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Prescription fill rates for acute and chronic medications in claims-EMR linked data

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Abstract

Nonadherence to prescribed medications poses a significant public health problem. Prescription data in electronic medical records (EMRs) linked with pharmacy claims data provides an opportunity to examine the prescription fill rates and factors associated with it.

Using a claims-EMR linked data, patients who had a prescription for either an antibiotic, antihypertensive, or antidiabetic in EMR were identified (index prescription). Prescription fill was defined as a pharmacy claim found within the 90 days following the EMR prescription. For each medication group, patient characteristics and fill rates were examined using descriptive statistics. Multivariate logistic regression was used to evaluate the association between fill rates and factors such as age, race, brand vs generic, and prior treatment during 365 days before the index date.

Among 77,996 patients with index antibiotic prescription, 78,462 with index antihypertensive prescription, and 24,013 with index antidiabetic prescription, the prescription fill rate was 73%, 74%, and 76%, respectively. Overall, African American race was negatively associated with fill rates (odds ratio [OR] 0.8 for all 3 groups). Prior treatment history was positively associated with antihypertensives (OR 5.6, 95% confidence interval [CI] 5.4–5.7) or antidiabetics (OR 4.1, CI 3.8–4.4) but negatively with antibiotics (OR 0.6, CI 0.6–0.6). Older age was an additional factor that was negatively associated with first time fill rate among patients without prior treatment.

Significant proportions of patients, especially patients with no prior treatment history, did not fill prescriptions for antibiotics, antihypertensives, or antidiabetics. The association between patient factors and medication fill rates varied across different medication groups.

Abbreviations: ACE inhibitors = angiotensin-converting enzyme, BB = beta-blockers, CED = claim EMR data, EMR = electronic medical records, NYISS = The New York State Identification and Intelligence System Phonetic Code, OR = odds ratio.

Keywords: drug utilization, electronic medical record-claims data, medication adherence

1. Introduction

Medication nonadherence is a major concern in public health. A large body of evidence shows that patients do not adhere to chronic medication such as antihypertensives or statins,[1,2] which can lead to undesirable health outcomes.[3–6] Understanding the extent of nonadherence as well as factors associated with it is therefore important to find effective intervention points for improving adherence.

Administrative claims data have been widely used for adherence studies, since it captures the medication filling events at pharmacy and is considered as more accurate than self-reports.[7] However, due to the nature of claims data where only "filled" events are recorded, it cannot be used to identify patients who never fill a doctor's prescription order. Due to this reason, a majority of prior research examined secondary nonadherence, defined as filling the initial prescription but do not persist to be adherent over a defined period of time. Medication fill rate is related to primary nonadherence in which patients do not fill the very first order for a medication.[8]

With the increasing use of electronic prescribing, electronic medical records (EMRs) linked with claims data are being utilized to investigate the primary nonadherence.[9–15] Since EMR contains information about what was prescribed by providers, subsequently identified pharmacy claim can be used to determine whether a patient has ever filled the prescribed medication. Linked data sets offer this opportunity to study the medication filling behavior of patients. In this study, we explored the fill rates including primary nonadherence to medications for 3 major health conditions using a large, nationwide linked data set.

2. Method

2.1. Data source and study cohort

IBM MarketScan Explorys Claims-EMR Data (CED) is a data set obtained through linkage between an EMR database (IBM Explorys Universe database) and a claims database (Truven MarketScan Research Databases). The IBM Explorys Universe database, EMR supplied by more than 300,000 health care providers, contains more than 315 billion clinical and operational data records from approximately 55 million unique patients.[16] The Truven MarketScan Research Databases, claims data supplied by more than 300 contributing employers and 40 contributing health plans,[17] captures more than 25 billion service records from 225 million unique individuals. Both databases have been de-identified, standardized, and normalized

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using common ontologies for secondary use. Social Security Number along with other demographic information and The New York State Identification and Intelligence System Phonetic Code (NYISS)[18] were used to link the raw data from the two sources, which was then de-identified. There were 4.4 million matched subjects in the linked data set. Ethical approval was not necessary due to the use of de-identified secondary database.

Patients with at least 1 electronic prescription record for any of the study drugs during the study period (index prescription), between January 1, 2014 and June 30, 2015, were included in the study. Patients were required to be continuously enrolled in a health insurance and to have at least 1 clinical activity per year (i.e., at least 1e record of office visit, admission, diagnosis, drug, immunization, observation, problem list, or procedure) between January 1, 2013 and December 31, 2015, which includes the baseline period (365 days before the index prescription) and 180 days after the index prescription.

2.2. Medication and adherence measure

We chose 3 medication groups used for 3 different health conditions to examine the medication fill rate, namely antihypertensive, antidiabetic, and antibiotics. Antihypertensive and antidiabetic were chosen because hypertension and diabetes are two of the most important chronic diseases for which significant degree of nonadherence have been previously reported, and the antibiotic was chosen for its high utilization[11] and the acute nature of use which is in contrast to chronic medications. Therapeutic classes in each group were defined using the RED BOOK (Truven Health Analytic), which classifies National Drug Codes into 31 therapeutic groups and 262 therapeutic classes. Antibiotic classes considered in the study included penicillin, tetracycline, cephalosporin and related agents, erythromycin and macrolides, and antifungals. We excluded the following classes: aminoglycoside due to limited usage in outpatient settings (1368 records), beta-lactam antibiotics (204 records), and miscellaneous (7107 records) due to nonspecific classification. As antihypertensive, we included diuretics (loop, potassium-sparing, and thiazide), angiotensin-converting enzyme (ACE) inhibitors, alpha-beta blockers, beta-blockers (BB), calcium channel blockers, hypotensive agents, and vasodilating agents. As antidiabetics, we included insulins, sulfonylureas, and others which includes the remaining types of medication, as was defined in RED BOOK.

Following the index prescription in the EMR, the first pharmacy claim for drugs within the same class as the index prescription was used to define medication fill. A medication order was considered filled if the first claim was found within the following 90 days.

2.3. Statistical analysis

We examined characteristics of patients in each of the 3 medication groups including demographics (age, gender, and race), specific therapeutic classes used, prior medication history, copay, insurance plan type (fee for service vs partially or fully capitated plans), and the time between electronic prescription order and filled date in claims. Prior use of medication was identified using both electronic prescription records and claims records during the baseline period. For each group, "any prior treatment" was defined as having at least 1 prescription or filling record for any medication in the same therapeutic group during the baseline period (e.g., use of any class of antihypertensive during baseline with an index antihypertensive prescription), and "same class prior treatment" was defined as having at least 1 prescription or filling record for the same therapeutic class medication during the baseline (e.g., use of a penicillin during baseline for an index penicillin prescription). We could not determine the level of copay and insurance plan types for patients not filling their index prescriptions. Thus, we reported the median copay level and proportion of each insurance plan type only among patients who filled medication.

To identify factors associated with the medication fill rate, we used multivariate logistic regression models including age, gender, race, brand vs generic drug use (based on a code identifying products as either original standard product or a generic copy), prior exposure to the same class, and number of distinct therapeutic classes used during baseline within the same therapeutic group (e.g., total number of antihypertensive classes used during the baseline period) as covariates. The models for each medication group and each therapeutic class was fitted separately because the factors affecting the adherence and the magnitude of effects can differ by clinical usage. A separate model was fit among the subgroup of patients without prior exposure to the same therapeutic class medication to examine whether the associated factors differ for first-ever prescriptions (i.e., primary adherence). We reported odds ratios and corresponding 95% of confidence intervals.

3. Results

From the linked data set, we identified 134,434 patients who met our study criteria. There were 77,996 patients who had an index antibiotic prescription, 78,462 patients who had an index antihypertensive prescription, and 24,013 patients who had an index antidiabetic prescription (Table 1). Majority of patients were Caucasians and had a traditional fee-for-service plans in all 3 groups. Patients were more likely to be female in the antibiotic and some of antihypertensive classes but not in the antidiabetic group.

The overall medication fill rate was 73% for the antibiotic, 74% for the antihypertensive, and 76% for the antidiabetic group (Table 2). The adherence rate was comparable in antibiotic group between patients who had prior treatment records with any antibiotic compared to patients who did not have any prior antibiotic treatment during baseline (74% vs 71%). However, a slightly lower adherence rate was observed for patients with index antibiotic prescription who had prior treatment with the same class antibiotic compared to those without same class prior treatment (69% vs 74%). Unlike antibiotics, adherence rate was higher among patients with any prior treatment compared to patients without prior treatment in the past year, in both antihypertensive (78% vs 41%, respectively) and antidiabetic groups (81% vs 48%, respectively). Similar pattern was observed with regard to the same class prior treatment. The mean time to fill was 1.7 days for antibiotic prescriptions and 13.5 days for both antihypertensives and antidiabetics (Table 2). As expected from the acute nature of use, antibiotics had much shorter time from prescription to filling compared to the chronic medications. Across the 3 medication groups, prior treatment history was associated with longer duration from the prescription to the filling.

In multivariate logistic regression models, different factors were associated with the medication fill rate in varying directions and degrees, even within the same therapeutic group depending on the therapeutic classes (Table 3). Overall, African American race was negatively associated with the fill rates, adjusting for other factors in the model. The age effect varied, with negative association observed in antibiotic group and no association observed in other medication groups. The number of medication classes used during baseline in the same therapeutic group was positively associated with the fill rates in all 3 medication groups.

Table 1

Patient characteristics in antibiotic, antihypertensive, and antidiabetic medication therapeutic groups[‡].

	N	Male	Age >65	Age 46–65	Age ≤45	Caucasians	African-American	Median Copay[*] ($)	Fee for service[†]
Antibiotics									
All	77,996	37%	19%	42%	39%	84%	12%	3.0	88%
Penicillins	30,883	37%	15%	40%	45%	84%	12%	3.0	89%
Tetracyclines	10,326	39%	22%	43%	35%	86%	11%	6.0	87%
Antifungals	10,074	15%	11%	43%	46%	79%	18%	3.0	90%
Cephalosporin and related	23,495	39%	25%	41%	34%	86%	11%	2.7	88%
Erythromycin and macrolide	27,707	36%	17%	45%	38%	84%	12%	3.0	88%
Antihypertensive drugs									
All	78,462	46%	39%	48%	13%	83%	15%	1.0	85%
Diuretics, loop diuretics	10,846	43%	65%	30%	5%	83%	16%	0.0	83%
Diuretics, potassium-sparing	7074	30%	39%	45%	16%	78%	20%	1.9	85%
Diuretics, thiazides, and related	12,708	39%	39%	51%	11%	78%	21%	0.0	85%
ACE inhibitors	31,454	54%	37%	52%	11%	84%	13%	0.0	85%
Alpha-beta blockers	3591	39%	30%	46%	24%	82%	17%	7.0	89%
Beta blockers	34,401	48%	48%	43%	10%	85%	13%	2.2	85%
Calcium channel blockers	23,092	48%	48%	44%	8%	76%	22%	1.9	85%
Hypotensive agents, NEC	8131	53%	51%	36%	12%	76%	22%	1.3	85%
Vasodilating agents, NEC	5925	53%	58%	36%	6%	82%	16%	1.5	86%
Antidiabetic drugs									
All	24,013	49%	38%	49%	13%	79%	17%	2.3	86%
Insulins	7005	50%	38%	47%	14%	77%	20%	33.7	85%
Sulfonylureas	7020	54%	49%	45%	7%	79%	17%	0.0	86%
Others	19,147	49%	36%	52%	13%	79%	17%	1.5	86%

ACE = angiotensin-converting enzyme, NEC = not elsewhere classified.

[*] Median copay is based on filled prescriptions only.

[†] Insurance type among patients who filled the index prescriptions.

[‡] Therapeutic group classification is based on the classification system in RED BOOK.

Table 2

Medication fill rate and mean time to fill index prescriptions, stratified by presence of prior treatment history.

	Medication fill rate					Mean time to fill, d				
	All	No prior any[*]	With prior any[†]	No prior same class[‡]	With prior same class[§]	All	No prior any[*]	With prior any[†]	No prior same class[‡]	With prior same class[§]
Antibiotics										
All	73%	71%	74%	74%	69%	1.7	0.8	2.3	0.8	4.3
Penicillins	77%	76%	77%	78%	73%	1.4	0.8	2	0.7	3.3
Tetracyclines	77%	76%	78%	81%	67%	3.1	0.9	4.2	0.8	10.7
Antifungals	76%	71%	78%	77%	73%	1.9	0.9	2.4	1	4.4
Cephalosporin and related	54%	50%	58%	55%	52%	2.4	1.4	3.1	1.7	5.6
Erythromycin and macrolide	81%	80%	82%	83%	74%	0.8	0.5	1.2	0.5	2.3
Antihypertensive drugs										
All	74%	41%	78%	48%	84%	13.5	4.3	14.2	4.5	15.6
Diuretics, loop diuretics	71%	40%	74%	57%	79%	15.4	4.5	16.1	5.5	19.5
Diuretics, potassium-sparing	80%	59%	82%	67%	85%	12.8	3.8	13.6	4.1	15.4
Diuretics, thiazides, and related	76%	56%	78%	60%	83%	10.9	2.6	11.7	2.6	13.9
ACE inhibitors	79%	52%	83%	58%	85%	12.8	4.1	13.6	4.1	14.5
Alpha-beta blockers	13%	3%	19%	4%	68%	13.3	3.5	14.1	3.9	16.4
Beta blockers	79%	44%	84%	51%	87%	14.7	5.4	15.3	5.6	16.1
Calcium channel blockers	79%	49%	83%	58%	86%	13.5	4.2	14.1	4.3	15.5
Hypotensive agents, NEC	53%	19%	60%	25%	81%	14.4	4.7	15	5.7	17
Vasodilating agents, NEC	51%	21%	56%	36%	70%	12.6	4.2	13.2	4.6	17.9
Antidiabetic drugs										
All	76%	48%	81%	52%	84%	13.5	5	14.4	5.5	15.1
Insulins	71%	17%	77%	35%	82%	15.2	13.7	15.3	9.5	16
Sulfonylureas	78%	38%	81%	62%	83%	14.2	6.7	14.5	4	16.5
Others	78%	55%	83%	55%	85%	12.7	4.3	14	5.1	14.3

ACE = angiotensin-converting enzyme, NEC = not elsewhere classified.

[*] No prior any: Having no prescription or filling records for any medication in the same therapeutic group during the baseline period.

[†] With prior any: Having at least one prescription or filling record for any medication in the same therapeutic group during the baseline period.

[‡] No prior same class: Having no prescription or filling record for the same therapeutic class medication during the baseline.

[§] With prior same class: Having at least one prescription or filling record for the same therapeutic class medication during the baseline.

Table 3

Factors associated with medication fill rate in each therapeutic group and each therapeutic class based on multivariate logistic regression models.

Antibiotics: odds ratio (95% confidence interval)

	All	Penicillins	Tetracyclines
Intercept	2.9 (2.8–2.9)	3.5 (3.4–3.7)	3.8 (3.4–4.2)
No. of therapeutic classes*	1.2 (1.2–1.2)	1.3 (1.2–1.3)	1.2 (1.1–1.3)
Same class prior treatment	0.6 (0.6–0.6)	0.6 (0.5–0.6)	0.4 (0.4–0.5)
Age†			
>65	0.8 (0.7–0.8)	0.9 (0.9–1.0)	1.0 (0.9–1.1)
46–65	1.0 (0.9–1.0)	1.1 (1.0–1.2)	1.1 (1.0–1.2)
Brand‡	1.2 (1.2–1.3)	0.8 (0.7–0.8)	0.7 (0.6–0.8)
Male	0.9 (0.9–0.9)	0.9 (0.9–1.0)	1.0 (0.9–1.1)
African-American	0.8 (0.7–0.8)	0.7 (0.7–0.8)	0.8 (0.7–0.9)

	Antifungals	Cephalosporin and related	Erythromycin and macrolide
Intercept	3.3 (3.0–3.6)	1.4 (1.3–1.5)	4.0 (3.7–4.2)
No. of therapeutic classes*	1.3 (1.3–1.4)	1.3 (1.2–1.3)	1.3 (1.3–1.4)
Same class prior treatment	0.6 (0.5–0.6)	0.7 (0.6–0.7)	0.4 (0.4–0.5)
Age			
>65	0.8 (0.7–0.9)	0.6 (0.6–0.7)	1.3 (1.2–1.4)
46–65	0.9 (0.8–1.0)	0.7 (0.7–0.8)	1.3 (1.2–1.4)
Brand‡	1.0 (0.9–1.1)	1.8 (1.7–2.0)	1.0 (0.9–1.1)
Male	0.7 (0.6–0.8)	0.9 (0.9–1.0)	1.0 (0.9–1.0)
African-American	0.8 (0.8–1.0)	0.7 (0.6–0.8)	0.7 (0.6–0.8)

Antihypertensive: odds ratio (95% confidence interval)

	All	Diuretics, loop diuretics	Diuretics, potassium-sparing	Diuretics, thiazides, and related	ACE inhibitors
Intercept	1.0 (0.9–1.0)	1.1 (0.9–1.3)	2.5 (2.1–3.0)	2.0 (1.8–2.3)	1.5 (1.4–1.6)
No of therapeutic classes*	1.0 (1.0–1.0)	1.2 (1.1–1.2)	1.1 (1.1–1.2)	1.0 (1.0–1.0)	1.1 (1.0–1.1)
Same class prior treatment	5.6 (5.4–5.7)	2.3 (2.1–2.5)	2.4 (2.1–2.8)	3.3 (3.0–3.6)	3.7 (3.4–3.9)
Age					
>65	1.0 (0.9–1.0)	1.0 (0.8–1.2)	0.7 (0.6–0.9)	0.8 (0.7–0.9)	1.0 (0.9–1.1)
46–65	0.9 (0.9–1.0)	0.9 (0.7–1.1)	0.7 (0.6–0.8)	0.8 (0.7–0.9)	0.9 (0.8–1.0)
Brand‡	1.1 (1.1–1.2)	1.3 (1.2–1.5)	1.0 (0.8–1.1)	1.3 (0.8–2.0)	1.1 (1.0–1.2)
Male	1.0 (1.0–1.0)	0.9 (0.9–1.0)	0.8 (0.7–1.0)	1.0 (0.9–1.1)	1.0 (0.9–1.0)
African-American	0.8 (0.8–0.8)	0.8 (0.7–0.9)	0.8 (0.7–0.9)	0.8 (0.7–0.9)	0.7 (0.7–0.8)

	Alpha-beta blockers	Beta-blockers	Calcium channel blockers	Hypotensive agents, NEC	Vasodilating agents, NEC
Intercept	0.1 (0.1–0.1)	1.1 (1.0–1.2)	1.7 (1.5–1.9)	0.3 (0.2–0.3)	0.2 (0.2–0.3)
No. of therapeutic classes*	1.2 (1.0–1.3)	1.1 (1.1–1.2)	1.1 (1.0–1.1)	1.2 (1.1–1.2)	1.2 (1.1–1.2)
Same class prior treatment	46.5 (34.8–62.8)	5.2 (4.9–5.6)	4.2 (3.9–4.5)	9.6 (8.5,10.8)	2.9 (2.6–3.4)
Age					
>65	0.3 (0.2–0.5)	1.0 (0.9–1.1)	0.7 (0.7–0.8)	0.9 (0.8–1.1)	2.4 (1.8–3.2)
46–65	0.3 (0.2–0.4)	0.9 (0.8–1.0)	0.8 (0.7–0.9)	0.8 (0.7–1.0)	1.9 (1.5–2.6)
Brand‡	4.1 (0.9–20.5)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	3.0 (2.3–4.0)	0.7 (0.6–0.8)
Male	0.9 (0.7–1.2)	1.0 (1.0–1.1)	0.9 (0.9–1.0)	1.2 (1.1–1.3)	1.2 (1.1–1.4)
African-American	1.3 (1.0–1.8)	0.7 (0.6–0.8)	0.8 (0.8–0.9)	1.0 (0.8–1.1)	0.6 (0.5–0.8)

Antidiabetic drug: odds ratio (95% confidence interval)

	All	Insulins	Sulfonylureas	Others
Intercept	1.2 (1.1–1.3)	0.4 (0.2–1.1)	1.5 (1.1–1.9)	1.3 (1.2–1.4)
No. of therapeutic classes*	1.1 (1.1–1.2)	1.5 (1.4–1.6)	1.3 (1.1–1.4)	1.1 (1–1.1)
Same class prior treatment	4.1 (3.8–4.4)	6.1 (5.4–7.1)	2.3 (1.9–2.7)	4.3 (3.9–4.8)
Age				
>65	1.0 (0.9–1.1)	1.0 (0.8–1.2)	1.0 (0.8–1.3)	1.0 (0.9–1.1)
46–65	0.9 (0.8–1.0)	0.9 (0.8–1.1)	0.8 (0.7–1.1)	0.9 (0.8–1.0)
Brand‡	0.8 (0.7–0.8)	1.0 (0.4–2.2)	1.2 (1.0–1.5)	1.0 (0.9–1.0)
Male	1.1 (1.0–1.1)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)
African-American	0.8 (0.7–0.8)	0.7 (0.6–0.8)	0.8 (0.7–0.9)	0.8 (0.7–0.9)

ACE = angiotensin-converting enzyme, NEC = not elsewhere classified.

* Number of therapeutic classes: The number of drugs in the same therapeutic group received during baseline.

† Reference age category is age 45 or less.

‡ Brand: Based on a code identifying products as either original standard product or a generic copy.

Same class prior treatment had the strongest association among the factors we examined. However, it was positively associated with the antihypertensive and the antidiabetic groups, whereas it was negatively associated with the antibiotics group.

The factors associated with primary adherence rate among patients who never received a same class treatment during the baseline were similar to those affecting medication fill rate in the entire study population (Table 4). One notable difference was the

Table 4

Factors associated with primary adherence rate in each therapeutic group and each therapeutic class based on multivariate logistic regression models.

Antibiotics: odds ratio (95% confidence interval)

	All	Penicillins	Tetracyclines
Intercept	2.8 (2.7–2.9)	3.4 (3.2–3.6)	3.2 (2.8–3.6)
No. of therapeutic classes*	1.3 (1.3–1.3)	1.3 (1.3–1.4)	1.5 (1.3–1.6)
Age†			
>65	0.8 (0.7–0.8)	1.0 (0.9–1.1)	1.1 (1.0–1.3)
46–65	1.0 (0.9–1.0)	1.2 (1.1–1.3)	1.2 (1.1–1.4)
Brand‡	1.2 (1.1–1.2)	0.7 (0.6–0.7)	0.5 (0.4–0.7)
Male	0.9 (0.9–0.9)	0.9 (0.9–1.0)	1.0 (0.9–1.1)
African-American	0.7 (0.7–0.8)	0.7 (0.6–0.8)	0.8 (0.7–1.0)

	Antifungals	Cephalosporin and related	Erythromycin and macrolide
Intercept	3.1 (2.8–3.4)	1.4 (1.3–1.5)	3.8 (3.5–4.1)
No. of therapeutic classes*	1.4 (1.3–1.6)	1.3 (1.2–1.3)	1.5 (1.4–1.5)
Age			
>65	0.8 (0.7–1.0)	0.6 (0.5–0.6)	1.4 (1.3–1.6)
46–65	0.9 (0.8–1.0)	0.7 (0.7–0.8)	1.3 (1.2–1.4)
Brand‡	1.0 (0.9–1.1)	2.0 (1.8–2.2)	0.9 (0.8–1.0)
Male	0.7 (0.6–0.8)	0.9 (0.9–1.0)	1.0 (0.9–1.1)
African-American	0.8 (0.7–1.0)	0.7 (0.6–0.7)	0.7 (0.6–0.7)

Antihypertensive: odds ratio (95% confidence interval)

	All	Diuretics, loop diuretics	Diuretics, potassium-sparing	Diuretics, thiazides, and related	ACE inhibitors
Intercept	1.1 (1.0–1.1)	1.2 (1.0–1.6)	3.1 (2.4–3.9)	2.7 (2.2–3.2)	2.0 (1.7–2.3)
No. of therapeutic classes*	1.2 (1.2–1.2)	1.3 (1.2–1.4)	1.4 (1.3–1.5)	1.2 (1.1–1.2)	1.3 (1.2–1.4)
Age					
>65	0.6 (0.6–0.7)	0.7 (0.5–0.9)	0.3 (0.2–0.4)	0.4 (0.3–0.5)	0.5 (0.4–0.6)
46–65	0.8 (0.7–0.8)	0.7 (0.5–0.9)	0.5 (0.3–0.6)	0.5 (0.4–0.6)	0.7 (0.6–0.8)
Brand‡	1.3 (1.3–1.4)	1.9 (1.6–2.3)	1.0 (0.8–1.3)	1.9 (1.1–3.7)	1.0 (0.8–1.2)
Male	1.0 (0.9–1.0)	0.9 (0.8–1.0)	0.9 (0.7–1.1)	0.9 (0.8–1.0)	0.9 (0.8–1.0)
African-American	0.8 (0.8–0.9)	0.8 (0.7–1.0)	0.8 (0.6–1.0)	0.7 (0.6–0.8)	0.7 (0.6–0.8)

	Alpha-beta blockers	Beta-blockers	Calcium channel blockers	Hypotensive agents, NEC	Vasodilating agents, NEC
Intercept	0.1 (0.1–0.1)	1.2 (1.1–1.4)	2.2 (1.9–2.6)	0.3 (0.2–0.3)	0.2 (0.1–0.3)
No. of therapeutic classes*	1.6 (1.4–1.8)	1.4 (1.3–1.5)	1.3 (1.2–1.4)	1.3 (1.2–1.4)	1.2 (1.2–1.3)
Age					
>65	0.1 (0.0–0.2)	0.5 (0.5–0.6)	0.4 (0.3–0.5)	0.6 (0.5–0.8)	2.3 (1.6–3.3)
46–65	0.1 (0.1–0.2)	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.6 (0.5–0.8)	2.1 (1.5–3.0)
Brand‡	14.6 (1.7–108.5)	1.2 (1.1,1.4)	1.2 (1–1.4)	9.7 (6.5–14.9)	0.9 (0.8–1.1)
Male	0.4 (0.3–0.7)	1.0 (0.9–1.1)	0.8 (0.7–0.9)	1.2 (1.1–1.4)	1.3 (1.2–1.5)
African-American	1.1 (0.7–1.7)	0.6 (0.5–0.7)	0.9 (0.8–1.0)	1.2 (1.0–1.5)	0.5 (0.4–0.6)

Antidiabetic drug: odds ratio (95% confidence interval)

	All	Insulins	Sulfonylureas	Others
Intercept	1.6 (1.5–1.9)	0.3 (0–1.5)	1.2 (0.9–1.8)	1.9 (1.7–2.2)
No. of therapeutic classes*	1.6 (1.5–1.7)	2.7 (2.4–3.2)	2.7 (2.2–3.3)	1.0 (0.9–1.2)
Age				
>65	0.6 (0.5–0.6)	0.6 (0.4–0.8)	0.5 (0.3–0.7)	0.6 (0.5–0.7)
46–65	0.7 (0.6–0.8)	0.8 (0.6–1.1)	0.5 (0.4–0.8)	0.7 (0.6–0.8)
Brand‡	0.4 (0.4–0.5)	1.0 (0.2–5.9)	1.5 (1.1–2.1)	0.6 (0.5,0.7)
Male	1.1 (1.0–1.2)	1.0 (0.8–1.3)	1.2 (1.0–1.5)	1.1 (1.0–1.2)
African-American	0.8 (0.7–0.9)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.8 (0.7–0.9)

ACE = angiotensin-converting enzyme, NEC = not elsewhere classified.

* No. of therapeutic classes: The number of drugs in the same therapeutic group received during baseline.

† Reference age category is age 45 or less.

‡ Brand: Based on a code identifying products as either original standard product or a generic copy.

effect of older age (>65), which was negatively associated with first-ever fill rate more than the overall fill rate.

4. Discussion

In a large linked data set, we observed that 24% to 27% of patients who were prescribed either an antibiotic, antihypertensive, or antidiabetic medication did not fill their prescriptions in the following 90 days. Notably, prior treatment history was associated with higher fill rates, suggesting that patients adhere better once the treatment begins, but adherence to the first-ever treatment is poorer.

The overall rate of prescription fill is comparable to what was reported earlier using a similar data set.[10,11] Previously reported rates of primary nonadherence for antimicrobial medications are around 23%, and for chronic medications the rates range from 3% to 4% to greater than 40%. Most of the previous studies were either done outside of the United States,[19,20] restricted to patients in a specific integrated managed care,[9,12,14,21] or restricted to a specific pharmacy benefit manager or insurance plan.[10,11,13] Lower nonadherence was seen in integrated managed systems, reflecting that better integration of care may lead to improved adherence in patients with chronic diseases.

Higher fill rates for medications that the patient had previously used was also observed in the previous studies.[11] An interesting exception to this observation was prior treatment with the same class antibiotic, which was associated with poorer adherence to subsequent antibiotic prescription. It may partly reflect the use of leftover antibiotics reported in a previous study.[22] This observation suggests that medication fill behaviors for acute and chronic medications can be associated with different factors, and methods to improve overall fill rates or primary adherence may need to differ depending on target drug.

One of the strengths of this study is the generalizability of the result to a larger population, because the study data set has contributions from multiple payers including large employers, managed care organizations, as well as Medicare and Medicaid. In addition, we were able to examine the difference in fill rates and factors associated with the fill rates at therapeutic class levels rather than at an aggregated level. However, this study is not without limitations. It was previously reported that adherence is higher for drugs on formulary[11] but we could not account for formulary in this analysis. In the presence of sample use obtained from physicians' offices, the fill rate would have been underestimated. But the effect of sample use is expected to be small since most samples do not last for extended period of time and we used 90-day period to capture the medication fill.

In conclusion, we observed that a significant proportion of patients did not fill their prescription for antibiotics, antihypertensives, or antidiabetics, and medication fill rate is strongly associated with the prior treatment history. The implication of the fact that a quarter of patients are not filling their prescriptions is significant with respect to both public health and policy point of view. Further research is needed to identify causal factors for nonadherence and targets for intervention to improve medication fill rates.

Author contributions

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Formal analysis: Hyuna Yang.
Methodology: Yoonyoung Park, Hyuna Yang.
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