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

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Keywords :	drug allergy, drug hypersensitivity, electronic health records, epidemiology

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 patient sex and race. 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 documented drug allergy with an average of 1.95 drug allergies per patient. The most commonly reported allergens in this population were penicillins (12.79%), sulfonamide antibiotics (7.36%), opiates (6.79%), and non-steroidal anti-inflammatory drugs (NSAIDs) (3.52%). 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 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 allergies to ACE inhibitors and statins is noteworthy.

Key words: drug allergy, drug hypersensitivity, electronic health records, epidemiology

Word count: 3,088

Abbreviations:

ADE – adverse drug event

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3 EHR – electronic health record
4 NSAID – non-steroidal anti-inflammatory drug
5 BWH – Brigham and Women’s Hospital
6 MGH – Massachusetts General Hospital
7 PEAR – Partners’ Enterprise-wide Allergy Repository
8 AHFS – American Hospital Formulary Service
9 ACE – angiotensin-converting enzyme
10 SSRI – selective serotonin reuptake inhibitor
11 MDIS – multiple drug intolerance syndrome
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For Peer Review

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 is 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 existing 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). Macy and Ho studied 478,283 patients with at least one allergy in EHRs, while other studies carried out surveys for 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. 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. 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).

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In this study, patients who visited BWH and/or MGH between 1990 and 2013 were included and their drug allergy information (also including unknown allergens and no-known allergies) was extracted from PEAR. We also collected all patients' demographic information, including sex and race, when available in the EHR systems.

While the majority (94%) of PEAR allergy records was 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 specific 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 allergens.

Drug allergy prevalence rates were calculated as the number of patients with a reported 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 race (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 0, 1, 2, 3... or 10+ drug allergies. The average number of drug allergies per patient was compared by sex and race.

The percentage of each specific 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 analysis was 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 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 (57.96%) were female, 742,374 (42.03%) were male, and 130 patients' sex information was missing. The majority of the patients were White (70.26%, n=1,241,012), followed by Hispanic (8.11%,

n=143,335), Black (7.12%, n=125,798), Asian (4.07%, n=71,860), and other (1.82%, n=32,218). There were 152,105 (8.62%) patients whose race information was unknown.

In total, there were 1,222,164 active drug allergy records. More than one-third of the patient population (35.49%, n=626,871) had at least one drug allergy documented in their EHR, 83,525 (4.73%) patients only had other types of allergies (i.e., food, environmental, and contrast media), and 1,055,932 (59.78%) patients had no known allergies.

Prevalence Rates of Drug Allergies

Table 1 shows the prevalence of the top 14 drug allergen classes. Individual drugs that made up 0.5% of all drug allergies were included in the table. Among the entire patient population (n=1,766,328), the most commonly reported allergens were penicillins (12.79%), sulfonamide antibiotics (7.36%) and opiates (6.79%). Other frequent drug allergies included NSAIDs (3.52%), macrolides (2.62%), angiotensin-converting enzyme (ACE) Inhibitors (2.03%), and cephalosporins (1.71%). The most commonly reported individual drugs were codeine (3.09%), amoxicillin (2.09%), and aspirin (1.63%). 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 drug allergy classes and individual drug allergies were significantly more prevalent among women (Table 1). Antibiotic drug classes were among the most prevalent drug allergies, including penicillins (15.22% in women vs. 9.45% in men, $p < .01$), sulfonamide antibiotics (10.36% vs. 3.23%, $p < .01$), macrolides (3.66% vs. 1.18%, $p < .01$), cephalosporins (2.19% vs. 1.05%, $p < .01$), fluoroquinolones (1.69% vs. 0.69%, $p < .01$), and tetracyclines (1.61% vs. 0.54%, $p < .01$).

NSAID allergies were more prevalent in women (4.38% vs. 2.33%, $p < .01$). Aspirin, the most common NSAID allergy in the population was found in 1.99% of women and 1.12% of men ($p < .01$). Ibuprofen was considerably more prevalent in women (0.84% vs. 0.45%, $p < .01$).

The overall prevalence rates of documented statin allergies were comparable between women and men (1.50% vs. 1.48%, $p = 0.30$), as were the rates for atorvastatin allergy (0.64% vs. 0.66%, $p = 0.10$). However, simvastatin allergy was significantly more prevalent among women (0.52% vs. 0.48%, $p < .01$). No drug allergies were significantly more prevalent in men compared to women.

Prevalence Rates by Race

White patients had significantly more reported drug allergies than other racial group (Table 2). Penicillins (14.28% in Whites vs. 7.93% in non-Whites, $p < .01$), sulfonamide antibiotics (8.74% vs. 2.87%, $p < .01$), and opiates (8.05% vs. 2.92%, $p < .01$) were among the most prevalent drug classes in Whites. Codeine (3.71% vs. 1.11%, $p < .01$) was the most prevalent individual drug in Whites, followed by amoxicillin (2.43% vs. 1.03%, $p < .01$), and erythromycin (1.77% vs. 0.49%, $p < .01$).

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Some allergens were significantly more prevalent in Black patients. These included NSAIDs (3.95% in Blacks vs. 3.52% in non-Blacks, $p < .01$), ACE inhibitors (2.55% vs 2.06%, $p < .01$), and thiazide diuretics (0.54% vs. 0.45%, $p < .01$). Common individual drugs within these classes were also more prevalent in Black patients, including aspirin (2.27% vs. 1.58%, $p < .01$), ibuprofen (0.85% vs. 0.67%, $p < .01$), lisinopril (1.53% vs. 1.26%, $p < .01$), and hydrochlorothiazide (0.51% vs. 0.42%, $p < .01$). Naproxen allergy, however, was significantly more prevalent in White patients (0.41% in Whites vs. 0.25% in non-Whites, $p < .01$). No drug class allergies or individual drug allergies were significantly more prevalent in any other race (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, 57.35% had only one drug allergy, 21.75% had two, and 9.47% 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 1.627 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. 1.977 in non-Hispanics, $p < .01$), 1.593 in Asians (vs. 1.970 in non-Asians, $p < .01$), and 1.67 in Other (vs. 1.96 in non-Other, $p < .01$).

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. Prevalence of sulfonamide antibiotic allergies also declined but remained the second most commonly reported antibiotic allergy (8% in 2013). After an initial increase (3.18% in 1992 and 3.81% in 1993 for macrolides and 2.19% in 1992 and 2.71% in 1993 for cephalosporins), prevalence rates of other antibiotics remained fairly constant. The prevalence of 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

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3 This study represents one of the largest EHR-based reports of drug allergy prevalence and
4 associated patient characteristics in a large health system (7). We found that antibiotics continue
5 to represent a large proportion of the medications involved. We also found that females and
6 White patients appeared to have more drug allergies than other patients.
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9 Our findings with respect to the medications involved are consistent with prior studies. A
10 study of self-reported drug allergy surveys in an adult Portuguese population found that the most
11 frequently reported drugs were penicillins or other beta-lactams, followed by aspirin or other
12 NSAIDs (5). Penicillins were also the most common drug class allergy in our results.
13 Cephalosporins and NSAIDs were amongst our top drug classes. Amoxicillin was the most
14 common penicillin drug allergy, which is consistent with other reports (16).
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17 Antibiotics have been reported as the majority of drug allergies documented, and we found
18 that antibiotic allergies accounted for 7 out of the top 14 drug classes (8). In a study of reported
19 antibiotic allergy incidence and prevalence using outpatient medical records, sulfonamide
20 antibiotics were found to be the most prevalent antibiotic allergy among both men and women,
21 followed by penicillins (8). Our results however showed the reverse; penicillins were the most
22 common antibiotic allergy followed by sulfonamide antibiotics. Our prevalence rates for both
23 penicillins and sulfonamide antibiotics were substantially higher than reported in the prior
24 antibiotic allergy study (8). Past reports have found that ciprofloxacin was the most prevalent
25 fluoroquinolone antibiotic allergy, which was consistent with our findings (4). Our higher
26 observed reported antibiotic allergy rates may be due to higher overall antibiotic exposure in
27 tertiary care hospitals (8, 17).
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31 NSAIDs were the 4th most common drug allergy reported in our data, with aspirin being the
32 most common individual drug in the class. Some studies have also found that aspirin was the
33 most common NSAID allergy, and others have found it to be naproxen (5, 18). In a 10-month
34 prospective cohort study on adverse cutaneous drug reactions (ACDRs) in hospitalized patients,
35 naproxen was found to be the 4th drug most frequently associated with ACDRs (18). In our data,
36 we found that naproxen (0.37%) was much less commonly reported compared to aspirin (1.62%)
37 and ibuprofen (0.68%).
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41 We found that two classes of antihypertensives were frequently documented as drug
42 allergies, ACE inhibitors and thiazide diuretics. Antihypertensives have been reported to be
43 frequent causes of hospitalizations due to adverse reactions (19). Common adverse reactions
44 include bradykinin-induced cough for ACE inhibitors and electrolyte imbalances (e.g.
45 hyponatremia and hypokalemia) for thiazide diuretics (20, 21). Although beta-blockers and
46 calcium channel blockers can also cause allergies and ADRs, we did not find these drug classes
47 to be as common as ACE inhibitors and thiazide diuretics in our study (19).
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51 Like many other studies, we found that drug allergies were significantly more prevalent
52 among females (5, 7, 8, 22). All drug classes and individual drugs were more commonly
53 reported in women with the exception of statins, which were comparable in both genders. Since
54 many patients may be intolerant to statins due to their common non immune-mediated adverse
55 events (e.g. myalgias and myositis), many of these reported allergies are not 'true' immune-
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3 mediated reactions (23). Females were also found to have more drug allergies documented per
4 patient than men on average.
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7 Our data showed that most of the top drugs documented were more prevalent in White
8 patients compared to other races. It also showed that White patients had more drug allergies
9 documented per patient than any other race. NSAIDs, ACE inhibitors, and thiazide diuretics,
10 however, were significantly more prevalent in Black patients. The high ACE inhibitor
11 prevalence may be due to the higher risk and prevalence of ACE inhibitor-induced angioedema
12 in Black patients (24). The racial difference in the reported drug allergies may potentially be
13 caused by provider documentation bias as reported in other studies (25-27).
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16 Over half of the patients with documented drug allergies had only one drug allergy. Even
17 though most patients only had one reported drug allergy, we found a much high number of
18 patients with multiple drug allergies compared to literature (7). Macy et al. reported that
19 multiple drug intolerance syndrome (commonly defined as reactions to three or more
20 medications) was present in 2.1% of their patient population at Kaiser Permanente (7, 28, 29).
21 We found that 7.41% of our total population had MDIS. This may be attributed to our
22 population being an urban tertiary care referral population that may be more sick (and therefore
23 have more medication exposure) than the population at Kaiser Permanente, since the largest risk
24 factor for reported drug allergy is drug exposure.
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28 Time prevalence trends over the last decade show how the prevalence of documented
29 allergies for different drug classes changed over time. Penicillin and sulfonamide antibiotic
30 allergies were shown to decline over time, but still remained the most commonly documented
31 allergies of all antibiotic classes. Macy et al. reported temporal trends of antibiotic usage in the
32 Kaiser Permanente San Diego area, which showed a decline in penicillin usage from 1995 –
33 2007 (8). Prevalence of opiate allergies has been consistently high compared to NSAID allergies
34 since about 1995. This is consistent with a reported increase in opioid prescribing and use in
35 past years (30, 31). While thiazide diuretics remained relatively stable throughout the years,
36 ACE inhibitor allergies have more than doubled since 2000. This may be because of an increase
37 in usage due to expansion of the drug group's indications (32). Reported statin allergies have
38 also doubled, since 2003. Studies on UK primary care databases showed a steady increase in
39 statin prescriptions due to statins being proven to be the most effective treatment for
40 hyperlipidemia (23, 33). These consistencies between reported drug usage and reported drug
41 allergies show that increased usage may be a risk factor for drug allergies.
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46 A limitation to this study is that patients tend to report and clinicians tend to document all
47 types of adverse drug reactions in the EHR allergy module including common side effects (e.g.
48 diarrhea or nausea), intolerances (e.g., gastro-intestinal upset or tinnitus) and immune-mediated
49 hypersensitivities (e.g., anaphylaxis or hives). Whether the reaction was immune-mediated or
50 whether a diagnostic test was performed was often not documented. It is likely that patients may
51 report drug allergies that have never been confirmed and may not be 'true' allergies. For
52 example, up to 90% of patients with a history of reported penicillin allergy are not actually
53 allergic when challenged with a skin-test (34). Another limitation is that data were only taken
54 from two institutions in the Boston area, with urban populations that may have more comorbid
55 patients. These patients may not be representative of a broader patient population.
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We found that sex and race were associated with a higher risk of drug allergies using a large population-based sample. Female and White patients were at a higher risk for experiencing an adverse drug event for most of the commonly reported drugs found in our patient population. The increasing number of some drug allergies may be due to an increased use of those or other drugs over time.

For Peer Review

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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 (12.79)	70,160 (9.45)	155,797 (15.22)
Amoxicillin	36,948 (2.09)	10,998 (1.48)	25,950 (2.53)
Sulfonamide Antibiotic	130,029 (7.36)	23,999 (3.23)	106,030 (10.36)
Trimethoprim/Sulfamethoxazole	21,682 (1.23)	4,224 (0.57)	17,458 (1.71)
Opiates	119,992 (6.79)	25,595 (3.45)	94,389 (9.22)
Codeine	54,609 (3.09)	9,667 (1.30)	44,942 (4.39)
Morphine	22,908 (1.30)	5,397 (0.73)	17,511 (1.71)
Oxycodone/Acetaminophen	18,678 (1.06)	3,791 (0.51)	14,887 (1.45)
Oxycodone	10,176 (0.58)	2,162 (0.29)	8,014 (0.78)
Meperidine HCl	7,028 (0.40)	1,333 (0.18)	5,695 (0.56)
Hydrocodone/Acetaminophen	7,021 (0.40)	1,494 (0.20)	5,527 (0.54)
NSAIDs	62,145 (3.52)	17,317 (2.33)	44,828 (4.38)
Aspirin	28,738 (1.63)	8,290 (1.12)	20,448 (1.99)
Ibuprofen	11,927 (0.68)	3,374 (0.45)	8,553 (0.84)
Naproxen	6,447 (0.37)	1,526 (0.21)	4,921 (0.48)
Macrolides	46,269 (2.62)	8,785 (1.18)	37,484 (3.66)
Erythromycin	25,905 (1.47)	4,547 (0.61)	21,358 (2.09)
Azithromycin	7,072 (0.40)	1,672 (0.23)	5,400 (0.53)
ACE Inhibitors	35,904 (2.03)	14,290 (1.92)	21,614 (2.11)
Lisinopril	21,794 (1.23)	8,345 (1.12)	13,449 (1.31)
Cephalosporins	30,272 (1.71)	7,812 (1.05)	22,460 (2.19)
Cephalexin	10,232 (0.58)	2,524 (0.34)	7,708 (0.75)
HMG CoA Reductase Inhibitors (Statins)	26,274 (1.49)	10,962 (1.48)	15,312 (1.50)
Atorvastatin	11,400 (0.65)	4,878 (0.66)	6,522 (0.64)
Simvastatin	8,912 (0.50)	3,550 (0.48)	5,362 (0.52)
Fluoroquinolones	22,417 (1.27)	5,156 (0.69)	17,261 (1.69)
Ciprofloxacin	12,080 (0.68)	2,709 (0.36)	9,371 (0.92)
Levofloxacin	7,942 (0.45)	1,927 (0.26)	6,015 (0.59)
Tetracyclines	20,454 (1.16)	4,016 (0.54)	16,438 (1.61)
Tetracycline	7,237 (0.41)	1,483 (0.20)	5,754 (0.56)
Selective Serotonin Reuptake Inhibitors (SSRIs)	10,526 (0.60)	2,728 (0.37)	7,798 (0.76)
Phenothiazines	9,129 (0.52)	1,450 (0.20)	7,679 (0.75)
Prochlorperazine	8,974 (0.51)	1,438 (0.19)	7,536 (0.74)
Thiazide Diuretics	7,726 (0.44)	2,527 (0.34)	5,199 (0.51)
Hydrochlorothiazide	7,309 (0.41)	2,384 (0.32)	4,925 (0.48)
Lincosamide Antibiotics	6,298 (0.36)	1,276 (0.17)	5,022 (0.49)
Clindamycin	6,216 (0.35)	1,254 (0.17)	4,962 (0.48)

1	Other	198,142 (11.22)	59,158 (7.97)	138,984 (13.57)
2	Acetaminophen	7,554 (0.43)	1,894 (0.26)	5,660 (0.55)

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

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

8 λ : all drug class and individual drug allergies were significantly more prevalent among women, except for
9 HMG CoA Reductase Inhibitors (statins) ($p = 0.30$) and Atorvastatin ($p = 0.10$).
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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 (%) ^B	Black (n = 125,798) n (%)	Hispanic (n = 143,335) n (%)	Asian (n = 71,860) n (%)	Other (n = 32,218) n (%)
Penicillins	177,216 (14.28)	10,516 (8.36)	10,735 (7.49)	5,468 (7.61)	2,864 (8.89)
Amoxicillin	30,156 (2.43)	1,132 (0.90)	1,433 (1.00)	905 (1.26)	389 (1.21)
Sulfonamide Antibiotic	108,464 (8.74)	4,163 (3.31)	2,895 (2.02)	2,486 (3.46)	1,185 (3.68)
Trimethoprim/Sulfamethoxazole	17,599 (1.42)	1,050 (0.83)	874 (0.61)	373 (0.52)	203 (0.63)
Opiates	99,901 (8.05)	5,082 (4.04)	3,540 (2.47)	1,243 (1.73)	1,047 (3.25)
Codeine	45,980 (3.71)	2,024 (1.61)	1,171 (0.82)	473 (0.66)	459 (1.42)
Morphine	19,261 (1.55)	906 (0.72)	675 (0.47)	183 (0.25)	208 (0.65)
Oxycodone/Acetaminophen	15,239 (1.23)	1,033 (0.82)	669 (0.47)	215 (0.30)	180 (0.56)
Oxycodone	8,171 (0.66)	682 (0.54)	456 (0.32)	156 (0.22)	81 (0.25)
Meperidine HCl	6,140 (0.49)	124 (0.10)	99 (0.07)	39 (0.05)	31 (0.09)
Hydrocodone/Acetaminophen	5,911 (0.48)	265 (0.21)	268 (0.19)	79 (0.11)	63 (0.20)
NSAIDs	44,552 (3.59)	4,969 (3.95)	4,859 (3.39)	1,954 (2.72)	1,005 (3.12)
Aspirin	19,069 (1.54)	2,852 (2.27)	2,833 (1.98)	1,014 (1.41)	596 (1.85)
Ibuprofen	8,255 (0.67)	1,066 (0.85)	1,038 (0.72)	441 (0.61)	205 (0.64)
Naproxen	5,036 (0.41)	362 (0.29)	354 (0.25)	163 (0.23)	54 (0.17)
Macrolides	39,340 (3.17)	1,434 (1.14)	845 (0.59)	668 (0.93)	373 (1.16)
Erythromycin	21,981 (1.77)	852 (0.68)	394 (0.27)	349 (0.49)	216 (0.67)
Azithromycin	5,925 (0.48)	224 (0.18)	222 (0.15)	140 (0.19)	55 (0.17)
ACE Inhibitors	27,302 (2.20)	3,207 (2.55)	1,935 (1.35)	1,128 (1.57)	373 (1.16)
Lisinopril	16,650 (1.34)	1,919 (1.53)	1,166 (0.81)	662 (0.92)	214 (0.66)
Cephalosporins	25,564 (2.06)	805 (0.64)	745 (0.52)	546 (0.76)	277 (0.86)
Cephalexin	8,710 (0.70)	264 (0.21)	222 (0.15)	152 (0.21)	81 (0.25)
HMG CoA Reductase Inhibitors (Statins)	22,090 (1.78)	1,157 (0.92)	817 (0.57)	395 (0.55)	209 (0.65)
Atorvastatin	9,645 (0.78)	507 (0.40)	306 (0.21)	175 (0.24)	91 (0.28)
Simvastatin	7,432 (0.60)	445 (0.35)	348 (0.24)	156 (0.22)	75 (0.23)
Fluoroquinolones	19,111 (1.54)	566 (0.45)	602 (0.42)	359 (0.50)	170 (0.53)
Ciprofloxacin	10,236 (0.82)	304 (0.24)	342 (0.24)	201 (0.28)	95 (0.29)
Levofloxacin	6,798 (0.55)	216 (0.17)	206 (0.14)	113 (0.16)	63 (0.20)
Tetracyclines	16,877 (1.36)	868 (0.69)	501 (0.35)	438 (0.61)	173 (0.54)
Tetracycline	6,031 (0.49)	276 (0.22)	133 (0.09)	118 (0.16)	56 (0.17)
Selective Serotonin Reuptake Inhibitors (SSRIs)	8,687 (0.70)	377 (0.30)	731 (0.51)	158 (0.22)	86 (0.27)
Phenothiazines	7,321 (0.59)	528 (0.42)	430 (0.30)	136 (0.19)	93 (0.29)
Prochlorperazine	7,226 (0.58)	524 (0.42)	421 (0.29)	132 (0.18)	86 (0.27)
Thiazide Diuretics	5,956 (0.48)	679 (0.54)	372 (0.26)	229 (0.32)	74 (0.23)

Allergy

1	Hydrochlorothiazide	5,625 (0.45)	641 (0.51)	350 (0.24)	226 (0.31)	71 (0.22)
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3	Lincosamide Antibiotics	5,336 (0.43)	239 (0.19)	172 (0.12)	114 (0.16)	51 (0.16)
4	Clindamycin	5,247 (0.42)	231 (0.18)	163 (0.11)	117 (0.16)	50 (0.16)
5						
6	Other	159,720 (12.87)	9,964 (7.92)	9047 (6.31)	4126 (5.74)	2030 (6.30)
7	Acetaminophen	5,635 (0.45)	561 (0.45)	459 (0.32)	209 (0.29)	104 (0.32)
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β : all drug class and individual drug allergies were significantly more prevalent among White patients expect NSAIDs, ACE Inhibitors, and Thiazide diuretics

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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 (57.35)	230,978 (53.32)	128,493 (66.34)	275,425 (55.65)	19,396 (62.01)	19,172 (67.22)	10,212 (68.54)	4,757 (64.97)
2	136,340 (21.75)	97,893 (22.60)	38,438 (19.85)	109,907 (22.21)	6,248 (19.97)	5,384 (18.88)	2,845 (19.09)	1,461 (19.95)
3	59,352 (9.47)	45,333 (10.47)	14,013 (7.23)	49,043 (9.91)	2,562 (8.19)	2,027 (7.10)	919 (6.17)	557 (7.61)
4	29,458 (4.70)	23,360 (5.39)	6,097 (3.15)	24,733 (5.00)	1,296 (4.14)	838 (2.94)	409 (2.74)	233 (3.18)
5	15,929 (2.54)	13,030 (3.01)	2,898 (1.50)	13,430 (2.71)	685 (2.19)	464 (1.63)	214 (1.44)	127 (1.74)
6	9,246 (1.47)	7,745 (1.79)	1,501 (0.78)	7,807 (1.58)	396 (1.27)	240 (0.84)	122 (0.82)	75 (1.02)
7	5,555 (0.89)	4,741 (1.09)	812 (0.42)	4,694 (0.95)	232 (0.74)	149 (0.52)	64 (0.43)	33 (0.45)
8	3,597 (0.57)	3,100 (0.72)	497 (0.26)	3,077 (0.62)	138 (0.44)	81 (0.28)	37 (0.25)	24 (0.33)
9	2,328 (0.37)	1,999 (0.46)	329 (0.17)	2,009 (0.41)	99 (0.32)	51 (0.18)	23 (0.15)	11 (0.15)
10+	5,566 (0.89)	4,985 (1.15)	581 (0.30)	4,768 (0.96)	228 (0.73)	116 (0.41)	55 (0.37)	44 (0.60)

€: 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

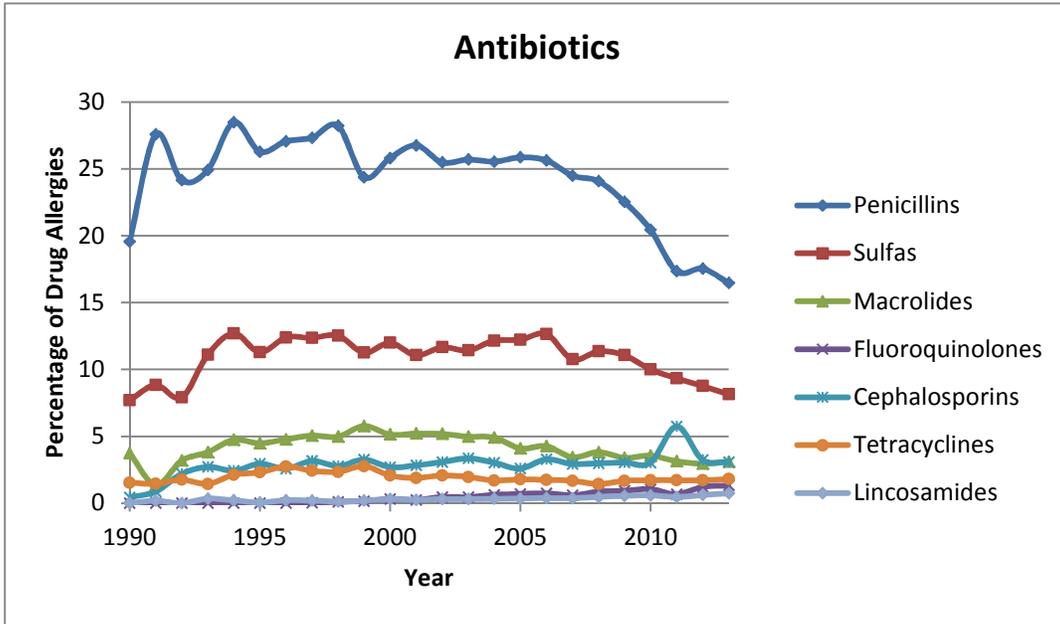
Figure 1A. Antibiotic drug allergies

Figure 1B. Analgesic drug allergies

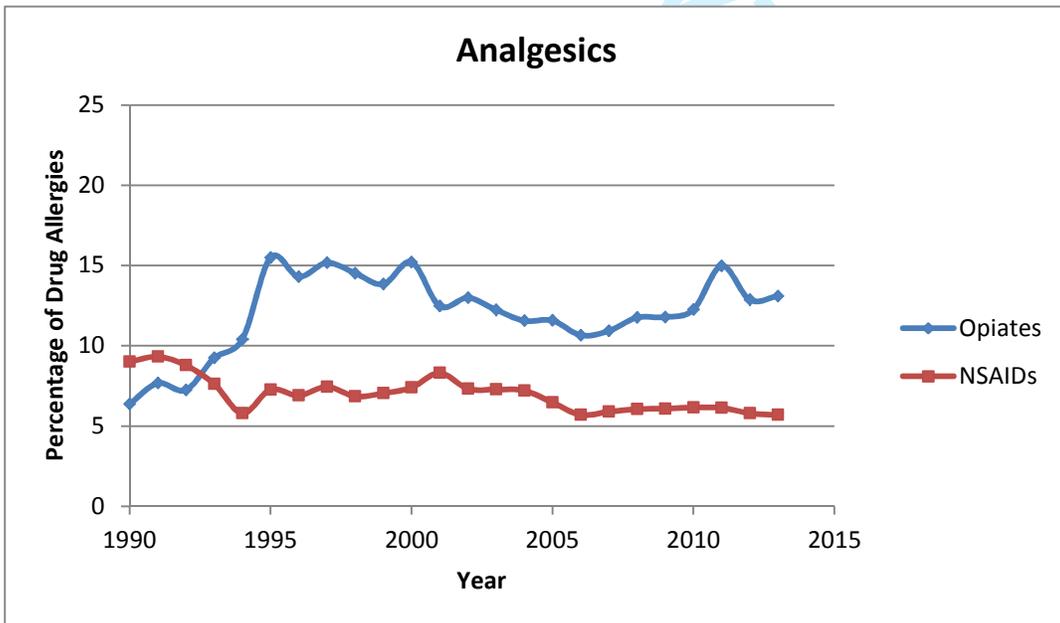
Figure 1C. Antihypertensive drug allergies

Figure 1D. Other drug allergies

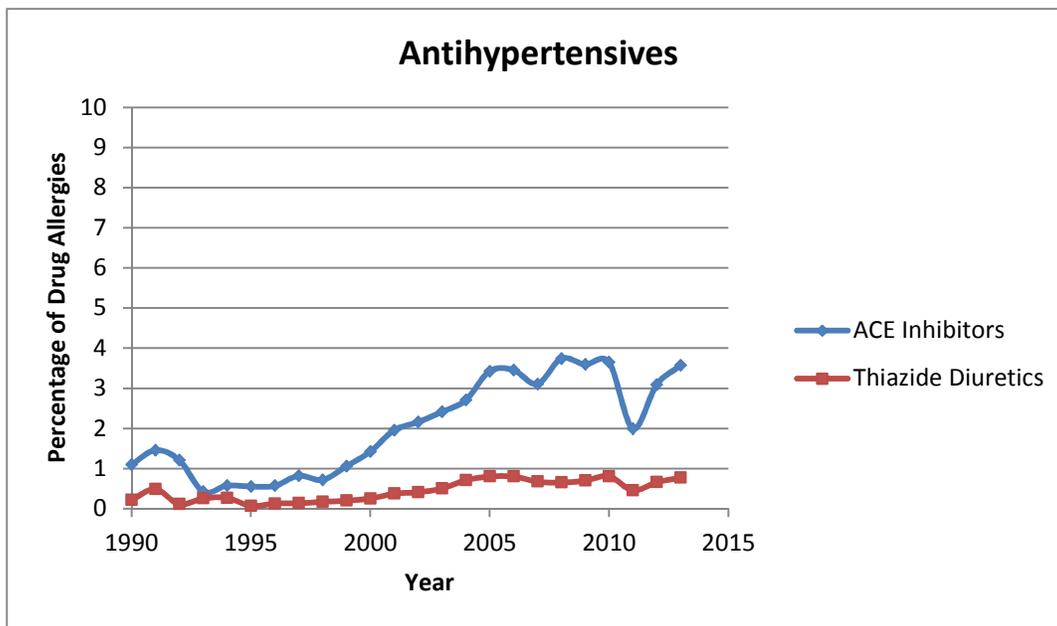
A.



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