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Drug Allergies Documented in Electronic Health Records of a Large Healthcare System

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Abstract

Background: The prevalence of drug allergies documented in electronic health records (EHRs) of large patient populations is understudied.

Objective: We aimed to describe the prevalence of common drug allergies and patient characteristics documented in EHRs of a large healthcare network over the last two decades.

Methods: Drug allergy data were obtained from EHRs of patients who visited two large tertiary care hospitals in Boston from 1990 to 2013. Prevalence of each drug and drug class was calculated and compared by sex and race/ethnicity. The number of allergies per patient was calculated and the frequency of patients having 1, 2, 3, or 10+ drug allergies was reported. We also conducted a trend analysis by comparing the proportion of each allergy to the total number of drug allergies over time.

Results: Among 1,766,328 patients, 35.4% of patients had at least one reported drug allergy with an average of 1.95 drug allergies per patient. The most commonly reported drug allergies in this population were to penicillins (12.8%), sulfonamide antibiotics (7.4%), opiates (6.8%), and non-steroidal anti-inflammatory drugs (NSAIDs) (3.5%). The relative proportion of allergies to angiotensin-converting enzyme (ACE) inhibitors and HMG CoA reductase inhibitors (statins) more than doubled since early 2000s. Drug allergies were most

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prevalent among females and white patients except for NSAIDs, ACE inhibitors, and Thiazide diuretics, which were more prevalent in black patients.

Conclusion: Females and white patients may be more likely to experience a reaction from common medications. An increase in reported allergies to ACE inhibitors and statins is noteworthy.

Key words: drug allergy, adverse drug event, drug hypersensitivity, electronic health records, safety

Abbreviations:

ADE – adverse drug event

EHR – electronic health record

NSAID – non-steroidal anti-inflammatory drug

BWH – Brigham and Women's Hospital

MGH – Massachusetts General Hospital

PEAR – Partners' Enterprise-wide Allergy Repository

AHFS – American Hospital Formulary Service

ACE – angiotensin-converting enzyme

SSRI – selective serotonin reuptake inhibitor

MDIS – multiple drug intolerance syndrome

Introduction

Adverse drug events (ADEs) are common in clinical practice, affecting 15-25% of patients (1). Most allergy-related ADEs are unpredictable given what is known today and are immunologically mediated (2). Allergic drug reactions can range from mild (e.g., itching) to life-threatening (e.g., anaphylaxis). They account for about 5-10% of all ADEs (3).

Most electronic health record (EHR) systems have an "Allergy" module (or list), where clinicians can document a patient's "allergies" reported by the patient or observed by the care provider. Although the "Allergy" module often contains other types of ADEs, such as drug intolerance, drug toxicity, drug idiosyncrasy and pseudoallergic reactions, it remains a rich and valuable data source for studying allergies. However, the use of large data sets from EHRs to describe trends across a broad spectrum of reported drug allergies is uncommon. Most previous epidemiological studies of drug allergies either relied on self-reported surveys or focused on a particular drug or drug class (4, 5). The most commonly studied drug allergens include antibiotics, such as penicillins, cephalosporins, and sulfonamides, and non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin (2, 6).

In addition, demographics and clinical characteristics of patients across all types of drug allergies have not been well documented in the US. Few studies have explored the relationship between racial groups or sex on documented allergy rates. Also, only a few studies have described the characteristics of patients with drug allergies in a given large population (7, 8). For example, while Macy and Ho studied 478,283 patients with at least one allergy in EHRs, other studies included smaller populations (5, 7) or described a population with documented anaphylaxis only (9-12). Further, the proportional changes of different drug allergies over time have not been well studied.

In this study, we aimed to describe the prevalence of various drug allergies documented in EHRs in a large patient population across a large healthcare delivery network over the past two decades. In particular, we described and compared each drug allergy by sex and race/ethnicity. We also conducted a trend analysis by comparing the percentages of commonly reported drug allergies by year.

Methods

Settings and Data Collection

Drug allergy data were collected from the Partners HealthCare System, which is an integrated healthcare delivery network in the Greater Boston area funded by the Brigham and Women's Hospital (BWH) and the Massachusetts General Hospital (MGH), and is composed by multiple community and specialty hospitals as well as community health centers. At Partners, patients' "allergy" information is documented by healthcare providers via the Allergy module of EHR systems used at each affiliated institution, and then integrated and stored in the Partners' Enterprise-wide Allergy Repository (PEAR) (13). Each patient has a longitudinal, common allergy record in their EHRs shared across the entire healthcare network. Healthcare providers are also able to deactivate (remove) an allergy from a patient's allergy list if the patient did not experience an adverse reaction during allergy work-up or accidental re-exposure. Our allergy data are similar to previous studies that also used allergy entries in EHRs, in that many "allergies" documented in patient's EHR allergy list are not immunologically mediated (7, 8) or confirmed by a diagnostic test; we therefore use the term "reported allergies" in this paper.

In this study, patients who visited BWH and/or MGH between 1990 and 2013 were included and their drug allergy information (also including unknown allergies and no-known allergies) was extracted from PEAR. A patient's drug allergy information includes a list of "allergens" (i.e. culprit drug), allergy status (active or deactivated), date/time reported or updated, and adverse reaction(s). Re-exposure to the same drug or drug class was not included in this analysis. We also collected all patients' demographic information, including sex and race/ethnicity, when available in the EHR systems. Contrast media was not included in this analysis, as they represent a distinct group of drugs used for procedures or imaging studies.

While the majority (94%) of PEAR allergy records were entered and stored in a coded format, 6% were entered using free-text (i.e., non-coded data). For free-text entries, we used natural language processing techniques in a semi-automated manner to normalize and "map" these entries to the coded form (14). We then manually reviewed all of the mappings.

Data Analysis

In EHRs, the documented drug allergen can be a specific drug or a drug class. We classified each allergen entry into a corresponding drug class using the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification for reporting prevalence (Tables 1-2), and then further manually classified some drug classes into broader ones (for example, 'cephalosporin antibiotics – 1st generation' and 'cephalosporin antibiotics – 2nd generation' into cephalosporins) (15). Under each class, we analyzed and presented the most common drug allergies.

Reported drug allergy prevalence rates were calculated as the number of patients with an active allergy to a drug or drug class divided by the total number of the patient population. We then calculated and compared the prevalence rates by sex (i.e., male and female) and racial/ethnic group (i.e., white, black, Asian, Hispanic, and other). We calculated the number of drug allergies documented per patient for the total population and reported the frequency of patients having 1, 2, 3... or 10+ drug allergies. The average number of reported drug allergies per patient was compared by sex and race/ethnicity.

The percentage of each suspected drug allergen class was calculated for each year by dividing the number of allergies documented for that drug class by the total number of documented drug allergies in the same year. We then conducted a trend analysis by comparing these percentages over the past two decades. Drug classes in each of four broader groups (antibiotics, analgesics, antihypertensives, and others) were presented together on separate time line graphs for comparison.

Statistical analyses were conducted using SAS statistical software (version 9.3; SAS Institute, Inc Cary, NC). Chi-square tests were used to compare prevalence rates across patient groups, t-tests were used to compare means (e.g., number of reported drug allergies across patient groups), and $p < .05$ was considered statistically significant. This study was approved by the Partners Institutional Review Board.

Results

General Description of the Patient Population

Among the total of 1,766,328 patients included in this study, 1,023,824 (58.0%) were female, 742,374 (42.0%) were male, and 130 patients' sex information was missing. The majority of the patients were white (70.3%, $n=1,241,012$), followed by Hispanic (8.1%, $n=143,335$), black (7.1%, $n=125,798$), Asian (4.1%, $n=71,860$), and other (1.8%, $n=32,218$). There were 152,105 (8.6%) patients whose race/ethnicity information was unknown. In total, there were 1,222,164 active drug allergy records. More than one-third of the population (35.5%, $n=626,871$) had at least one drug allergy documented.

Prevalence Rates of Drug Allergies

Table 1 shows the prevalence of the top 14 reported drug allergen classes. Individual drugs that made up 0.5% of all reported drug allergies were included in the table. Among the entire patient population ($n=1,766,328$), the most commonly reported allergens were penicillins (12.8%), sulfonamide antibiotics (7.4%) and opiates (6.8%). Other frequently reported drug allergies included NSAIDs (3.5%), macrolides (2.6%), angiotensin-converting enzyme (ACE) Inhibitors (2.0%), and cephalosporins (1.7%). The most commonly reported individual drugs were codeine (3.1%), amoxicillin (2.1%), and aspirin (1.6%). Although selective serotonin re-uptake inhibitor (SSRI) antidepressants were a commonly reported drug class, no individual SSRI was documented in more than 0.5% of all drug allergy records.

Drug Allergy Prevalence Rates by Sex

Almost all of the reported drug allergy classes and individual drug allergies were significantly more prevalent among women (Table 1). Antibiotic drug classes were among the most prevalent reported drug allergies, including penicillins (15.2% in women vs. 9.5% in men, $p < .01$), sulfonamide antibiotics (10.4% vs. 3.2%, $p < .01$), macrolides (3.7% vs. 1.2%,

$p < .01$), cephalosporins (2.2% vs. 1.0%, $p < .01$), fluoroquinolones (1.7% vs. 0.7%, $p < .01$), and tetracyclines (1.6% vs. 0.5%, $p < .01$).

Reported NSAID allergies were more prevalent in women (4.4% vs. 2.3%, $p < .01$). Aspirin, the most commonly reported NSAID allergy in the population was found in 2.0% of women and 1.1% of men ($p < .01$). Ibuprofen was considerably more prevalent in women (0.8% vs. 0.5%, $p < .01$).

The overall prevalence rates of reported statin allergies were comparable between women and men (1.5% vs. 1.5%, $p = 0.30$), as were the rates for reported atorvastatin allergy (0.6% vs. 0.7%, $p = 0.10$). However, reported simvastatin allergy was significantly more prevalent among women (0.52% vs. 0.48%, $p < .01$). No reported allergies to any drug or drug class were significantly more prevalent in men compared to women.

Prevalence Rates by Race/Ethnicity

White patients had significantly more reported drug allergies than any other racial group (Table 2). Penicillins (14.3% in whites vs. 7.9% in non-whites, $p < .01$), sulfonamide antibiotics (8.7% vs. 2.9%, $p < .01$), and opiates (8.1% vs. 2.9%, $p < .01$) were among the most prevalent reported drug classes in whites. Codeine (3.7% vs. 1.1%, $p < .01$) was the most prevalent reported individual drug in whites, followed by amoxicillin (2.4% vs. 1.0%, $p < .01$), and erythromycin (1.8% vs. 0.5%, $p < .01$).

Some reported allergens were significantly more prevalent in black patients. These included NSAIDs (4.0% in blacks vs. 3.5% in non-blacks, $p < .01$), ACE inhibitors (2.6% vs. 2.1%, $p < .01$), and thiazide diuretics (0.54% vs. 0.45%, $p < .01$). Commonly reported individual drugs within these classes were also more prevalent in black patients, including aspirin (2.3% vs. 1.6%, $p < .01$), ibuprofen (0.9% vs. 0.7%, $p < .01$), lisinopril (1.5% vs. 1.23%, $p < .01$), and hydrochlorothiazide (0.5% vs. 0.4%, $p < .01$). Reported naproxen allergy, however, was significantly more prevalent in white patients (0.4% in whites vs. 0.3% in non-whites, $p < .01$). No reported drug class allergies or individual drug allergies were significantly more prevalent in any other race/ethnicity (i.e., Hispanic, Asian, or other).

Number of Drug Allergies per Patient

Among the 626,871 patients who had at least one drug allergy documented in their EHRs, 57.4% had only one drug allergy, 21.8% had two, and 9.5% had three (Table 3). On average, patients with at least one allergy had 1.95 drug allergies documented. Female and white patients had significantly higher numbers of allergies compared to other groups. On average, female patients had 2.09 drug allergies documented compared to 1.63 drug allergies documented in male patients ($p < .01$). White patients had 2.00 drug allergies documented on average (vs. 1.71 in non-whites, $p < .01$), 1.83 in blacks (vs. 1.97 in non-blacks, $p < .01$), 1.64 in Hispanics (vs. 1.98 in non-Hispanics, $p < .01$), 1.59 in Asians (vs. 1.97 in non-Asians, $p < .01$), and 1.67 in others (vs. 1.96 in non-others, $p < .01$).

Percentages of Drug Allergen Classes Reported Each Year

In recent years, reported penicillin allergies have declined but still remained the most commonly reported antibiotic allergy (Figure 1A). Penicillins still made up 16% of reported drug allergies in 2013. The prevalence of sulfonamide antibiotic allergies also declined but this remained the second most commonly reported antibiotic allergy (8% in 2013). After an initial increase (3.2% in 1992 and 3.8% in 1993 for macrolides and 2.2% in 1992 and 2.7% in 1993 for cephalosporins), the prevalence rates for other antibiotics remained fairly constant.

The prevalence of reported tetracyclines, fluoroquinolones, and clindamycin allergies remained constant over the study period and are of the least reported antibiotic allergies.

Until 1993, NSAIDs were the more commonly reported analgesic allergy (Figure 1B). Recently however, opiates have become the more frequently reported allergy. Opiates have made up 10 – 15% of reported drug allergies in the last 13 years, and NSAIDs have only made up 5 – 8%.

Thiazides remained fairly constant throughout the years, and make up one of the lowest reported drug classes out of the most frequent (<1% every year) (Figure 1C). In contrast, ACE inhibitors have been steadily increasing starting from 2000 (1.4% in 2000 and 3.6% in 2013).

Phenothiazines and SSRI prevalence rates have been relatively constant (phenothiazines with a slight decrease and SSRIs with a slight increase) (Figure 1D). Statins however, have been reported more frequently over the years and have doubled since 2003 (1.5% in 2003 and 3.4% in 2013).

Discussion

This study represents one of the largest EHR-based reports of drug allergy prevalence and associated patient characteristics in a large health system (7). We found that antibiotics continue to represent a large proportion of the medications involved. Also, females and white patients had more drug allergies documented than other patients.

Our findings with respect to the medications involved are consistent with prior studies. A study of self-reported drug allergy surveys in an adult Portuguese population found that the most frequently reported drugs were penicillins or other beta-lactams, followed by aspirin or other NSAIDs (5). Penicillins were also the most commonly reported drug class allergy in our results. Cephalosporins and NSAIDs were among our top drug classes. Amoxicillin was the most common penicillin drug allergy, which is consistent with other reports (16).

Antibiotics have been reported as the majority of drug allergies documented, and we found that antibiotics accounted for 7 out of the top 14 drug classes (8). In a study of reported antibiotic allergy incidence and prevalence using outpatient medical records, sulfonamide antibiotics were found to be the most prevalent antibiotic allergy among both men and women, followed by penicillins (8). Our results however showed the reverse; penicillins were the most commonly reported antibiotic allergy followed by sulfonamide antibiotics. Our prevalence rates for both penicillins and sulfonamide antibiotics were substantially higher than reported in the prior antibiotic allergy study (8). Past reports have found that ciprofloxacin was the most prevalent fluoroquinolone antibiotic allergy, which was consistent with our findings (4). Our higher observed reported antibiotic allergy rates may be due to higher overall antibiotic exposure in tertiary care hospitals (8, 17).

NSAIDs were the 4th most common drug allergy reported in our data, with aspirin being the most common individual drug reported in the class. Some studies have also found that aspirin was the most common NSAID allergy, and others have found it to be naproxen (5, 18). In a 10-month prospective cohort study on adverse cutaneous drug reactions (ACDRs) in hospitalized patients, naproxen was found to be the 4th drug most frequently associated with ACDRs (18). In our data, naproxen (0.4%) was much less commonly reported compared to aspirin (1.6%). Ibuprofen was found to be the most common NSAID involved

with drug hypersensitivity reactions (DHRs) in a 6-year study of a large population, but our data showed reported ibuprofen allergies (0.7%) to be less common than reported aspirin allergies (19).

Two classes of antihypertensives were frequently documented as drug allergies, ACE inhibitors and thiazide diuretics. Antihypertensives have been reported to be frequent causes of hospitalizations due to adverse reactions (20). Common adverse reactions include bradykinin-induced cough for ACE inhibitors and electrolyte imbalances (e.g. hyponatremia and hypokalemia) for thiazide diuretics (21, 22). Although beta-blockers and calcium channel blockers can also cause allergies and ADRs, we did not find these drug classes to be as common as ACE inhibitors and thiazide diuretics in our study (20).

Like many other studies, we found that reported drug allergies were significantly more prevalent among females (5, 7, 8, 23). Females were also found to have more drug allergies documented per patient than men on average. All drug classes and individual drugs were more commonly reported in women with the exception of statins, which were comparable in both genders. This exception may be because males have been more likely to be prescribed a statin compared to females, shown by studies of statin prescribing patterns in recent years (24, 25). An increased usage of statins could have reflected a higher prevalence of reported statin allergies. Also, since many patients may be intolerant to statins due to their common non immune-mediated adverse events (e.g. myalgias and myositis), many of these reported allergies are not 'true' immune-mediated reactions (26).

Our data showed that most of the top drugs documented were more prevalent in white patients compared to other races/ethnicities. White patients also had more drug allergies documented per patient than any other race/ethnicity. NSAIDs, ACE inhibitors, and thiazide diuretics, however, were significantly more prevalent in black patients. The high ACE inhibitor prevalence may be due to the higher risk and prevalence of ACE inhibitor-induced angioedema in black patients (27). The racial difference in the reported drug allergies may be caused by provider documentation bias as reported in other studies (28-30).

Over one-third of the population had at least one reported drug allergy. This is a higher prevalence rate compared to other studies that reported 20-25% (7, 31). More than half of the patients with reported drug allergies had only one drug allergy. However, we found a much higher number of patients with multiple drug allergies compared to literature (7). Macy et al. reported that multiple drug intolerance syndrome (MDIS; commonly defined as reactions to three or more chemically unrelated medications) was present in 2.1% of their patient population at Kaiser Permanente (7, 32, 33). We found that 7.4% of our total population had MDIS. This may be attributed to our population being an urban tertiary care referral population that may be sicker (and therefore have more medication exposure) than the Kaiser Permanente population, since the largest risk factor for reported drug allergy is drug exposure.

Time prevalence trends showed that reported penicillin and sulfonamide antibiotic allergies declined over time, but still remained the most commonly reported allergies of all antibiotic classes. Macy et al. reported temporal trends of antibiotic usage in the Kaiser Permanente San Diego area, which showed a decline in penicillin usage from 1995 – 2007 (8). Prevalence of reported opiate allergies has been consistently high compared to reported NSAID allergies since about 1995. This is consistent with a reported increase in opioid prescribing and use in past years (34, 35). While thiazide diuretics remained relatively stable

throughout the years, reported ACE inhibitor allergies have more than doubled since 2000. This may be because of an increase in usage due to expansion of the drug group's indications (36). Reported statin allergies have also doubled, since 2003. Studies on UK primary care databases showed a steady increase in statin prescriptions due to statins being proven to be the most effective treatment for hyperlipidemia (26, 37). These consistencies between reported drug usage and reported drug allergies show that increased usage may be a risk factor for drug allergies.

It is worth mentioning that systems such as Vigibase (the World Health Organization Global Individual Case Safety Reports database) collect spontaneous ADE reports (38). Compared to the allergy entries in EHRs, the type and severity of reported adverse drug reactions and reported pharmacological groups may be different. For example, the majority of ADEs in Vigibase were reported for nervous system medications, followed by cardiovascular medicines (38).

A limitation to this study is that patients tend to report and clinicians tend to document other types of adverse drug reactions in the EHR allergy module including common side effects (e.g. diarrhea), intolerances (e.g., gastro-intestinal upset) and immune-mediated hypersensitivities (e.g., anaphylaxis). Whether the reaction was immune-mediated or whether a diagnostic test was performed was often not documented. It is likely that patients may report drug allergies that have never been confirmed and may not be 'true' allergies. Further, the quality of the allergy entries in EHRs often depends on clinicians' expertise and interpretation, which may result in incongruent or unspecific data. Additionally, in this study, prevalence rates were calculated as the number of patients with a reported allergy divided by the total number of the patient population; however, it would also be important to consider patients' drug exposure by using prescription data. This would allow us to compare results against prescriptions as correlations between gender, race/ethnicity, time trends and drug allergy reports can probably be explained by different patterns in prescription and drug intake in different subpopulations. This represents an important area of future research. Another limitation is that data were only taken from two institutions in the Boston area, with urban populations that may have more comorbid patients. These patients may not be representative of a broader patient population.

In summary, we found that female and white patients were at a higher risk of experiencing an adverse drug event for most of the commonly reported drugs found in our patient population. The increasing number of reported drug allergies to some of these commonly reported drugs may be due to an increased exposure and usage over time. Clinicians should be wary of this, especially in female and white patients, as many of these commonly reported drugs are the foundation of modern-day medical therapies. In addition, geographical, environmental and patient population characteristics may contribute to these differences. Future studies should consider these factors in their analysis.

Author Contributions

LZ collected the data, and designed and supervised the study. ND performed the data analysis. ND and LZ analyzed and interpreted the findings and drafted the initial manuscript. KB, FG, MT, SS, and DB assisted in the interpretation of findings and critical review of the manuscript. All of the authors approved the final manuscript.

Conflict of Interest

All of the authors declare no conflicts of interest.

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Table 1. Drug allergy prevalence among the entire patient population by drug class and patient's sex

Drug Class and Allergen	Total (n = 1,766,328)* ^π n (%)	Male (n = 742,374) n (%)	Female (n = 1,023,824) n (%) [†]
Penicillins	225,957 (12.8)	70,160 (9.5)	155,797 (15.2)
Amoxicillin	36,948 (2.1)	10,998 (1.5)	25,950 (2.5)
Sulfonamide Antibiotic	130,029 (7.4)	23,999 (3.2)	106,030 (10.4)
Trimethoprim/Sulfamethoxazole	21,682 (1.2)	4,224 (0.6)	17,458 (1.7)
Opiates	119,992 (6.8)	25,595 (3.5)	94,389 (9.2)
Codeine	54,609 (3.1)	9,667 (1.3)	44,942 (4.4)
Morphine	22,908 (1.3)	5,397 (0.7)	17,511 (1.7)
Oxycodone/Acetaminophen	18,678 (1.1)	3,791 (0.5)	14,887 (1.5)
Meperidine HCl	12,938 (0.7)	2,478 (0.3)	10,460 (1.0)
Oxycodone	10,176 (0.6)	2,162 (0.3)	8,014 (0.8)
Hydrocodone/Acetaminophen	7,021 (0.4)	1,494 (0.2)	5,527 (0.5)
NSAIDs	62,145 (3.5)	17,317 (2.3)	44,828 (4.4)
Aspirin	28,738 (1.6)	8,290 (1.1)	20,448 (2.0)
Ibuprofen	11,927 (0.7)	3,374 (0.5)	8,553 (0.8)
Naproxen	6,447 (0.4)	1,526 (0.2)	4,921 (0.5)
Macrolides	46,269 (2.6)	8,785 (1.2)	37,484 (3.7)
Erythromycin	25,905 (1.5)	4,547 (0.6)	21,358 (2.1)
Azithromycin	7,072 (0.4)	1,672 (0.2)	5,400 (0.5)
ACE Inhibitors	35,904 (2.0)	14,290 (1.9)	21,614 (2.1)
Lisinopril	21,794 (1.2)	8,345 (1.1)	13,449 (1.3)
Cephalosporins	30,272 (1.7)	7,812 (1.1)	22,460 (2.2)
Cephalexin	10,232 (0.6)	2,524 (0.3)	7,708 (0.8)
HMG CoA Reductase Inhibitors (Statins)	26,274 (1.5)	10,962 (1.5)	15,312 (1.5)
Atorvastatin	11,400 (0.7)	4,878 (0.7)	6,522 (0.6)

Simvastatin	8,912 (0.5)	3,550 (0.48) ^μ	5,362 (0.52) ^μ
Fluoroquinolones	22,417 (1.3)	5,156 (0.7)	17,261 (1.7)
Ciprofloxacin	12,080 (0.7)	2,709 (0.4)	9,371 (0.9)
Levofloxacin	7,942 (0.5)	1,927 (0.3)	6,015 (0.6)
Tetracyclines	20,454 (1.2)	4,016 (0.5)	16,438 (1.6)
Tetracycline	7,237 (0.4)	1,483 (0.2)	5,754 (0.6)
Selective Serotonin Reuptake Inhibitors (SSRIs)	10,526 (0.6)	2,728 (0.4)	7,798 (0.8)
Phenothiazines	9,129 (0.5)	1,450 (0.2)	7,679 (0.8)
Prochlorperazine	8,974 (0.5)	1,438 (0.2)	7,536 (0.7)
Thiazide Diuretics	7,726 (0.4)	2,527 (0.3)	5,199 (0.5)
Hydrochlorothiazide	7,309 (0.4)	2,384 (0.3)	4,925 (0.5)
Lincosamide Antibiotics	6,298 (0.4)	1,276 (0.2)	5,022 (0.5)
Clindamycin	6,216 (0.4)	1,254 (0.2)	4,962 (0.5)
Other	198,142 (11.2)	59,158 (8.0)	138,984 (13.6)
Acetaminophen	7,554 (0.4)	1,894 (0.3)	5,660 (0.6)

*: sex information was missing for 130 patients and not included in this table.

π: number of allergies to a specific drug class may be less than the total number of individual drugs within the class due to patients having more than one documented drug allergy.

£ : all drug class and individual drug allergies were significantly more prevalent among women, except for HMG CoA Reductase Inhibitors (statins) (p = 0.30) and Atorvastatin (p = 0.10).

μ: percentages for Simvastatin were presented as hundredths to show significant difference between genders.

Table 2. Drug allergy prevalence among the entire patient population by drug class and patient's race

Drug Class and Allergen	White (n = 1,241,012) n (%) ^β	Black (n = 125,798) n (%)	Hispanic (n = 143,335) n (%)	Asian (n = 71,860) n (%)	Other (n = 32,218) n (%)
Penicillins	177,216 (14.3)	10,516 (8.4)	10,735 (7.5)	5,468 (7.6)	2,864 (8.9)
Amoxicillin	30,156 (2.4)	1,132 (0.9)	1,433 (1.0)	905 (1.3)	389 (1.2)
Sulfonamide Antibiotic	108,464 (8.7)	4,163 (3.3)	2,895 (2.0)	2,486 (3.5)	1,185 (3.7)
Trimethoprim/Sulfamethoxazole	17,599 (1.4)	1,050 (0.8)	874 (0.6)	373 (0.5)	203 (0.6)
Opiates	99,901 (8.1)	5,082 (4.0)	3,540 (2.5)	1,243 (1.7)	1,047 (3.3)
Codeine	45,980 (3.7)	2,024 (1.6)	1,171 (0.8)	473 (0.7)	459 (1.4)
Morphine	19,261 (1.6)	906 (0.7)	675 (0.5)	183 (0.3)	208 (0.7)
Oxycodone/Acetaminophen	15,239 (1.2)	1,033 (0.8)	669 (0.5)	215 (0.3)	180 (0.6)
Meperidine HCl	11,233 (0.9)	293 (0.2)	186 (0.1)	95 (0.1)	79 (0.3)
Oxycodone	8,171 (0.7)	682 (0.5)	456 (0.3)	156 (0.2)	81 (0.3)
Hydrocodone/Acetaminophen	5,911 (0.5)	265 (0.2)	268 (0.2)	79 (0.1)	63 (0.2)
NSAIDs	44,552 (3.6)	4,969 (4.0)	4,859 (3.4)	1,954 (2.7)	1,005 (3.1)
Aspirin	19,069 (1.5)	2,852 (2.3)	2,833 (2.0)	1,014 (1.4)	596 (1.9)
Ibuprofen	8,255 (0.7)	1,066 (0.9)	1,038 (0.7)	441 (0.6)	205 (0.6)
Naproxen	5,036 (0.4)	362 (0.3)	354 (0.3)	163 (0.2)	54 (0.2)
Macrolides	39,340 (3.2)	1,434 (1.1)	845 (0.6)	668 (0.9)	373 (1.2)
Erythromycin	21,981 (1.8)	852 (0.7)	394 (0.3)	349 (0.5)	216 (0.7)
Azithromycin	5,925 (0.5)	224 (0.2)	222 (0.2)	140 (0.2)	55 (0.2)
ACE Inhibitors	27,302 (2.2)	3,207 (2.6)	1,935 (1.4)	1,128 (1.6)	373 (1.2)
Lisinopril	16,650 (1.3)	1,919 (1.5)	1,166 (0.8)	662 (0.9)	214 (0.7)
Cephalosporins	25,564 (2.1)	805 (0.6)	745 (0.5)	546 (0.8)	277 (0.9)
Cephalexin	8,710 (0.7)	264 (0.2)	222 (0.2)	152 (0.2)	81 (0.3)
HMG CoA Reductase Inhibitors (Statins)	22,090 (1.8)	1,157 (0.9)	817 (0.6)	395 (0.6)	209 (0.7)
Atorvastatin	9,645 (0.8)	507 (0.4)	306 (0.2)	175 (0.2)	91 (0.3)
Simvastatin	7,432 (0.6)	445 (0.4)	348 (0.2)	156 (0.2)	75 (0.2)
Fluoroquinolones	19,111 (1.5)	566 (0.5)	602 (0.4)	359 (0.5)	170 (0.5)
Ciprofloxacin	10,236 (0.8)	304 (0.2)	342 (0.2)	201 (0.3)	95 (0.3)
Levofloxacin	6,798 (0.6)	216 (0.2)	206 (0.1)	113 (0.2)	63 (0.2)
Tetracyclines	16,877 (1.4)	868 (0.7)	501 (0.4)	438 (0.6)	173 (0.5)
Tetracycline	6,031 (0.5)	276 (0.2)	133 (0.1)	118 (0.2)	56 (0.2)
Selective Serotonin Reuptake Inhibitors (SSRIs)	8,687 (0.7)	377 (0.3)	731 (0.5)	158 (0.2)	86 (0.3)

Phenothiazines	7,321 (0.6)	528 (0.4)	430 (0.3)	136 (0.2)	93 (0.3)
Prochlorperazine	7,226 (0.6)	524 (0.4)	421 (0.3)	132 (0.2)	86 (0.3)
Thiazide Diuretics	5,956 (0.5)	679 (0.5)	372 (0.3)	229 (0.3)	74 (0.2)
Hydrochlorothiazide	5,625 (0.5)	641 (0.5)	350 (0.2)	226 (0.3)	71 (0.2)
Lincosamide Antibiotics	5,336 (0.4)	239 (0.2)	172 (0.1)	114 (0.2)	51 (0.2)
Clindamycin	5,247 (0.4)	231 (0.2)	163 (0.1)	117 (0.2)	50 (0.2)
Other	159,720 (12.9)	9,964 (7.9)	9047 (6.3)	4126 (5.7)	2030 (6.3)
Acetaminophen	5,635 (0.5)	561 (0.5)	459 (0.3)	209 (0.3)	104 (0.3)

β : all drug class and individual drug allergies were significantly more prevalent among White patients except NSAIDs, ACE Inhibitors, and Thiazide diuretics.

Table 3. Number of drug allergies documented per patient by race and sex among patients with at least one drug allergy

	Overall n (%)	Sex[€] n (%)		Race^α n (%)				
Number of Drug Allergies	Overall (n = 626,871)	Female (n = 433,164)	Male (n = 193,659)	White (n = 494,893)	Black (n = 31,280)	Hispanic (n = 28,522)	Asian (n = 14,900)	Other (n = 7,322)
Mean (95% CI)	1.95(1.95-1.95)	2.09 (2.09-2.10)	1.63 (1.62-1.63)	2.00 (2.00-2.01)	1.83 (1.81-1.84)	1.64 (1.62-1.65)	1.59 (1.57-1.61)	1.70 (1.67-1.73)
1	359,500 (57.4)	230,978 (53.3)	128,493 (66.3)	275,425 (55.7)	19,396 (62.0)	19,172 (67.2)	10,212 (68.5)	4,757 (65.0)
2	136,340 (21.8)	97,893 (22.6)	38,438 (19.9)	109,907 (22.2)	6,248 (20.0)	5,384 (18.9)	2,845 (19.1)	1,461 (20.0)
3	59,352 (9.5)	45,333 (10.5)	14,013 (7.2)	49,043 (9.9)	2,562 (8.2)	2,027 (7.1)	919 (6.2)	557 (7.6)
4	29,458 (4.7)	23,360 (5.4)	6,097 (3.2)	24,733 (5.0)	1,296 (4.1)	838 (2.9)	409 (2.7)	233 (3.2)
5	15,929 (2.5)	13,030 (3.0)	2,898 (1.5)	13,430 (2.7)	685 (2.2)	464 (1.6)	214 (1.4)	127 (1.7)
6	9,246 (1.5)	7,745 (1.8)	1,501 (0.8)	7,807 (1.6)	396 (1.3)	240 (0.8)	122 (0.8)	75 (1.0)
7	5,555 (0.9)	4,741 (1.1)	812 (0.4)	4,694 (1.0)	232 (0.7)	149 (0.5)	64 (0.4)	33 (0.5)
8	3,597 (0.6)	3,100 (0.7)	497 (0.3)	3,077 (0.6)	138 (0.4)	81 (0.3)	37 (0.3)	24 (0.3)
9	2,328 (0.4)	1,999 (0.5)	329 (0.2)	2,009 (0.4)	99 (0.3)	51 (0.2)	23 (0.2)	11 (0.2)
10+	5,566 (0.9)	4,985 (1.2)	581 (0.3)	4,768 (1.0)	228 (0.7)	116 (0.4)	55 (0.4)	44 (0.6)

€: sex information was missing for 48 patients.

α: race information was missing for 49,954 patients.

Figure 1. A-D display percentages of common drug allergies over all reported drug allergies annually between 1990-2013

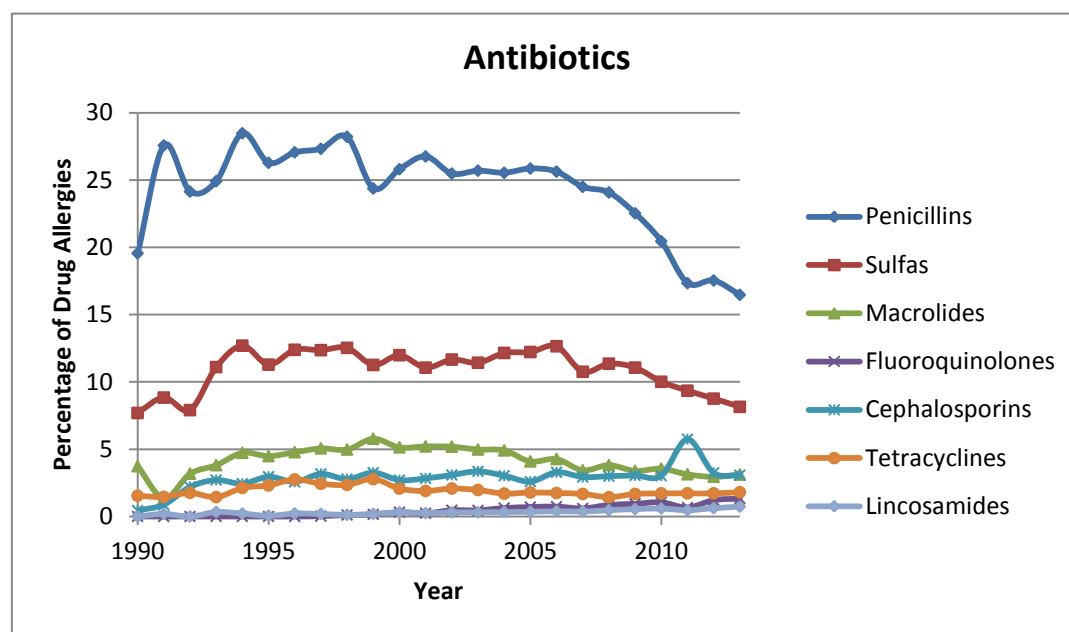
Figure 1A. Antibiotic drug allergies

Figure 1B. Analgesic drug allergies

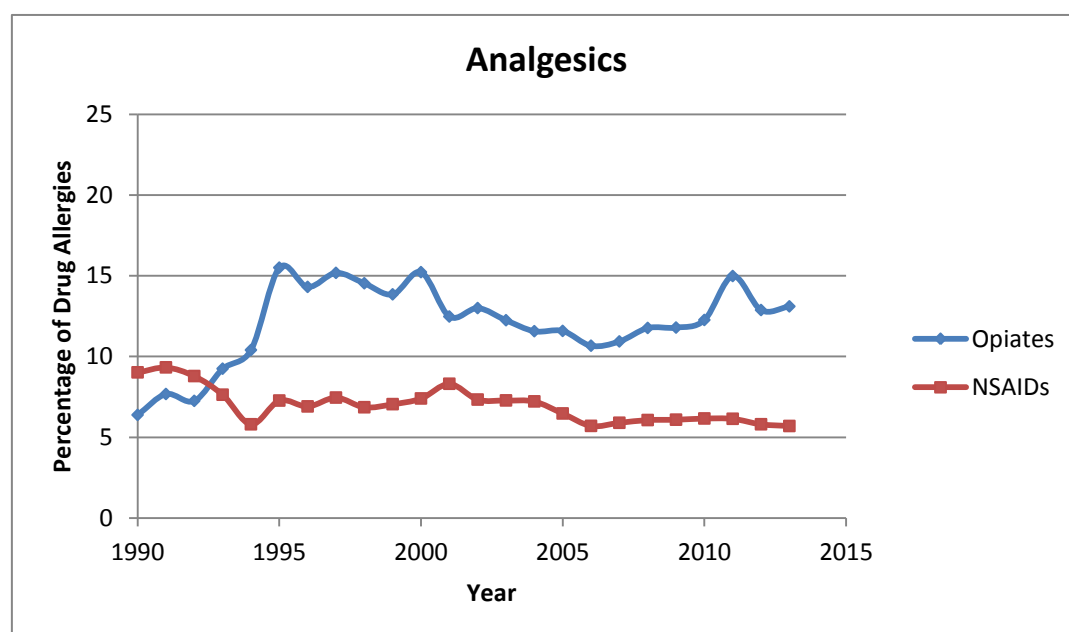
Figure 1C. Antihypertensive drug allergies

Figure 1D. Other drug allergies

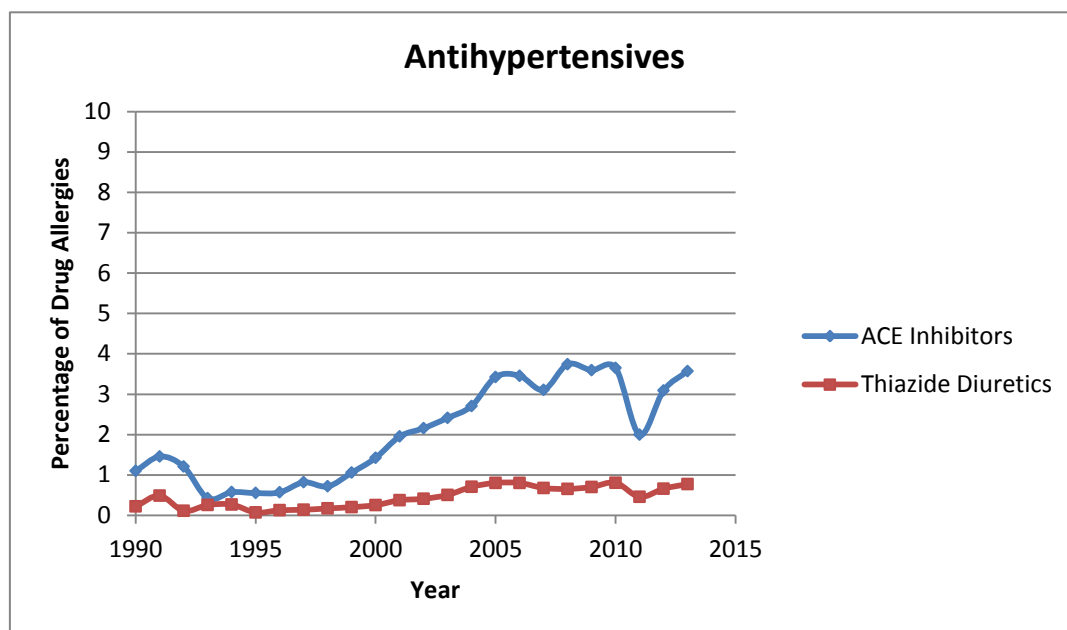
A.



B.



C.



D.

