

Difference in rural and urban Medicare prescription pattern for Parkinson's disease in Hawai'i

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ABSTRACT

Background: Medical management of Parkinson's Disease (PD) is becoming complex. Increasing evidence suggests that patients have better outcomes when they are managed by neurologists. However, access to neurologists can be limited in rural areas. Analysis of prescription pattern can provide insight into access gap rural patients face.

Methods: This retrospective observational study used National Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use Files from 2013 to 2018. Query was made for levodopa, dopamine agonists and other antiparkinsonian medications. The data elements obtained included drug name, number of prescribers, prescriber specialty, number of claims, number of standardized 30-day Part D prescriptions, and number of Medicare beneficiaries in the state of Hawai'i. Individual prescribing providers were categorized as urban or rural based on their cities of practice. Prescription patterns of urban and rural providers in Hawai'i as well as difference in provider specialty were compared, using standardized 30-day prescriptions as the primary measure of utilization.

Results: Practice patterns differed between rural and urban areas. In rural Hawai'i, Rytary, Rotigoitne and selegiline were rarely prescribed. Levodopa percentage was higher in urban Hawai'i. In urban Hawai'i, 74.4% of the prescriptions were provided by movement disorders and general neurologists. In rural Hawai'i, 25.1% of the prescriptions were written by neurologists and 74.9% by general practitioners.

Conclusions: In the state of Hawai'i, there is an urban–rural access gap to neurologists as evidenced by Medicare prescription pattern. Further study is needed to understand the reasons for rural–urban differences in prescription patterns and their impact on outcomes.

1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disease, estimated to affect 1–2% of population over 65 [1]. Medical management of PD is becoming increasingly complex. There are >25 FDA approved treatments for the motor symptoms of PD [2]. Increasing evidence suggests that patients have better outcomes when their conditions are managed by neurologists who specialize in movement disorders [3]. Regular neurologist care in PD is associated with lower risk of hospitalizations and re-hospitalizations for several PD related illness [4]. However, access to subspecialty neurologists or general neurologists can be limited in more rural areas. Previous studies

demonstrated an urban–rural divide for neurological care across US. The mean density of neurologists varied nearly 4-fold from the lowest (9.7/100,000 Medicare beneficiaries) to the highest (43.1/100,000 Medicare beneficiaries) quintile [5]. In multiple sclerosis (MS), another chronic neurological condition, significantly larger proportions of people with MS in rural areas had a family or general practitioner as their primary physician while a significantly larger proportion of people with MS in urban areas had a neurologist as their primary physician [6,7]. Of patients with neurological conditions such as dementia, chronic pain, and stroke, there was a notable disparity in neurologists' involvement between low- and high-density areas. However, for PD, a remarkably high proportion (>80%) of neurologist involvement was seen even in the

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lowest quintile regions [5]. In another study, primary care clinicians provided more neurological care than neurologists in many neurological conditions, including dizziness and headaches, but PD care was predominantly provided by neurologists (75.6%) vs primary care clinicians (20.8%) [8]. Beyond this, there are not many studies examining the access gap and urban–rural disparity patients with PD face.

Hawai'i is the only island state in the US. It consists of 4 major islands (O'ahu, Island of Hawai'i, Maui, and Kaua'i) and many other less populated islands. Amongst the US 50 states, Hawai'i is the eighth smallest state in area, but with 1.3–1.4 million people, ranks 13th in population density [9]. Two-thirds of the population lives on O'ahu [10], home to the state's capital and largest city, Honolulu, where most neurologists practice. The federal government uses few different definitions of "rural," including those produced by the U.S. Census Bureau, the Office of Management and Budget (OMB), and by rural–urban commuting area (RUCA) code created by US department of Agriculture [11,12]. The state of Hawai'i has three US urbanized areas (an urban area with 50,000 or more people per US census bureau): two in O'ahu (spanning the majority population of O'ahu) and the Kahului/Wailuku area in Maui [9]. Based on OMB and RUCA definitions, only O'ahu is considered urban, and the three neighbor islands (Island of Hawai'i, Maui, and Kaua'i) are all considered rural [11]. Living in rural Hawai'i has unique challenges; for residents of Kaua'i and the Island of Hawai'i, the only way to access an urbanized area is flying.

Studying the epidemiology of islands can help biogeographical research [13]. The state of Hawai'i is 2000 miles from continental US and patients rarely receive prescriptions from out of state providers: this geographical isolation makes Hawai'i an ideal contained system to analyze prescription pattern as a proxy for practice pattern. Medicare Part D prescription data are publicly available, and a previous study showed geographic variation in outpatient antibiotic prescription using this data source [14]. Another study, analyzing VA data identified rural–urban variation in opioid prescribing patterns in veterans [15]. It is estimated that 19% of the US population, approximately 60 million people, live in rural US [12], and understanding the urban–rural disparities in PD care can have implications beyond local practice in Hawai'i.

This study examines variation in prescription of motor symptoms control medications related to rurality by analyzing Medicare Part D prescription data from Hawai'i.

Pharmacologic treatments for Parkinson disease motor symptoms are primarily dopamine based [2]. Levodopa, a precursor to dopamine, is the gold standard for treatment of Parkinson's disease (PD). Levodopa is extremely effective, but may lead to dyskinesias and motor complications.

Dopamine agonists can improve motor function by directly stimulating the post-synaptic dopamine receptors. In early 2000s, clinical practice shifted to using more dopamine agonists in attempt to delay motor complications [16]. More recently, adverse effect of dopamine agonists, such as impulse control disease (eg, gambling, compulsive spending, abnormal sexual and eating behaviors, compulsive medication use, hobbyism) is recognized [2].

Recent evidence shows that Levodopa is the best medications to treat motor symptoms of PD [17–19]. Although previously many physicians avoided levodopa for early Parkinson disease treatment, recent research does not support this approach.

Various medications are useful adjuncts to levodopa. Catechol-O-methyltransferase (COMT) inhibitors and Monoamine oxidase (MAO) B inhibitors block enzymes that degrade dopamine, prolonging the benefits of levodopa. Amantadine has mild parkinsonian effect, as well as improving dyskinesias. For young individuals with prominent tremor, anticholinergic trihexyphenidyl can be considered [2].

2. Methods

We performed a retrospective observational study using National

Medicare Provider Utilization and Payment Data: Part D Prescriber Public Use Files from 2013 to 2018, obtained from the Centers for Medicare and Medicaid Services (CMS). These datasets aggregate all outpatient medications covered under the Part D benefit nationally, by state, and by prescriber including their National Provider Identifier (NPI). As these files were publicly available and de-identified, IRB approval was not needed.

Query was made for FDA approved medications for motor symptoms control of PD as of 2018. We divided the medications into 3 categories: 1) Levodopa [carbidopa/levodopa, carbidopa/levodopa ER, carbidopa/levodopa/entacapone, Rytary (combination carbidopa/levodopa immediate release and extended release)]; 2) Dopamine agonists (pramipexole, ropinirole and rotigotine); and 3) Others [COMT inhibitor (entacapone), MAO inhibitors (selegiline, rasagiline), amantadine, and trihexyphenidyl].

The data elements obtained for Hawai'i include state, drug name (brand and generic), number of prescribers, prescriber specialty, number of Medicare Part D claims, number of standardized 30-day Part D prescriptions, number of Medicare beneficiaries, and aggregate cost paid for Part D claims. In addition, we queried individual provider data, including provider's NPI, name, and city.

Based on the US census designation, we divided the providers into urban providers (all O'ahu, except Hale'iwa, Kahuku, and Laie and Kahului/Wailuku providers from Maui) and rural providers (Hale'iwa, Kahuku, and Laie from O'ahu, rest of Maui except Kahului/Wailuku and all the Island of Hawai'i and Kaua'i).

Variation in prescription patterns (drug type) and the specialty of prescribers were examined in urban vs rural areas. Our primary measure of utilization in this study was the standardized 30-day prescriptions, calculated by CMS as the number of days' supply divided by 30 days. This is preferred to examining the number of prescriptions because prescriptions can vary in their days' supply. For example, if we were to have merely counted prescriptions, a 90-day prescription would have been counted the same as a 5-day prescription.

For this data source, the number of beneficiaries was not recorded when a provider prescribes medication for <10 beneficiaries/year. Therefore, we were not able to obtain precise number of beneficiaries for urban vs rural providers. To ascertain whether there was a difference between urban vs rural providers who prescribed a particular drug to <10 beneficiaries per year, (we suspect this is more common for rural providers who are asked to provide general care for broader range of patients, and may lead to unfamiliarity with each medication), we calculated the percentage of standardized 30-day prescriptions that was written for <10 beneficiaries vs total 30-day prescriptions.

For provider specialist, movement disorder specialist was identified by fellowship training for movement disorder. In addition, one neurologist was identified as a movement disorder specialist based on expert knowledge. This practitioner has been practicing movement disorder focused neurology for over 25 years.

We created a heat map using the city of the provider. We calculated the average standardized 30-day prescriptions/year/1,000 people for each city and mapped the value using Microsoft Excel program.

2.1. Statistical analysis

We used Microsoft Excel to analyze the data. We used descriptive statistics to examine the data. Chi-Squared tests were used to determine whether differences in type of medication prescribed, and prescriber specialty differed by urban/rural status. P value < 0.05 was deemed statistically significant.

3. Results

3.1. Study population and outcomes

According to 2019 Census data, there were 1,154,807 (81.3%)

residents living in urban Hawai'i and 272,114 (18.7%) in rural Hawai'i [9]. Medicare beneficiaries numbers were obtained from CMS 2018 data. We used data from previous study to estimate the number of appropriate neurologists [5] (Table 1).

From 2013 to 2018, 133,795.6 Standard 30-day Part D prescriptions were identified in the state of Hawai'i. 116,453.6 (87.0%) prescriptions were prescribed by urban providers and 17,342 (13.0%) prescriptions were prescribed by rural providers (Table 1). There were 5 movement disorder specialist neurologists, 29 general neurologists and 436 general practitioners, who prescribed medications for PD over the course of 6 years. The prescription number was relatively stable over the 6 years (Supplemental Fig. 1).

3.2. Beneficiaries

We were not able to ascertain the exact number of beneficiaries receiving the prescriptions from urban vs rural providers. This was because the number of beneficiaries were not recorded when a provider writes a prescription for a particular drug for <10 beneficiaries/year. Therefore, we calculated the percentage of 30-day Part D prescriptions written for <10 beneficiaries/year. Rural providers wrote more prescriptions for <10 beneficiaries/year in all drug categories (Table 1, depicted as “% of <10”).

3.3. Subgroup analysis

3.3.1. Specialty data

All five movement specialists and majority of the neurologists were practicing in urban areas. In urban Hawai'i, 34.6% of the prescriptions were written by movement specialists and 39.8% by neurologists (Fig. 1). Together, 74.4% of the prescriptions were provided by neurologists. In rural areas 25.1% of the prescriptions were written by neurologists and 74.9% by general practitioners, including family medicine (37.2%), internal medicine (27.0%), and advance practice providers (nurse practitioners and physician assistants) (6.4%). There was a statistically significant difference in the composition of specialists between urban and rural Hawai'i ($p < 0.001$).

3.3.2. Medication subcategories

For urban providers, levodopa was the highest prescribed medication, consisting of 56.2% of prescriptions, followed by dopamine agonists, 27.6% (Fig. 2). For rural providers, levodopa and dopamine agonist prescriptions were nearly equal, prescribed 43.1% and 43.3% of prescriptions respectively. Some medications were rarely prescribed by rural providers including rural neurologists. Rytary was never prescribed by rural providers, and Rotigotine and selegiline prescriptions were low. There was a statistically significant difference in the drug types prescribed between urban and rural providers ($p < 0.001$).

3.3.3. Heat map

Fig. 3 shows the heat map of average 30-day standardized prescriptions/year/1,000 people. We identified 41 different cities for the providers. The value for average 30-day standardized prescriptions/year/1,000 people varied by 300-fold, from 0.28 in Kula, Maui, to 102.91 in Lihue, Kaua'i.

4. Discussion

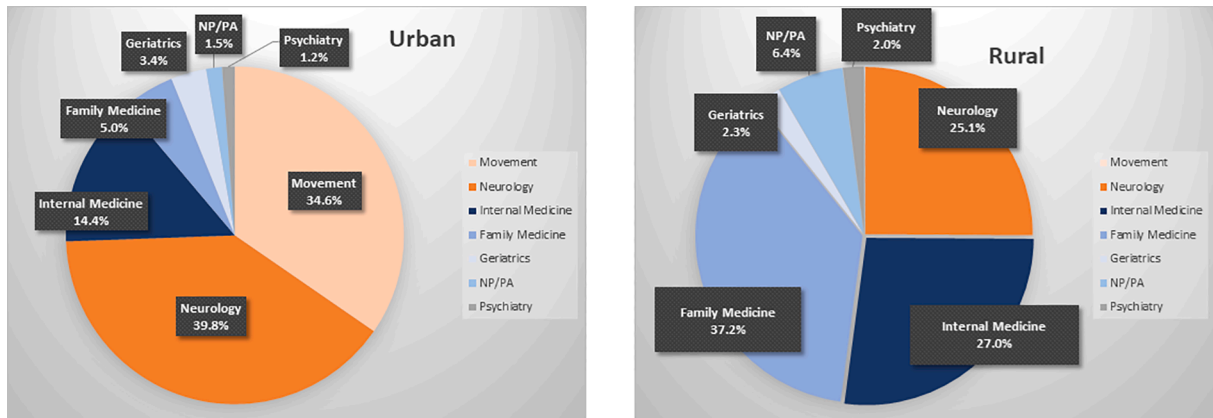
We sought to analyze Medicare Part D prescription data from 2013 to 2018, to understand the pharmacological treatment Medicare patients with PD are receiving in the state of Hawai'i. Due to geographic isolation, Hawai'i residents rarely receive their prescriptions from providers of another state: thus, Hawai'i is an ideal state to study urban-rural difference within a contained system. Our hypothesis was that rural patients have limited access to neurologists, and prescription data will help us understand these disparities.

Table 1
Characteristics of Urban vs Rural Providers in the state of Hawai'i and 30-day standardized Prescriptions between 2013 and 2018.

		Urban	Rural	Total
	Population ¹	1,154,807 (81.3%)	272,114 (18.7%)	1,148,443
	Male/Female Ratio ¹	50.7%/ 49.3%	50.0%/ 50.0%	50.6%/ 49.4%
	Ratio of age over 65 ¹	16.4%	21.7%	17.0%
	Estimated Medicare Beneficiaries ²	209,104 (18.1%)	57,836 (21.8%)	266,940 (18.8%)
	Calculated Neurologist per capita ³	20.3–90.1	5.6–24.9	25.9–115.1
Prescribers	Movement Neurologist	5 (100.0%)	0 (0.0%)	5
	Neurologist General Practitioner	26 (89.7%) 278 (63.8%)	3 (10.3%) 158 (36.2%)	29 436
Drug Class				
L-Dopa	Total 30-day standardized Prescriptions Beneficiaries/year	64446.1 (90.2%)	7039.7 (9.8%)	71485.8 1834.8
	Carbidopa/Levodopa	61482.6 (90.5%)	6461.3 (9.5%)	67943.9
	% of <10*(see below)	21.9%	55.3%	
	Carbidopa/Levodopa/Entacapone	2049.9 (78.0%)	578.4 (22.0%)	2628.3
	% of <10*	49.6%	37.3%	
	Rytary	913.6 (100.0%)	0 (0%)	913.6
	% of <10*	88.7%	N/A	
Dopamine Agonist	Total 30-day standardized Prescriptions Beneficiaries/year	33080.7 (80.3%)	8107.3 (19.7%)	41,188 1398.3
	Pramipexole	15839.8 (83.1%)	3227.7 (16.9%)	19067.5
	% of <10*	55.4%	81.3%	
	Ropinirole	14,167 (74.5%)	4839.6 (25.5%)	19006.6
	% of <10*	55.0%	91.8%	
	Rotigotine	3073.9 (98.7%)	40 (1.3%)	3113.9
	% of <10*	41.3%	100.0%	
Other	Total 30-day standardized Prescriptions Beneficiaries/year	18926.8 (89.6%)	2195 (10.4%)	21121.8 699.7
	Amantadine	4168.7 (89.0%)	512.7 (11.0%)	4681.4
	% of <10*	44.2%	100.0%	
	Entacapone	4372.5 (88.3%)	580.8 (11.7%)	4953.3
	% of <10*	55.9%	34.8%	
	Rasagiline	7293.3 (96.9%)	230 (3.1%)	7523.3
	% of <10*	59.5%	100.0%	
	Selegiline	871.2 (96.2%)	34 (3.8%)	905.2
	% of <10*	33.5%	100.0%	
	Trihexyphenidyl	2221.1 (72.6%)	837.5 (27.4%)	3058.6
	% of <10*	96.5%	100.0%	
Total		116453.6 (87.0%)	17,342 (13.0%)	133795.6

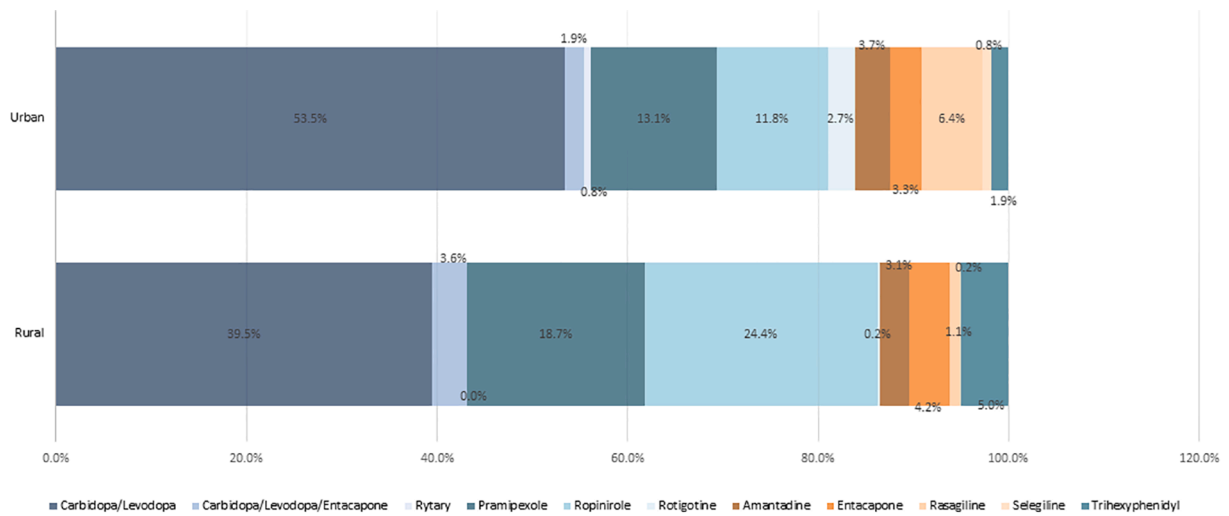
¹ US Census Data 2019, ² CMS Total Medicare Enrollment Data 2018, ³9.7–43.1/100,000 Medicare beneficiaries (ref.7), *Percentage of Standard 30-

day Prescriptions written by providers who wrote for beneficiaries <10 prescriptions.



Difference between Urban vs Rural specialty p<0.001

Fig. 1. Prescriber Specialist Comparison of Urban vs Rural Standardized 30-day prescriptions.



Difference between Urban vs Rural p<0.001

Fig. 2. Drug Class Comparison of Urban vs Rural Standardized 30-day Prescriptions.

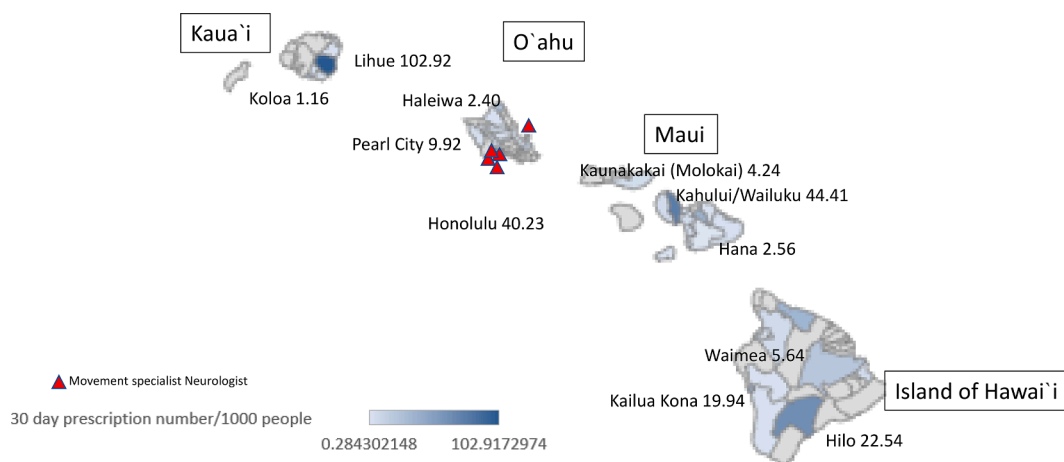


Fig. 3. Heat Map of Hawaiian Islands based on Standard 30-Day Prescriptions/Year/1,000 people by Provider Zip Code.

Although over 20% of the population resides in a rural area, 87% of the prescriptions were written by urban providers. In the urban areas, 74.4% of the prescriptions were provided by neurologists, compatible with previous studies showing that even in an area with low density of neurologists, high proportion (75–80%) of PD care is provided by neurologists [5–8]. This was in contrast with rural areas of Hawai'i, where only 25.1% of the prescriptions were written by neurologists. Geographic trends of specialists contribute to this disparity. All movement disorder neurologists and majority of general neurologists were practicing in urban areas. There were only 3 neurologists who prescribed PD medications in rural Hawai'i. Previous national data identified current neurologists' distribution to be 9.7–43.1 per 100,000 Medicare beneficiaries [5]. Based on these numbers, estimated projection of neurologists for urban Hawai'i is 20.3–90.1 and 5.3–24.9 for rural Hawai'i. Thus having only 3 neurologist prescribing PD medications in rural Hawai'i demonstrates substantial lack of access to outpatient neurologists for patients with PD, even though we understand that not all neurologists prescribe PD medications. (Some neurologists specialize in inpatient neurology or other subspecialties). This void was filled by general practitioners, including family medicine, internal medicine, and advanced practitioners (nurse practitioners and physician assistance) writing PD prescriptions. In rural Hawai'i, there was high percentage of prescription written by providers writing the specific drug for <10 beneficiaries/year, suggesting lack of familiarity and expertise with many PD medications.

A recent study by Singh et al highlighted 3 major concerns that rural PD communities face in obtaining medical care: disease specific challenges (mobility and progression), limited access (information, provider and stakeholders), and disease related stigma [20]. This mirrors the result of a meta-synthesis of rural patients with chronic disease [21]. Geography (distance from services poses access barriers, worsened by transportation problems or weather conditions), limited availability of health care professionals (coupled with low education or lack of peer support), and rural culture (patients may feel culturally marginalized in the urban health care context, especially if health literacy is low; a culture of self-reliance and community belonging in rural areas may incline patients to do without distant care and may mitigate feelings of vulnerability) emerged as 3 challenges rural patients face. Another study examined barriers in rural and urban areas from a healthcare provider's point of view. Rural areas struggle more with healthcare barriers especially resource limitations, confidentiality limitations, overlapping roles, provider travel, service access, and training constraints. The smaller a provider's practice community, the greater the reports of barriers, with the most severe barriers reported in small rural communities [22].

Patients with PD living in rural Hawai'i are likely receiving PD care from general practitioners, or alternatively seek care from movement disorder specialists and neurologists on O'ahu or Maui, an hour flight away from each of the neighbor islands. Air travel is a significant burden for patients afflicted with a disorder that limits their mobility and a burden for their family. Unexpectedly, we did find Lihue in Kaua'i to have the highest 30-day prescription rate per 1000 people (Fig. 3). Even though Lihue is not an urbanized area, Lihue has one neurologist and may be acting as a hub to attract patients residing in the entire island of Kaua'i. Advancement of telehealth is expected to fill some of the gaps rural communities are facing [23]. However, technological challenge and gap remains for rural communities to adopt telehealth [24,25]. We need to urgently develop programs to educate rural providers, improve communications and remove access barriers to neurologists/specialty care. For example, such programs may include, but not limited to educational programs, community partnership for ancillary service, telehealth infrastructure and travel grants.

Another finding from this study is that the prescription pattern and distribution of PD medicine was different between urban and rural providers. Urban prescribers prescribed more levodopa and less dopamine agonist compared to rural providers when examining the

distribution of PD medication. This pattern mirrored our recent study results analyzing Medicare Part D prescriber data for PD medications across the 50 states of the U.S. States: states with higher proportion of neurologists had a higher proportion of levodopa prescriptions (Pearson correlation coefficient of 0.82) [26].

There has been a somewhat confusing pendulum swing on levodopa vs dopamine agonist debate [19]. Levodopa is extremely effective, but liberal usage may lead to dyskinesias and motor complications. Practice pattern shifted to the use of dopamine agonists in the 2000s. However, recent studies show that dopamine agonists are less effective in controlling the motor symptoms of PD and produce undesirable side effects. More recent guidelines recommend levodopa over dopamine agonists to treat early PD motor symptoms [18]. Studies suggest that limiting levodopa can leave patients with greater net disability and poorer quality of life than necessary, and may lead to complications such as falls [17]. Yet, considerable "Levodopa phobia" still exists in the community, as well as in prescribing physicians [16,27].

Certain medications were rarely prescribed by rural practitioners and were predominantly prescribed by urban providers. They were: Rytary, rotigotine patch, and rasagiline. Rytary is a combination carbidopa/levodopa IR and ER approved in 2015 [28] which is commonly used to mitigate the motor complications of long term use of levodopa. Rotigotine patch and rasagiline may also be used in combination therapy for increased efficacy in treating motor symptoms [29]. Rural practitioners may not be comfortable with using newer agents or combination therapies. While difference in patient population may account for difference in prescription pattern (rural general practitioners may be comfortable providing care for simple PD patients, but may refer more complicated PD patients to urban movement disorder neurologists or general neurologists), having to seek specialist care in a different island is a significant burden for PD patients and their families, and we believe our study highlighted the interisland gap and neurologist density gap.

There are limitations in our study. Medicare prescription data is aggregated at the provider, state, or national level and does not contain any patient-specific information such as diagnoses. Some of the medications in this study of PD are prescribed for other movement disorders. Dopamine agonists are commonly prescribed for restless leg syndrome [30]. Trihexyphenidyl is prescribed for dystonia [31] and tardive dyskinesia, although the clinical benefit is unclear [32]. Levodopa maybe prescribed for other parkinsonian syndromes, including Parkinson-plus syndrome, vascular parkinsonism, and dopa-responsive dystonia. Transdermal selegiline patch (EMSAM) patch is prescribed for refractory depression [33]. Selegiline prescriptions were generally few, and psychiatrists prescribing EMSAM was negligible in our study. Another limitation is that Medicare only covers approximately 19% of Hawai'i residents, and that the data reported here are not representative of general population of the state. However, PD predominantly affect seniors over age 65, and it is estimated that 88.5% of PD patients have Medicare [34] thus analyzing Medicare data do have relevance for PD care. Lastly, not all Part D plan cover prescriptions the same way, and difference in plans and coverage may affect the drug utilization.

A recent statewide initiative analyzed 50 health and socio-economic indicators by geographic communities in Hawai'i and found significant difference in demographics and health characteristics [35]. Even though the ratio of seniors (>65) or ratio of cardiovascular co-morbidities (obesity, diabetes and hypertension) did not differ significantly amongst each island, neighbor island (Island of Hawai'i, Maui and Kaua'i) populations had consistently higher mortality from heart disease, cancer, stroke and unintentional injuries compared to O'ahu [35]. While socioeconomic and neighborhood factors [36] may play a role in this disparity, in the state of Hawai'i, only Island of Hawai'i has the lowest median household income (59,297) below US average (63,179) with the highest poverty rate of 16.6% (US average 8.8%). O'ahu, Maui and Kaua'i did not differ significantly in the median household income (84,423, 82,885 and 80,921 respectively, all above US average), suggesting that factors other than income, including access gap to medical

care may account for health disparity. The state currently does not track statewide data for PD patients, but in the future, we hope to study the health outcomes on rural vs urban PD patients. Further studies are urgently needed to understand PD care in Hawai'i, as well as urban–rural disparities PD patients face nationally. We hope to explore other data in the future, including insurer data, hospitalization data and telemedicine data to see if we can understand the gap patients with PD and their family residing in rural community face.

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CRedit authorship contribution statement

Michiko K. Bruno: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft. **Gina Watanabe:** Data curation, Formal analysis, Software. **Fay Gao:** Methodology, Writing – review & editing. **Todd Seto:** Supervision, Resources, Writing – review & editing. **Kazuma Nakagawa:** Methodology, Writing – review & editing. **Connie Trinacty:** Methodology, Writing – review & editing. **Stacy Brown:** Methodology, Writing – review & editing. **Deborah A. Taira:** Conceptualization, Methodology, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.prdoa.2022.100144>.

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