Prescribing of Alzheimer's Disease Treatments by Provider Type and Geographic Region: A Comparison among Physicians, Nurse Practitioners, and Physician Assistants

Yeonhee Jenny Park

A thesis
submitted in partial fulfillment of the
requirements for the degree of

Master of Science

University of Washington
2021

Committee:
Zachary Marcum
David Veenstra

Program Authorized to Offer Degree:
Pharmacy

University of Washington

Abstract

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Yeonhee Jenny Park

Chair of the Supervisory Committee:
Zachary Marcum
The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute

Background: The U.S. healthcare workforce is insufficient to handle the increasing Alzheimer's Dementia (AD) caseload. While nurse practitioners (NPs) and physician assistants (PAs) are increasingly delivering primary care to patients with chronic diseases, the nature of their prescribing of AD treatments is largely unknown.

Objective: The primary objective of this study was to compare the prescribing of AD medicines across provider types (physician, NP, and PA) and geographic regions.

Methods: We conducted a retrospective cohort study using IBM MarketScan® commercial and Medicare supplemental claims to examine unique AD prescriptions prescribed between January 1, 2016, and December 31, 2019. Food and Drug Administration (FDA) indicated AD prescriptions were identified and prescribing patterns were descriptively analyzed by provider type and metropolitan statistical area (MSA). Parallel analysis of prescriptions for another geriatric condition, osteoporosis (OP), was also conducted for comparison.

Results: A total of 103,067 AD prescriptions and 131,773 OP prescriptions were included in our analyses. Physicians, NPs, and PAs prescribed 95.65%, 3.37%, and 0.98% of AD prescriptions, respectively. NPs and PAs prescribed a significantly higher (95% CI: 0.018, 0.028) proportion of

AD prescriptions in rural (5.84%) as compared to urban areas (3.56%). A significantly higher proportion of AD prescriptions were prescribed by NPs and PAs (95% CI: 0.004, 0.008) and specialists (95% CI: 0.185, 0.191) compared to OP prescriptions.

Conclusion: The proportion of AD prescriptions prescribed by NPs and PAs is relatively low, especially in urban areas. Further research assessing AD health outcomes and costs by provider type and geographic region is necessary to better guide healthcare workforce planning for patients with AD.

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Introduction

Alzheimer's Disease (AD) is a neurodegenerative disease currently ranked as the sixth leading cause of death in the United States (1). Over six million Americans age 65 and older, roughly one in nine seniors, currently live with AD (1). The number of patients with AD is expected to more than double to 13.5 million by 2050 (2).

A simulation analysis assessing the effect of capacity constraints on access to care for patients with AD revealed that the U.S. health care system is unprepared and insufficient to handle the increasing AD caseload (3). The increasing number of patients with AD requires more diagnosing, prescribing, and monitoring for treatment and management. Although the workforce issues are multifaceted, the most pressing constraint may be the inadequate supply of geriatrics and dementia specialists to treat patients (4). Under current circumstances, a patient with dementia is projected to wait 18.6 months on average to get diagnosed or treated by a dementia specialist (3). Over 2.1 million patients with mild cognitive impairment (MCI) would develop AD during such a delay from 2020 to 2040 (3).

Nurse practitioners (NPs) and physician assistants (PAs) may play critical roles in alleviating wait times and providing access to care for patients with AD (6, 18). NPs and PAs are increasingly serving as primary care providers (PCPs) for patients with chronic diseases (5). The proportion of NPs and PAs providing primary care for patients with AD is expected to vary by geographic region due to state regulations regarding scope-of-practice and varying access to care by

rurality (7, 14). However, the nature of NP and PA involvement in treating and managing AD is largely unknown. Potential differences in NP and PA prescribing of AD treatments in relation to that of physicians (including specialists) are also unexamined.

Objective

The primary objective of this study was to compare the prescribing of AD medicines across provider types (physicians, NPs, and PAs) and geographic regions. Secondary objectives were to compare the prescribing of AD medicines against that of osteoporosis (OP), another geriatric condition, and describe the proportion of patients with AD that underwent neuroimaging within 90 days prior to a documented AD diagnosis.

Methods

Study Design and Data Source

A retrospective cohort study using medical and pharmacy claims was performed using the IBM MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases (8). The IBM MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases are composed of de-identified patient-level health data regarding the annual medical utilization and expenditures for inpatient, outpatient, and prescription claims for over 90 million employees, their spouses, and their dependents who are covered under employer-sponsored private health insurance or Medicare supplemental insurance in the United States.

Eligibility Criteria

All Food and Drug Administration (FDA) indicated AD and OP prescriptions (Table 1) filled between 2016 to 2019 were included. AD prescriptions were comprised of cholinesterase inhibitors and memantine, an NMDA receptor antagonist. OP prescriptions included antiresorptive agents (bisphosphonates, denosumab, selective estrogen receptor modulators) and anabolic agents (romosozumab).

Inpatient prescriptions, duplicates, refills, and prescriptions for which the pharmacy fill date did not exactly match an outpatient service date were excluded from the analysis. Prescriptions missing enrollee ID data, metropolitan statistical area (MSA) data, and provider type data were also excluded. Finally, prescriptions for which the listed provider type was an agency, facility, or a provider type lacking independent prescriptive authority were excluded.

Prescriptions meeting the prespecified eligibility criteria were then compared against all unique AD and OP prescriptions to assess potential differences. Unique prescriptions were defined as prescriptions without missing data that were not refills or duplicates. Differences in patient demographics (age and gender) and prescription characteristics (proportion of each drug prescribed and days supply) were assessed.

Data Collection: Variables and Measures

Due to a lack of provider type data in the pharmacy claims database within MarketScan, we estimated provider type by identifying the enrollee's nearest preceding outpatient service claim. We assumed that if an enrollee had visited an outpatient clinic on the same day that a unique prescription was filled for that enrollee at a pharmacy, then the provider seen at the outpatient clinic was most likely to have prescribed the unique prescription.

Similar methods were used to analyze AD and OP prescriptions. However, specialist MDs were defined as neurologists for AD and endocrinologists or rheumatologists for OP.

We first identified the total number and proportions of prescriptions written by physicians, NPs, and PAs. The top five physician subtypes prescribing AD and OP prescriptions were also identified. Prescriptions were then grouped by provider type to describe the proportions of each medicine prescribed by provider type. We compared the proportions of physician specialists and NPs/PAs prescribing AD and OP medicines and the proportions of each medicine prescribed by NPs and PAs against that of physicians (e.g., the proportion of donepezil prescribed by NPs and PAs compared to MDs).

Regional Analyses

The proportions of AD and OP medicines prescribed by physician specialists, NPs, and PAs were assessed by MSA. MSAs are delineated by the U.S. Office of Management and Budget to encompass a cluster of counties around a densely populated core region (21). In an effort to

identify potential regional patterns of physician specialist prescribing, heat maps were generated to visually depict the proportion of medicines in each MSA prescribed by physician specialists.

MSAs were grouped according to rurality to assess differences in AD prescribing between rural and urban areas. MSA-level data was divided into county-level data using the National Bureau of Economic Research (NBER) Census Core-Based Statistical Area (CBSA) to Federal Information Processing Series (FIPS) County Crosswalk (10). Counties were then classified into one of six rurality categories using the National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties (11). MSAs not listed in the NBER crosswalk were excluded from rurality analyses.

Some MSAs encompassed counties with different rurality categories. The most common rurality category for such MSAs was set as the rurality category for the whole MSA. Because MSAs by definition require counties to be near an urbanized area with a population greater than 50,000, some US counties are not part of an MSA. Prescriptions written in rural areas that were not geographically classified into an MSA were separately placed into their own rurality category: rural. Including the pre-designated 'rural' category, each prescription was classified into one of seven total rurality categories. The rurality categories in the order of lowest to highest population density were rural, non-core, micropolitan, small metro, medium metro, large fringe metro, and large central metro.

We identified and compared the proportion of prescriptions written by specialist physicians, NPs, and PAs in each rurality category. We also descriptively compared characteristics of the top 5% of counties with the highest proportion of prescriptions prescribed by NPs and PAs against the bottom 5% of counties with the lowest proportion of prescriptions prescribed by NPs and PAs.

Exploratory Analysis

We estimated the proportion of patients with AD that had a neuroimaging procedure documented in their claims within 90 days prior to an AD diagnosis. All enrollees with at least one AD diagnosis recorded in their outpatient claims between January 1, 2016 and December 31, 2019 were identified. The following International Classification of Disease, 10th revision (ICD-10) codes were used to identify AD diagnoses: G30.0, G30.1, G30.8, and G30.9. We then calculated the proportion of enrollees who had at least one documented neuroimaging record within 90 days prior to the AD diagnosis. Neuroimaging was defined as any magnetic resonance imaging (MRI), PET or CT scan of the brain. The following CPT codes were used to identify the neuroimaging in MarketScan: 70551, 70553, 70544, 78608, 70460, 70470, and 70480 (Appendix 6).

Statistical Analysis

Due to the relatively smaller number of prescriptions written by NPs and PAs, prescriptions written by NPs/PAs were combined into one group (non-physician providers) for statistical analyses. Two-sample independent z-tests were performed to detect any statistically significant

differences in the following outcomes: (1) the proportion of AD prescriptions prescribed by MDs, specialist MDs, NPs, and PAs as compared to that of OP medications; (2) the proportion of each AD and OP medicine prescribed by MDs as compared to that prescribed by NPs and PAs; and (3) the proportions of specialist physicians and NPs/PAs prescribing amongst the most rural and most urban rurality categories. For all statistical analyses, we set alpha at 0.05 and obtained 95% confidence intervals (CI).

Software

SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for constructing the analytic dataset and R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) for statistical analyses and generating heat maps. Microsoft PowerPoint version 16.49 and Microsoft Excel version 16.49 (Microsoft Corporation., Redmond, WA) were used to generate tables and figures.

Results

Of 1,966,057 AD and 2,958,050 OP FDA-indicated prescriptions in MarketScan from 2016 to 2019, 103,067 AD and 131,773 OP prescriptions were included for analysis (Figure 1). The most common reasons for exclusion of AD and OP prescriptions were due to the exclusion of refills (60.73% of AD prescriptions and 65.60% of OP prescriptions) and prescriptions for which the fill date did not exactly match an outpatient service date (28.31% of AD prescriptions and 25.19% of OP prescriptions).

Enrollees included in our analytic cohort for AD prescriptions were relatively younger compared to enrollees of all unique AD prescriptions (Table 2). A higher proportion of donepezil and combination donepezil/memantine and a lower proportion of galantamine and memantine were observed in our analytic cohort as compared to all unique AD prescriptions. Patient demographics of our OP cohort were similar to that of all unique OP prescriptions. A higher proportion of alendronate and lower proportions of denosumab and teriparatide were observed in our analytic cohort as compared to all unique OP prescriptions.

Figure 2 depicts the proportion of AD and OP prescriptions written by NPs, PAs, MDs, and MD specialists. Physicians and NPs/PAs prescribed 95.65% and 4.34% of AD prescriptions, respectively. NPs/PAs prescribed a statistically significantly (95% CI: 0.004, 0.008) higher proportion of AD prescriptions (4.35%) as compared to OP prescriptions (3.75%). The five MD specialties prescribing the largest proportions of AD prescriptions were family practice, neurology, internal medicine, multispecialty, and psychiatry. Physician specialists prescribed 23.21% of AD prescriptions, which was statistically significantly (95% CI: 0.185, 0.191) higher than the proportion of OP prescriptions prescribed by physician specialists (10.29%).

The proportions of AD and OP medicines prescribed by NPs, PAs, and MDs are presented in Figure 3. Overall, donepezil was the most frequently prescribed AD medicine followed by memantine, rivastigmine, galantamine, and combination donepezil and memantine. NPs/PAs prescribed significantly lower proportions of donepezil (95% CI: -0.071, -0.041) and significantly

higher proportions of memantine (95% CI: 0.030, 0.059) and combination donepezil and memantine (95% CI: 0.008, 0.014) as compared to physicians.

Alendronate was the most frequently prescribed OP medicine followed by ibandronate, raloxifene, risedronate, denosumab, teriparatide, abaloparatide, zoledronic acid, and combination alendronate and cholecalciferol. Compared to physicians, NPs/PAs prescribed significantly lower proportions of alendronate (95% CI: -0.046, -0.018) and significantly higher proportions of raloxifene (95% CI: 0.004, 0.022) and risedronate (95% CI: 0.011, 0.025).

A total of 90,657 (88%) AD prescriptions and 115,331 (87.5%) OP prescriptions were included in regional analyses after excluding prescriptions with MSAs not listed in the NBER crosswalk. AD and OP prescriptions were similarly distributed across the rurality categories (Figure 4). Most of the AD (32.41%) and OP (37.45%) prescriptions were filled in MSAs with populations greater than one million. Very few prescriptions were filled in micropolitan areas, and none of the prescriptions were filled in non-core areas.

NPs/PAs prescribed a significantly (95% CI: 0.018, 0.028) higher proportion of AD prescriptions in rural MSAs (5.84%) as compared to urban MSAs (3.56%). The proportion of AD prescriptions prescribed by specialists did not significantly (95%CI: -0.021, 0.0002) differ between rural (21.86%) and urban areas (22.88%). In the top 5% of counties with the highest proportion of AD prescriptions prescribed by NPs/PAs, NPs/PAs prescribed 17.30% of all AD prescriptions (Figure 5). In the bottom 5% of counties with the lowest proportion of AD prescriptions prescribed by

NPs/PAs, NPs and PAs prescribed 0.9% of all AD prescriptions. The counties in the top 5% had a bigger population and slightly lower median household incomes as compared to the bottom 5%.

NPs/PAs prescribed a significantly (95% CI: 0.064, 0.069) higher proportion of OP prescriptions in rural MSAs (7.75%) as compared to urban MSAs (1.30%). Physician specialists prescribed a significantly (95% CI: 0.027, 0.036) lower proportion of OP prescriptions in rural MSAs (6.95%) as compared to urban MSAs (3.82%). No apparent geographic variation was evident regarding the proportion of NPs/PA prescribing AD and OP medicines (Figure 6).

Exploratory Analyses

A total of 70,771 enrollees had an AD diagnosis documented in their outpatient claims between January 1, 2016, and December 31, 2019. A total of 1,785 enrollees (2.52%) had records of at least one neuroimaging procedure within 90 days before an AD diagnosis. Of 2,362 total neuroimaging procedures, 1338 (56.65%) were magnetic resonance imaging (MRI) which was the most common method of neuroimaging used.

Discussion

This study evaluated prescribing patterns for AD among provider types and across geographic regions. NPs/PAs and physician specialists prescribed significantly higher proportions of AD prescriptions as compared to OP prescriptions. Statistically significant differences in the proportions of some AD medicines prescribed by NPs/PAs and physicians were also identified; however, these differences are numerically small. There was no apparent geographic variation

in physician specialist prescribing. However, NPs/PAs prescribed a significantly higher proportion of AD prescriptions in rural areas compared to urban areas.

Our results imply there is opportunity for increased involvement of NPs and PAs in AD care. While a statistically significantly higher proportion of prescriptions were written by NPs and PAs in the AD cohort (4.35%) as compared to the OP cohort (3.75%), the proportion of AD prescriptions prescribed by NPs and PAs is small compared to that of other diseases. For example, approximately 21.8% of patients with diabetes are managed by NPs and PAs (14), and 23% of antibiotics are prescribed by NPs and PAs (16). Since 2000, the number of geriatricians per 10,000 adults 65 years and older has decreased (19); the U.S. Department of Health and Human Services suggests that increasing the number of NPs and PAs to provide primary care can alleviate the projected shortage of physicians for managing AD (18).

Recent scope-of-practice regulations allowing NPs and PAs to prescribe without physician oversight has demonstrated positive impacts on costs and patient outcomes. Practitioner labor costs per visit along with total labor costs per visit are significantly lower among practices with greater NP and PA involvement as primary care providers (13). In one study, patients taking anti-diabetic medications had significantly higher medication adherence rates and probabilities of good adherence in states that expanded NP scope of practice (12). In a literature review, three studies reported significantly greater primary care access in states where NPs have full practice authority (14). With our aging population, we expect an increased need for diagnosing, prescribing, and monitoring for patients with AD. Roughly 16% of the US senior population is

expected to have AD in 2050 (2), and proactive solutions – such as expanding scope of practice for NPs and PAs – are necessary to ensure timely and quality care for older adults.

These results should be interpreted in the context of important limitations. First, selection bias may be a concern as included prescriptions represented roughly 5% of all AD and OP prescriptions identified from MarketScan during this time period. As such, our results can be generalized to unique prescriptions for AD, not refills. Moreover, there were some minor differences in age and proportions of certain medicines when comparing included versus excluded prescriptions. However, these differences were minor and unlikely to significantly skew our results. Second, the lack of provider type data in the pharmacy claims database within MarketScan may have resulted in the incorrect matching of provider data for some prescriptions. Incorrectly matching provider data to prescriptions may reduce the internal validity of this study. To minimize the risk of incorrectly matching providers to prescriptions, we used the most conservative method of only including prescriptions for which the pharmacy fill date was the same day as a documented outpatient service claims date for the same enrollee. Finally, our analytic cohort included data from those with employer-sponsored supplemental Medicare coverage, which is representative of 29% of all Medicare beneficiaries (17).

Conclusion

We conducted a retrospective cohort study using insurance claims data and descriptively assessed the prescribing of AD treatments by provider type and geographic region. NPs and PAs prescribe roughly 4% of AD prescriptions, and their involvement in AD prescribing is greater in

rural areas as compared to urban areas. NPs and PAs may effectively help alleviate projected workforce constraints and delays in access to care for patients with AD. Further research comparing AD health outcomes and costs by provider type and geographic region may be necessary to more effectively increase the capacity of our current workforce to provide timely care for patients with AD.

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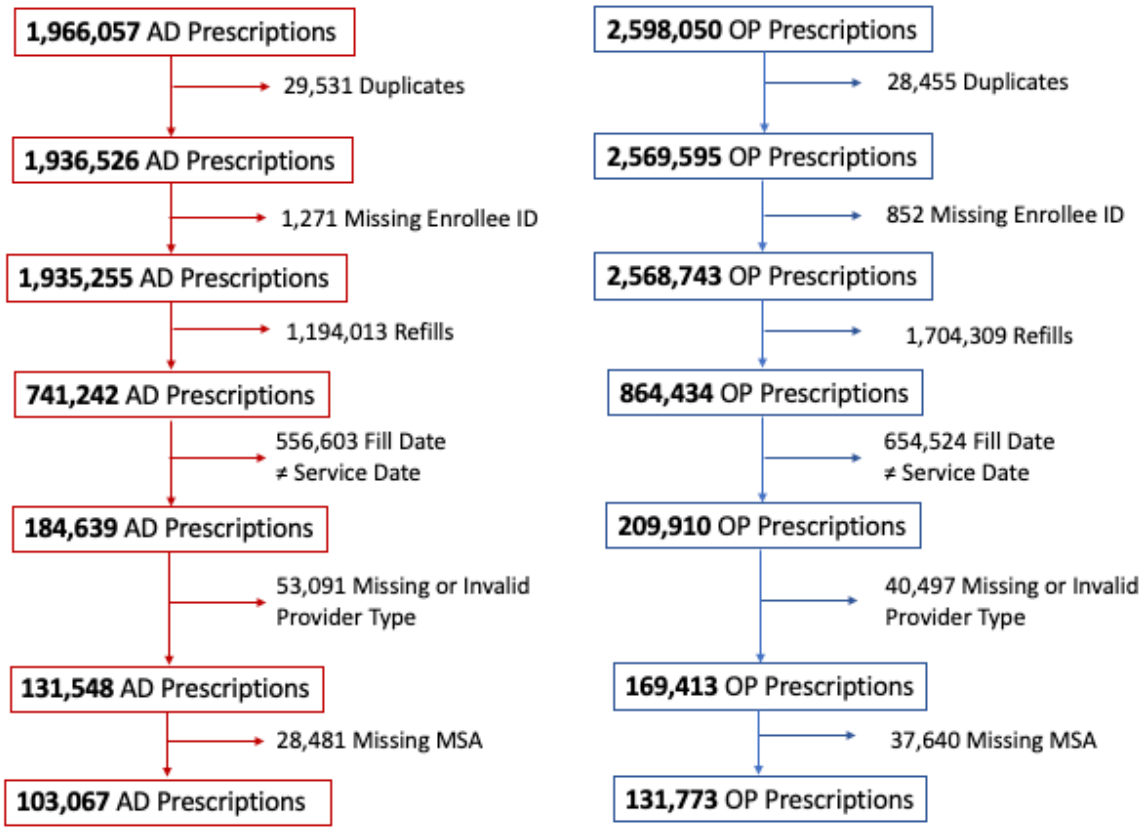
Figures and Tables

Table 1: Generic Names of AD and OP medicines	
Alzheimer's Disease (AD)	**Osteoporosis (OP)**
Donepezil	Abaloparatide
Galantamine	Alendronate
Rivastigmine	Alendronate and Cholecalciferol
Memantine	Denosumab
Donepezil and Memantine	Ibandronate
	Raloxifene
	Risedronate
	Teriparatide
	Zoledronic Acid

Figure 1: Cohort Selection Flowchart



Abbreviations: AD = Alzheimer's Dementia, OP = Osteoporosis, ID = Identification, MD = Medical Doctor, NP = Nurse Practitioner, PA = Physician Assistant

Table 2: Demographic and Clinical Characteristics of Analytic Sample

Alzheimer's Disease Cohort		
	Included in Analysis	All Unique Prescriptions
Patient Demographics		
Age: Mean (SD)	75.22 (13.91)	78.86 (12.43)
Gender (% Female)	57.64%	58.12%
Prescriptions (n (%))		
Donepezil	57,749 (56%)	375,576 (50%)
Galantamine	1,463 (1%)	14,210 (2%)
Rivastigmine	7,664 (8%)	61,521 (8%)
Memantine	34,555 (34%)	276,092 (37%)
Donepezil and Memantine	1,306 (1%)	1,935 (0.3%)
Total	103,067	744,180
Days Supply: Mean (SD)	44.71 (30.00)	42.37 (31.10)

Osteoporosis Cohort		
	Included in Analysis	All Unique Prescriptions
Patient Demographics		
Age: Mean (SD)	63.59 (10.32)	64.54 (10.70)
Gender (% Female)	92.66%	92.82%
Prescriptions (n (%))		
Abaloparatide	229 (0.2%)	2832 (0.4%)
Alendronate	80,539 (61%)	395,836 (56%)
Alendronate/Cholecalciferol	120 (0.1%)	964 (0.1%)
Denosumab	3,280 (2%)	36,970 (5%)
Ibandronate	18,585 (14%)	90,178 (13%)
Raloxifene	16,704 (13%)	102,461 (14.5%)
Risedronate	10,766 (8%)	57,811 (8%)
Teriparatide	1,362 (1%)	17,624 (2%)
Zoledronic Acid	185 (0.1%)	1,734 (0.25%)
Romosozumab-aqqg	3	35
Total	131,773	706,445
Days Supply: Mean (SD)	60.65 (33.67)	62.72 (37.21)

Abbreviations: SD = Standard Deviation

Figure 2: The proportion of AD and OP prescriptions written by NPs, PAs, MDs and MD subtypes.

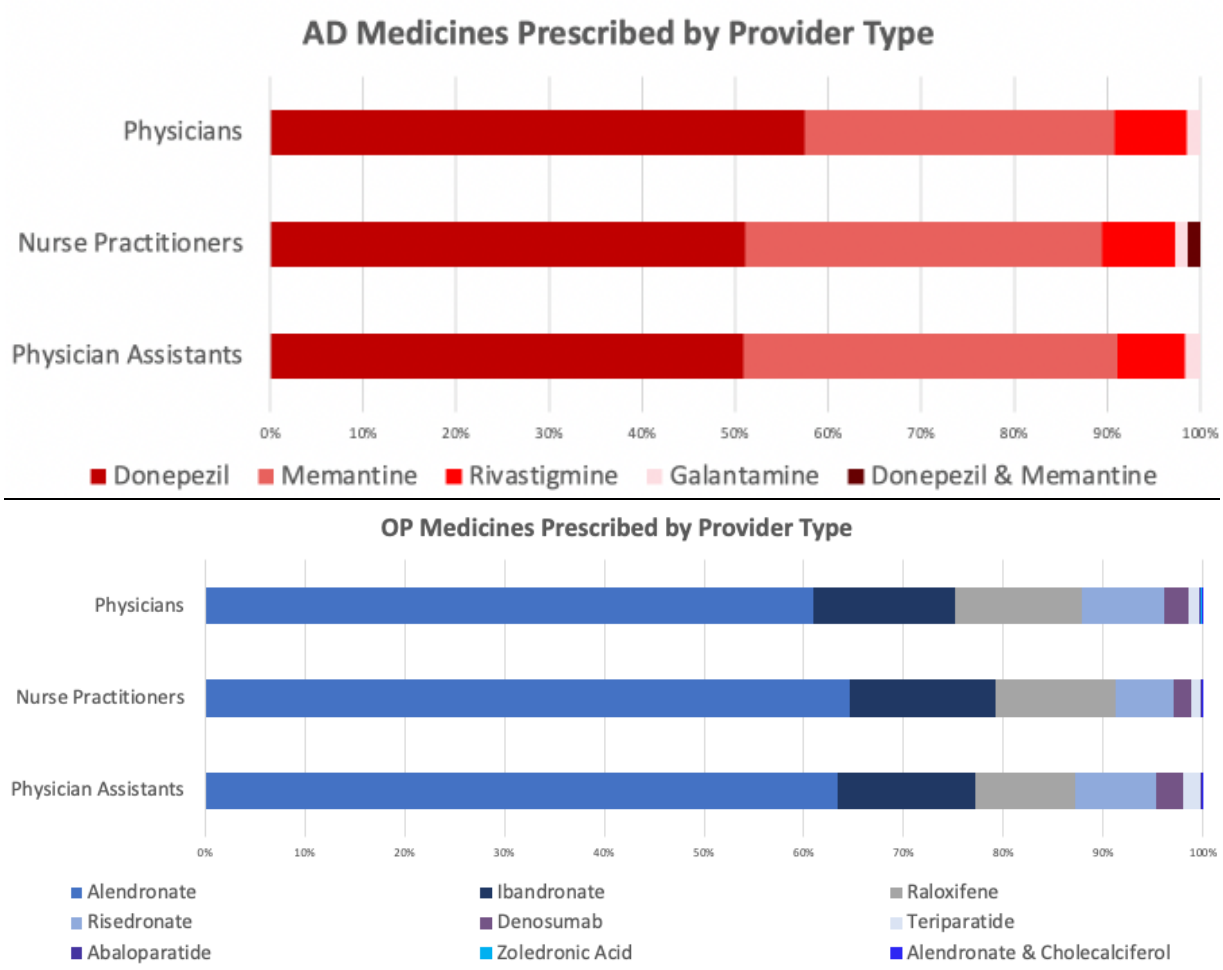
Alzheimer's Disease Prescriptions		
	Count	Percentage of All Prescriptions
Physicians	**98,588**	**95.65%**
Family Practice	29,655	28.77%
Neurology	23,924	23.21%
Internal Medicine	16,254	15.77%
Multispecialty	8,867	8.60%
Psychiatry	5,459	5.30%
Geriatric Medicine*	813	0.79%
Other	13,616	13.21%
Non-Physician Professionals	**4,479**	**4.35%**
Nurse Practitioner	3,477	3.37%
Physician Assistant	1,002	0.98%
Total	**103,067**	**100%**

Not top 5 but relevant and important

Osteoporosis Prescriptions		
	Count	Percentage of All Prescriptions
Physicians	**126,836**	**96.25%**
Family Practice	39,137	29.70%
Internal Medicine	30,005	22.77%
Obstetrics & Gynecology	10,179	7.72%
Rheumatology	7,804	5.92%
Multispecialty	6,183	4.69%
Endocrinology & Metabolism*	5,763	4.37%
Geriatric Medicine*	194	0.15%
Other	27,571	20.92%
Non-Physician Professionals	**4,937**	**3.75%**
Nurse Practitioner	3,465	2.63%
Physician Assistant	1,472	1.12%
Total	**131,773**	**100%**

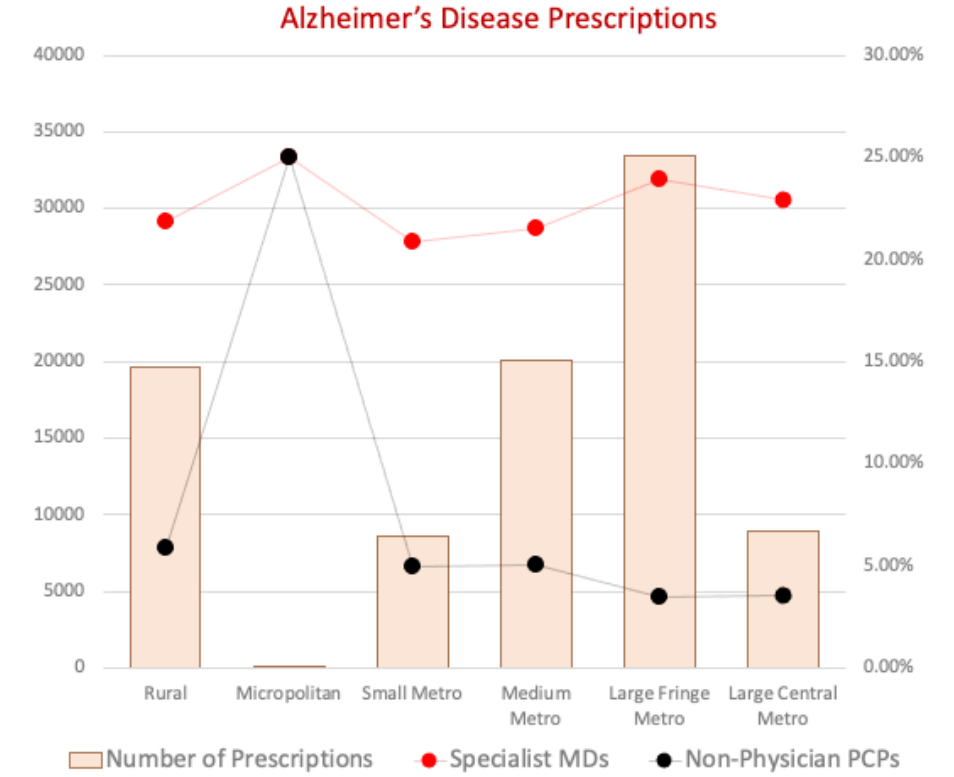
Abbreviations: AD = Alzheimer's Disease, NP = Nurse Practitioner, PA = Physician Assistant

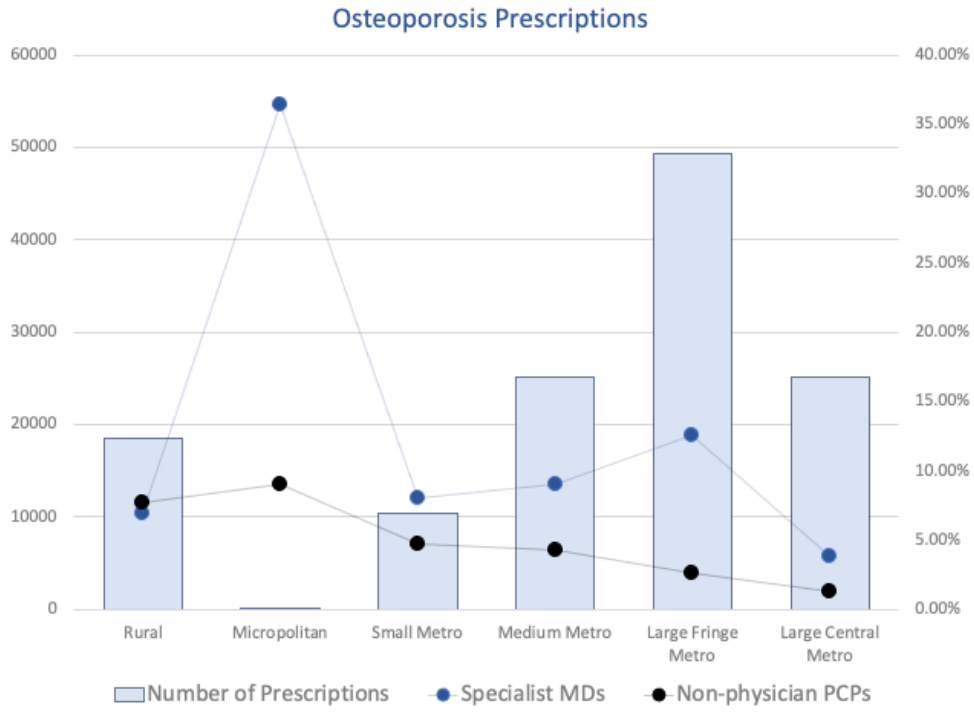
Figure 3: Proportions of AD and OP medicines prescribed by NPs, PAs, and MDs.



Abbreviations: AD = Alzheimer's Dementia, OP = Osteoporosis, MD = Medical Doctor, NP = Nurse Practitioner, PA = Physician Assistant

Figure 4: The distribution of prescriptions and proportion of prescriptions written by non-physician PCPs (NPs/PAs) or specialist MDs by rurality.





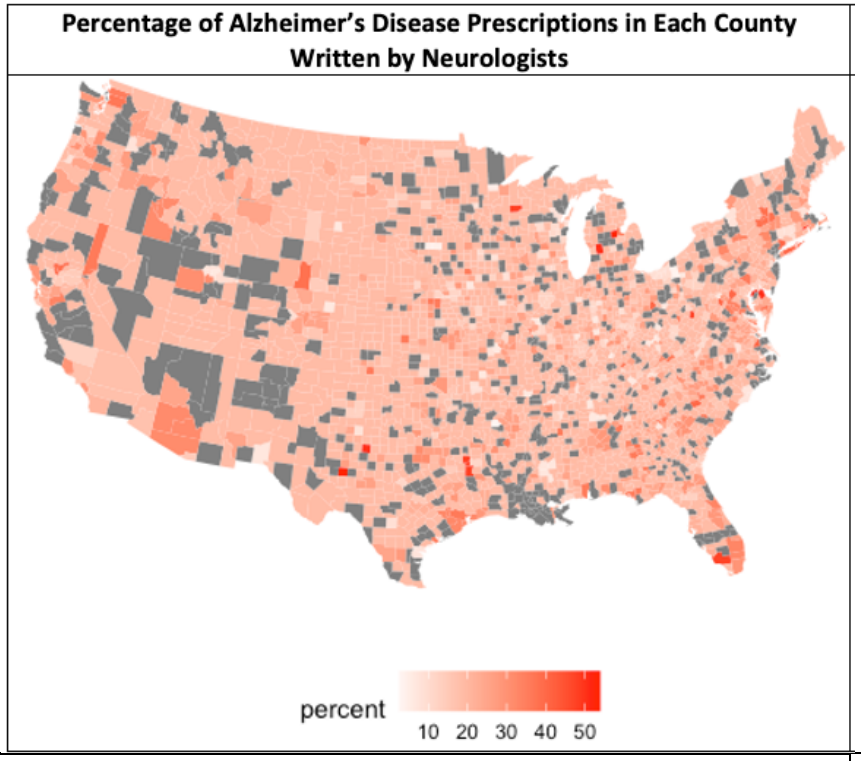
Abbreviations: PCP = Primary Care Provider, NP = Nurse Practitioner, PA = Physician Assistants, MD = Medical Doctor

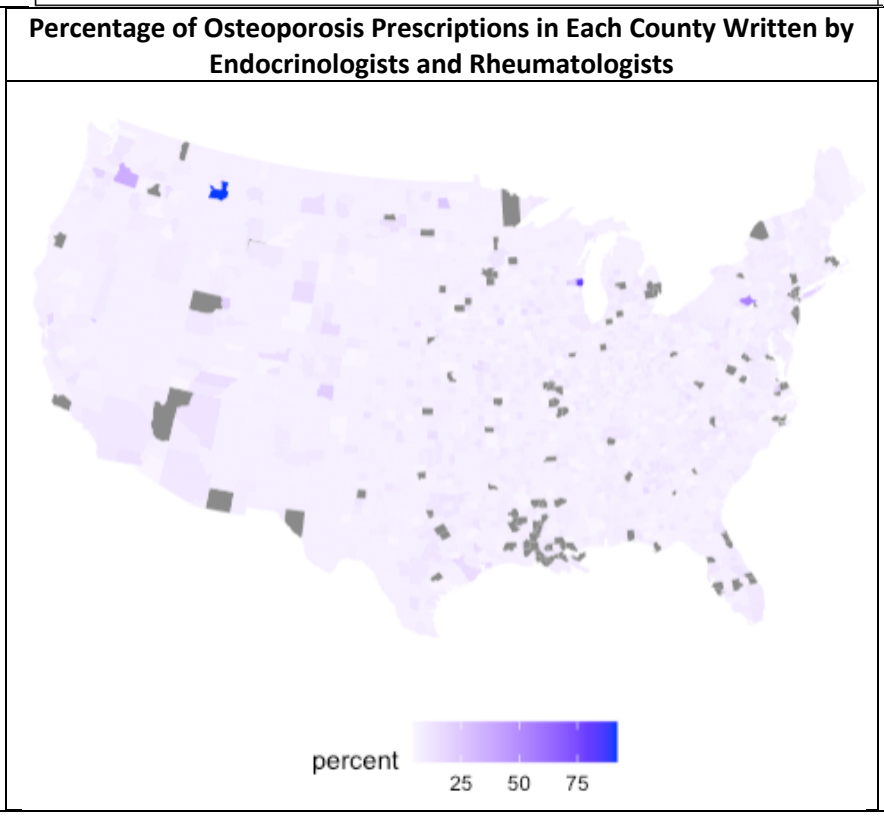
Figure 6: Comparing county characteristics between the top 5% and bottom 5% of counties with the highest and lowest proportion of prescriptions prescribed by NPs and PAs

	Top 5%	Bottom 5%
Percent of all prescriptions written by NPs and PAs	17.30%	0.9%
County population	135,103	680,809
Median Household Incomes	$62,642	$67,509

Abbreviations: NPs = Nurse Practitioners, PAs = Physician Assistants

Figure 5: Heat maps depicting the proportion of prescriptions prescribed by specialist MDs in each county.

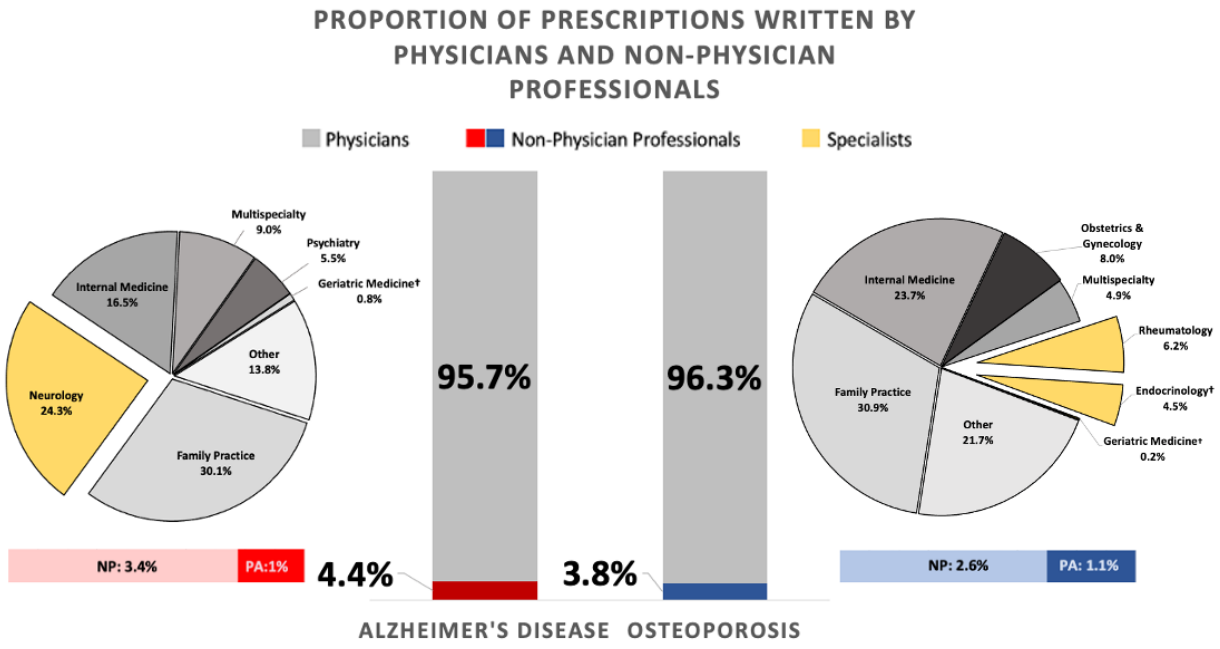




Abbreviations: MDs = Medical Doctors

Appendix

Appendix 1: Visual representation of the proportions of AD and OP prescriptions written by NPs, PAs, MDs and MD subtypes.



†: Not top five but relevant and important

Abbreviations: AD = Alzheimer's Disease, NP = Nurse Practitioner, PA = Physician Assistant

Appendix 2: Data for Figure 3

Alzheimer's Disease					
	Donepezil	Memantine	Rivastigmine	Galantamine	Donepezil & Memantine
PA	50.90%	40.22%	7.29%	1.60%	0.00%
NP	52.14%	39.09%	8.02%	1.38%	1.41%
MD	57.47%	33.34%	7.74%	1.42%	0.03%

Osteoporosis									
	Alendronate	Ibandronate	Raloxifene	Risedronate	Denosumab	Teriparatide	Abaloparatide	Zoledronic Acid	Alendronate & Cholecalciferol
PA	63.38%	13.86%	9.99%	8.02%	2.79%	1.70%	0.14%	0	0.14%
NP	64.53%	14.66%	12.01%	5.77%	1.76%	0.95%	0.23%	0.03%	0.06%
MD	61%	14.09%	12.73%	8.24%	2.51%	1.03%	0.17%	0.15%	0.09%

Appendix 3: Data for Figure 4

Rurality (NCHS)	Alzheimer's Disease				Osteoporosis			
	Total	Specialists	NP	PA	Total	Specialists	NP	PA
MSA = 0	19638	4292	858	289	18554	1290	1026	411
1	8906	2038	221	96	25093	959	205	120
2	33402	7986	910	236	49351	6217	907	395
3	20064	4318	776	237	25093	2278	764	311
4	8643	1804	359	67	10363	830	370	120
5	4	1	1	0	11	4	1	0
6	0	0	0	0	0	0	0	0
Excluded*	12410				16442			

*MSA not listed in the Census Bureau Crosswalk
National Center for Health Statistics (NCHS) Rurality Classification: (1: Large central metro, 2: Large fringe metro, 3: Medium Metro, 4: Small Metro, 5: Micropolitan, 6: Non-Core)

Abbreviations: NCHS = National Center for Health Statistics, NP = Nurse Practitioner, PA = Physician Assistant

Appendix 4: Regional Top and Bottom Analysis

	AD Top 5%		AD Bottom 5%	
	Mean	SD	Mean	SD
Percent NP/PA	17.30%	2.41	0.9%	0.04
County Population	135,103	173,109	680,809	1,923,149
Median Household Income	$62,642	8,909	$67,509	15716
Unemployment	3.57%	0.76	3.37%	0.51
% High School	9.4%	4.1	12.86%	4.33
% College	30.20%	11.6	27.91%	12.67

Abbreviations: AD = Alzheimer's Disease, SD = Standard Deviation, NP = Nurse Practitioner, PA = Physician Assistant

Appendix 5: Results of the 2-sample independent z-tests

Test	Coefficient	Result (p-value and 95% CI)
Provider type proportions: AD compared to OP		
Specialists*	0.188	p-value < 0.001 | (0.185, 0.191)
Nurse Practitioners*	0.007	p-value < 0.001 | (0.006, 0.008)
Physician Assistants*	-0.004	p-value < 0.001 | (-0.002, -0.0006)
NPs/PAs*	-0.0013	p-value < 0.001 | (0.004, 0.008)
Medicines prescribed: physicians compared to NPs/PAs		
Donepezil*	0.056	p-value < 0.001 | (0.041, 0.071)
Memantine*	-0.0445	p-value < 0.001 | (-0.059, -0.030)
Rivastigmine	-0.001	p-value = 0.815 | (-0.009, 0.007)
Galantamine	0	p-value = 1 | (-0.004, 0.004)
Donepezil & Memantine*	-0.011	p-value < 0.001 | (-0.014, -0.008)
Medicines prescribed: physicians compared to NPs/PAs		
Alendronate*	0.032	p-value < 0.001 | (0.018, 0.046)
Ibandronate	0.003	p-value = 0.527 | (-0.007, 0.013)
Raloxifene*	-0.013	p-value = 0.007 | (-0.022, -0.004)
Risedronate*	-0.018	p-value < 0.001 | (-0.025, -0.011)
Denosumab	-0.0046	p-value =0.058 | (-0.009, -0.0002)
Teriparatide	0.011	p-value = 0.3534| (0.012, 0.010)
Abaloparatide	0.0005	p-value = 0.738 | (-0.001, 0.002)
Zoledronic Acid	-0.0005	p-value = 0.035 | (-0.002, -0.001)
Alendronate & Cholecalciferol	0.001	p-value = 1 | (0.001, 0.001)
Rural vs. Large Fringe Metro		
AD Non-Physician PCPs*	0.023	p-value < 0.001 | (0.018,0.028)
AD Nurse Practitioners*	0.0175	p-value < 0.001 | (0.014, 0.023)
AD Physician Assistants*	0.004	p-value = 0.009 | (0.001, 0.007)
AD Specialists	-0.0104	p-value = 0.055 | (-0.021, 0.0002)
OP Non-Physician PCPs*	0.0665	p-value < 0.001 | (0.064, 0.069)
OP Nurse Practitioners*	0.0472	p-value < 0.001 | (0.0434, 0.051)
OP Physician Assistants*	0.0035	p-value = 0.009 | (0.002,0.005)
OP Specialists*	0.0315	p-value = 0.001 | (0.027, 0.036)

*: Significant at alpha=0.05

Abbreviations: CI = Confidence Interval, AD = Alzheimer's Disease, OP = Osteoporosis, NP = Nurse Practitioner, PA = Physician Assistant

Appendix 6: CPT Codes

Imaging		CPT Code
Magnetic Resonance	MRI Brain, IAC's or Pituitary without contrast	70551
		70553
	MRA Brain without contrast	70544
PET	Brain Imaging NM	78608
CT	Head Brain with contrast	70460
	Head Brain without contrast	70450
	Head Brain with or without contrast	70470

Abbreviations: CPT = Current Procedural Terminology, MRI = Magnetic Resonance Imaging, IAC = Internal Auditory Canal, w/o = Without, PET = Positron Emission Tomography, NM = Nuclear Medicine, CT = Computerized Tomography