4)	**Itchy watery eyes**	3,423 (0.6)
19	**Bronchospasm**	4,726 (0.4)	Myalgia	3,217 (0.5)
20	Fever	4,191 (0.3)	**Swollen tongue**	2,421 (0.4)
21	Hypotension	3,751 (0.3)	Palpitations	2,403 (0.4)
22	Dystonia	2,991 (0.2)	Fever	2,274 (0.4)
23	Anxiety	2,968 (0.2)	**Confusion**	2,198 (0.4)
24	**Wheezing**	2,960 (0.2)	**Congestion nose**	2,114 (0.4)
25	Dizziness	2,698 (0.2)	Arrhythmia	2,089 (0.4)
26	**Renal toxicity**	2,340 (0.2)	**Agitation**	2,088 (0.4)
27	**Hepatoxicity**	2,272 (0.2)	**Edema**	2,014 (0.3)
28	Dermatitis	2,210 (0.2)	**Watering eyes**	1,644 (0.3)
29	Seizures	1,570 (0.1)	Seizures	1,514 (0.4)
30	Arrhythmia	1,174 (0.1)	**Respiratory distress**	1,453 (0.2)
31	**Maculopapular rash**	1,137 (0.09)	**Asthma**	1,429 (0.2)
32	Thrombocytopenia	741 (0.06)	Flushing	1,315 (0.2)
33	**Rigor**	685 (0.06)	**Itching of mouth**	1,261 (0.2)
34	**Erythema multiforme**	430 (0.03)	**Bleeding**	1,247 (0.2)
35	**Acute generalized exanthematous pustulosis**	422 (0.03)	**Fatigue**	1,230 (0.2)
36	Lightheadedness	414 (0.03)	**Airway obstruction**	1,212 (0.2)
37	Photosensitivity	388 (0.03)	**Chest pain**	1,135 (0.2)
38	Tinnitus	338 (0.03)	Hypotension	1,069 (0.2)
39	Anemia	330 (0.03)	**Eye swelling**	1,037 (0.2)

Table 3 (*Continued*)

Ranking	BWH ($n = 1{,}230{,}165$)		UCH ($n = 586{,}750$)	
	Reaction[a]	***n* (%)**	**Reaction**[a]	***n* (%)**[b]
40	**Fixed drug eruption**	244 (0.02)		
	Other (see comments)[d]	217,904 (17.7)	Other (see comments)[d]	19,444 (3.3)
	Unknown	171,529 (13.9)	Unknown	9,693 (1.7)
	Null	147,720 (12.0)	Null	171,871 (29.3)

Abbreviations: BWH, Brigham and Women's Hospital; GI, gastrointestinal; UCH, University of Colorado Hospital.
[a]Bold formatting denotes structured reaction terms that do appear on the other institution's reaction picklist.
[b]Reported allergic drug reaction prevalences were calculated as the number of patients with a documented reaction considering the study population with at least one reported reaction.
[c]GI is an abbreviation for gastrointestinal.
[d]"Other (see comments)" refers to other reactions where free text was entered.

in the picklist may not only influence reaction documentation but also downstream clinical decision-making and analyses of EHR ADR data for drug surveillance and research. For studies involving secondary use of EHR data, researchers should consider potential biases in clinical documentation due to EHR design when interpreting results related to reactions.

With respect to documented causative drugs, our findings are consistent with prior studies. Historically, antibiotics have accounted for a majority of documented drug allergies.[13] A previous study conducted utilizing EHR data from 1990 to 2013 showed the most frequently reported drug class allergen was penicillins, followed by sulfonamide antibiotics.[11] Our study found that this is still true today for penicillins; however, opioids replaced sulfonamides as the second most commonly reported drug class allergen at both sites. This shift may be due to higher overall opiate exposure in patients in the United States.[14] Interestingly, we determined that the frequency of documented opioid allergies was considerably higher at UCH than at BWH (11.9 vs. 9.3%, respectively), and the number of opioid prescriptions per 100 persons in Colorado (52.9) is greater than that in Massachusetts (40.1).[15] Overall, the rates of all reported drug class allergens were comparable between the two institutions. This similarity could potentially be attributed to BWH and UCH using the same commercial medication data dictionary for drug allergens (i.e., First Databank Inc.), which may prompt similar documentation patterns, enabling more accurate and feasible comparisons across sites.

Table 4 Examples of allergen drug reactions being recorded as structured entry versus free text between the two institutions[a]

	BWH ($n = 3{,}174{,}702$)	UCH ($n = 846{,}465$)
	Structured entry *n* (%)	**Free-text entry *n* (%)**
Angioedema	18,816 (0.6)	1,126 (0.1)
Mental status change	17,492 (0.6)	1,957 (0.2)
Musculoskeletal pain	6,262 (0.2)	2 (0.0002)
Bronchospasm	4,726 (0.1)	863 (0.1)
Wheezing	2,960 (0.09)	455 (0.05)
	Free-text entry *n* (%)	**Structured entry *n* (%)**
Throat swelling	11,107 (0.3)	6,079 (0.7)
Abdominal cramping/pain	7,846 (0.2)	5,972 (0.7)
Hallucination	15,756 (0.5)	5,416 (0.6)
Blistering	7,243 (0.2)	4,113 (0.4)
Itchy watery eyes	4,548 (0.1)	3,423 (0.4)

Abbreviations: BWH, Brigham and Women's Hospital; UCH, University of Colorado Hospital.
[a]"*n*" delineates the total number of instances an allergen drug reaction is mentioned, within both structured entry and free-text entry, from that specific institution.

While BWH and UCH share a common dictionary for allergen documentation, the two health care centers, despite utilizing the same EHR system, have institution-specific reaction picklists. At the time of this study, there were 48 reactions on BWH's picklist but 160 on UCH's. Perhaps due to the picklist differences, there were several notable differences in the specific coded reactions reported at the two sites. For example, swelling was more commonly reported across all the top drug classes at UCH than at BWH. The current reaction picklist at BWH had both "angioedema" and "swelling" as coded reactions, while UCH had "swelling," "throat swelling," and "swollen tongue." Thus, clinicians at BWH may differentiate between etiologies of swelling (angioedema vs. edema) when entering reaction details, whereas clinicians at UCH differentiate swelling by location (e.g., "throat swelling" and "swollen tongue"). Indeed, when comparing only the "swelling" coded reactions between BWH and UCH for ACE inhibitors, it initially appears that swelling is reported considerably more frequently at UCH for that drug class. However, after aggregating the "swelling" and "angioedema" coded reactions at BWH, the sum was comparable to "swelling" at UCH in response to ACE inhibitors.

Many reactions were entered in the allergy EHR module only as free-text comments. At BWH, 17% of reactions were entered as free text compared with only 3% at UCH. A possible reason for the higher number of free-text reactions at BWH

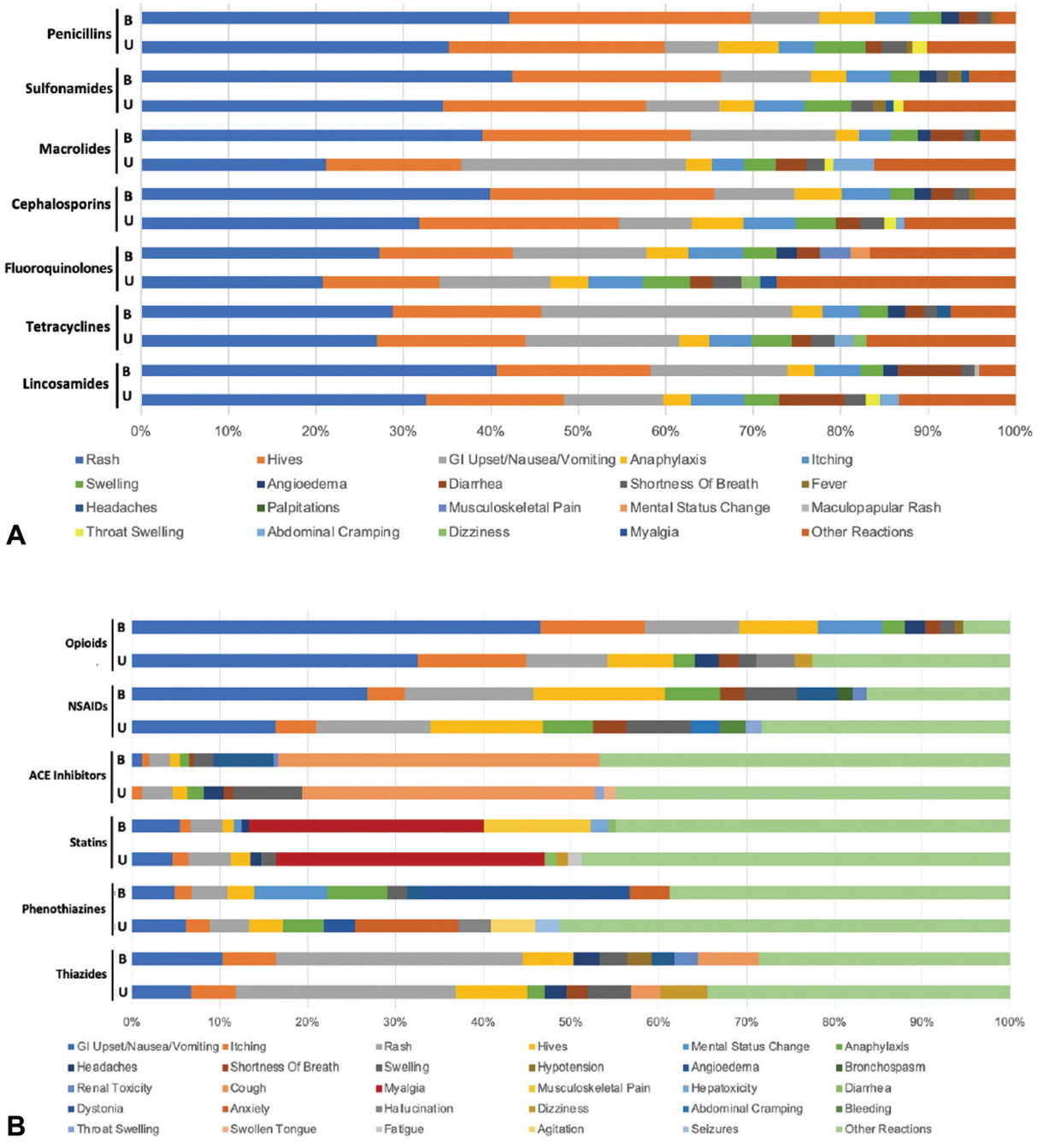

Fig. 1 (**A**) For the antibiotics listed below, we demonstrate the most common reactions at BWH (B) and UCH (U). A majority of the reported reactions to antibiotic drug classes were hypersensitivity reactions (e.g., rash and hives) which appear on both institutions' picklists. Across all antibiotic drug classes, rash was reported more at BWH than at UCH. While angioedema was reported across all drug classes at BWH, it was not reported at UCH as it is not a coded reaction term on UCH's picklist. "Other reactions" includes coded reactions that do not comprise the top 10 frequently reported reactions, excluding "null," "other: see comments," and "unknown." (**B**) For the drugs listed below, we demonstrate the most common reactions at BWH (B) and UCH (U). Rash to opioids, NSAIDs, and thiazide diuretics was reported considerably more at BWH than at UCH. While mental status change to opioids was reported at BWH, this term is not included on UCH's picklist. Instead, hallucinations to opioids were reported at UCH. The sum of "swelling" and "angioedema" reported reactions to ACE inhibitors at BWH is comparable to "swelling" at UCH, as angioedema does not exist on UCH's reaction picklist. In addition to myalgia, musculoskeletal pain was reported in response to statins at BWH but does not exist on UCH's picklist. Dystonia to phenothiazines was reported considerably more at BWH than at UCH. Other Reactions includes coded reactions that do not comprise the top 10 frequently reported reactions, excluding "null," "other: see comments," and "unknown."

may be due in part to the diversity of reactions available in the picklist (40 vs. 160 at UCH). There are certain reactions that have a structured entry option in one institution's picklist but not in that of the other institution. Because of this, clinicians in the other institution, whose picklist does not contain the structured entry option, must utilize free-text comments to record the specific reaction. We conducted free-text extraction and analysis to compare reactions' presence as structured entry versus as free text between the two institutions. This was conducted using a natural language

processing tool and a reaction lexicon consisting of 469 uniquely identified reaction concepts.[16] As shown, having a structured entry option for an ADR may promote increased documentation for that specific reaction.

Further, free-text comments are encouraged for complete documentation by the Allergy Clinical Consensus Group within BWH's health care system.[17] Along this line, a drug allergy practice parameter—developed by the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology—advises that a relevant drug-allergy history should include ample details such as the symptoms' timing, onset, duration, relationship with medication use while also discussing the history of previous reactions, and their management.[17] Documenting these details requires documentation beyond Epic's coded fields. Furthermore, it is critical to consider the balance between documenting enough details to guide proper management and doing so in a means that is easy enough for patients to fill out and without contributing to clinician burnout.

Another possible explanation for the variation is different allergy documentation policies at the two institutions. Registered nurses and physicians are the primary clinicians who enter reactions at BWH, while this role is primarily held by medical assistants or nurses at UCH. A previous study conducted at Mass General Brigham using EHR data from 2005 to 2012 found that it was most often nonallergist physicians who interfaced with the EHR allergy module and that most of the team members lack sufficient drug allergy knowledge. The allergy/ADR classification was customized from the AHFS, which was developed by pharmacists who serve as patient care providers in hospitals, health systems, ambulatory clinics, and other health care settings. This highlights a potential knowledge gap between pharmacists, who are developing the allergy/ADR classification found within the EHR module and the nonpharmacist clinicians who are most frequently interfacing with the EHRs allergy modules and documenting ADRs. Our data indicate that pharmacists only accounted for 1.5% of free-text entries at BWH and 3.1% at UCH, while the majority of free text was entered by registered nurses, physicians, and medical assistants (see ►**Appendix**). Standardization of the nomenclature and clear understanding of the classification between pharmacists and the clinicians in charge of documentation is critical. The different roles might, therefore, contribute to the differences in documentation. To improve the quality and utility of the EHR allergy module, more allergy education and training of best practices for allergy documentation is needed.[18]

Standardization of reaction picklists would substantially enhance the interoperability of EHR systems and allow providers and organizations to exchange electronic health information easily and accurately.[19] Having a common reaction terminology and picklist is important on both the patient and population level. Many patients visit more than one hospital or clinic throughout their course of care,[8] and incomplete or inaccurate carryover of reaction information may result in duplicated documentation or clinical testing.[20] On the population level, standardized reaction picklists enable accurate comparison and pooling of EHR data from multiple institutions to study true epidemiological trends, as opposed to differences observed due to picklist variation. Furthermore, reaction list standardization as a gateway for more accurate documentation is particularly relevant for drug safety surveillance, including the Food and Drug Administrations' Adverse Event Reporting System.[10]

Development of a standardized reaction picklist that captures the most frequently documented reactions would be valuable for improving ADR documentation and promoting the use of coded fields over free-text entries which will help improve the specificity of allergy alerts. Current drug-allergy alerting mechanisms in the EHR do not consider the type and severity of the reaction (e.g., mild nausea vs. anaphylaxis). Future improvement on alerting that considers these factors would allow more specificity and potentially reduce the number of alerts and clinician alert fatigue.

However, a picklist that is granular and lengthy forces clinicians to scroll, which is time-consuming. To mitigate the concerns with a lengthy picklist, we developed a dynamic, data-driven reaction picklist that automatically generates commonly reported reactions to a particular allergen—based on statistical association methods (e.g., support, lift, derived term frequency inverse document frequency).[16] Thus, optimizing the user interface of the ADR field, together with the picklist, could facilitate the accuracy of ADR documentation. Multiple factors including the granularity and length of the picklist, as well as the coded reactions available, impact the accuracy of documentation. Future research could utilize natural language processing to compare notes and laboratory data (i.e., renal function and liver function) within the EHR with the coded ADR list to detect discrepancies and prompt clinicians to reconcile such discrepancies and thus improve the accuracy of ADR documentation.

Although this study highlighted the diversity of reactions documented in EHRs that utilize institution-specific picklists, there are several limitations worth noting. First, many different types of ADRs are documented in the EHR, such as common side effects (e.g., diarrhea), intolerances (e.g., GI upset), and immune-mediated hypersensitivities (e.g., anaphylaxis). Although it is possible to specify the "reaction type" in the EHR, this field is rarely used by clinicians. Even when a documented reaction is potentially immune mediated, it is rarely confirmed with specialist assessment or diagnostic testing. Thus, the EHR allergy module houses a myriad of reactions that may not be "true" allergies. Furthermore, the quality of documentation is reliant on the knowledge of the person entering the data.[17] Prior studies evaluating the accuracy and effectiveness of ADR documentation have identified discrepancies in ADR documentation within hospital systems and the process of transferring ADR information into the EHR.[21] Additional studies have demonstrated widespread under-reporting of ADRs including serious or severe ADRs.[22]

Thus, it is important to consider the accuracy of the EHR allergy records and the distinction between true allergies versus ADRs. This discussion raises the question about

whether ADRs should be documented within allergy fields and how to best utilize the module to differentiate among the entries. One possible solution is to promote and train clinicians documenting allergies, ADRs and other adverse reactions to utilize the "type" field within the allergy module. Currently, four types of reactions (allergy, intolerance, contraindication, unknown) are available and can help differentiate from true allergies.

These data additionally include just two large academic health care centers that are not representative of the broader patient population. Future studies of reaction picklists across more academic and community hospitals are needed to confirm these initial observations.

Conclusion

Even when using the same commercial EHR system, hospitals and health care systems often adopt institution-specific allergy reaction picklists. The availability and granularity of the reactions in the picklist likely influence ADR documentation and contribute to the variations of frequencies and proportions of reported reactions across EHR systems. Different picklists make it difficult to share records or conduct comparisons across multiple institutions and, hence, affect downstream analyses of EHR data. Future work must focus on methods to standardize reaction picklists to improve the accuracy and completeness of ADR documentation as it relates to clinical care and patient safety. Furthermore, it is critical to develop methods to improve documentation without contributing to clinician burnout.

Clinical Relevance Statement

Accurate documentation of adverse reactions to medications, foods, and other substances is critical to ensure quality and safety of care. Differences in coverage and granularity of reaction picklists impact how health care providers document ADRs in the EHR and may contribute to variations in reported ADRs across health care systems. Standardized reaction picklists may facilitate more efficient sharing and comparison of allergy and ADR information across sites.

Multiple Choice Questions

1. Which of the following describes a benefit of standardized reaction picklists compared with proprietary picklists?
   a. Standardized picklists increase the specificity of reaction documentation.
   b. Standardized picklists increase interoperability between EHRs.
   c. Standardized picklists are shorter.
   d. Standardized picklists are better at capturing reaction severity and type.

   Correct Answer: The correct answer is option b. Standardized coded reaction lists are not necessarily more or less specific than existing coded reaction lists, which may be more or less specific/granular by location. Standardized picklists do increase interoperability and facilitate sharing, transfer, and comparison of allergy documentation across different sites. Because proprietary picklists currently vary greatly in length, a standardized picklist may be longer or shorter depending on the location. A standardized reaction picklist would only include reaction names; reaction severity and type (e.g., allergy or intolerance) would still need to be documented separately.

2. Which of the following describes a difference between coded reactions compared with reactions documented in free text?
   a. Coded reactions are more accurate.
   b. Coded reactions are automatically visible in the EHR, while free-text reactions are not.
   c. Coded reactions are easier to use in downstream applications.
   d. Coded reactions can be entered by clinicians of all roles, while only physicians can add free-text comments.

   Correct Answer: The correct answer is option c. Coded reactions are not necessarily more or less accurate than reactions documented in free text. The visibility of coded reactions and reactions documented in free-text comments depends on the EHR system in use and is not inherent to the method of documentation. Coded reactions can more easily be used in downstream applications such as allergy alerts and other automated clinical decision support tools in the EHR. Whether or not clinicians of different roles (e.g., nurses, medical assistants, or physicians) can enter reaction information is determined by institution-specific policies and is not inherent to the method of documentation.

Author Contributions

S.Y. conducted study design, data acquisition, analysis, and interpretation, drafted the article, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. S.N.S. contributed to data interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. S.V.B. contributed to data analysis and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. C.A.O. contributed to data analysis and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. K.G.B. contributed to study design, data analysis, and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. F.G. contributed to study design, data acquisition, analysis, and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or

integrity. D.L.S. contributed to data analysis and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. P.G.W. contributed to data interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. C.M.M. contributed to data analysis, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. D.W.B. contributed to data interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity. L.Z. conducted study conception and design, contributed to data analysis and interpretation, reviewed the manuscript, gave final approval of the manuscript, and agrees to be accountable for all aspects of the work related to its accuracy or integrity.

Protection of Human and Animal Subjects

This study was approved by the Mass General Brigham Human Research Committee and the Colorado Multiple Institutional Review Board.

Funding

This research was supported with funding from the U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality, grant R01HS025375.

Conflict of Interest

None declared.

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