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Abstract

Purpose: To determine if there is a geographic variation in antipsychotic prescribing in Medicare recipients in 10 US divisions. **Methods:** Data was collected in the Microsoft Excel format from the Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use File for 2013 CMS data. Antipsychotics were sorted and downloaded into separate excel formats. The states were separated into the 10 geographic according to the US Census Bureau to identify prescribing trends. The primary endpoint was to determine the difference in the rates of CMS Medicare Part D utilizers who had antipsychotic prescriptions in each of the 10 geographic divisions. The rate of antipsychotic prescribing was calculated by determining the number of prescription claims for each antipsychotic for the division and dividing by the number of people utilizing Medicare Part D in each division. Data was converted to SPSS (version19, Armonk, NY) for further analysis. ANOVA was used to compare the differences. **Results:** Approximately 35 million claims were included in the data set. Antipsychotics comprised 4.75% of the total spending on medications for Medicare Part D. New England was found to have the highest rate of claims at 0.83. No statistically significant differences in the rate of antipsychotic prescribing across geographic regions was observed; however, a statistically significant difference was observed for total claims ($P<0.001$) and total antipsychotic costs ($P<0.017$) across regions. **Conclusion:** Additional studies need to be conducted to determine if there is a difference in antipsychotic prescribing in the United States.

Keywords: antipsychotics, Medicare Part D, geographic variation

Introduction

Antipsychotic medications are some of the most commonly prescribed drugs in the country. In fact, quetiapine, aripiprazole, olanzapine, ziprasidone, and risperidone were represented on the list of the Top 200 Drugs for 2013.[1] Aripiprazole accounted for $6.5 billion in sales in 2013. A total $2.1 billion was filed under Medicare Part D for aripiprazole and this product represents about 2% in total sales for all Part D medications.[2] When combined, antipsychotics comprise a significant portion of the Medicare Part D expenditures.

These drugs are used for a variety of indications and prescribing seems to be varied across the nation. Prescribing differences between metropolitan and non-metropolitan areas have been found in prescribing concomitant antipsychotics in patients with psychiatric disorders. Prescribers in cities were more likely to prescribe more than one antipsychotic than those in rural areas.[3] There have been studies on antipsychotics in general, and clozapine, in specific, has been evaluated to determine if geographic variations exist. Geographic differences in prescribing characteristics of antipsychotics have also been observed in depot antipsychotics in Medicaid patients with schizophrenia.

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Despite risks of using antipsychotics in the elderly, there has been variation found in the nursing home setting.[6,7] A study using Missouri Medicaid data described the prescribing differences between state-defined mental health service areas of the state based upon zip codes where the number of prescriptions was determined for each section, based on zip code differences.[8] One article discussed regional variation of antipsychotic use in four states in adolescents in residential treatment facilities. Investigators determined the percent of antipsychotic use in the facilities evaluated and compared the states to each other.[9] Another investigator used prescription counts from IMS LifeLink LRx Longitudinal Prescription database to evaluate geographic variations based on three-digit zip code in antipsychotic, antidepressant, and stimulant use, but it was limited due to insurance restraints and patient population.[10] Geographic differences in antipsychotic prescribing, however, have not been extensively researched in the nationwide Medicare Part D population.

Clinical practice guidelines (CPGs) are developed as a result of a larger quality improvement program that is geared to ensure appropriate therapeutic outcomes. When CPGs are circumvented, there may be issues with respect to how patients are treated and a resultant reduction in favorable outcomes. Therefore, differences in prescribing may reflect noncompliance with CPGs and result in lower quality evidence, if any, used to make therapeutic decisions. Differences in geographic variations are important to document because these differences may allude to noncompliance with clinical guidelines or disparities with respect to use of antipsychotic therapy. These differences in prescribing may impact mental

health patients, in general. As a result, increased public health programs and policies to address differences in quality in this patient population may need to be developed.[11] The Centers for Medicare and Medicaid Services (CMS) released prescribing information from 2013 in order to increase understanding of prescribing patterns for Medicare/Medicaid beneficiaries in America. The public release of the 2013 *Medicare Provider Utilization and Payment Data* from CMS can assist in investigating regional variation in prescribing antipsychotics. The purpose of this retrospective database review was to determine if geographic variation exists in use of antipsychotics in Medicare Part D patients.

Methods
This study was a retrospective, descriptive analysis of geographic trends in prescribing of antipsychotics by prescribers, as reported by the CMS during 2013. The MS Excel 2013 CMS data was downloaded from the CMS website via the *Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use File (PUF).*[12]The PUF comprises data that was retrieved from CMS's National Claims History (NCH) Standard Analytic Files (SAFs). The claims within this file had been completed. Claim discrepancy adjustments were acknowledged through June 30, 2014. The updated data set, which included prescription drug events (PDEs) of 35.7 million Part D beneficiaries (68% of total Medicare beneficiaries), contained completely resolved fee-for service claims. Claims associated with fewer than 10 prescriptions were excluded from the CMS Excel spreadsheet and were not available for analysis. The antipsychotic medications (aripiprazole, asenapine maleate, clozapine, iloperidone, lurasidone HCl, olanzapine, olanzapine pamoate, olanzapine/fluoxetine HCl, paliperidone, paliperidone palmitate, quetiapine fumarate, risperidone, risperidone microspheres, ziprasidone HCl, and ziprasidone mesylate) were searched from each Excel spreadsheet that was categorized by prescriber's last name, and the information was downloaded in a separate file. Separate files were compiled that focused on different aspects of the data including division totals for cost, type of antipsychotics, and brand-generic composition of antipsychotic prescriptions nationwide. This was to allow for the cost of both brand and generic to be evaluated along with the geographic trends. The states were separated into the ten geographic divisions, according to the US Census Bureau, and the U.S. territories to identify prescribing trends.[12] Divisions were New England: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Middle Atlantic: New Jersey, New York, and Pennsylvania; East North Central: Illinois, Indiana, Michigan, Ohio, and Wisconsin; West North Central: Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota; South Atlantic: Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, and West Virginia; East South Central:

Alabama, Kentucky, Mississippi, and Tennessee; West South Central: Arkansas, Louisiana, Oklahoma, and Texas; Mountain: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming; Pacific: Alaska, California, Hawaii, Oregon, and Washington; and US territories including Puerto Rico.

The primary endpoint was to determine the difference in the rates of CMS Medicare Part D utilizers who had antipsychotic prescriptions in each of the ten geographic divisions. The total number of claims was divided by the population of total Medicare Part D utilizers in order to account for each of the areas having different populations. The secondary endpoints were the differences in percentage of antipsychotic spending in each division in relation to total spending for Medicare Part D, total cost of generics versus brand name drugs, and the number of prescriptions for a variety of specialists. Demographic information was determined including: number of antipsychotic prescriptions per division, absolute number of antipsychotic prescriptions and total antipsychotic medication cost, number of prescriptions and costs of brand versus generic drugs, percentage of brand spending versus generic spending, percentage of Medicare Part D spent on antipsychotics versus total costs, and number of prescriptions per prescriber specialty. Prescriber specialty was based loosely on American Medical Association practitioner fields. The rate of antipsychotic use was evaluated in relation to the active Medicare Part D population of the division by utilizing the 2013 CMS data. The rate of antipsychotic prescribing was calculated by determining the number of prescriptions for each antipsychotic for the division and dividing by the number of people utilizing Medicare Part D. The data was converted to SPSS (version 19, Armonk, NY) for further data analysis, which included ANOVA.

Results
Approximately 35 million claims of antipsychotic prescriptions via the Medicare Part D program in 2013 were documented. Tables 1 and 2 provide the demographics of the claims. The New England division was found to have the highest rate of patients receiving an antipsychotic at 0.83 and West North Central was at 0.73. The Mountain division had the lowest rate at 0.46. The nationwide rate was at 0.58 and several divisions such as the Pacific, West South Central, East South Central, South Atlantic, East North Central, and Middle Atlantic were close to this amount. No significant differences in the rate of antipsychotic prescriptions per division were observed (P=0.484). Table 2 demonstrates the number of claims per division and the rate of patients with claims in each of these divisions.

There was about $4.9 billion spent on antipsychotics in the patient population. Table 1 demonstrates the demographics

of Medicare Part D spending on antipsychotics. The percentage of spending on antipsychotics by Medicare Part D was approximately 4.75% of the $103 billion. The total cost for the brand name antipsychotics was approximately $3.5 billion versus $1.4 billion for the generics. Approximately 72% of the cost represented brand name drugs. The antipsychotic generics in descending order of number of claim counts were quetiapine, risperidone, olanzapine, aripiprazole, clozapine, ziprasidone, paliperidone, lurasidone, asenapine maleate, iloperidone, and lastly olanzapine-fluoxetine. In addition, over 50% of the claims were for quetiapine and risperidone. There was a significant difference seen between the numbers of prescriptions for the various brands of antipsychotics (P=0.017). Total antipsychotic cost was the most in the East North Central part of the country, with the total cost of $854 million, followed by the South Atlantic ($827 million), Middle Atlantic ($719 million), and Pacific regions ($657 million). The lowest total antipsychotic cost was observed in the US territories ($35 million) followed by the Mountain area ($224 million).

The percentages of the numbers of prescriptions per prescriber specialty was evaluated and is shown in Table 3. Mental health professionals were associated with 47% of antipsychotic prescribing. Family and general practice physicians prescribed about 17% of the antipsychotics. Internal medicine doctors were responsible for about 17% of antipsychotic prescriptions as well. Neurology and geriatric medicine specialists were each accountable for about 1.5% each. Mid-level prescribers (limited-scope prescriptive authority) were responsible for about 12% of the antipsychotic prescriptions. Nurses were responsible for about 2% of the total prescriptions. Most of the other prescribers not included in these groups were writing less than 1% of the total prescriptions.

When different divisions were compared for prescribing characteristics based on generic prescription counts interesting trends emerged. Every division had the same top two most prescribed drugs (e.g., quetiapine and risperidone). The third and fourth most commonly prescribed drugs by region varied between olanzapine and aripiprazole, and the majority of the divisions had olanzapine as their third most prescribed drug. Exceptions to this included: West South Central, East South Central, South Atlantic, and West North Central divisions. With the exception of the US territories, the top six most prescribed drugs were all the same in these divisions, but there were slight inconsistencies in their order. These additional two drugs were ziprasidone and clozapine with the "alternative" top six drugs being rounded out by paliperidone and ziprasidone in the US territories. Olanzapine-fluoxetine was the least prescribed drug in every division except for US territories.

Discussion

There were no statistically significant differences in prescribing patterns of antipsychotics in the geographic divisions. New England and West North Central should be further evaluated to evaluate why these areas have rates that are so much above the national average. The rates of these areas were 0.83 and 0.73, respectively, which was above the nation average of 0.58. The percentage of the cost of antipsychotics at 4.75% was a significant portion of the budget. Brand name drugs consisted of 72% of the cost for antipsychotics. As these medications become available as generic products, the spending on antipsychotic medications by Medicare Part D will be reduced. For example, this study was based on 2013 data and aripiprazole was only available as a brand at that time. Generics that were available include: clozapine, olanzapine, olanzapine-fluoxetine, quetiapine, risperidone, and ziprasidone.

Mental health professionals prescribed the highest percentage of prescriptions for antipsychotics. Family/general doctors and internal physicians comprised 34% of the claims written for antipsychotics. This is likely because patients often see these doctors more regularly than their specialists, and thus asked their primary care physicians for refills on their medications. Additionally, these doctors often serve as resident physicians for nursing homes. Geriatric and neurology specialists made up 3% of the claims. Mid-level prescribers prescribed 12% of the claims. This is a significant group, and worth further investigation, as these prescribers may not be as familiar with antipsychotics.

Although geographic variation of antipsychotics has been evaluated, our study has several differences compared to previously published data. Rawal et al., found percentages of youth receiving antipsychotics in each of the treatment facilities. Investigators determined percentages of patients receiving antipsychotics because researchers performed chart reviews at facilities and determined the number of patients receiving antipsychotics.[9]

In the current study, the number of people who were taking antipsychotics is unknown because only number of claims being processed and total number of Medicare Part D utilizers was known. Each division was normalized by dividing the number of claims by the Medicare Part D population. Rawal et al found that the southwestern states included had the largest percentage of antipsychotic use which is counter to the current finding of the New England division having the largest rate of prescription claims. The patients in this study were adolescent, unlike in the Medicare Part D study, which could have resulted in this difference.[9] King et al found the number of patients that filled at least one antipsychotic in 2008 with a database that included over 60% of all retail prescriptions in

the US.[10] Therefore, this study did not take into all retail sources or other sources, and there was not a specific population type being taken into account. While the current study indicated that New England was the area with the highest rate of antipsychotic use, the study conducted by King et al did not include any of the states within the division of New England as an area of heavy antipsychotic use. However, the study by King et al displayed results via maps, which may have biased the data to the East due to population centers. Our study, on the other hand, evaluated each division individually and reported data nationally in tables instead of maps. [10]

Additionally, geographic variation of prevalence of all mental illnesses in adults 18 or older in 2012 and 2013 was reported which should have an effect on the cause of geographic distribution of antipsychotic use.[13] When comparing this to the results of the current study, it is found that there is not a direct correlation with rates of antipsychotic use in Medicare Part D and the rates of mental illnesses in the various divisions. This can be a result of including all patients aged 18 and older instead of only the Medicare Part D population which consists mostly of patients that are 65 or older.

There were limitations to the study. The data did not include doses of the medications which would have assisted in interpreting why they were being prescribed. When evaluating the different prescribers, there were a few categories (e.g., driver and adult companion) that did not seem to be accurate so coding errors could have been present within the data. It is unknown whether or not CMS was able to capture all Pharmacy Benefit Management data. Therefore, it is possible that not all Medicare Part D utilizers were included in the study. Practitioners who prescribed fewer than ten prescriptions were excluded. This may not have had an impact on the current results unless a significant number of practitioners were included in this exclusion. Zip codes, rather than geographic regions may provide a better indication of geographic variation of antipsychotic use. Zip codes may provide a more meaningful way to characterize geographic variation rather than geographic regions. Zip codes will allow more targeting of efforts aimed at reducing geographic variation.

Conclusions

Geographic variation does not appear to exist in antipsychotic prescribing between the ten divisions in the utilizers of Medicare Part D; however, statistically significant differences in total antipsychotic claims and costs were observed. The divisions with the highest rates of claims were New England (0.83), West North Central (0.73), and East North Central (0.63). Additional studies need to be conducted to assess the impact of differences in total antipsychotic claims and costs over the United States.

Conflict of Interest: "We declare no conflicts of interest or financial interests that the authors or members of their immediate families have in any product or service discussed in the manuscript, including grants (pending or received), employment, gifts, stock holdings or options, honoraria, consultancies, expert testimony, patents and royalties".

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Table 1: Medicare Part D antipsychotic medication use, 2013

Total Number of Antipsychotic Prescriptions	20,381,015
Number of Brand Name Prescriptions	4,878,594
Cost of Brand Name Products	$3,511,550,311.29
Number of Generic Prescriptions	15,502,421
Cost of Generic Products	$1,398,372,070.84
Percent of Cost on Brand Name Products	71.52%
Total Cost of Antipsychotics	$4,909,922,382.13
Percent of Antipsychotic Cost versus Total Cost	~4.75%

Table 2: United States' geographic distribution of antipsychotic use, 2013

	P	M	WSC	ESC	SA	WNC	ENC	MA	NE	UST
Medicare Part D Utilizer Population[a]	5.1	2.1	3.5	2.4	6.8	2.4	5.4	5.0	1.7	0.57
Total Antipsychotic Claims [a,b]	2.6	9.7	1.8	1.4	3.5	1.7	3.4	3.1	1.4	0.28
Rate[c]	0.51	0.46	0.53	0.58	0.52	0.73	0.63	0.62	0.83	0.5
Aripiprazole	328,248	121,213	244,928	173,292	430,962	243,052	439,761	426,285	189,130	24,534
Asenapine maleate	14,195	4,875	12,725	11,975	17,886	10,517	21,236	12,945	4,359	584
Clozapine	163,005	51,538	59,669	31,442	131,344	130,665	233,696	223,587	140,103	2,071
Iloperidone	7,695	1,600	8,282	3,747	7,497	6,774	13,193	5,063	959	48
Lurasidone	42,081	10,825	26,376	13,364	33,413	34,840	55,407	25,956	12,558	355
Olanzapine	416,256	146,343	233,913	167,198	415,174	233,444	466,479	464,147	215,078	27,369
Olanzapine-fluoxetine	861	620	1,971	1,824	3,848	1,303	2,772	2,572	327	438
Paliperidone	60,146	25,953	58,142	38,407	87,412	58,837	106,741	52,436	26,033	2,472
Quetiapine[a]	0.84	0.31	0.69	0.53	1.2	0.57	1.06	1.0	0.44	0.12
Risperidone	621,748	242,618	427,566	341,253	928,964	405,169	828,923	802,975	328,841	96,599
Ziprasidone	111,680	51,427	95,018	80,274	175,767	81,248	159,488	113,948	49,060	7,068
Total Antipsychotic Cost (in millions)[a,d]	$657	$224	$475	$330	$827	$464	$854	$719	$321	$35

aResults recorded in millions; bP<0.001; cP=0.484; dP<0.017

Pacific (P): Alaska, California, Hawaii, Oregon, and Washington; Mountain (M): Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming; West South Central (WSC): Arkansas, Louisiana, Oklahoma, and Texas; East South Central ESC) :Alabama, Kentucky, Mississippi, and Tennessee; South Atlantic (SA): Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, and West Virginia; West North Central (WNC): Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota; East North Central (ENC): Illinois, Indiana, Michigan, Ohio ,and Wisconsin; Middle Atlantic (MA): New Jersey, New York, and Pennsylvania; New England: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; US Territories (UST): Any US territory including Puerto Rico

Table 3: Number of prescriptions per prescriber specialty, 2013

Prescriber Type	Number of Prescriptions	Percent of Overall Total Prescriptions
Mental Health	9,663,331	47.41%
Family/General Practice	3,488,160	17.11%
Internal Medicine	3,408,932	16.73%
Neurology	297,184	1.46%
Geriatric Medicine	288,811	1.42%
Mid Level/Limited Scope Prescribers	2,405,838	11.80%
Nurses	395,492	1.94%

Mental Health: Psychiatry, Neuropsychiatry, Geriatric Psychiatry, Psychologist, Counselor, Clinical Psychologist, Clinical Neuropsychologist, Psychoanalyst, Behavioral Analyst, Marriage & Family Therapist; **Family/General Practice**: Family Practice, General Practice, Family Practice; **Internal Medicine**: Internal Medicine, Pulmonary Disease, Nephrology, Infectious Disease, Gastroenterology, Rheumatology, Critical Care; **Neurology**; **Geriatric Medicine**; **Mid Level/Limited Scope Prescribers**: Nurse Practitioner, Physician Assistant, Dentist, Pharmacist, Licensed Clinical Social Worker, Podiatry, Chiropractic