

Correlation of Antimicrobial Prescription Rate and Socioeconomic Status

and

The role of socioeconomic status on brand-name vs. generic drug prescriptions:
A county-level, U.S.-wide analysis based in Medicare Part D claims

By:

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TABLE OF CONTENTS

COORELATION OF ANTIMICROBIAL PRESCRIPTION RATE AND SOCIOECONOMIC STATUS.....	1
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ABSTRACT.....	2
INTRODUCTION.....	4
METHODS.....	5
RESULTS.....	7
DISCUSSION.....	11
FIGURE 1.....	16
FIGURE 2.....	17
TABLE 1.....	18
TABLE 2.....	19
TABLE 3.....	20
REFERENCES.....	22

THE ROLE OF SOCIOECONOMIC STATUS ON BRAND NAME VS. GENERIC PRESCRIPTIONS: A COUNTY-LEVEL, U.S.-WIDE ANALYSIS BASED IN MEDICARE PART D CLAIMS.....	25
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ABSTRACT.....	26
INTRODUCTION.....	28
METHODS.....	29
RESULTS.....	31
DISCUSSION.....	36
FIGURE 1.....	40
TABLE 1.....	41
TABLE 2.....	42
TABLE 3.....	43
TABLE 4.....	44
TABLE 5.....	45
TABLE 6.....	46
REFERENCES.....	47

Correlation of Antimicrobial Prescription Rate and Socioeconomic Status

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ABSTRACT

Background: Excessive antimicrobial agent usage plays a key role in antimicrobial resistance.

Objective: To examine whether socioeconomic status has an impact on the likelihood of being prescribed an antimicrobial agent.

Design: Cross-sectional study.

Setting: United States, 2015.

Data Sources: We used combined data from Medicare Part D Public Use File (PUF) and the US Census Bureau. The 2015 Medicare Part D PUF data quantified the antimicrobial prescription rate in a county level cross-sectional study while data from the US Census Bureau provided information on socioeconomic status at the county level.

Study Selection: The analysis of this study included counties in the United States who had available data containing information on levels of income and the number of antimicrobial agents prescribed. In total, we gathered data from 807 counties.

Main Outcomes and Measures: The primary outcome variable was percentage of antimicrobial agent claims from the medical prescriber. All original and refill antimicrobial prescription claims included in the Medicare Part D PUF were used in this study.

Results: We analyzed 54,382,436 outpatient antimicrobial prescription claims from 36 million Medicare Part D recipients. Interestingly, at the county level, 48% of the variance in antimicrobial rate was explained by socioeconomic status, age, gender, and race ($P_{\text{model}} < 0.001$, $R^2 = 0.48$). More specifically, 26% of the variance in antimicrobial rate was explained by socioeconomic status ($P_{\text{model}} < 0.001$, $R^2 = 0.26$) and a trend was noted revealing that as income increased, correlation with antimicrobial prescription rate decreased. This trend was evident

given a downward trend in coefficient values for our ascending income brackets. We noted that a 1 SD increase in percentage of individuals in the income bracket of \$24,999 or less in a given county yielded a 0.21 increase in total antimicrobial prescription rate. This was compared to those in our highest income bracket ($\geq \$65,000$), where a 1 SD increase yielded an increase of 0.11 in antimicrobial prescription rate. Multivariable analysis including sociodemographics (age, % male, % white) revealed a significant negative relationship between our highest income bracket and the rate of antimicrobial agents prescribed. Age, gender, and race, were also associated with antimicrobial prescription rate. An increase of 1 SD in percentage of persons in the age 18-24 bracket in a given county yielded a 0.76 increase in rate of antimicrobial prescription. Moreover, a 1 SD increase in percentage of males in a county were found to have a -0.2 decrease in antimicrobial prescription rate while an increase of 1 SD in percentage of individuals of white race in a county were found to have a 0.35 increase in antimicrobial prescription rate.

Conclusions and Relevance: Socioeconomic factors influence the prescription of antimicrobial agents. Interventions should consider these factors in order to effectively evaluate antimicrobial prescription methods.

Introduction

The World Health Organization (WHO) has recognized antimicrobial resistance as a leading threat to public health [1] and there is a link between adverse health outcomes related to antimicrobial resistant bacteria and antimicrobial agent consumption [2]. The Center for Disease Control (CDC) reported that over 50% of antimicrobial agents prescribed in the United States are not correctly prescribed [3] and studies research have confirmed higher rates of resistance in countries that have a higher amount of antimicrobial agents prescribed [4-7] concluding that the misuse and overuse of antimicrobials is a primary cause in the emergence of antimicrobial resistant bacteria [8, 9].

A better understanding of factors that influence antimicrobial prescription is needed in order to efficiently mitigate rates of antimicrobial agents prescribed. Sociodemographic factors influence the level of care received and overall health outcomes [10] and low-income populations are at considerably increased risk of health care inequities when compared to higher income individuals [11]. While research has shown an association between income inequality and antimicrobial resistance [12-14], little research exists which examines the role socioeconomic status has on antimicrobial agent prescription rate.

The prescription of antimicrobials is influenced by several factors, including: background of country, clinical autonomy, patient's cultural beliefs and demands, the background of the prescriber, and general sociocultural factors [15]. However, the role socioeconomic factors have on being prescribed an antimicrobial has been rarely studied. An examination of this relationship is vital in order to suggest effective public health intervention. The purpose of this study, therefore, was to examine the relationship between antimicrobial agent prescription rates and socioeconomic status.

Methods

This cross-sectional study used data from two publicly available datasets. Datasets included the Medicare Provider Utilization and Payment Data: Part D [16] and the American Community Survey (ACS) from the U.S. Census Bureau [17].

The primary outcome variable of interest in this study was the percentage of antimicrobial agent claims prescribed per 10,000 people in a county. This estimate was done using the 2015 Medicare Part D Prescriber Public User File (PUF). Medicare Part D offers outpatient prescription drug coverage to the disabled and elderly [18]. Medicare Part D Prescriber PUF provides information on prescription drug counts from 36 million Medicare beneficiaries with a part D prescription drug plan [16]. We isolated information related to the total claims of antimicrobials, including refills, from providers listed in the PUF. These data allowed us to obtain the number of antimicrobial claims given by prescribers. We then summarized claims by the provider's zip code. Finally, we matched each zip code with its corresponding county in order to summarize claims per county. To estimate the antimicrobial prescription rate, we summarized antimicrobial prescription drug claims per county, divided by county population, and multiplied by 10,000.

The primary exposure variable of interest was socioeconomic status. This was assessed using estimated income levels using county data from the 2012-2016 American Community Survey (ACS) 5-year estimate dataset [17]. Socioeconomic information was obtained for each county from the 2012-2016 ACS 5-Year estimates and is a component of the publicly available data provided by the U.S. Census Bureau [17]. Income was examined at the county level and was given specific median income ranges [19]. Annual household income was grouped into the following brackets: \$24,999 or less, \$25,000-34,999, \$35,000-\$64,999, and \$65,000 or more.

We further examined the role other sociodemographic characteristics have on antimicrobial prescription rate. The ACS was used to obtain additional sociodemographic information [17]. The following explanatory variables were included in our analysis: a) Age, b) Percentage of males, and c) Percentage of white population.

The number of antimicrobial agents prescribed has been shown to vary according to age group [20]. Age was grouped into seven brackets (Age: 5 to 17, 18 to 24, 25 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 and over) in order to examine antimicrobial rates for several age ranges. Previous reports suggest that women are more likely to be prescribed antimicrobials than men [20]. Therefore, men were examined with women used as the reference group. Little literature exists that examines the role race has on prescription rates. However, recent studies have shown that white patients are more likely to be prescribed antimicrobials [21, 22]. Thus, for the purposes of this study, white individuals were used as the reference group.

The analysis of this study is limited to counties in the U.S. who had available data containing information on levels of income and the number of antimicrobial agents prescribed. Of the counties (n = 3,141) in the 50 states and District of Columbia, 807 counties included data on number of antimicrobial prescriptions and sociodemographics of interest and were therefore included in our eligible sample.

Statistical analysis: The county population was used as a weight for study analysis in order to account for oversampling. Descriptive statistics and bivariate correlations were utilized for all study variables. Linear regression analyses examined relationships between socioeconomic status and rate of antimicrobial agents prescribed. A univariable regression was used to determine the unadjusted relationship between income and antimicrobial prescription rates. Multivariable linear regressions were completed in order to examine a cross-tabulation of the outcome, age, gender,

and race by the exposure (Table 1). A P value of < 0.05 was used to indicate statistical significance and statistical tests were two-sided. All statistical analyses were performed using Stata 14.0 [23] and accounted for complex survey design. We also conducted a hot spot analysis to obtain a visual relationship of counties and antimicrobial prescription rate on a national level. Values in the analysis represent z-scores, with positive z-scores indicating hot spots and negative z-scores indicating cold spots.

Results

We analyzed 54,382,436 prescriptions reported by health providers in the 2015 Medicare Part D dataset, that were prescribed in 807 counties to nearly 36 million beneficiaries. The overall average annual antimicrobial prescription rate was 1.30 claims per beneficiary that received a prescription for an antimicrobial agent.

A univariable linear regression was first performed to examine the relationship between the main exposure and outcome of interest. Income was broken down into four ascending brackets of income levels and served as our proxy for socioeconomic status. All income brackets showed statistical significance with a prediction, $p < .05$ (Table 2). In a county level, 26% of the variance in antimicrobial agent rate was associated with socioeconomic status ($P_{\text{model}} < 0.001$, $R^2 = 0.26$).

Interestingly, the coefficient for each income bracket tended to lower given increase in income. An overall trend was noted in the brackets revealing that as income increased, the correlation with rate of antimicrobial prescription decreased (Figure 1). Our lowest income bracket (\$24,999 or less) yielded a 0.21 increase in the total antimicrobial prescription rate per 1 SD increase in percentage of individuals included in this income in a given county. At the county level, the coefficient nearly halved to 0.11 for an increase in percentage of individuals in our highest income bracket (\$65,000 or more). Meaning that a 1 SD increase in percentage of individuals in a

given county whom reported an income of \$65,000 or more yielded only a 0.11 increase in total antimicrobial prescription rate.

Additional univariable linear regressions were performed to identify other sociodemographics that were believed to be significantly associated with antimicrobial prescription rates. The number of antimicrobials prescribed were seen to be positively associated with age and race (% of white population). For our analysis, age was ordered into seven ascending range brackets. Conversely, a negative association was found related to the number of antimicrobial prescribed and gender (% of male population). Multivariable linear regressions at the county level were then performed with the significant predictors to evaluate for potential associations between antimicrobial prescription rate and socioeconomic status.

At the county level, 37% of the variance in antimicrobial prescription rate was explained by socioeconomic status and age ($P_{\text{model}} < 0.001$, $R^2 = 0.37$). Multivariable analysis revealed the seven age brackets to add statistical significance to the prediction, $p < .05$. However, only two of the income brackets (\$24,999 or less and \$35,000-64,999) continued to add significance (Table 3A). Similar to the univariable regression done examining socioeconomic status, the coefficients of the income brackets decreased as the income range increased. Further, the lowest income bracket continued to provide our most evident positive effect. Where, given age constant, a 1 SD increase in percentage of persons in a given county whom reported an income of \$24,999 or less yielded a 0.12 increase in total antimicrobial prescription rate.

As in the univariate analysis, age was positively associated with antimicrobial prescription rate. When examining age and socioeconomic status in multivariable analysis, results indicated the strongest positive association to be for those aged 18 to 24. We found that a 1 SD increase of individuals in this age range in a county yielded a 0.76 increase in total antimicrobial prescription

rate. The coefficient of this result directly precedes the regressions finding for those aged 25 to 44. Where, as percentage of individuals aged 25 to 44 increased by 1 SD in a given county, an increase of 0.64 in total antimicrobial prescription rate was observed.

We then examined antimicrobial prescription rates given income, age, and gender (% of male population). The gender variable added statistical significance to the prediction, $p < .05$ while all of the age variables and three of the income variables (\$24,999 or less, \$25,000-34,999, and \$35,000-64,999) continued to provide statistical significance (Table 3B). At the county level, 43% of the variance in antimicrobial rate is explained by income, age, and gender ($P_{\text{model}} < 0.001$, $R^2 = 0.43$). The most significant association was again seen to be for those in our lowest income bracket. More specifically, with gender and age constant, a 1 SD increase in percentage of individuals in a county with an income of \$24,999 or less yielded a 0.11 increase in total antimicrobial prescription rate. As seen in the univariate analysis, gender was negatively associated with rate of antimicrobial prescription. When included in multivariable analysis, results found an increase of 1 SD in % of males in a county to yield a -0.2 decrease in antimicrobial prescription rate.

Moreover, we performed a multivariable linear regression that examined antimicrobial prescription rates given income, age, gender, and race (% of white population). At the county level, 48% of the variance in antimicrobial rate can be explained by these sociodemographics ($P_{\text{model}} < 0.001$, $R^2 = 0.48$). Race was seen to add statistical significance to the prediction, $p < .05$. However, the only additional variables that continued to provide significance were gender and a reported income of \$65,000 or more (Table 3C). Notably, white individuals were found to have a 0.35 increase in antimicrobial prescription rate per 1 SD increase in percentage of white populace in a county.

By our third regression, the remaining statistically significant income brackets lost their positive relationship with our main exposure of interest. However, with the addition of race in multivariable analysis, results determined a negative association concerning antimicrobial prescription rate and our highest income bracket. At the county level, this analysis determined that with gender, race, and age held constant, a 1 SD increase in percentage of individuals with an income of \$65,000 or more in a county yielded a decrease of -0.15 in total antimicrobial prescription rate.

While the lowest income bracket lost its significance in this regression, the reemergence of significance for the highest income bracket warrants further examination. An income of \$65,000 or more was the bracket which lost significance in our previous multivariable analyses. Unlike other income brackets (\$25,000-34,999 & \$35,000-64,999), the highest income bracket did not regain significance in the multivariable regressions concerning age and gender. However, with the addition of race in analysis, the $\geq \$65,000$ bracket was the only income range to have a significant association. Further, the association was found to have a negative relationship with antimicrobial prescription rate. This differed from the positive relationship that was yielded in the initial univariate linear regression on socioeconomic status.

Finally, we examined the remaining significant variables (Table 3D). At the county level, 44% of the variance in antimicrobial prescription rate was explained by gender, race, and an income of \$65,000 or more ($P_{\text{model}} < 0.001$, $R^2 = 0.44$). Race was still seen to be positively associated with antimicrobial prescription rate whereas gender and an income of \$65,000 or more continued to be negatively associated. This analysis indicates that, given race and gender constant, a 1 SD increase in percentage of individuals with an income of \$65,000 or more in a given county yielded a -0.17 decrease in rate of antimicrobials prescribed.

The findings from the hot spot analysis were visually apparent (Figure 2). From a national perspective, we see that the Southwest and Rocky Mountain region of the U.S. were mostly determined to have a non-significant relationship between rates of antimicrobial prescriptions and county cluster. However, we found a cluster of counties with low (cold spots) antimicrobial prescription rates in the Northeast and the Pacific Coast that were highly significant. Conversely, we determined a highly significant cluster of counties with high (hot spots) antimicrobial prescription rates primarily in the Southeast. The hot spot analysis suggests that the Southeast region of the U.S. is most likely to have a large cluster of counties with high rates of antimicrobial prescriptions.

Discussion

A CDC report indicates that the majority of antimicrobial agents to be inappropriately prescribed [3], with research showing most antimicrobials prescribed being at the outpatient setting [24]. Antimicrobial use is the most critical modifiable factor in addressing antimicrobial agent resistance [25]. An understanding of antimicrobial prescription patterns at the outpatient level is thus vital in order to decrease the excessive rate at which antimicrobial agents are prescribed. Previous research has indicated certain factors that can influence prescription of antimicrobial agents [15]. However, the role socioeconomic status has on prescription rates has seldom been examined.

Our study combined data from the Medicare Part D PUF and the US Census Bureau to further examine a potential relationship. Results found socioeconomic factors to account for a considerable amount of the variation in antimicrobial prescription rate at the county level. For this study, socioeconomic status was examined in four ascending brackets of income values. The coefficients in income brackets generally decreased given higher income bracket. Given previous research showing an association between income inequality and antimicrobial resistance globally

[12-14], we predicted a higher antimicrobial prescription rate for individuals of lower income. Our findings also revealed rates of antimicrobial prescriptions in a given county to be positively associated with age and race (% white) of patients but negatively associated with gender (% male) of patients. Additionally, analysis showed that with these sociodemographics held constant, an increase in percentage of individuals with an income of \$65,000 or more in a county was found to result in lower rates of antimicrobial prescriptions.

This analysis demonstrates the importance socioeconomic factors have on rates of antimicrobial prescriptions. Prior to this study, the association between socioeconomic status and antimicrobial prescription rate in the U.S. had not been examined in such a large level. The main finding from this study provides novel insight as to an important sociodemographic in need of additional attention when considering antimicrobial agent reduction. A better understanding as to how antimicrobials are prescribed can help focus policies that moderate antimicrobial prescription rates effectively. This study provides evidence that a patient's income should be considered when attempting to address the high number of antimicrobial agents inappropriately prescribed.

This finding can be explained using a syndemic model of health. Typically, a person's likelihood of disease decreases as their income increases [26]. Health is consistently worse for those of lower income with research showing that people with a higher SES report fewer adverse health outcomes than those of lower SES [27]. The syndemic framework hypothesizes that health consists of interactions involving the environment, social factors, and negative effects of disease interaction [28]. Using a syndemic approach, individuals of lower income may be at higher need of antimicrobials compared to individuals of higher income because they are more likely to seek medical treatment in which antimicrobial agents are typically prescribed.

The multivariable linear regressions performed using age differed from consistent findings in previous literature. Typically, the elderly have a higher likelihood of being prescribed antimicrobials [20]. However, this study found that counties with a higher percentage of individuals aged 18 to 24 had the highest increase in total antimicrobial prescription rate compared to those of all other age groups in a county. Further, the second highest age group were those aged 25 to 44. This study finding may relate to research showing that the highest percentage of unnecessary antimicrobial prescriptions are for individuals in these age ranges [29].

This study provided interesting findings related to race. While previous research has found patients from disadvantaged areas, identify as a minority, or are older, are groups that are more often prescribed antimicrobial agents [30], more recent research has found that white individuals are more likely to be prescribed such agents [21, 22]. Our study determined that an increase in percentage of white individuals in a county was associated with an increased risk of being prescribed antimicrobial agents when compared to individuals of other racial backgrounds. This finding is perhaps explained given disparities in health coverage by race and ethnicity. In the U.S., whites are more likely than any other racial or ethnic group to have health insurance [31]. These disparities extend to the Medicare dataset used as white individuals comprise 76% of Medicare beneficiaries [32]. Further, a recent study found that racial minorities who have Medicare are less likely to utilize health services [33].

Gender has been associated with differences in outpatient drug prescriptions [34]. We determined that an increase in percentage of men in a county resulted in a lower likelihood of being prescribed an antimicrobial agent. This finding matches well with a recent meta-analysis that determined women received a significantly higher number of prescriptions of outpatient antimicrobial agents compared to men [34]. This disparity in prescribing is predicted to be

primarily due to behavioral and social differences. Research has shown that men have a higher reluctance to attend health appointments and engage in health behaviors [35]. A gap in seeking treatment makes men less likely to receive an antimicrobial prescription.

Our hot spot analysis provides a national visual of the substantial geographic variation in antimicrobial prescription rates. The Southeast region had a large cluster of counties with a high rate of antimicrobial prescriptions. This is extremely relevant to our main study finding as the highest incidence of poverty in the U.S. is concentrated in this region [36]. Moreover, the Northeast and the Pacific Coast were likely to have high cluster of counties with lower antimicrobial prescription rates. The Northeast result is of particular importance as this is the region that has the greatest number of high-SES counties in the U.S. [37].

Limitations exist with the datasets used for the purposes of this study. The cross-sectional nature of our study impairs our ability to infer casual relationships. Further, the data used in this study relied on self-reported measures, including information on income. A common problem in survey research is the overestimation of income [38]. Therefore, the number of income brackets may be overestimated with the data on people in the lowest income bracket being most distorted. Also, the findings from this study lack the ability to be generalizable given data from individual cases was not available for analysis. Instead, the study relied on data collected at the county level. Additionally, the data are limited to the years 2012-2016 for the sociodemographic data and 2014-2015 for the Medicare data and may not accurately represent the general populace. However, the Medicare data used on antimicrobial agent claims includes information on Part D beneficiaries, who comprise nearly two-thirds of those who received Medicare and comprise 15% of the total US population [39]. Moreover, while the final models included three variables for analysis, there is the possibility of other variables contributing to rates of antimicrobial agents prescribed.

In conclusion, examining the way that antimicrobial agents are prescribed is a prudent step in addressing the crisis of antibiotic resistance. This study was one of the first to show an association between socioeconomic status and antimicrobial prescription rate and found a county-level association between lower socioeconomic status and rate of antimicrobial prescriptions. We also determined the Southeast to be the region at highest risk of having a high rate of antimicrobial prescriptions. Findings from this study can help guide intervention efforts which aim to minimize the number of inappropriate antimicrobials prescribed, such as antimicrobial stewardship programs. Effective interventions have the capability of decreasing levels of inappropriate antimicrobials prescribed and prevent future cases of resistance.

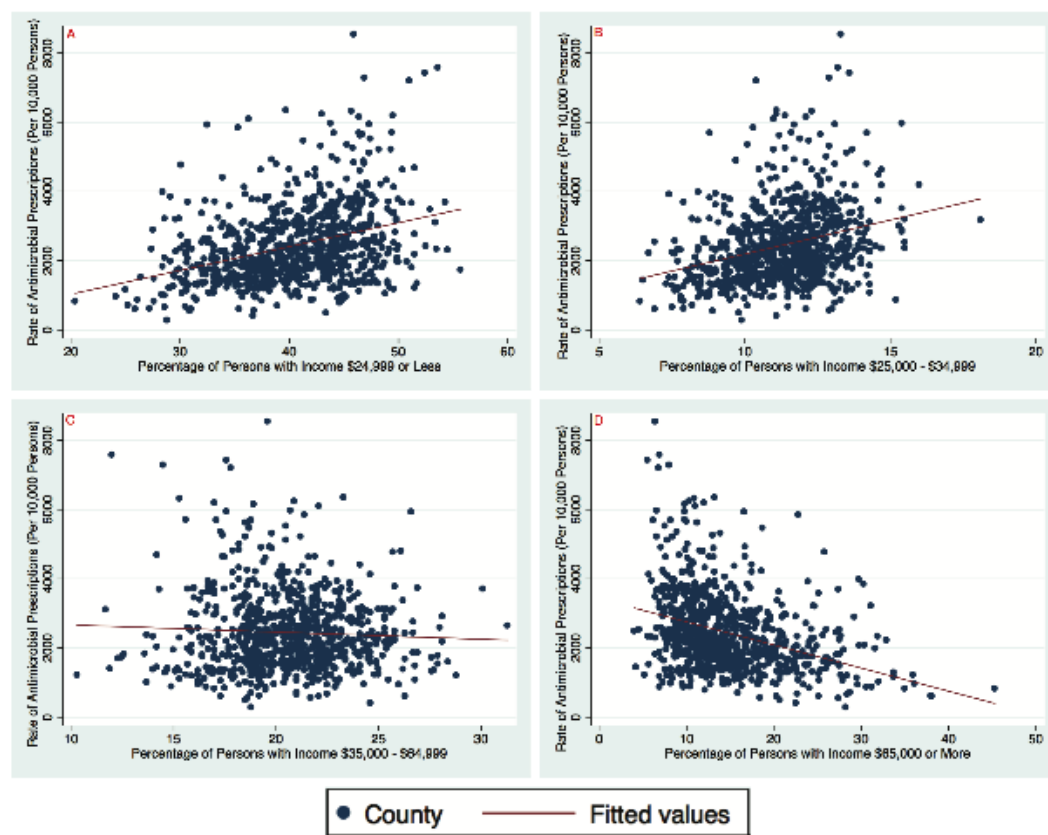


Figure 1:
Scatter Plot(s) of Bivariate Data Visualizing Relationship Between Antimicrobial Agent Prescription Rate and Socioeconomic Status

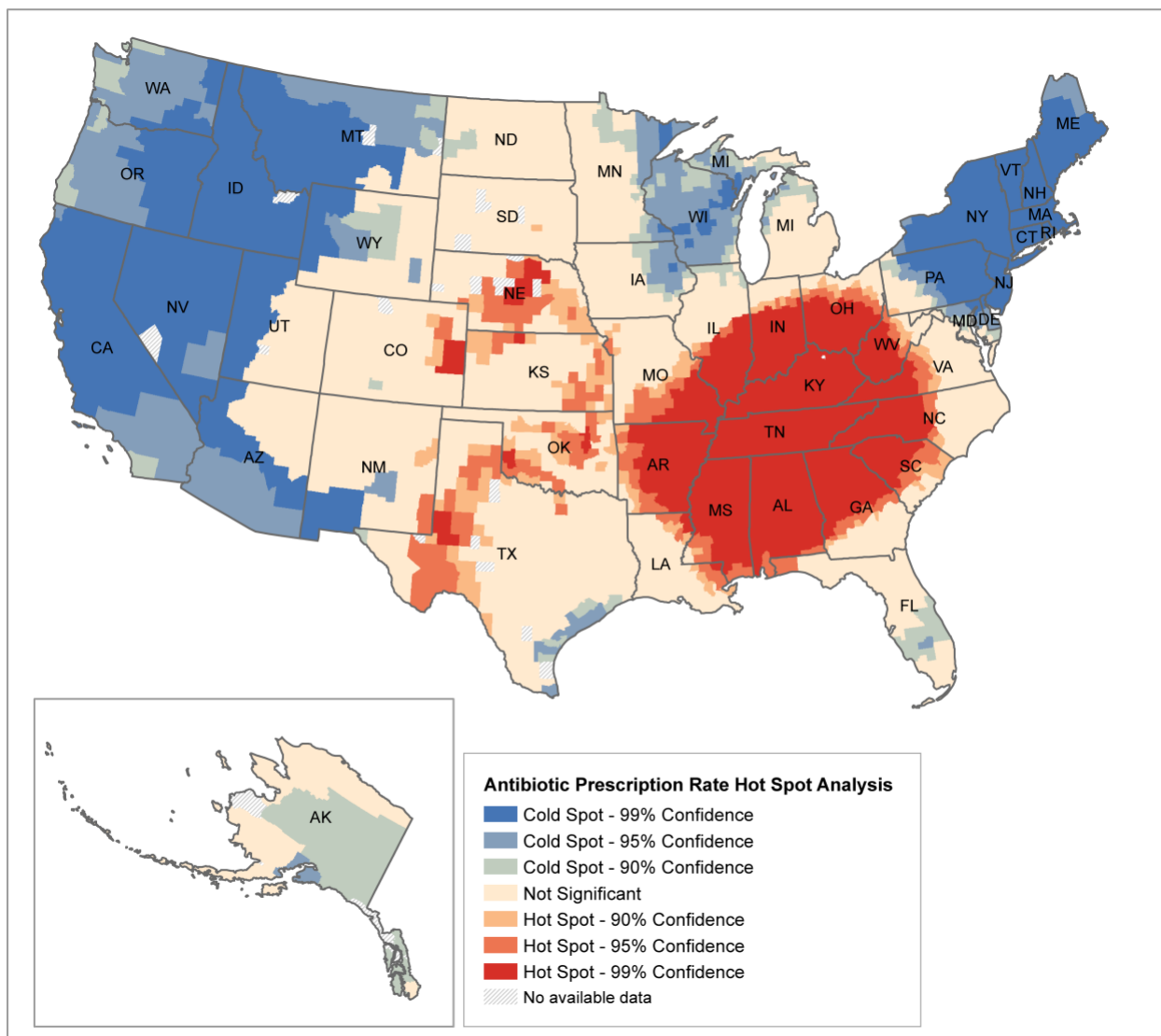


Figure 2:
Hot Spot Analysis of Antimicrobial Prescription Rates, 2015.

Table 1 Summary of variables:

Variable	Mean (SD)
SES:	
\$24,999 or less	40.59 (5.69)
\$25,000-34,999	11.29 (1.69)
\$35,000-64,999	20.64 (2.91)
\$65,000 or more	14.59 (5.91)
Age:	
5 to 17	16.74 (2.34)
18 to 24	10.28 (3.80)
25 to 44	25.27 (3.06)
45 to 54	13.32 (1.54)
55 to 64	12.98 (1.72)
65 to 74	8.97 (2.28)
75 and over	6.43 (1.95)
Gender:	
Male	49.24 (1.22).
Race:	
White	70.93 (18.71)

Table 2 Univariable regression model

	Coeff	<i>p</i> value	SE	<i>t</i> statistic	R ²	<i>p</i> value (model)
<i>A. Association of total antibiotic prescription rate with socioeconomic status</i>						
					0.26	<0.001
\$24,999 or less	0.21	<0.001	0.02	8.66		
\$25,000-34,999	0.14	0.001	0.04	3.41		
\$35,000-64,999	0.09	<0.001	0.02	4.22		
\$65,000 or more	0.10	0.001	0.03	3.26		

SE standard error, *Coeff* coefficient

Table 3 Multivariable regression models:

	Coeff	p value	SE	t statistic	R ²	p value (model)
<i>A. Association of total antibiotic prescription rate with socioeconomic status and age</i>						
SES:					0.37	<0.001
\$24,999 or less	0.12	<0.001	0.03	4.17		
\$25,000-34,999	0.10	0.016	0.04	2.42		
\$35,000-64,999	0.07	0.003	0.02	3.02		
\$65,000 or more	-0.02	0.519	0.03	-0.65		
Age:						
5 to 17	0.56	0.001	0.16	3.47		
18 to 24	0.76	<0.001	0.20	3.84		
25 to 44	0.64	0.001	0.18	3.49		
45 to 54	0.31	<0.001	0.07	4.28		
55 to 64	0.42	<0.001	0.11	3.79		
65 to 74	0.41	0.001	0.12	3.43		
75 and over	0.57	<0.001	0.13	4.44		
<i>B. Association of total antibiotic prescription rate with socioeconomic status, age and gender</i>						
SES:					0.41	<0.001
\$24,999 or less	0.11	<0.001	0.03	4.01		
\$25,000-34,999	0.12	0.002	0.04	3.13		
\$35,000-64,999	0.06	0.004	0.02	2.86		
\$65,000 or more	-0.01	0.736	0.03	-0.34		
Age:						
5 to 17	0.62	<0.001	0.16	3.97		
18 to 24	0.85	<0.001	0.19	4.41		
25 to 44	0.68	<0.001	0.18	3.81		
45 to 54	0.32	<0.001	0.07	4.57		
55 to 64	0.42	<0.001	0.11	3.86		
65 to 74	0.49	<0.001	0.12	4.28		
75 and over	0.55	<0.001	0.13	4.40		
Gender:						
Male	-0.20	<0.001	0.03	-7.15		
<i>C. Association of total antibiotic prescription rate with socioeconomic status, age, gender and race</i>						
SES:					0.48	<0.001
\$24,999 or less	0.01	0.75	0.03	0.32		
\$25,000-34,999	0.06	0.11	0.04	1.60		
\$35,000-64,999	-0.05	0.02	0.02	-2.29		
\$65,000 or more	-0.15	<0.001	0.02	-4.67		
Age:						
5 to 17	0.22	0.14	0.15	1.47		
18 to 24	0.31	0.10	0.19	1.63		
25 to 44	0.35	0.04	0.17	2.06		
45 to 54	0.17	0.009	0.07	2.62		
55 to 64	0.14	0.17	0.10	1.37		
65 to 74	0.15	0.17	0.11	1.36		
75 and over	0.33	0.006	0.12	2.73		

Gender:

Male	-0.25	<0.001	0.03	-9.49
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Race:

White	0.35	<0.001	0.03	10.85
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D. Association of total antibiotic prescription rate with income of \$65,000-74,999, gender and race

SES:

	0.44	<0.001
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\$65,000 or more	-0.17	<0.001	0.01	-14.58
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Gender:

Male	-0.29	<0.001	0.03	-11.58
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Race:

White	0.36	<0.001	0.02	20.06
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SE standard error, *Coeff* coefficient

References:

1. World Health Organization. *Antibiotic resistance* 2017; Available from: <http://www.who.int/mediacentre/factsheets/antibiotic-resistance/en>.
2. Kåhrström, C.T., *Entering a post-antibiotic era?* Nature Reviews Microbiology, 2013. **11**(3): p. 146-146.
3. Centers for Disease Control and Prevention. *Antibiotic/Antimicrobial Resistance*. 2017; Available from: <https://www.cdc.gov/drugresistance/about.html>.
4. Austin, D.J., K.G. Kristinsson, and R.M. Anderson, *The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance*. Proc. Natl. Acad. Sci. USA., 1999. **96**(3): p. 1152-1156.
5. Goossens, H., et al., *Outpatient antibiotic use in Europe and association with resistance: a cross-national database study*. The Lancet, 2005. **365**(9459): p. 579-587.
6. Hicks, L.A., et al., *Outpatient antibiotic prescribing and nonsusceptible Streptococcus pneumoniae in the United States, 1996–2003*. Clin. Infect. Dis., 2011. **53**(7): p. 631-639.
7. Riedel, S., et al., *Antimicrobial use in Europe and antimicrobial resistance in Streptococcus pneumoniae*. Eur J Clin Microbiol Infect Dis, 2007. **26**(7): p. 485.
8. Lee, G.C., et al., *Outpatient antibiotic prescribing in the United States: 2000 to 2010*. BMC Med, 2014. **12**(1): p. 96.
9. Ventola, C.L., *The antibiotic resistance crisis: part 1: causes and threats*. Pharm. Ther., 2015. **40**(4): p. 277.
10. National Academies of Sciences Engineering and Medicine, *Accounting for Social Risk Factors in Medicare Payment*. 2017: National Academies Press.
11. Berenson, J., et al., *Achieving better quality of care for low-income populations: the roles of health insurance and the medical home in reducing health inequities*. Issue Brief (Commonw Fund), 2012. **11**: p. 1-18.
12. Alvarez-Uria, G., S. Gandra, and R. Laxminarayan, *Poverty and prevalence of antimicrobial resistance in invasive isolates*. Int J Infect Dis., 2016. **52**: p. 59-61.
13. Kirby, A. and A. Herbert, *Correlations between income inequality and antimicrobial resistance*. PloS one, 2013. **8**(8): p. e73115.
14. Nomamiukor, B.O., et al., *Living conditions are associated with increased antibiotic resistance in community isolates of Escherichia coli*. J. Anat, 2015. **70**(11): p. 3154-3158.
15. Llor, C. and L. Bjerrum, *Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem*. Ther Adv Drug Saf., 2014. **5**(6): p. 229-241.
16. Centers for Medicare & Medicaid Services. *Part D Prescriber Data CY 2015*. 2015; Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/PartD2015.html>.
17. United States Census Bureau. *General Economic Characteristics (2015 ACD, DPO3)*. 2016; Available from: <https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml>.
18. Jung, J.K., et al., *Coverage for hepatitis C drugs in Medicare Part D*. Am J Manag Care, 2016. **22**(6 Spec No.): p. SP220-6.
19. Berkowitz, S.A., et al., *Evaluating Area-Based Socioeconomic Status Indicators for Monitoring Disparities within Health Care Systems: Results from a Primary Care Network*. Health Serv. Res., 2015. **50**(2): p. 398-417.
20. Centers for Disease Control and Prevention. *Outpatient antibiotic prescriptions-United States, 2013 (Vol. 24, pp. 303)*. 2016; Available from: <https://www.cdc.gov/antibiotic->

- [use/community/programs-measurement/state-local-activities/outpatient-antibiotic-prescriptions-US-2011.html](https://www.cdc.gov/drugresistance/threat-report-2013/).
21. Gerber, J.S., et al., *Racial differences in antibiotic prescribing by primary care pediatricians*. J Pediatr, 2013. **131**(4): p. 677-684.
 22. Goyal, M.K., et al., *Racial and ethnic differences in antibiotic use for viral illness in emergency departments*. J Pediatr, 2017: p. e20170203.
 23. StataCorp, *Stata Statistical Software: Release 14*. Texas USA: StataCorp LP, 2015.
 24. Hersh, A.L., et al., *Antibiotic prescribing in ambulatory pediatrics in the United States*. J Pediatr, 2011. **128**(6): p. 1053-1061.
 25. Centers for Disease Control and Prevention. *Antibiotic Resistance Threats in the United States*. 2013; Available from: <http://www.cdc.gov/drugresistance/threat-report-2013/>.
 26. Schiller, J.S., J.W. Lucas, and J.A. Peregoy, *Summary health statistics for US adults: national health interview survey, 2011*. 2012.
 27. Adler, N.E. and D.H. Rehkopf, *US disparities in health: descriptions, causes, and mechanisms*. Annu. Rev. Public Health, 2008. **29**: p. 235-252.
 28. Singer, M., et al., *Syndemics and the biosocial conception of health*. The Lancet, 2017. **389**(10072): p. 941-950.
 29. Centers for Disease Control and Prevention. *Antibiotic Use in the United States, 2017: Progress and Opportunities 2017*; Available from: <https://www.cdc.gov/antibiotic-use/stewardship-report/index.html>.
 30. Ackerman, S. and R. Gonzales, *The context of antibiotic overuse*. Ann. Intern. Med., 2012. **157**(3): p. 211-212.
 31. Artiga, S., J. Stephens, and A. Damico, *The impact of the coverage gap in states not expanding Medicaid by race and ethnicity*. Henry J. Kaiser Family Foundation. October, 2015.
 32. Kaiser Family Foundation. *Profile of Medicare Beneficiaries by Race and Ethnicity: A Chartpack*. 2016; Available from: <https://www.kff.org/report-section/profile-of-medicare-beneficiaries-by-race-and-ethnicity-tables/>.
 33. Gandhi, K., et al., *Racial Disparities in Health Service Utilization Among Medicare Fee-for-Service Beneficiaries Adjusting for Multiple Chronic Conditions*. J Aging Health, 2017: p. 0898264317714143.
 34. Schröder, W., et al., *Gender differences in antibiotic prescribing in the community: a systematic review and meta-analysis*. J. Antimicrob. Chemother, 2016. **71**(7): p. 1800-1806.
 35. Rosu, M.B., J.L. Oliffe, and M.T. Kelly, *Nurse Practitioners and Men's Primary Health Care*. AJMH, 2017. **11**(5): p. 1501-1511.
 36. Farrigan, T. *Geography of Poverty*. 2017; Available from: <https://www.ers.usda.gov/topics/rural-economy-population/rural-poverty-well-being/geography-of-poverty.aspx>.
 37. CDC. *Median household income by county for 2010-2014* 2016; Available from: <https://www.census.gov/library/visualizations/2015/acs/2010-2014-acs-hh-income.html>.
 38. Shengelia, B., et al., *Health systems performance assessment: debates, methods and empiricism*. Health systems performance assessment: debates, methods and empiricism, 2003.

39. Hoadley J., C.J., Neuman T. *Medicare Part D in 2016 and Trends Over Time*. 2016; Available from: <http://www.kff.org/medicare/report/medicare-part-d-in-2016-and-trends-over-time/>.

The role of socioeconomic status on brand-name vs. generic drug prescriptions: A county-level, U.S.-wide analysis based in Medicare Part D claims

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ABSTRACT

Background: Brand-name drugs lead to higher health care expenditures nationally.

Objective: To determine whether socioeconomic parameters impact brand-name drug prescription patterns among several medical specialties with high brand-name outpatient prescription patterns.

Design: Cross-sectional.

Setting: United States, 2015.

Data Sources: We used combined data from the US Census Bureau and Medicare Part D Public Use File. Data from the US Census bureau provided information on socioeconomic status while the 2015 Medicare Part D Public Use File quantified the brand-name prescription claims in a county level cross-sectional study.

Methods: The analysis included counties in the United States who had available data containing information on income, the number of brand-name drugs prescribed, and whether a county had the medical specialty of interest. Depending on the specialty, we gathered data from around 1,077-2,907 counties. Income was broken down into four ascending brackets of income levels and served as our variable for socioeconomic status. Univariable analysis also included regressions involving age, gender, and race.

Main Outcomes and Measures: The primary outcome variable was percentage of brand-name claims from a medical prescriber. All original and refill claims included in the Medicare Part D Public Use File were used in this study.

Results: We analyzed 3,821,523 brand-name claims and 14,088,613 generic claims reported by health providers from 40 specialties as provided by the 2015 Medicare Part D dataset. Internal Medicine, Family Practice, General Practice, Cardiology, and Ophthalmology accounted for

71% of the total amount of brand-name drugs prescribed under Medicare Part D in 2015. At the county level, univariable analysis revealed that an income of \$100,000 or more was significantly associated with a larger number of brand-name drugs prescribed for these five specialties ($R^2 = 0.003-0.08$). As the presence of individuals with an income $\geq \$100,000$ increased in a given county, the likelihood of receiving a brand-name prescription claim increased ($R^2 = 0.01-0.12$). Other parameters, such as percent of non-White population and percent of individuals 18 to 64 or ≥ 65 years old had a smaller impact. The influence of these sociodemographics was highest in Cardiology where 12% of the county level variance in brand-name prescription claims among cardiologists was associated with an income $\geq \$100,000$, an age of 18 to 64, and a race of 'Other' ($P_{\text{model}} < 0.001$, $R^2 = 0.12$).

Conclusions and Relevance: At a county level, socioeconomic factors, in addition to other sociodemographics, influence outpatient brand-name drug prescription patterns. Future interventions should consider these factors in order to reduce number of brand-name drugs prescribed and decrease health care expenditures.

Introduction

United States spends more money on prescription medications than any other advanced industrialized country [1]. A 20% increase in prescription drug spending in the U.S. occurred from 2013 to 2015 [2], leading to an 11% increase in health care expenditures [3]. Between 2008 to 2015, prices for popular brand-name drugs increased by 164% [4] with escalating prices for commonly used brand-name drugs being cited as a major reason for this upsurge [5]. In 2015, although brand-name drugs comprised only 11% of the total prescription rate in the U.S., they accounted for 73% of prescription drug spending [6].

Availability of generic medicines and inclination of a health practitioner to prescribe a generic over a brand-name drug is essential in reducing prescription drug net prices [4]. Generic drugs are produced by multiple manufacturers from a brand-name equivalent and are considerably less costly [7]. According to the U.S. Food & Drug Administration, the same active ingredients from brand-name drugs are used to create generics [8]. Thus, generics are considered to be clinically identical in terms of benefits and risks as its brand-name equivalent [8].

Despite the potential economic benefits, generic drugs remain relatively underused [9]. A recent meta-analysis found six key factors that determine the influence of generic drug prescription patterns, including: cost control factors, educational activities, insurance policies, promotional activities, patient sociodemographic factors, and technology [10]. The findings from this analysis were generally based upon qualitative findings [10]. The role of sociodemographic factors on prescribing a brand-name over a generic has rarely been studied at the quantitative level. A quantitative examination of these relationships is vital when considering interventions whose aim is to increase the usage of generic over brand-name drugs. The purpose of this study, therefore,

was to examine the relationship between brand-name drugs prescribed and sociodemographic factors among several medical specialties at the county level.

Methods

The datasets for this cross-sectional study included the Medicare Provider Utilization and Payment Data: Part D [11] and the American Community Survey from the U.S. Census Bureau [12]. The outcome variable of primary interest in this study was the percentage of brand-name claims prescribed per 10,000 people in a county. The 2015 Medicare Part D Prescriber Public User File was used to determine this estimate. Medicare Part D offers outpatient prescription drug coverage to the disabled and elderly [13] and information from 36 million Medicare beneficiaries with a part D prescription drug plan are included in the Part D Public User File [11]. We obtained data related to the total claims of brand-name drugs, including refills, from providers listed in the Public User File. These data provided us information related to the number of brand-name drugs prescribed by prescribers. Claims were then summarized by the provider's zip code. In order to summarize claims per county, each zip code was then matched with its corresponding country. Finally, we summarized brand-name drug claims per county and divided by total brand claims in order to obtain the percentage of brand-name drugs.

Socioeconomic status was our primary exposure of interest. County data from the 2012-2016 American Community Survey 5-year estimate dataset was used to determine socioeconomic status [12]. Socioeconomic status information was acquired for each county from the 2012-2016 American Community Survey 5-Year estimates and is a component of the publicly available data provided by the U.S. Census Bureau [12]. We grouped income into specific median income ranges and examined socioeconomic status at the county level [14]. Research shows that a higher income is associated with better health outcomes [15] and less overall prevalence of disease [16]. Data

from the Center for Disease Control and Prevention show this disparity to be greatest in households of annual income of less than \$35,000 compared to income of \$100,000 or more [18]. Therefore, annual household income was grouped into the following brackets: \$34,999 or less, \$35,000-59,999, \$60,000-\$99,999, and \$100,000 or more.

The role that other sociodemographic characteristics have on brand-name prescription patterns was also examined. The American Community Survey was used to obtain additional sociodemographic information [12]. The following explanatory variables were included in our analysis: a) Age, b) Gender, and c) Race. The number of prescriptions prescribed has been shown to vary according to age group [17]. Age was grouped into three brackets (5 to 17, 18 to 64, and 65 and over) in order to examine number of brand-name drugs prescribed for several age ranges. Gender has historically been viewed as an important determinant of health behavior [18]. Research regarding gender differences in prescription drug dispensing trends are conflicted [19]. Moreover, little literature exists that examines the role race has on brand-name prescription patterns [20]. In this study, race was examined in three categories: White, Black, and Other. Study analysis is limited to counties in the U.S. who had available data containing information on levels of income and the number of brand-name drugs prescribed.

Statistical analysis: Bivariate correlations and descriptive statistics were used for all study variables. Linear regression analyses examined relationships between number of brand-name drugs prescribed and socioeconomic status. Univariable regressions were used to determine the unadjusted relationship between sociodemographics and number of brand-name drugs. Multivariable linear regressions were completed in order to examine a cross-tabulation of the outcome and significant sociodemographic variables by the exposure. A P value of <0.05 was used to indicate statistical significance and statistical tests were two-sided. All statistical analyses were

performed using Stata 14.0 [21] and accounted for complex survey design. We also conducted a hot spot analysis to obtain a visual relationship of counties and brand-name prescriptions on a national level. Values in the analysis represent z-scores, with positive z-scores indicating hot spots and negative z-scores indicating cold spots.

Results

We first examined the relationship between the number of brand-name drugs prescribed compared to generic drugs among several medical specialties. In order to perform this analysis, a paired t-test was performed on medical specialties for which sufficient data was available. In total, we ran paired t-test analysis for 40 unique specialties (Table 1) and analyzed 3,821,523 brand-name claims and 14,088,613 generic claims as reported by health providers from these specialties in the 2015 Medicare Part D dataset. These drugs were prescribed throughout the U.S to nearly 36 million beneficiaries. The number of counties ranged from 1,077 counties (Cardiology) to 2,907 (Family Practice) and was dependent on whether a given county had data for that particular medical specialty.

From our paired t-test analysis, we determined that Internal Medicine, Family Practice, General Practice, Cardiology, and Ophthalmology to be five medical specialties of high concern based upon the number of brand-name prescription claims. These five categories accounted for 71% of the total amount of brand-name drugs prescribed to Medicare Part D beneficiaries in 2015. For these five specialties, univariable linear regressions were performed to examine the relationship between our main exposure and outcome of interest at the county level.

Internal Medicine was the specialty with the highest number of brand-name prescription claims. Overall, 21% of prescriptions from this specialty were brand-name. Univariable analysis for Internal Medicine determined three out of the four income brackets to show statistical

significance with a prediction $p < 0.05$ (Table 2A). Regression revealed a positive coefficient for those in our highest income bracket, \$100,000 or more ($R^2 = 0.03$). The coefficient of this bracket was found to be 0.13. Meaning that a 1-unit increase in percentage of individuals in a given county whom reported an income of $\geq \$100,000$ yielded a 0.13% increase in brand-name prescriptions from an internal medicine practitioner. Interestingly, two preceding income brackets yielded a significant negative value. Thus, we determined that internal medicine physicians were more likely to prescribe brand name-drugs as individuals with an income of $\geq \$100,000$ increased in a given county when compared to other income groups.

Moreover, univariable regressions involving the Internal Medicine specialty revealed significant differences in outpatient prescription patterns based upon age and race. At the county level, those aged 65 and over were found to be less likely to have brand-name drug prescriptions prescribed compared to generics ($R^2 = 0.008$). A 1-unit increase in percentage of individuals aged ≥ 65 in a given county yielded a 0.08% decrease in brand-name prescription claims from an internal medicine specialist.

Analysis involving race determined individuals of a race ‘Other’ than ‘White’ or ‘Black’ to have a significant positive coefficient ($R^2 = 0.008$). A 1-unit increase in percentage of individuals in a given county of a race of ‘Other’ yielded a 0.04% increase in brand-name prescriptions from an internal medicine practitioner. We then conducted a multivariable analysis (Table 2B) for three high-interest variables from our univariate analysis. At the county level, 2% of the variance in brand-name prescription claims among internal medicine practitioners was associated with an income of $\geq \$100,000$, an age of ≥ 65 , and a race of ‘Other’ ($P_{\text{model}} < 0.001$, $R^2 = 0.02$).

Family Practice analysis found 19% of prescribed drugs in this specialty to be brand-name. Results were similar to our findings for Internal Medicine (Table 3A) and again provided statistical significance with a prediction $p < 0.05$ and explained up to 3% of the variance. As seen in our analysis for Internal Medicine, other significant income brackets were found to have a negative coefficient except for the bracket of \$100,000 or more ($R^2 = 0.003$). We determined that a 1-unit increase in percentage of individuals in a given county whom reported an income of $\geq \$100,000$ yielded a 0.07% increase in family practice prescribed brand-name prescription claims.

Differences were again present in prescription patterns involving race and gender. However, the only variables to provide significance were the variables: age 65 and over ($R^2 = 0.002$) and a race of 'Other' ($R^2 = 0.008$). For those aged ≥ 65 , a 1-unit increase in percentage of individuals in this age group yielded a 0.03% decrease in amount of brand-name prescription claims from a family practice practitioner. Whereas, a 1-unit increase in percentage of individuals with a race of 'Other' yielded a 0.04% increase in amount of brand-name prescription claims from a family practice practitioner. A multivariable regression was run for the variables found to be of high significance during univariable analysis (Table 2B). This regression demonstrated that 1% of the variance in brand-name prescription claims among family practice practitioners can be associated with an income of $\geq \$100,000$, an age of ≥ 65 , and a race of 'Other' ($P_{\text{model}} < 0.001$, $R^2 = 0.01$).

Next, we examined the relationship between sociodemographics and outcome among general practice practitioners (Table 4A). Among the overall prescriptions prescribed in this specialty, 19% were found to be brand-name. Statistical significance was displayed with a prediction $p < 0.05$. However, the only significant income bracket to yield a positive coefficient was \$100,000 or more ($R^2 = 0.008$). The income bracket \$34,999 or less ($R^2 = 0.007$) had a

significant negative coefficient value. The only other variable determined to be significant by univariable analysis was a race of ‘Other’ ($R^2 = 0.003$). A multivariable analysis was run with key variables (Table 4B). At the county level, only 1% of the variance in brand-name prescription claims among general practice practitioners was associated with an income of $\geq \$100,000$ and a race of ‘Other’ ($P_{\text{model}} < 0.001$, $R^2 = 0.01$).

In Cardiology, 22% of the drugs prescribed were brand-name and all income levels showed statistical significance with a prediction $p < 0.05$, explaining up to 8% of the variance (Table 5A). As previously seen, regression revealed a positive coefficient for those in our highest income bracket, \$100,000 or more ($R^2 = 0.08$). A 1-unit increase in percentage of individuals in a given county whom reported an income of $\geq \$100,000$ yielded a 0.11% increase in brand-name prescriptions from a cardiologist. Additionally, outpatient prescription patterns were seen to differ based upon other sociodemographics. At the county level, those aged 18 to 64 were more likely to have a higher amount of brand-name drug prescriptions compared to generics ($R^2 = 0.04$). An increase in 1-unit in percentage of individuals aged 18 to 64 in a given county yielded a 0.24% increase in brand-name prescription claims from a cardiologist. Univariable analysis involving race determined ‘White’ to have a negative coefficient ($R^2 = 0.01$) while ‘Black’ ($R^2 = < 0.001$) and ‘Other’ ($R^2 = 0.03$) were shown to have a positive coefficient. This finding was most apparent for those of ‘Other’ race, where a 1-unit increase in percentage of individuals in a given county of a race of ‘Other’ yielded a 0.10% increase in brand-name prescriptions from a cardiologist. We then conducted a multivariable regression (Table 5B) for three high-interest univariate variables. At the county level, 12% of the variance in brand-name prescription claims among cardiologists was associated with an income of $\geq \$100,000$, an age of 18 to 64, and a race of ‘Other’ ($P_{\text{model}} < 0.001$, $R^2 = 0.12$).

In Ophthalmology, univariable regression determined three out of the four income brackets to be statistically significant with a prediction $p < 0.05$ (Table 6A) and explained up to 2% of the variance. Additional univariate tests determined a race of ‘Other’ ($R^2 = 0.004$) to be the only other resulting significant variable in this specialty. Out of the medical specialties examined, Ophthalmology was unique in that brand-name drugs accounted for more than half of the prescription drugs prescribed. Our paired t-test analysis revealed that 54% of drugs prescribed under this specialty were brand-name. Analysis determined a similar trend as to what was noted in our previous regressions from the other medical specialties examined. Again, the only positive coefficient found during univariable regression was for the highest income bracket ($R^2 = 0.02$). At the county level, we determined that a 1-unit increase in percentage of people with an income of \$100,000 or more yielded a 0.48% increase in brand-claim prescriptions from an ophthalmologist. We then conducted a multivariable analysis (Table 6B) for two high-interest univariate regression variables. At the county level, 2% of the variance in brand-name prescription claims among ophthalmologists was associated with an income of $\geq \$100,000$ and a race of ‘Other’ ($P_{\text{model}} < 0.001$, $R^2 = 0.02$).

Findings from the hot spot analysis offered a visual as to what counties in the U.S. had high amounts of brand-name drugs prescribed (Figure 1). We determined a highly significant cluster of counties with high (hot spots) antimicrobial prescription rates throughout the U.S. From a national perspective, we see that the Midwest, Southwest, and regions of the Mid-Atlantic/Northeast to have a large number of counties with high brand-name drugs prescribed clustered together. Moreover, we found a cluster of counties with low (cold spots) antimicrobial prescription rates spread throughout the U.S. that were highly significant.

Discussion

The Medicare Part D program spent over \$397 billion on prescription drugs between 2012 and 2015 [22] and projections predict expenditures to increase by 77% over the next decade [23]. As medication use continues to rise [24], preferential increase in usage of generic medications is required in order to achieve a reduction in pharmaceutical health care expenditure [5]. Further, utilization of generics can help patients display greater medication adherence due to its cost-effectiveness [25] and greater adherence leads to additional cost-benefits with reduced hospitalization rates [26]. Research has shown that certain demographics can influence generic drug prescription [10] but this research has largely been qualitative and the role of socioeconomic status on the number of brand-name drugs prescribed has rarely been studied. Thus, additional research is needed to strengthen knowledge related to outpatient drug prescription patterns.

The combination of data from the Medicare Part D Public Use File and the U.S. Census Bureau allowed us to further identify if a relationship exists involving the prescription of brand-name drugs and socioeconomic status. Study findings from regression analysis using our exposure provided insight as to what income brackets at the county level have greater likelihood of receiving a brand-name prescription. Overall, there was variability found in the number of brand-name drugs prescribed among Medicare Part D beneficiaries based upon income status. Analyses also provided useful information into other sociodemographics of particular concern for each medical specialty observed. Our main finding for the medical specialties examined revealed an increased likelihood of a medical practitioner prescribing a brand-name drug as the percentage of individuals with an income of \$100,000 or more increased in a given county. Interestingly, this finding was seen in all analyses, regardless of the number of generics prescribed over brand-name and despite the

inclusion of general specialties (General Practice, Internal Medicine and Family Practice), a subspecialty (Cardiology) and a focused surgical specialty (Ophthalmology).

Part D plans are delivered primarily in two distinct forms, fee-for-service or Medicare Advantage with 61% of Part D beneficiaries enrolled in fee-for-service plans [27]. Medicare Advantage is associated with lower out-of-pocket costs of managed care compared to fee-for-service [28] and is popular among lower income groups [29]. Medicare Advantage beneficiaries are usually concentrated among a subset of medical providers in inner-city or rural communities [30]. This is relevant to our hot-spot analysis finding as we determined many rural areas and counties surrounding major cities to have a large cluster of counties with a high rate of brand-name drugs. Moreover, Medicare Advantage beneficiaries may elect to enroll for a low-income subsidy which restricts them from utilizing certain medications [30] and some plans prevent beneficiaries from receiving brand-name drug prescriptions [32]. Individuals of higher income are less likely to qualify for subsidies associated with restrictions on brand-name drug prescriptions [31]. As a result, the structure of these plans might incentivize some patients to request generic drugs.

The willingness of a health practitioner to prescribe brand-name medications over generics is influenced by several factors. First, prescribers may have negative views on generics and view them as inferior substitutes [32] and this negative outlook may also be shared by patients [33]. For example, the strongest correlation in our study came from the examination of the relationship of our outcome and exposure amongst Cardiologists. This may be the result of the popularity of Lipitor, a brand-name statin that has become the best-selling prescription drug of all-time [34] and further, dispensing of its generic has not been widely utilized [35]. This suggests that the availability of a suitable generic may not be sufficient to achieve a reduction in the prescription of

brand-name medications. Nevertheless, increased utilization of generic drugs is necessary to reduce costs for patients and payers [36].

In 2017, the FDA approved more generic drugs than any prior year in an effort to decrease cost and improve patient health outcomes [37]. The generic prescriptions approved by the FDA account for nearly 90% of the overall amount of prescriptions prescribed annually [37]. An increase in approved generic drugs should allow for practitioners of all specialties to reduce the number of brand-name drugs prescribed. However, as evidenced by our study, additional understanding into outpatient prescription drug patterns is needed given the rising costs associated with the prescription of brand-name drugs. A better comprehension of these patterns, in cohesion with the efforts from FDA, will allow for maximal success in interventions aimed at reducing health care costs by decreasing the number of brand-name drugs prescribed.

There are limitations to our study. Data were collected at the county level since data from individual cases were not available for analysis. Moreover, the data used for analysis are limited to the years 2014-2015 for the Medicare data and 2012-2016 for the sociodemographic data and has the potential to not accurately represent the U.S. population. However, the beneficiaries of Medicare Part D are an especially significant population to consider as they consist of nearly two-thirds of those who receive Medicare and comprise 10-15% of the total US population [38]. Furthermore, analysis into Medicare spending revealed that the substitution of 62 generic medications to a brand-name alternative using Part D beneficiaries could result in a savings of \$3.4 billion [33]. Also, although we controlled for three variables in our final model analysis, the possibility of other confounders that contribute to a higher likelihood of brand-name drugs exists. Finally, cross-sectional study design prevents causality in our results. Despite these limitations,

this was one of the first known studies to determine a quantitative county-level association between patient income and outpatient brand-name drug prescription patterns.

In conclusion, we found socioeconomic factors, in addition to other sociodemographics, to influence brand-name drug prescription in a wide range of medical specialties. At the county-level, this effect was most closely associated with an increase in the percent of individuals with an income of $\geq \$100,000$. We determined that an increase of individuals in this income group is more likely to result in higher brand-name prescription claims in a given county. Additional research is needed in order to evaluate causality. However, the consideration of sociodemographics, particularly patient income, may be a key component in achieving a reduction in brand-name drug prescriptions. Interventions that aim to reduce the number of brand-name prescriptions can benefit from our study findings with the implementation and delivery of successful interventions having the capability of decreasing patient costs and significantly reducing health care expenditures at the national level.

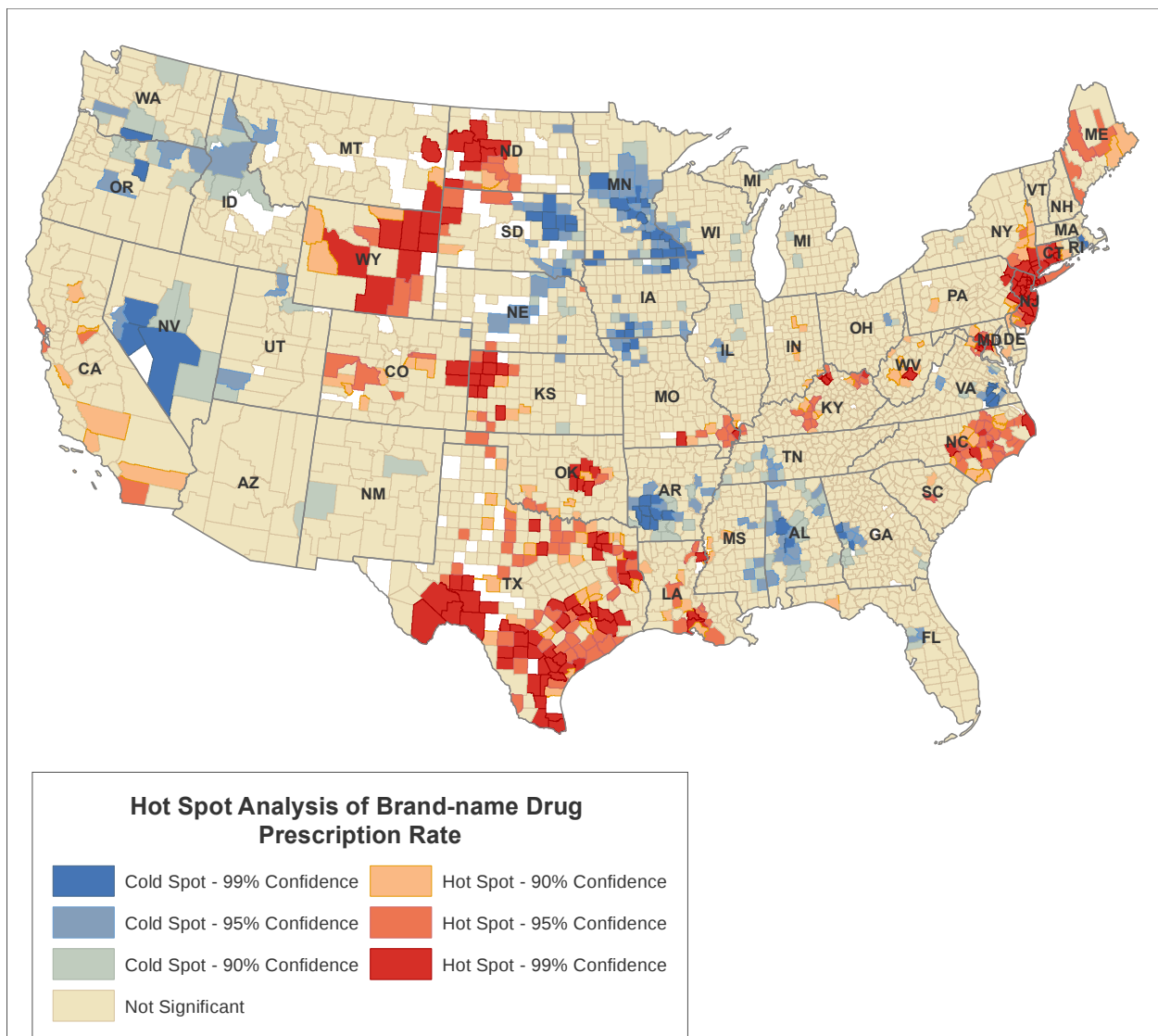


Figure 1:
Hot Spot Analysis of Brand-name Drugs, 2015.

Table 1. Paired *t*-test of brand-name and generic drug claims from medical specialties, mean (Ratio; SD).

Specialty	Brand Claims	Generic Claims	<i>t</i> -value	<i>p</i> -value
Optometry	45,530 (53%; 45,594)	38,945 (47%; 35,131)	3.09	0.0032
Ophthalmology	157,632 (54%; 217,443)	135,469 (46%; 174,763)	2.89	0.0056
Pulmonary Disease	92,808 (49%; 100,274)	95,439 (51%; 123,927)	-0.44	0.6600
Pharmacist	2,977 (40%; 10,726)	4,406 (60%; 19,211)	-1.10	0.2782
Intensivists	7,245 (47%; 9,101)	8,187 (53%; 13,258)	-1.12	0.2683
Endocrinology	116,096 (48%; 141,951)	124,886 (52%; 157,114)	-1.96	0.0553
General Practice	106,485 (19%; 252,850)	449,931 (81%; 1,177,945)	-2.70	<0.001
Registered Nurse	1,161 (19%; 2,390)	4,930 (81%; 9,2650)	-3.81	<0.001
Podiatry	6,592 (14%; 10,924)	39,540 (86%; 66,289)	-4.35	<0.001
Thoracic Surgery	567 (19%; 1,652)	2,370 (81%; 5,095)	-4.48	<0.001
Preventive Medicine	1,412 (22%; 2,241)	5,053 (78%; 7,584)	-4.55	<0.001
Plastic Surgery	68 (16%; 107)	352 (84%; 491)	-4.55	<0.001
Infectious Disease	23,617 (40%; 35,344)	35,716 (60%; 52,869)	-4.71	<0.001
Neuropsychiatry	1,677 (15%; 2,598)	9,678 (85%; 14,511)	-4.74	<0.001
Palliative Care	1,438 (21%; 2,122)	5,444 (79%; 7,441)	-4.88	<0.001
Colorectal Surgery	1,111 (27%; 1,393)	3,015 (73%; 3,777)	-5.29	<0.001
Vascular Surgery	707 (12%; 1,127)	5,151 (88%; 7,866)	-5.86	<0.001
Allergy/Immunology	15,588 (38%; 18,310)	25,611 (62%; 26,698)	-5.98	<0.001
Anesthesiology	10,276 (14%; 13,886)	65,804 (86%; 92,217)	-5.18	<0.001
Nephrology	47,730 (25%; 81,451)	143,275 (75%; 208,290)	-5.46	<0.001
Cardiac Surgery	877 (17%; 1,219)	4,214 (83%; 5,287)	-5.54	<0.001
Dermatology	14,074 (14%; 19,248)	83,907 (86%; 109,257)	-5.63	<0.001
Gastroenterology	40,285 (30%; 55,458)	92,319 (70%; 120,487)	-5.75	<0.001
Hematology	9,179 (22%; 16,281)	33,399 (78%; 55,007)	-6.01	<0.001
Internal Medicine	1,408,719 (21%; 1,917,686)	5,449,084 (79%; 6,862,665)	-6.13	<0.001
Cardiology	92,442 (22%; 175,998)	337,451 (78%; 579,398)	-6.18	<0.001
Psychiatry	34,407 (13%; 67,685)	229,775 (87%; 446,164)	-6.18	<0.001
Otolaryngology	10,249 (15%; 13,090)	60,059 (85%; 70,936)	-6.23	<0.001
Pediatric Medicine	8,301 (22%; 9,573)	29,951 (78%; 34,767)	-6.24	<0.001
Geriatric Medicine	44,603 (21%; 50,822)	164,271 (79%; 184,768)	-6.36	<0.001
Urology	21,784 (21%; 27,681)	83,587 (79%; 97,886)	-6.40	<0.001
Physical Medicine	12,204 (15%; 14,822)	71,769 (85%; 86,317)	-6.40	<0.001
Emergency Medicine	33,510 (17%; 41,667)	164,038 (83%; 192,657)	-6.40	<0.001
Hematology/Oncology	15,272 (21%; 19,607)	56,179 (79%; 64,595)	-6.55	<0.001
Orthopedic Surgery	9,106 (10%; 11,083)	86,731 (90%; 96,650)	-6.56	<0.001
Pain Management	8,111 (13%; 11,758)	52,301 (87%; 79,269)	-6.61	<0.001
Obstetrics/Gynecology	23,313 (32%; 29,388)	49,783 (68%; 57,595)	-6.70	<0.001
Rheumatology	28,292 (22%; 34,482)	102,843 (78%; 110,498)	-6.92	<0.001
General Surgery	11,259 (18%; 12,901)	50,248 (82%; 53,927)	-6.94	<0.001
Family Practice	1,319,404 (19%; 13,888,384)	5,540,935 (81%; 5,662,061)	-7.31	<0.001
Neurology	34,567 (19%; 54,678)	147,497 (81%; 208,133)	-7.59	<0.001

Table 2 Regression model(s) – Medical Specialty: Internal Medicine.

	Coeff	p value	SE	t statistic	R ²
B. Association of brand claims with sociodemographics (Univariable)					
SES:					
\$34,999 or less	-0.25	0.002	0.79	-3.11	0.007
\$35,000-59,999	-0.24	0.149	0.17	-1.44	<0.001
\$60,000-99,999	0.41	0.765	0.14	0.30	<0.001
\$100,000 or more	0.25	0.001	0.78	3.18	0.008
Age:					
5 to 17	0.01	0.893	0.09	0.13	<0.001
18 to 64	0.07	0.267	0.64	1.11	<0.001
65 and over	-0.08	0.120	0.05	-1.56	0.002
Gender:					
Male	-0.12	0.260	0.11	-1.13	0.001
Race:					
White	-0.01	0.355	0.01	-0.93	<0.001
Black	<0.001	0.978	0.02	-0.03	<0.001
Other	0.05	0.039	0.03	2.07	0.003
C. Association of brand claims with selected sociodemographics (Multivariable)					
SES:					0.01
\$100,000 or more	0.24	0.002	0.08	3.08	p value (model) = 0.011
Race:					
Other	0.04	0.058	0.03	1.90	
SE standard error, Coeff coefficient					

SE standard error, *Coeff* coefficient

Table 3 Regression model(s) – Medical Specialty: Family Practice.

	Coeff	p value	SE	t statistic	R ²
<i>A. Association of brand claims with sociodemographics (Univariable)</i>					
SES:					
\$34,999 or less	-0.07	0.003	0.02	-2.96	0.003
\$35,000-59,999	-0.05	0.271	0.04	-1.10	<0.001
\$60,000-99,999	-0.04	0.233	0.04	-1.19	<0.001
\$100,000 or more	0.07	0.003	0.02	2.96	0.003
Age:					
5 to 17	0.01	0.632	0.02	0.48	<0.001
18 to 64	0.03	0.089	0.02	1.70	0.001
65 and over	-0.03	0.017	0.01	-2.40	0.002
Gender:					
Male	0.04	0.155	0.03	1.42	<0.001
Race:					
White	-0.01	0.154	0.01	-1.42	0.007
Black	-0.01	0.426	0.01	-0.80	<0.001
Other	0.04	<0.001	0.01	4.89	0.008
<i>B. Association of brand claims with selected sociodemographics (Multivariable)</i>					
SES:					0.01
\$100,000 or more	0.06	0.012	0.02	2.52	p value (model) = <0.001
Age:					
65 and over	-0.01	0.567	0.01	-0.57	
Race:					
Other	0.03	<0.001	0.03	4.42	

SE standard error, *Coeff* coefficient

Table 4 Regression model(s) – Medical Specialty: General Practice.

	Coeff	<i>p</i> value	SE	<i>t</i> statistic	R ²
<i>A. Association of brand claims with sociodemographics (Univariable)</i>					
SES:					
\$34,999 or less	-0.25	0.002	0.79	-3.11	0.007
\$35,000-59,999	-0.24	0.149	0.17	-1.44	<0.001
\$60,000-99,999	0.41	0.765	0.14	0.30	<0.001
\$100,000 or more	0.25	0.001	0.78	3.18	0.008
Age:					
5 to 17	0.01	0.893	0.09	0.13	<0.001
18 to 64	0.07	0.267	0.64	1.11	<0.001
65 and over	-0.08	0.120	0.05	-1.56	0.002
Gender:					
Male	-0.12	0.260	0.11	-1.13	0.001
Race:					
White	-0.01	0.355	0.01	-0.93	<0.001
Black	<0.001	0.978	0.02	-0.03	<0.001
Other	0.05	0.039	0.03	2.07	0.03
<i>B. Association of brand claims with selected sociodemographics (Multivariable)</i>					
SES:					0.01
\$100,000 or more	0.24	0.002	0.08	3.08	<i>p</i> value (model) = 0.011
Race:					
Other	0.04	0.058	0.03	1.90	

SE standard error, *Coeff* coefficient

Table 5 Regression model(s) – Medical Specialty: Cardiology.

	Coeff	<i>p</i> value	SE	<i>t</i> statistic	R ²
<i>A. Association of brand claims with sociodemographics (Univariable)</i>					
SES:					
\$34,999 or less	-0.48	<0.001	0.05	-9.18	0.07
\$35,000-59,999	-0.88	<0.001	0.10	-9.00	0.07
\$60,000-99,999	-0.33	<0.001	0.09	-3.52	0.01
\$100,000 or more	0.41	<0.001	0.04	9.88	0.08
Age:					
5 to 17	-0.16	0.003	0.05	-2.94	0.008
18 to 64	0.24	<0.001	0.04	6.86	0.04
65 and over	-0.12	<0.001	0.03	-3.93	0.01
Gender:					
Male	0.11	0.0015	0.09	1.27	0.002
Race:					
White	-0.03	<0.001	0.01	-3.80	0.01
Black	0.01	<0.001	0.01	0.81	<0.001
Other	0.10	<0.001	0.02	5.85	0.03
<i>B. Association of brand claims with selected sociodemographics (Multivariable)</i>					
SES:					0.12
\$100,000 or more	0.34	<0.001	0.04	8.01	<i>p</i> value (model) = <0.001
Age:					
18 to 64	0.16	<0.001	0.03	4.49	
Race:					
Other	0.07	<0.001	0.02	4.35	

SE standard error, *Coeff* coefficient

Table 6 Regression model(s) – Medical Specialty: Ophthalmology.

	Coeff	p value	SE	t statistic	R ²
<i>A. Association of brand claims with sociodemographics (Univariable)</i>					
SES:					
\$34,999 or less	-0.69	<0.001	0.15	-4.57	0.02
\$35,000-59,999	-0.61	0.023	0.27	-2.28	0.005
\$60,000-99,999	0.17	0.508	0.25	0.66	<0.001
\$100,000 or more	0.48	<0.001	0.10	4.21	0.02
Age:					
5 to 17	-0.11	0.445	0.14	-0.76	<0.001
18 to 64	0.15	0.116	0.09	1.57	0.002
65 and over	-0.07	0.408	0.08	-0.83	<0.001
Gender:					
Male	0.36	0.114	0.23	1.58	0.002
Race:					
White	-0.02	0.376	0.02	-0.89	<0.001
Black	<0.001	0.807	0.02	-0.24	<0.001
Other	0.09	0.031	0.01	2.16	0.04
<i>B. Association of brand claims with selected sociodemographics (Multivariable)</i>					
SES:					0.02
\$100,000 or more	0.45	<0.001	0.12	3.92	p value (model) = <0.001
Race:					
Other	0.07	0.128	0.05	1.53	

SE standard error, *Coeff* coefficient

References:

1. Quon, B.S., R. Firszt, and M.J. Eisenberg, *A comparison of brand-name drug prices between Canadian-based Internet pharmacies and major US drug chain pharmacies*. *Annals of Internal Medicine*, 2005. **143**(6): p. 397-403.
2. Aitken, M., et al., *Medicines Use and Spending in the US: A Review of 2015 and Outlook to 2020*. IMS Institute for Healthcare Informatics, Parsippany, NJ, 2016.
3. Keehan, S.P., et al., *National health expenditure projections, 2014–24: spending growth faster than recent trends*. *Health Affairs*, 2015. **34**(8): p. 1407-1417.
4. Express Scripts. *Express Scripts 2015 Drug Trend Report*. 2016 Available from: <http://lab.express-scripts.com/lab/drug-trend-report>
5. Kesselheim, A.S., J. Avorn, and A. Sarpatwari, *The high cost of prescription drugs in the United States: origins and prospects for reform*. *Jama*, 2016. **316**(8): p. 858-871.
6. Arnoff, S. *Generic Drugs Continue to Deliver Billions in Savings to the U.S. Healthcare System, New Report Finds*. 2015; Available from: <https://www.gphaonline.org/gpha-media/press/generic-drugs-continue-to-deliver-billions-in-savings-to-the-u-s-healthcare-system-new-report-finds/>.
7. Dentali, F., et al., *Brand name versus generic warfarin: a systematic review of the literature*. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 2011. **31**(4): p. 386-393.
8. Administration, U.S.F.D. *Generic Drug Facts*. 2017 Available from: <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm167991.htm>.
9. Summers, A., et al., *Examining patterns in medication documentation of trade and generic names in an academic family practice training centre*. *BMC medical education*, 2017. **17**(1): p. 175.
10. Howard, J.N., et al., *Influencers of generic drug utilization: A systematic review*. *Research in Social and Administrative Pharmacy*, 2017.
11. Centers for Medicare & Medicaid Services. *Part D Prescriber Data CY 2015*. 2015; Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/PartD2015.html>.
12. United States Census Bureau. *General Economic Characteristics (2015 ACD, DPO3)* 2016; Available from: <https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml>.
13. Jung, J.K., et al., *Coverage for hepatitis C drugs in Medicare Part D*. *The American journal of managed care*, 2016. **22**(6 Spec No.): p. SP220-6.
14. Berkowitz, S.A., et al., *Evaluating Area-Based Socioeconomic Status Indicators for Monitoring Disparities within Health Care Systems: Results from a Primary Care Network*. *Health services research*, 2015. **50**(2): p. 398-417.
15. Pollack, C.E., et al., *Do wealth disparities contribute to health disparities within racial/ethnic groups?* *J Epidemiol Community Health*, 2013: p. jech-2012-200999.
16. Woolf, S.H., *How are income and wealth linked to health and longevity?* 2015.
17. Barrett, L.L., *Prescription drug use among midlife and older Americans*. 2005: AARP, Knowledge Management.
18. Grossman, M., *On the concept of health capital and the demand for health*. *Journal of Political economy*, 1972. **80**(2): p. 223-255.

19. Hellerstein, J.K., *The importance of the physician in the generic versus trade-name prescription decision*. The Rand journal of economics, 1998: p. 108-136.
20. Chen, A.Y. and S. Wu, *Dispensing pattern of generic and brand-name drugs in children*. Ambulatory Pediatrics, 2008. **8**(3): p. 189-194.
21. StataCorp, *Stata Statistical Software: Release 14*. Texas USA: StataCorp LP, 2015.
22. Centers for Medicare & Medicaid Services. *2015 Medicare Drug Spend Data*. Available from: <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/2015MedicareData.html>.
23. Congressional Budget Office. *The Budget and Economic Outlook: 2015-2025* Available from: <https://www.cbo.gov/sites/default/files/114th-congress-2015-2016/reports/49892-Outlook2015.pdf>.
24. Kleinrock, M. *Medicine Use and Spending in the U.S.* . 2018; Available from: <https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-review-of-2017-outlook-to-2022>.
25. Shrank, W.H., et al., *The implications of choice: prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions*. Archives of internal medicine, 2006. **166**(3): p. 332-337.
26. Gagne, J.J., et al., *Comparative effectiveness of generic and brand-name statins on patient outcomes: a cohort study*. Annals of internal medicine, 2014. **161**(6): p. 400-407.
27. Hoadley, J., J. Cubanski, and T. Neuman, *Medicare Part D at ten years: the 2015 marketplace and key trends, 2006-2015*. Kaiser Family Foundation Report, 2015.
28. Atherly, A. and K.E. Thorpe, *Value of Medicare Advantage to Low-Income and Minority Medicare Beneficiaries*. Emory University, September, 2005. **20**: p. 7.
29. Weech-Maldonado, R., et al., *Do racial/ethnic disparities in quality and patient experience within Medicare plans generalize across measures and racial/ethnic groups?* Health services research, 2015. **50**(6): p. 1829-1849.
30. Buntin, M.B. and J.Z. Ayanian, *Social risk factors and equity in Medicare payment*. New England Journal of Medicine, 2017. **376**(6): p. 507-510.
31. The Centers for Medicare and Medicaid Services, *Guidance to States on the Low-Income Subsidy* 2009.
32. Emery, J., A. McKenzie, and C. Bulsara, *Controversy over generic substitution*. BMJ: British Medical Journal (Online), 2010. **341**.
33. Himmel, W., et al., *What do primary care patients think about generic drugs?* International Journal of Clinical Pharmacology & Therapeutics, 2005. **43**(10).
34. Luo, J., et al., *Effect of generic competition on atorvastatin prescribing and patients' out-of-pocket spending*. JAMA internal medicine, 2016. **176**(9): p. 1317-1323.
35. Warraich, H.J., et al., *Trends in Use and Expenditures of Brand-name Atorvastatin After Introduction of Generic Atorvastatin*. JAMA internal medicine, 2018.
36. Liu, Q., et al., *The adoption of generic immunosuppressant medications in kidney, liver, and heart transplantation among recipients in Colorado or nationally with Medicare part D*. American Journal of Transplantation, 2018.
37. Uhl, K. *2017 Was Another Record-Setting Year for Generic Drugs*. 2018; Available from: <https://blogs.fda.gov/fdavoices/index.php/2018/02/2017-was-another-record-setting-year-for-generic-drugs/>.

38. Hoadley J., C.J., Neuman T. *Medicare Part D in 2016 and Trends Over Time*. 2016;
Available from: <http://www.kff.org/medicare/report/medicare-part-d-in-2016-and-trends-over-time/>.