Factors that affect the employability of patients with epilepsy in Hawaii: A look at race, comorbidities, and marital status

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Background

Epilepsy is a common chronic neurological disease that affects approximately 3.4 million people in America and 15,000 people in Hawaii. However, despite many advances in treatment options, epilepsy remains a debilitating disease that has significant impacts on quality of life.[1] Numerous studies have found increased rates of psychiatric comorbidities, single status, and unemployment among patients with epilepsy (PWE).[2,3] However, no such study has been completed in Hawaii. Hawaii offers unique perspectives on this problem because of its diverse population which can help identify whether epilepsy affects certain races disproportionately. Employment is an important indicator of quality of life, therefore, analyzing the factors that affect employment and identifying ways to increase employment are vital to improving the care of PWE.[4]

This study focused on a patient population in Hawaii and looked at the rates of unemployment among patients with epilepsy compared to patients with other neurological diagnoses and to the general public. Factors that affected employability of these patients and variation in employment rates between patients of different racial backgrounds were also explored.

Objectives

The objective of this study was to establish the rate of unemployment among patients with epilepsy in Hawaii and identify key factors that affected employability. In analyzing what factors affected employment rates, the aim was to identify ways to help PWE increase their independence and quality of life.

Methods

An IRB approved retrospective chart review of 500 PWE at Hawaii Pacific Neuroscience (HPN) was performed. Patients were identified using ICD-10 codes for epilepsy and were included in the study if they were seen at HPN in the last year, reported employment status, and were at least 18 years of age. 510 controls were randomly selected from the patients at HPN and were included if they reported employment status, were at least 18, and were not diagnosed with epilepsy. Both groups were comparable in age, sex, and race. Statistical analyses were performed using the $\chi 2$ test, Tukey's HSD multiple comparison test (ANOVA), and independent sample T-tests. For all tests, an alpha of .05 was used to indicate significance and were performed using SPSS.

Employment status was classified into one of the following: employed, unemployed, retired, disabled, housewife, and student. Seizure level of control were classified into one of three categories: (1) seizure free (no seizure in the last year), (2) breakthrough seizures (one to three seizures per year), and (3) poorly controlled (monthly or weekly seizures).

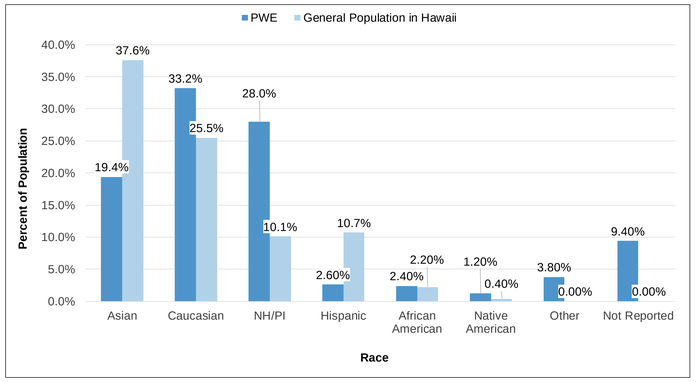

Figure 1. Percent of Population by Race for PWE and General Population of Hawaii.[5]

Results

- Of the 500 PWE, 45.2% reported to be unemployed or disabled while only 28.2% were employed. This differed significantly from the reference group wherein only 20.9% were unemployed or disabled and 49.4% were employed ($p < 0.001$).
- There was found to be a significant difference in employment rates between racial groups (p=.034). Asians were found to have higher employment rates than both the Caucasian group (p=.037) and Native Hawaiian or other Pacific Islander (NH/PI) group (p=.017) as noted in [Figure 2].
- Of the PWE, 46.8% were single and only 35.0% were married, whereas in the reference group only 33.0% were single and 47.0% were married. It was also found that patients were more likely to be employed if they were married than if they were single ($p < 0.001$) or widowed (p=.011).
- Patients with poorly controlled seizures had higher unemployment rates than those with well controlled seizures (p=.001) and sporadic seizures (p=.012). They were also more likely to be single (p=.007).
- PWE were not only more likely to have multiple comorbidities ($p < 0.001$), but it was also demonstrated that PWE were more likely to be unemployed when compared to reference patients with the same number of comorbidities.
- Furthermore, PWE were more likely to be depressed (OR=1.32; 95% CI 1.00-1.74; $p < 0.001$) or have other psychiatric disorders compared to the reference group [Figure 3].

	Epilepsy N=500		Reference N=510	
	n	(%)	n	(%)
Sex				
Male	243	48.6%	250	49.0%
Female	257	51.4%	260	51.0%
Age				
18-29	81	16.2%	90	17.6%
30-39	77	15.4%	56	11.0%
40-49	80	16.0%	84	16.5%
50-64	129	25.8%	119	23.3%
65+	133	26.6%	161	31.6%
Marital Status				
Single	242	48.4%	169	33.1%
Married	176	35.2%	239	46.9%
Divorced/ Separated	49	9.80%	65	12.7%
Widowed	33	6.60%	34	6.67%
Not Reported	0	0.00%	3	0.59%

Table 1. Basic characteristics of study population.

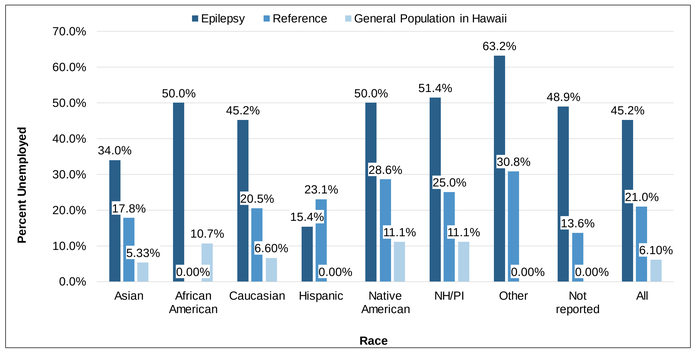

Figure 2. Rate of unemployment by race in PWE, reference group, and general population in Hawaii.[6] Hispanic and Other race rates of unemployment were not reported for general population.

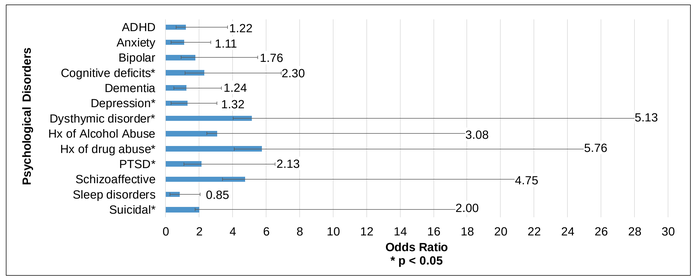

Figure 3. Odds of psychological disorders among PWE.

Discussion

This was the first study to look at employment rates of PWE in Hawaii, and many of the findings corroborated prior studies done both within the United States and throughout the world. It was demonstrated that not only were PWE more likely to be unemployed, they were also more likely to be single and to have multiple comorbidities.

One of the main factors found to affect employability was marital status, as a positive correlation was found between being married and employed. The stigmatization surrounding epilepsy often creates a social barrier which may prevent some PWE from finding partners as well as employment. A study done in 2018 found that many PWE felt "ashamed" of the disease both in work and social settings.[7] In addition, patients with a lower level of control were more likely to be unemployed and single, emphasizing the importance of achieving adequate seizure control in PWE.

Psychological comorbidities including, but not limited to, PTSD, depression, schizoaffective disorder, and dysthymic disorder were found to affect PWE at disproportionate rates. Given that PWE are also more likely to be unemployed, they are further faced with the challenge of finding mental health providers who are willing to accept their insurance or lack thereof. Without adequate care and treatment these psychiatric disorders may contribute to the increased rates of unemployment of PWE.

These findings highlight the need to have appropriate support systems in place to assist PWE in preparing for and finding employment opportunities that suit their needs and to also aid in connecting patients who need mental health care with facilities that can supply necessary care. PWE face many challenges on a daily basis, making it imperative that health care providers work together in order to improve their quality of life by connecting patients to appropriate employment opportunities, and by providing access to quality mental health care.

Limitations of this study include the reference group being selected from patients that are under the care of Hawaii Pacific Neuroscience (HPN) for other neurological disorders that may also affect employability and rate of psychiatric disorders compared to the general public.

Future Directions

- Future work can be done to conduct phone surveys with PWE in order to assess their level of social support, quality of life, and employment status. This work could also identify why patients are unemployed and determine if they have been directed to support systems who can assist them with finding employment opportunities.
- Further studies should also be done to examine what factors positively influence employability in PWE.

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Disclosures/Correspondence

All authors reported no conflicts of interest.
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An Assessment of the Shift in Neurological Care Toward Telemedicine during the COVID-19 Pandemic

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Background

The novel coronavirus of 2019 (COVID-19) pandemic and the establishment of social distancing measures nationwide called for a substantial change in the delivery of healthcare. Many healthcare organizations began to implement telehealth services in response. Telemedicine is the remote diagnosis and treatment of patients. Telemedicine can be divided into two categories: synchronous and asynchronous. Synchronous refers to telemedicine that occurs in real-time, both audio and/or video. Asynchronous telemedicine can include emails, text messages, or remote monitoring of patients. The use of telemedicine has previously been proven successful in remote locations where there is a lack of medical personnel, and its validity has been tested in headaches, multiple sclerosis, Parkinson's, and acute stroke for neurology.

Hawaii Pacific Neuroscience (HPN), an outpatient neurology provider with locations in West Oahu, Honolulu, Windward Oahu, and Hawaii island, was among the healthcare organizations that offered telemedicine services in response to the social distancing restrictions in Hawaii. Officially, HPN conducts synchronous, video and audio telehealth appointments via the *eClinicalWorks* Healow app. During the pandemic, insurance companies began covering telehealth appointments using any video and audio capable platform (i.e. Zoom, Facetime, Google Duo, Google Meet, Skype). The usability and patient satisfaction of these platforms have yet to be tested in a predominantly older patient population similar to that of HPN.

Objective

To assess the use and satisfaction of telemedicine during the COVID-19 pandemic in neurological patients seen at HPN.

Methods

A telephone survey was conducted with 367 HPN patients who were seen between 4/22/2020-5/18/2020 that addressed four areas related to their outpatient experience: delivery of care, general well-being, experience with telemedicine, and disease-specific questions. 182 patients who have participated in a telemedicine appointment during the pandemic were additionally asked about ease, satisfaction, and comparability to a regular face-to-face appointment. A retrospective chart review was then conducted to collect patients' diagnoses, demographics (age, gender, race / ethnicity, marital status, insurance type), duration of care at HPN, and distance from the nearest HPN clinic location. Patient zip codes and US Census data were used to obtain average education level and median household income in their census tract. Zip code tabulation area (ZCTA) maps were used to determine the density of confirmed COVID-19 cases in patients' geographical region. Patients' characteristics were summarized using descriptive statistics and bivariate associations with the status of telemedicine usage were examined using Mann-Whitney U test or Fisher's exact test. A multivariable logistic regression model was developed for the status of telemedicine usage. In the 182 telemedicine patients, bivariate associations were further explored between the location where they utilized telemedicine and their satisfaction with the telemedicine experience. Statistical analyses were conducted using R, and a p-value of less than 0.05 was considered statistically significant.

Table 1: Patient Demographics

Category	No Telemedicine (n = 185)	Used Telemedicine (n = 182)	p-value
COVID-19 Job Status (reference: Employed)			0.2893
Employed	104 (56.22%)	87 (47.80%)	
Otherwise Unemployed	16 (8.7%)	17 (9.3%)	0.7653
Retired	37 (20.0%)	51 (28.0%)	0.1467
Lost job	28 (15.1%)	27 (14.8%)	0.9130
Age			0.5129
< 40 years	46 (24.9%)	41 (22.5%)	
40 - 55 years	46 (24.9%)	48 (26.4%)	
55+ years	93 (50.3%)	93 (51.1%)	
Mean (SD)	52.99 (18.6)	52.22 (18.4)	
Gender			0.2700
Female	102 (55.1%)	110 (60.4%)	
Male	83 (44.9%)	72 (39.6%)	
Marital Status (reference: married)			0.3770
Married	84 (45.4%)	85 (46.7%)	
Single	63 (34.0%)	48 (26.4%)	0.5486
Unknown	11 (6.0%)	16 (8.8%)	0.1603
Div / Sep	16 (8.7%)	23 (12.6%)	0.3231
Widowed	11 (6.0%)	10 (5.5%)	0.5558
Ethnicity / Race (reference: white)			0.5671
White	55 (29.73%)	63 (34.62%)	
NHOPI	56 (30.3%)	43 (23.6%)	0.7552
Asian	31 (16.8%)	37 (20.3%)	0.5527
Other	15 (8.1%)	14 (7.7%)	0.7850
Not Reported	28 (15.1%)	25 (13.7%)	0.5930

Results

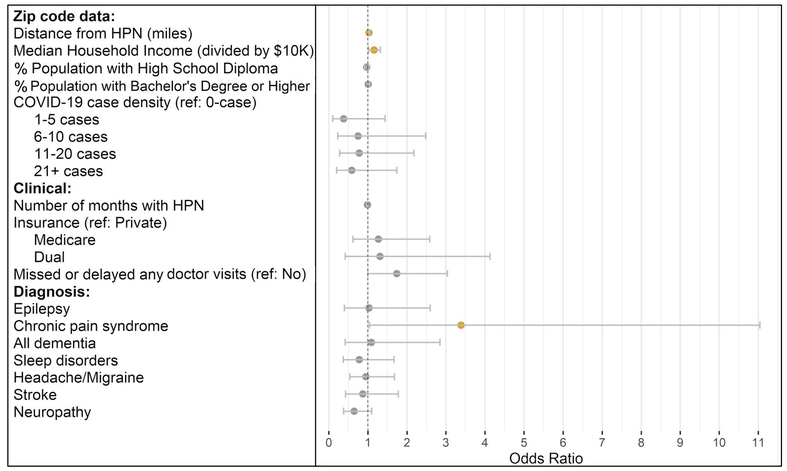

Figure 1: Odds of Using Telemedicine Based on Zip Code Data, Clinical Data, or Diagnosis
Yellow = $p < 0.05$

The logistic regression results suggest that for each one mile increase in distance from the nearest HPN location, the odds of using telemedicine increased by 3% (OR=1.03; 95% CI=1.01-1.05) after adjusting for other confounding variables. In addition, as the median household income of a patient increases by $10,000, the odds of the patient participating in telemedicine increased by 16% (OR=1.16; 95% CI=1.02-1.32). It was also found that patients with chronic pain syndrome are 3.39 times more likely to use telemedicine compared to patients without chronic pain syndrome (OR=3.39; 95% CI=1.04-11.04).

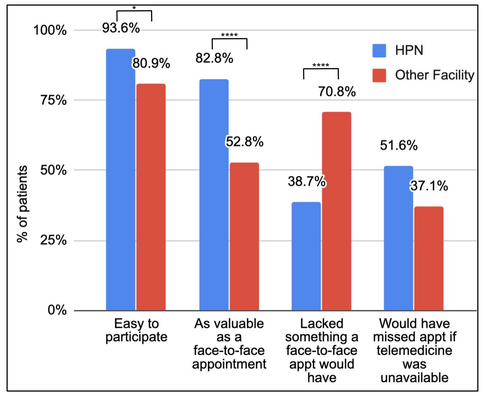

Figure 2: Telemedicine Satisfaction
*p < 0.05, ****p < 0.0001

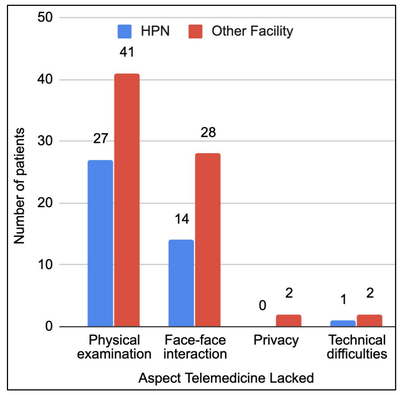

Figure 3: Telemedicine Criticisms

Data was collected for the 367 patients who responded to the survey questions; 182 patients participated in telemedicine while 185 patients did not. Of the 182 patients who participated in telemedicine, 93 of them participated in telemedicine at HPN, while the other 89 patients participated in telemedicine at a different facility. HPN telemedicine patients were more likely to find telemedicine appointments easy to participate in (94% vs. 81%; $p = 0.013$) and as valuable as face-to-face appointments (83% vs. 53%; $p < 0.001$), compared to telemedicine patients at other facilities. Furthermore, telemedicine patients at other facilities were more likely than HPN telemedicine patients to find that their telemedicine appointment lacked something compared to a regular face-to-face appointment (71% vs. 39%; $p < 0.001$). Largely, patients stated that telemedicine lacked an opportunity for physical exam and/or a face-to-face interaction.

Discussion and Conclusions

Overall, patients were satisfied with their telemedicine experiences during the COVID-19 pandemic. Telemedicine was deemed useful for patients that are farther away from HPN locations and patients diagnosed with chronic pain syndrome, suggesting that telemedicine is a fair healthcare delivery alternative to mitigate any travel inconveniences. Less costly telehealth modalities (emailing, text messaging, phone calls, etc.) may help providers reach patients in lower income brackets. To address patients' concerns about physical examination, providers could offer patients' caregivers or family members tools and education for them to perform simple physical exams. Moreover, it may be helpful for providers to receive training on online interpersonal relations to address the lack of face-to-face interaction patients' reported. Nevertheless, patients seen at HPN rated their telemedicine experience higher than other facilities, perhaps due to the familiarity and established relations patients have with their providers and the flexibility of telemedicine platforms. However, surveying only patients seen at HPN may add bias. Other limitations include the demographic information obtained from US Census Data is the average income and education level of each patient's geographical area and does not represent each patient's exact information. Furthermore, only surveying patients who visited HPN, in person or virtually, during the survey period. Telephone contact was established with 46% patients seen during this period, with an 86% response rate. Therefore, the results of this study do not represent the entire patient population at HPN.

Future Directions

Future work can focus on conducting a follow-up survey with a larger sample size that includes inquiry of pertinent data to forgo the use of US Census Data. This would allow a comparison between patients' conditions in the middle of the first wave of COVID-19 cases wherein there were strict restrictions versus the second wave wherein the restrictions have been relatively lenient.

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The Efficacy of Mono versus Dual Antiplatelet Therapy for Recurrent Ischemic Stroke Prevention in Hawaii

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Background

Stroke affects approximately 7 million people across the U.S. and is the leading cause of disability in Hawai'i[1,2]. This study focuses on the most common subtype, ischemic stroke, which accounts for 87% of all strokes. The risk of having a recurrent stroke within the first 3 months of the initial event is 10-20%[1].

Currently, the gold standard for secondary stroke prevention is the prescription of aspirin as a mono antiplatelet therapy (MAPT). However, recent literature has suggested that the combination of aspirin with clopidogrel, as a dual antiplatelet therapy (DAPT), can reduce the risk of a subsequent stroke with a higher success than MAPT[3,4]. Clopidogrel is a platelet aggregation inhibitor that has proven to decrease ischemic events in previous studies, but can cause significant cranial bleeding when combined with aspirin[1,4,5].

The aim of this study is to explore the efficacy of these two therapies for ischemic stroke patients in Hawai'i and determine whether or not our results are consistent with current research and literature. Understanding the effectiveness of each therapy is important for improving secondary stroke prevention as well as the quality of care for stroke patients in Hawai'i.

Hypothesis

Among patients with acute ischemic stroke, DAPT will be more effective than MAPT in reducing stroke recurrence.

Methods

This study was a single-centered, retrospective medical chart review of stroke patients seen at Hawaii Pacific Neuroscience over a 10 year period from 2010 to 2020. Patients were initially screened using ICD codes specific to ischemic stroke and cerebrovascular accidents (CVA). They were then categorized by prescribed treatment which included mono therapy (aspirin only) and dual therapy (aspirin and clopidogrel/Plavix). Patients receiving alternative treatments were excluded from the study. The date of first stroke, treatment start date, and dates for any subsequent strokes within 365 days of treatment start were recorded for each patient. The frequency of recurrent strokes for each treatment along with the time difference between dates for recurrent strokes and treatment start date were calculated and used to estimate efficacy within a given time frame of 30, 90, 200, and 365 days. Statistical significance of the data was calculated using the Fisher's exact test with an alpha of 0.5.

Results

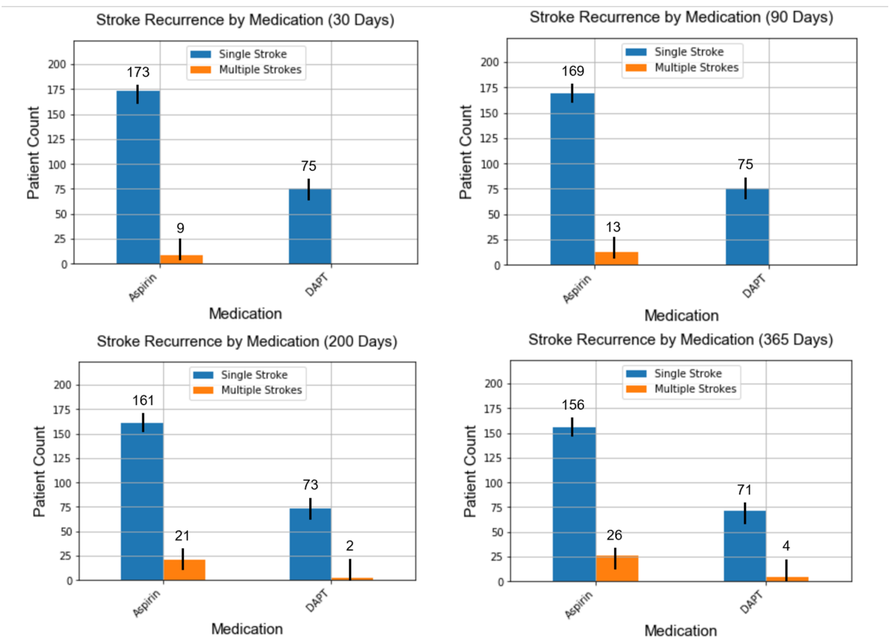

Fig. 1. Stroke recurrence for patients treated with DAPT was infrequent enough compared to Aspirin to suggest dual treatment for ischemic stroke better prevents subsequent CVAs (p-values = 0.062, 0.012, 0.028, 0.053 respectively).

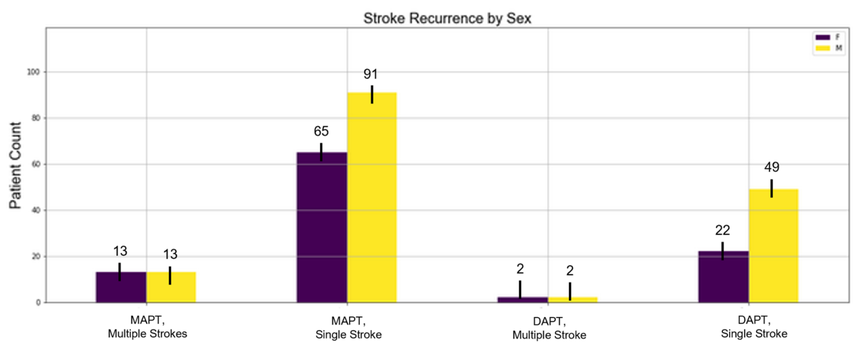

Fig. 2. Stroke treatment and outcome at 365 days, stratified by gender.

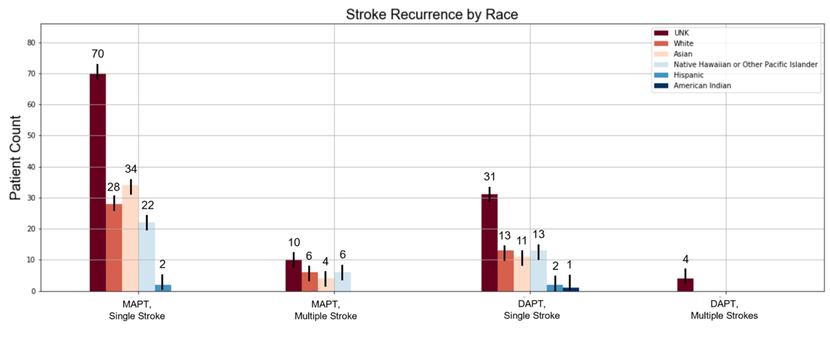

Fig. 3. Stroke treatment and outcome at 365 days, stratified by ethnicity.

Discussion/Conclusion

Consistent with our hypothesis, the combination treatment of aspirin and clopidogrel had a greater efficacy for secondary stroke prevention than treatment of aspirin alone over the course of 12 months. We found a significant difference in efficacy up to 200 days after an initial stroke, compared to 90 days in current literature[4]. One potential explanation could be the synergistic effect of two antiplatelet agents inhibiting a range of pathways for platelet aggregation[3].

However, our results are limited to a small population of patients at HPN. Since the proportion of HPN patients that suffered a recurrent stroke parallels proportions published in current literature, we believe that statistical significance would have been seen at shorter time frames if a larger sample population was used. Access to data was limited by information provided in the patient charts. If care was sought outside of HPN or follow-up visits discontinued before 12 months, the patient was excluded out of the data analysis of recurrent stroke events. In addition, patients treated at HPN for recurrent strokes but had missing information on their initial stroke were excluded from the study.

While unrelated to our main objective, we thought it was interesting that male were prescribed DAPT at up to twice the rate of females. We also included a distribution of treatment and outcomes stratified by race.

Future Directions

Future studies should include larger sample sizes, stratification based on dosage and treatment duration, stratification of race to acknowledge Hawai'i's unique racial/ethnic communities, and stratification based on prevalence of specific comorbidities within these subpopulations.

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Disclosure/Correspondence

All other authors reported no conflicts of interest.

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Hawaii Neuroscience Research Internship Program
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Association of Parkinson's Disease Progression and Gastrointestinal Dysfunction

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Background

Parkinson's Disease is a progressive disorder involving neurodegeneration of dopaminergic (DA) neurons in the brain. This can lead to symptoms such as shuffling gait, tremor, muscle rigidity, bradykinesia, mood changes, cognitive impairment and postural instability[1].

Clinical indicators of PD progression include changes in motor function (captured by the Unified Parkinson's Disease Rating Scale, UPDRS Section III), drug dosage (Levodopa Equivalent Daily Dose, LEDD) and impairment of daily living activities (dementia, falls)[4].

The UPDRS Section III motor examination is a clinically validated method utilized to analyze PD progression by comparing scores over time; higher UPDRS scores are characteristic of progressing PD[4]. Anti-parkinsonian medications may be quantified using Levodopa equivalent daily dose (LEDD) which is the sum of all dopaminergic medication converted to equivalents of levo-dopa. Increases in LEDD is indicative of worsening PD[4, 6]. The combination of LEDD and UPDRS motor scores has been used as a more accurate representation of progression, as LEDD influences severity of motor symptoms[5]. Dementia and the presence of falls are also good clinical indicators of worsening PD. Dementia requires special consideration as high doses increase the risk for psychosis in patients with cognitive impairment, and therefore directly influences LEDD. The presence of falls is the culmination of severe balance issues, body bradykinesia, and tremor indicative of severe PD[4].

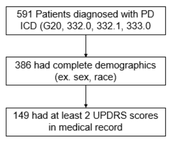
There is an increasing interest in GI dysfunction and PD. Manifestations include symptoms of dysphagia, nausea, constipation, drooling, abdominal pain, and more[8]. The pathology underlying GI dysfunction is thought to be related to the loss of dopaminergic neurons in the enteric nervous system and/or loss of DA neurotransmission in the dorsal motor vagus neurons[2,9]. Studies on the microbiota-gut-brain axis have found significant differences in distribution and frequency of various microbiota communities based on PD progression rates[5], as well as their involvement in changes of behavior and neurochemical brain activity since the presence and absence of certain bacteria are associated with various motor disturbances[3].

By broadening knowledge on the microbiota-gut-brain axis and its role in PD, further details of the relationship between the two may be elucidated and aid in identifying new clinical indicators for PD. The present study seeks to analyze correlations between the frequency and significance of GI dysfunction and PD progression in the Hawai'i population.

Objectives

- Evaluate relationships between gastrointestinal dysfunction and Parkinson's disease progression in the Hawai'i population
- Identify possible correlations between individual PD motor symptoms and GI dysfunction symptoms within differing demographics

Methods



A retrospective medical chart review of 149 patients diagnosed with Parkinson's Disease (using ICD-9 and ICD-10 codes: 332.0, 332.1, 333.0, G20) at Hawaii Pacific Neuroscience between June 2010 and July 2020 was conducted. Variables collected include: patient demographics (age, race, sex, vital status), first and last recorded UPDRS score (grouped categories + composite), PD medication dosage and intake, GI-related medications, GI ICD code diagnoses, presence of falls, dementia diagnosis, and frequency and type of GI related issues reported/addressed during clinic visits between the first and last recorded UPDRS scores (inclusive).

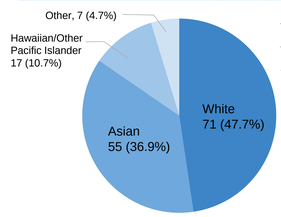
A PD progression/severity score was calculated by adding the following: (1) the change in UPDRS Scores divided by time in between (min-max normalization, -1-1pts), (2) the change in LEDD, representing the sum of PD medications multiplied by their respective conversion factors[6] divided by the time in between (min-max normalization, -1-1 pts), (3) diagnosis of dementia before last UPDRS score (1pt), and (4) falls reported during last UPDRS score (1pt).

A GI progression/severity score was calculated by adding the following: (1) the percentage of appointments a patient reported a GI-related symptom up to the last recorded UPDRS score (0-1pts), and (2) GI-related ICDs assigned prior to the last UPDRS score date (1pt each). GI symptoms explicitly related to medications were excluded. We then conducted regression analysis between PD severity and GI severity scores using a Wald Test with t-distribution of test statistic and alpha of 0.05 for statistical significance.

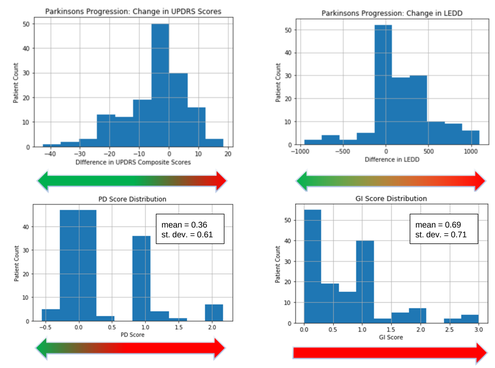
Further, scores for specific PD motor symptoms (ex. tremor) were calculated by taking the difference between the last and first UPDRS score specific to the symptom, dividing by the total number of days between scores, and normalizing. Lastly, scores for individual GI dysfunction symptoms (ex. constipation) were calculated in the same way as the general GI progression/severity score but specific to the symptom in reported issue and assigned ICD. Scores for specific PD motor and GI dysfunction symptoms were plotted against one another in search of trends. Analysis was further broken down by sex and race.

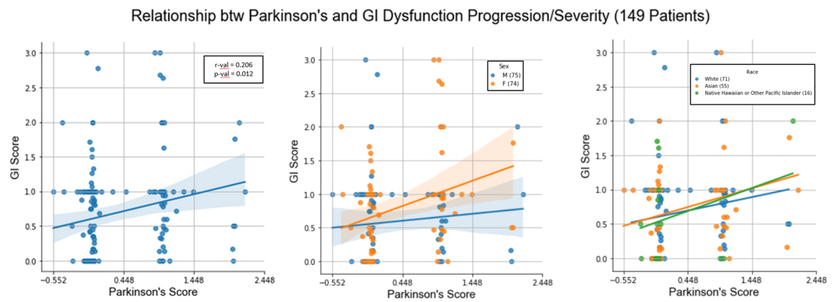
Results

Scoring criteria	-	+
Increase in UPDRS Score	100	49 (33%)
Increase in LEDD	55	94 (63%)
Presence of Falls	110	39 (26%)
Dementia Diagnosis	133	16 (11%)
Reported GI-related Issues	46	103 (69%)
GI-related ICD	126	23 (15%)

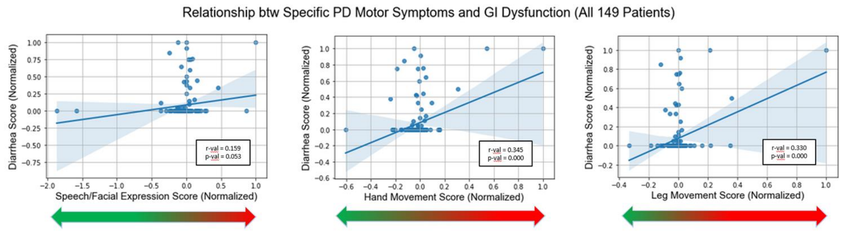


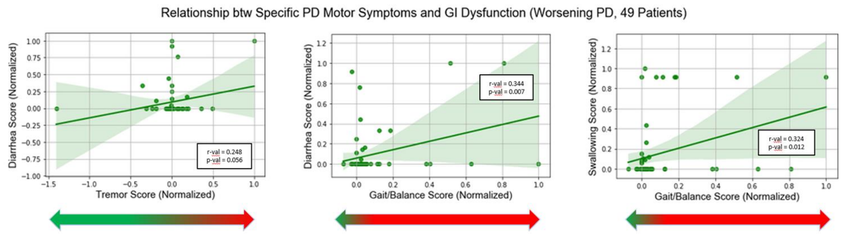
	#
Male	75
Female	74

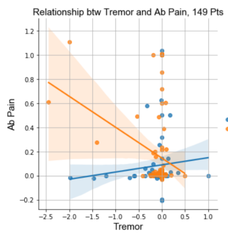




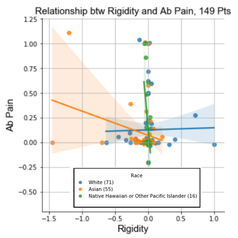
Results indicate a positive relationship between PD progression score and GI severity score among the 149 patients reviewed (r=0.21, p=0.01). Of note, females appeared to have a stronger positive correlation (r = 0.30, p= 0.01). Regarding race, Whites, Asians, and Native Hawaiian/Other Pacific Islanders appeared to have similar correlation patterns.







Comparison	Variable	r-val	p-val
Tremor vs. Ab Pain	M	0.10	0.40
Tremor vs Ab Pain	F	-0.31	0.01
Rigidity vs Ab Pain	White	0.18	0.14
Rigidity vs Ab Pain	Asian	-0.25	0.06
Rigidity vs Ab Pain	NH/Other PI	-0.52	0.04



Conclusions/Discussion

There is a positive relationship between PD progression score and GI severity score. These findings on the Hawai'i population support current literature of the correlation between progression of GI symptom severity and PD severity[5,8]. Females had a stronger positive correlation than males, which aligns with previously reported trends of higher GI symptom prevalence in females. Furthermore, there were stark differences observed between specific motor and GI symptoms between sexes. For instance, females showed a strong negative correlation between abdominal pain and tremor while males presented the opposite. These variances can be explained by biological differences and observed tendencies with respect to how the sexes appraise and report severity of symptoms[10].

Additionally, findings showcase a relationship between diarrhea and several motor symptoms (speech/facial expression, hand movement, and leg movement). Diarrhea is included in few PD studies and frequently used questionnaires such as NMSS do not include questions about diarrhea, indicating that it may be under recognized in PD patients. Of patients with worsening motor symptoms, there appeared to be positive correlations between tremor and diarrhea, gait/balance and diarrhea, and gait/balance and swallowing. These findings could work alongside the gut microbiota-PD literature to provide explanations for concurrent GI and motor symptoms[3].

There were some limitations posed on this study, the first of which was accessibility to complete medical records (ex. care sought outside of HPN or prior to June 2010). Additionally, PD progression scores and GI scores do not differentiate between acute and chronic GI symptoms, frequency of falls, and severity of dementia diagnosis. Clinical indicators of PD progression were also only collected at the date of first and last UPDRS score which does not account for any potential fluctuations in condition. The full understanding of GI symptoms and their role with PD is limited, as their onset could stem from a variety of factors (ex. age) not directly related to PD. GI symptoms were generally assumed to be related to PD unless otherwise stated in patient charts. The present study provides valuable insight on how the PD population is affected by GI dysfunction in a wide range of Hawaii PD patients to include military, private insurance, and the uninsured, which are often unaccounted for in studies done in the continental US.

Future Directions

Given that this is a single-centered study collecting data on only 149 patients at HPN who fit the inclusion criteria, future longitudinal studies with a larger sample size should be conducted to evaluate the validity of the correlations and to study trends between sexes, races, and various demographics. Further work could include more frequent clinical assessments to lessen the effect of fluctuations. As PD condition fluctuates, collecting UPDRS scoring within the first and last examinations, as well as changes in medication dosages, fall frequency, and severity of dementia may provide useful insight. Additionally, focusing on frequency of falls and severity of dementia along with differentiating between acute and chronic GI symptoms may provide a more holistic understanding of the PD and GI relationship. Given the observed correlation between diarrhea and individual motor symptoms, future studies should include more detailed information on GI symptoms beyond merely presence of constipation to include straining, pain, diarrhea, bloating, etc. which can be collected through implementing more GI questions in questionnaires such as the NMSS.

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Disclosure/Correspondence

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A Retrospective Analysis of the Association Between Economic Status and Severity of Disease in MS Patients in Hawaii

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Background

Multiple sclerosis (MS) is a chronic neurodegenerative disease that affects the central nervous system through nerve demyelination, inflammation, gliosis, and lesion formation.[1] The exact causes of MS remain unknown, yet certain risk factors can be postulated. In Hawaii, high taxes on low-income households and rising costs of living have resulted in significant income inequality.[2] Economic disparities being present, patients may experience financial burden due to treatment costs. Low-income patients with public insurance (such as Medicare and Medicaid) find it harder for their plans to cover treatment costs than patients with private insurance.[3] The current literature and research suggest that higher severity and worse outcome of a disease are linked to a higher poverty level and lower economic status.[4] We predict that patients of lower economic status will have greater self-reporting of severe pain, higher incidences of disease worsening, and higher rates of abnormal ambulatory status.

Objectives

The aim of this study is to determine if an association between multiple sclerosis severity and factors indicating economic status exists in Hawaii MS patients.

Methods

- Retrospective data was reviewed from Multiple Sclerosis (MS) patients seen at Hawaii Pacific Neuroscience (HPN) between 2010-2020.
- Patient data was obtained from *eClinicalWorks* using ICD-10 code (G35).
- Sample exclusion criteria: insufficient clinical data, unclear diagnosis, absence of insurance, less than two clinical visits and out-of-state residence.
- Information collected from patient records included: insurance coverage, ambulatory status, self-reported number on the pain scale, and "worsening" of MS.
  - Clinical "worsening" categorized as mention of previous "exacerbation," "relapse", "flare-up," "attack" or the word "worsening," within the physician's progress notes.
  - Ambulatory status was quantified by recording and ranking patient levels of mobility/gait using the verified Disease Steps (DS) scale.
- MS severity was measured in three ways:
  - Presence of severe pain (self-reported pain scale >5) within the last physician visit
  - Presence of "relapses", "exacerbations", "attacks", "flare-ups", or "worsenings" within the past year of the last HPN appointment
  - Presence of an abnormal ambulatory status using Disease Steps scale (scores >1) within last physician visit
- Patient insurance coverage was considered as a surrogate indicator of the economic status.
  - Patients grouped into public (Medicaid, Medicare, TriCare, and Quest) and private insurance categories (lower and higher economic statuses respectively)
- Statistical analysis was performed using a Chi-Square Test.

Results

N=74 MS HPN patients, 18 private insurance (24.32%), 56 public insurance (75.68%)

Reported Severe Pain vs Insurance Type

A greater proportion of public insurance patients reported severe pain compared to private insurance patients (public insurance = 37.5% versus private insurance = 5.6%). This finding was statistically significant, X^2 (1, N=74)=6.654, p=.01.

Insurance Type * Reported Severe Pain in Past Visit Crosstabulation

			Reported Severe Pain in Past Visit		
			No	Yes	Total
Insurance Type	Private	Count	17	1	18
		Expected Count	12.6	5.4	18.0
	Public	Count	35	21	56
		Expected Count	39.4	16.6	56.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.654[a]	1	.010		

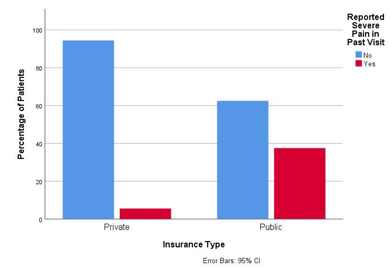

Figure 1. Percentage of patients reporting severe pain based on insurance type.

Reported Worsening vs Insurance Type

A greater proportion of private insurance patients reported worsening of their multiple sclerosis in the past year compared to public insurance patients (private insurance = 44.4% versus public insurance = 28.6%). This finding was not statistically significant, X^2 (1, N=74)=1.566, p=.211.

PastYearofRelapse * Insurance Type Crosstabulation

			Insurance Type		
			Private	Public	Total
PastYearofRelapse	No	Count	10	40	50
		Expected Count	12.2	37.8	50.0
	Yes	Count	8	16	24
		Expected Count	5.8	18.2	24.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.566[a]	1	.211		

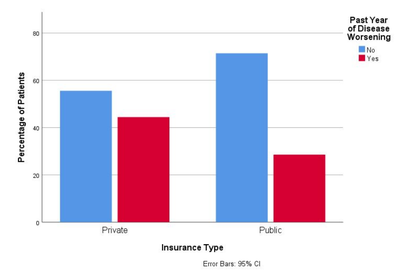

Figure 2. Percentage of patients with clinical worsening based on insurance type.

Ambulatory Status vs Insurance Type

A greater proportion of public insurance patients displayed abnormal ambulatory status when compared to private insurance patients (public insurance = 44.6% versus private insurance = 22.2%). The relation between these variables was borderline significant, X^2 (1, N=74)=2.873, p=0.09.

Non-Normal Ambulatory Status * Insurance Type Crosstabulation

			Insurance Type		
			Private	Public	Total
Non-Normal Ambulatory Status	no	Count	14	31	45
		Expected Count	10.9	34.1	45.0
	yes	Count	4	25	29
		Expected Count	7.1	21.9	29.0

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.873[a]	1	.090		

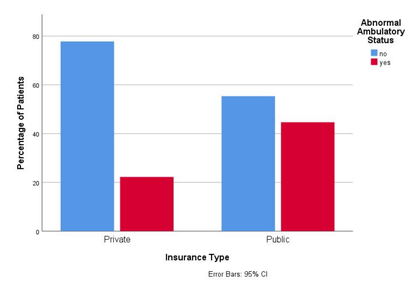

Figure 3. Percentage of patients with a change in ambulatory status based on insurance type.

Conclusions/Discussion

Based on our findings, there are differences in disease severity between MS patients of different economic backgrounds in Hawaii. MS patients of a lower economic status are more likely to report severe pain (p=0.01) when compared to patients of a higher economic status. These results affirm one of our three hypotheses and correspond to the current literature.[5] In contrast, the presence of abnormal ambulation (p=0.09) and clinical worsening (p=0.211) were not significantly linked to differences in economic status. The current literature does not support this finding; in previous published studies, associations were found for both areas.[6] A possible explanation lies in our simple categorized use of insurance as a measure of economic status; economic status is far more complex and there are multiple factors that haven't been included in this study. The social factors needed to measure for socioeconomic status could not be obtained from the HPN database and thus omitted. Based on the data it cannot be strongly concluded that the severity of MS is affected by economic status. This is mainly an exploratory study. Limitations include a small sample size, inconsistent follow-up time, unequal groups, inconsistent wording in the patient documents, and the use of multiple researchers to score ambulatory status and "clinical worsening."

Future Directions

Future studies with a larger sample size, standardized patient records, and inclusion of social factors in the determination of economic status (such as education, occupation, ethnicity, and area of residence) should be conducted to obtain more representative results.

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Disclosure/Correspondence

All authors reported no conflicts of interest.

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A Comparative Analysis of Alzheimer's Disease Presentation in the Asian, Caucasian, and Native Hawaiian Populations of Hawai'i

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Background

Alzheimer's Disease (AD) is a progressive neurodegenerative disorder that has been observed to disproportionately affect minority racial groups (1). Although racial disparity in AD incidence has been identified across the Caucasian, African American, and Hispanic populations, there has yet to be adequate inclusion of Native Hawaiians and Asians in these comparative analyses. Hawai'i provides the optimal environment to fill these gaps in research, with a population that is 37.6% Asian, 21.7% Caucasian, and 10.1% Native Hawaiian (2). Comparison of AD presentation across these groups will provide valuable insight into existing disparities that have not been acknowledged. Disease presentation can first be described in terms of group characteristics at diagnosis, such as age and body mass index (BMI). This will provide the foundation for further observation of cognitive impairment and behavioral disturbance in each group. The Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) will serve as measures of cognitive impairment severity, while behavioral disturbance intensity can be gauged in two ways. The Geriatric Depression Scale (GDS) can first be used to assess depressive severity, as depression is the second most common neuropsychiatric symptom of AD (1). Due to lapses in the validity of the GDS when reported by individuals with severe cognitive impairment, usage of antidepressants, antipsychotics, or anxiolytics that are prescribed to assuage abnormal behaviors will act as a secondary indicator (5). Upon comparison, it is expected that differences in AD presentation will arise across the Asian, Caucasian, and Native Hawaiian populations in Hawai'i.

Objectives

- To identify differences in AD presentation across the Asian, Caucasian, and Native Hawaiian populations in Hawai'i through comparison of: diagnosis characteristics, cognitive impairment severity, and behavioral disturbance intensity, across each group
- To provide data for underrepresented races in AD literature
- To highlight the influence race/culture has on overall health

Methods

- HPN patient records from 2010 - 2020 were accessed for analysis
- **Inclusion Criteria:**
  - Late onset AD (G30.1*)
  - Reported Race of Asian, Caucasian, or Native Hawaiian
- **Exclusion Criteria:**
  - Early onset AD (G30.0*)
  - Unspecified AD (G30.9*)
  - Reported Race of African American or Hispanic
- Mixed patients were classified according to their primary race
- Date of G30.1* addition to diagnosis list was set as diagnosis date
- MoCA scores were converted to MMSE equivalents (3)
- GDS scores were converted to describe depressive severity (4)
- Patients with an MMSE of <15 were omitted from GDS analysis (5)
- Medications needed to be associated to G30.1* or another code for a common behavioral symptom of AD to be counted

*denotes International Classification of Diseases, Tenth Revision (ICD-10) code

Results

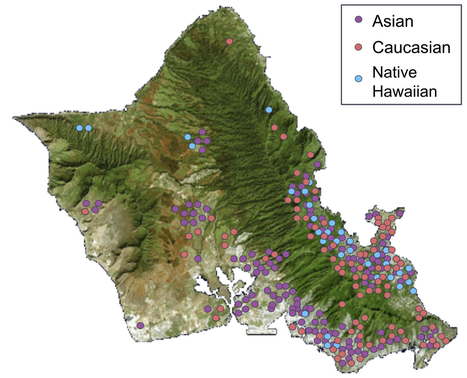

Figure 1: Geographical Distribution. This study included 142 Asians (50.5%), 103 Caucasians (36.7%), and 36 Native Hawaiians (12.8%). Most resided in Honolulu (31.3%), Kaneohe (20.6%), and Kailua (19.5%).

Racial Group	Average Diagnosis Age	Average Diagnosis BMI
Asian (n = 133)	79.9	23.54
Caucasian (n = 102)	80.7	24.66
Native Hawaiian (n = 35)	79.8	25.93

Table 1: Diagnosis Characteristics. Average diagnosis ages fell within a year of each other. Asians averaged the lowest BMI, but are in the normal weight category. Native Hawaiians, with the highest BMI, fall into the overweight range.

Racial Group	Average MMSE Score	AD Severity Stage
Asian (n = 92)	21.1	Mild
Caucasian (n = 72)	22.4	Mild
Native Hawaiian (n = 23)	18.2	Moderate

Table 2: Cognitive Impairment Severity. Native Hawaiians post an average MMSE in the moderate AD severity range, scoring 4.2 points less than Caucasians, and 2.9 points less than Asians.

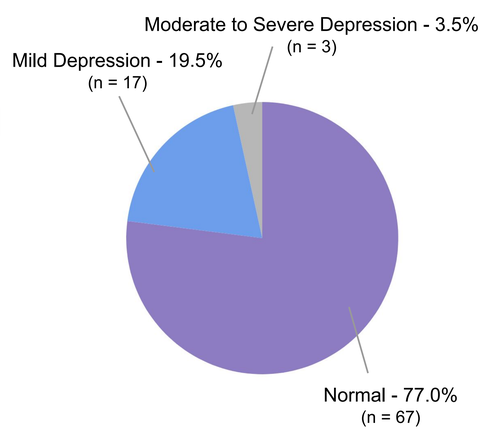

Figure 2: Behavioral Disturbance Intensity Measured by the GDS. Only 87 patients were eligible for GDS analysis, 20 of which reported some degree of depressive severity. The small overall sample made further comparison across race insignificant.

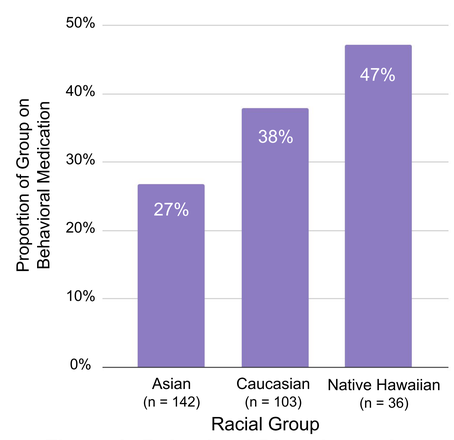

Figure 3: Behavioral Disturbance Intensity Measured by Medication Use. The proportion of patients on antidepressants, antipsychotics, or anxiolytics was highest in Native Hawaiians and lowest in Asians. Antidepressant use was most common in all racial groups.

Conclusions/Discussion

- MMSE comparison (p = 0.003894) suggests that Native Hawaiians experience the most severe cognitive impairment, possibly resulting from higher BMI and lower socioeconomic status.
- GDS analysis indicated no significant difference in depressive severity, but behavior medication analysis (chi-square: 6.823) showed significantly higher usage in Native Hawaiians, indicating more intense behavioral disturbances in this group.
- The GDS should not be used as a measurement of behavioral disturbance, as MMSE cutoffs may exclude more cognitively impaired patients that display behavioral disturbance. Mental illness stigma may have also decreased the willingness to report depressive thought patterns, further proving the inadequacy of the GDS, as it is subjected to much bias. A more appropriate depression assessment should be implemented for use in AD/demented patients.
- Asians may experience more severe cognitive impairment than Caucasians, but seem to encounter less intense behavioral disturbance, shown by lower medication use in the group.
- It can be concluded that AD presentation does differ amongst the Asian, Caucasian, and Native Hawaiian populations in Hawai'i, with Native Hawaiians presenting with the greater cognitive impairment severity and behavioral disturbance intensity than Asians or Caucasians diagnosed around the same age.

Future Directions

- Outreach should be directed to the Native Hawaiian population to disseminate AD information, offer earlier diagnostic testing, and push for regulation of modifiable risk factors to slow AD progression
- Exploration into the physiological differences in the onset of brain changes in these groups could expand upon the observed disparity
- Replication of the study with a less limited depression assessment, such as the Cornell Scale for Depression in Dementia, could better depict differences in depressive behavioral disturbances
- Further stratification into ethnicities could potentially unveil more nuanced disparities within the each of the studied racial groups

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Disclosure/Correspondence

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The Efficacy of Anti-CGRP Monoclonal Antibody Monotherapy in Comparison to Anti-CGRP and Botox Dual Therapy For Migraine Patients

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Background

Migraines are a neurological disorder characterized by moderate to severe, recurrent headaches, further classified as episodic or chronic depending on the number of migraine days per month a patient experiences. Two preventative treatments for migraines include anti-CGRP monoclonal antibodies (anti-CGRP mAbs), approved in 2018, and Botulinum Neurotoxin Type A (botox), approved in 2010. The four FDA approved anti-CGRP mAbs are erenumab, galcanezumab fremanezumab, and eptinezumab. Both anti-CGRP mAbs and Botox reduce migraine pain by acting on sensory nerve fibers in the trigeminal nervous system to inhibit the release of calcitonin gene-related peptides (CGRPs). At the receptor and ligand level, both therapies aim to lower CGRP concentration in the blood, a migraine characteristic that correlates with increased migraine pain. Prior to this study, there has been little research that thoroughly examined the relationship between the two treatments, especially from a clinical perspective.

Patients with chronic or episodic migraines typically attribute 50% reductions in migraine severity to Anti-CGRP medications in a three month period. However, a significant percentage of patients do not achieve appreciable benefits and may benefit from dual therapy with Botox. Two treatments in combination could result in synergistic effects because anti-CGRP mAbs prevent CGRP from binding to its receptor, while Botox inhibits the release of CGRP itself. Furthermore, one noteworthy study suggested that fremanezumab selectively inhibited the activation of Aδ- fibers, while Botox selectively inhibited C-fibers. Both Aδ- fibers and C-fibers contain CGRP receptors in their axonal synapses, directly influencing pain transmission during a migraine. Hence, our study aims to use clinical data to show whether anti-CGRP mAbs and botox dual therapy achieves better efficacy than anti-CGRP mAb monotherapy.

Methods

- This study was within-subjects, repeated measures and counterbalanced. A total of 41 out of 95 patients met our inclusion criteria at Hawaii Pacific Neuroscience, using the eClinicaWorks 11e database. These patients, ages 20 to 73, included 4 males and 37 females, of a variety of races.
- A review of the Hawaii Pacific Neuroscience patient database was conducted from June 2020 to August 2020.
  - Inclusion Criteria:
    - Patients diagnosed with chronic migraine and/or episodic migraines, and prescribed an anti-CGRP mAb drug between May 2018 and June 2020. The anti-CGRP medications analyzed in this study were Emgality, Aimovig and Ajovy.
  - Exclusion Criteria:
    - Patients missing quantifiable initial and/or final measurements for migraine days or severity.
    - Newly prescribed anti-CGRP patients, without follow up data.
- Since our study analyzed the efficacies of various treatments, migraine conditions were collected from each patient before and after treatment implementation.
  - Before treatment conditions were defined on the day of prescription, and after treatment conditions were determined approximately 1-6 months after beginning the treatment.
  - Conditions consisted of the number of migraine days and migraine severity.
    - A migraine day was defined as a day with more than four hours of headache pain and recorded out of 30 days.
    - Migraine severity was measured on a 10-point pain scale, defined by the physician at Hawaii Pacific Neuroscience. To counter subjectivity, each rating was compared to the Boston Scientific Corporation's Pain Scale, based on patient symptoms and descriptions of pain.
      - If a patient failed to specify intensity but reported improvements, their final score was determined by multiplying the average reduction of the specific anti-CGRP to the patient's initial score, subtracting the value from the original.

Objectives

- This study provides a holistic examination of the effectiveness of anti-CGRP mAbs in their treatment in migraines. This study can be used to strengthen the pre-existing knowledge of the use of mAbs with and without botox in migraine treatment.
- The primary objective of this study was to determine the difference in effectiveness of mAbs monotherapy versus botox and mAbs dual therapy among different age groups.

Data Analysis

- Change in migraine severity and headache days were calculated using the percent change of the initial and final values, after a 1-6 month period.
- Statistical analyses were run using IMB SPSS Statistics 25.0. A paired t-test was used to determine a statistical difference between the percent change of headache days and severity after 3-6 months of dual-therapy versus monotherapy. P-values of $p<.05$ were considered significant for all tests.
- Patients were further divided into severe (25-30 initial migraine days) and moderate (25+ migraine days) groups for migraine days; and severe (9-10 points) and moderate (8+ points) groups for migraine severity. A paired t-test was used to determine a statistical difference between dual and mono- therapy within such groups.
- Patients were also divided into groups by age of onset: child (0-18) and adult (18+). A paired t-test was used to determine a statistical difference between monotherapy and dual therapy within such groups.

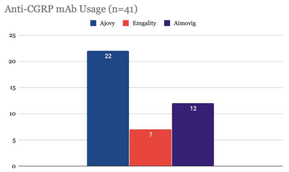

Figure 1. Anti-CGRP distribution amongst out patient population .

Results

Medication	Average % Reduction of Migraine Days	Average % Reduction of Migraine Severity
Mono therapy (n=19)	50.5 ± 40.4	55.8 ± 32.2
Dual therapy (n=20)	40.1 ± 32.0	39.1 ± 32.8
P-value (two-tailed)	*0.366*	*0.109*

Chart 1. Average percent reduction means between mono- and dual therapy.

- Patient's mean percent changes in severity, after 1-6 month of treatment, were not significantly different between the dual and monotherapy ($p=0.054$). Similarly, mean percent changes in migraine days, after 1-6 months of treatment, were not significantly different between dual and monotherapy ($p=0.185$).
- Significant differences were determined in the percent reduction of migraine severity between dual ($m=31.7 \pm 42.4$) and mono- therapy ($m=62.5 \pm 26.5$), for patients who reported a childhood onset of migraines ($p=.042$), where monotherapy had a significantly greater reduction in severity
- Patients with a childhood onset of migraines also experienced significant differences in their percent reduction of migraine days between dual ($m=28.7 \pm 38.4$) and mono- therapy ($m=65.5 \pm 25.9$). Similarly, monotherapy has a significantly greater reduction in migraine days ($p=.021$).
- Furthermore, significant differences were determined in the percent reduction of migraine severity between dual ($m=20.7 \pm 39.1$) and mono- therapy ($m= 51.1 \pm 29.7$), for patients who reported moderate initial migraine severity and days. Monotherapy demonstrated significantly greater percent reductions in severity ($p=.05$). However, there was no significant difference in the percent reduction of migraine severity and days between dual and mono-therapy for the groups who reported a severe initial severity and days.

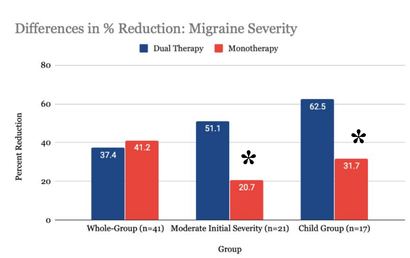

Figure 2. Average percent reductions in migraine severity between dual and mono therapy. Significant differences marked with an asterisk.

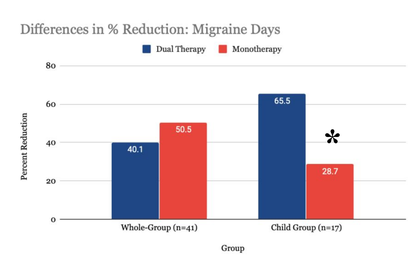

Figure 3. Average percent reductions in migraine days between dual and mono therapy. Significant differences marked with an asterisk.

Conclusions/Discussion

- The drastically unequal amount of female versus male patients featured in this study can be attributed to the significant hormonal fluctuations that females experience; on average, females suffer from migraines three times as often as males because of estrogen related changes.
- Patients with an initial moderate severity experienced a significantly greater reduction in migraine severity from monotherapy compared to dual therapy.
  - If administered early in treatment before a patient's symptoms progress to severe, anti-CGRP mAbs could prevent patients from having the burden of taking two medications in order to achieve the same efficacy in migraine reduction.
- Monotherapy yielded significantly greater reduction in migraine days and severity for patients with a childhood onset of migraines.
  - The reason for this is unclear and warrants further investigation. It may be attributed to adult onset migraines having a more progressive nature.
- There was no evidence to suggest a significant difference in migraine severity and frequency reduction between dual and monotherapy within our entire sample.
  - There is currently only indirect clinical evidence to propose a synergistic effect between anti-CGRP mAbs and Botox. This study showed no significant clinical data to support this theory. Moreover, physicians should exercise caution when prescribing these medications concurrently.

Future Research

- Investigate mono- and dual therapy:
  - In a larger sample size
  - Over a more extended period
  - Within different populations
  - In exclusively chronic migraine patients
  - Utilizing a more objective pain scale
  - With Eptineuzumab - the most recent FDA approved anti-CGRP mAb

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Disclosure/Correspondence

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