# 2022 - 2023

# Neuroscience Research Publications, Presentations with Focus on

### **Native Hawaiian and Pacific Islanders**









# Improving Neuroscience Care & Access Meeting Unmet Needs in Hawaii & Pacific Regions

Aloha Friends,

According to <u>NIH NIMHD</u> (<u>National Institute on Minority Health & Health Disparities</u>), one of America's greatest challenges is reducing the profound disparity in health status of its racial and ethnic minority, rural, low-income, and other underserved populations. Hawaii can play an important role in reducing the disparity in care for minority groups as defined by <u>NIH National</u> Institute on Minority Health & Health Disparities (NIMHD) with its:

- Asian Americans (7% of US & over 40% of Hawaii's population)
- Native Hawaiians and Pacific islanders (NHPI) (25% of Hawaii's population)
- Underserved rural population (94% Hawaii's landmass)

According to <u>FDA Clinical Trial Diversity site</u> "people from racial and ethnic minority and other diverse groups are underrepresented in clinical research. This is a concern because people of different ages, races, and ethnicities may react differently to certain medical products." Take for example a drug like Lecanemab that was approved by FDA in 2023 based on the CLARITY data, out of the 1795 participants, only 1 subject was NHPI from our Memory Disorder Ctr.

It is therefore our goal and our "kuleana" to not only take interest, but to engaged, promote, inspire, mentor and invest in the next generations of clinicians and scientists, residents and students in promoting research in underserved minority populations especially NHPI & lowering the barriers to access to care and representation in clinical trials. We are particularly excited to partner with the Dept. Native Hawaiian Health to collaborate "laulima" together,

### Aloha,



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### Welina me ke aloha,

Native Hawaiians and Pacific Islanders are at an increased risk for many neurological disorders, such as stroke, head and spinal cord injuries, and Alzheimer's disease and related dementias (ADRD), compared to non-Hispanic Whites and other racial and ethnic groups. They are also diagnosed with these conditions at considerably younger ages. For some neurological disorders, such as stroke and ADRD, their higher risk is attributed to the high prevalence of cardiometabolic and vascular risk factors, such as diabetes, hypertension, obesity, and dyslipidemia. And, there are also behavioral factors, such as substance use, interpersonal violence, and not using a seatbelt – factors that can lead to head and spinal cord injuries.

If we go "upstream," we will find that the risk factors for many neurological disorders are associated with socioeconomic factors, such as financial hardship, food insecurity, and stressors associated with economic deprivation. There are sociocultural and psychosocial factors, such as racism, acculturation-related stressors, and social isolation. Many of these socioeconomic and psychosocial factors are associated with obesity, diabetes, and hypertension in Native Hawaiians and Pacific Islanders.

Neighborhood factors can also affect their risk for neurological conditions. Exposure to environmental toxins can lead to Parkinson's disease and ADRD. Native Hawaiians and Pacific Islanders are more likely to live in areas where they are exposed to environmental toxins. These "upstream" factors are the social determinants of health – the conditions under which people are born, grow, learn, live, work, and age that impact their morbidity and mortality.

Despite all this, there remains a dearth of research on Native Hawaiians and Pacific Islanders regarding neurological disorders. The research being conducted by the clinician-scientists, and the students and residents they mentor, at the Center for Neuroscience Diversity are filling the important gaps in our clinical and scientific understanding of neurological-related disparities and their risk and protective factors as exemplified in the collection of research here. They are building the next generation of clinician-scientists who can help advance health equity for Native Hawaiians and Pacific Islanders.

### Kihe, mauli ola!



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## 2023 Hawaii Neuroscience Research Plenary Sessions Keynote Lecture

### August 19<sup>th</sup>, 2023 Honolulu, Hawaii



# Hoʻi Hou iā Mauli Ola Achieving Health Equity for Native Hawaiians and Pacific Islanders

Native Hawaiians and Pacific Islanders (NHPI) are at an increased risk for many neurological disorders (e.g., stroke and Alzheimer's disease and related dementias [ADRD]), and their vascular risk factors (e.g., hypertension, diabetes, and obesity). They are also diagnosed with these conditions at younger ages and are less likely to have these conditions well managed or treated than other racial/ethnic groups.

This keynote presentation highlighted the social and cultural determinants of NHPI health and the need for culturally responsive interventions aimed at preventing chronic diseases, such as cardiovascular disease (CVD) and ADRD. To illustrate these points, the adverse effects of racism on several cardiometabolic (i.e., hypertension and obesity) and mental health (e.g., depression)

conditions and physiological stress response, were presented based on research with NHPI communities. Also shared was a culturally grounded intervention that leveraged hula, the traditional dance of Native Hawaiians, to improve blood pressure control and 10-year CVD risk in Native Hawaiians and Pacific Islanders with previously uncontrolled hypertension.



In a randomized controlled trial (RCT) of 240 adult NHPI, the 6-month hula-based intervention,

called Ola Hou I ka Hula (retorting health through hula), was found superior to an education-only waitlist control group in improving blood pressure control and reducing 10-year CVD risk. It was explained how this successful hula- based intervention is now being applied to improve the vascular risk factors of ADRD and cognitive functioning in NHPI participants of a current, ongoing RCT.

### Key takeaways of this keynote lecture were:

- 1) NHPI are diverse in languages, cultures, and political statuses.
- 2) The need for NHPI data disaggregation in clinical research,
- 3) Racism is a significant social determinant of health impacting NHPI, and
- 4) Culturally grounded health promotion strategies are importance and effective in addressing the vascular factors associated with ADRD and other neurological disorders for NHPI communities.



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### **Journal of Stroke and Cerebrovascular Diseases**



# Native Hawaiian And Other Pacific Islanders' Leading Risk Factors For Ischemic Stroke: A Comparative Ethnographic Study

Ogasawara R, Kang E, Among J, Oyadomari K, Capitaine J, Regaspi N, Borman P, Viereck J, Carrazana E, Liow KK. Native Hawaiian and Other Pacific Islanders' Leading Risk Factors for Ischemic Stroke: A Comparative Ethnographic Study. J Stroke Cerebrovasc Dis. 2022 Jun;31(6):106433. doi: 10.1016/j.jstrokecerebrovasdis.2022.106433. Epub 2022 Mar 24. PMID: 35339856.

Hawaii is a multicultural state with many different ethnicities, including Native Hawaiians and other Pacific Islanders (NHOPI). This demographic has not been thoroughly studied, despite its significantly higher prevalence of stroke. This study aimed to characterize risk factors for ischemic stroke in NHOPI compared to other ethnicities.

### **Methods:**

An Institutional Review Board (IRB) sanctioned retrospective chart review was conducted at a multi-site community neurology clinic from June 2017 through June 2019. Prospective patients were identified from the database using the International Classification of Diseases 10th Edition (ICD-10) codes for ischemic stroke. 326 patients (99 NHOPI, 116 Asian, 111 Caucasian) with a history of ischemic stroke met the inclusion criteria. Risk factors were determined based on the American Stroke Association guidelines; ethno-racial grouping was based on self-identification; and average household income levels were estimated based on patient zip codes US Census Bureau data. Continuous variable risk factors were analyzed using an analysis of variance (ANOVA) and post-hoc pairwise comparisons using Tukey-Kramer; a multivariate analysis was conducted.

### **Results:**

Compared to Asians and Caucasians, NHOPI patients were on average 11 years younger at the onset of stroke and more likely to be women. The NHOPI group also had the highest rates of diabetes and obesity. NHOPI average income was significantly lower compared to the Caucasian group. Hypertension and hyperlipidemia were found to be higher in the Asian population. Alcohol consumption was reported more frequently among Caucasian patients.

### **Conclusions:**

These results better-characterized risk factors for ischemic stroke among NHOPI in Hawaii. The younger age of stroke onset in NHOPI patients is likely due to the higher burden of cardiovascular risk factors like obesity, smoking, and diabetes. Identifying such disparities in associated risk for NHOPI and other ethnicities can allow targeted stroke prevention and outpatient care in a multicultural setting



### Clinical Neurology and Neurosurgery

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journal homepage: www.elsevier.com/locate/clineuro



# Identification of risk factors and distinguishing psychogenic nonepileptic seizures from epilepsy: A retrospective case-control study

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**Introduction:** Patients with psychogenic non-epileptic seizures (PNES) experience significant morbidity and early mortality, secondary to delayed diagnosis. Better characterizing risk factors and exploring how PNES differentially affects sex and racial strata may facilitate earlier diagnosis.

**Methods:** From a Hawai'i neuroscience institution, 101 PNES patients were investigated in relation to sociodemographic and medical comorbidities. Cases were compared to 202 sex-, age-, and race-matched controls—representing patients with neurological disorders (general controls)—, as well as 404 unmatched epilepsy controls.

Results: Relative to general controls, PNES patients had increased odds (p < 0.05) of being: female, younger age, Native Hawaiian or other Pacific Islander (NHPI), suburban origin, from the lowest income quartile, Medicaid, beneficiaries, homeless, current/former smoker, illicit drug users (marijuana, opioids/narcotics, polysubstance abuse), have anxiety, depression, post-traumatic stress disorder, bipolar disorder, traumatic history, World Health Organization obesity class 3, traumatic brain injury, epilepsy, and somatoform disorder. In relation to epilepsy controls, PNES patients exhibited increased odds of being: employed, having attention-deficit/hyperactivity disorder, asthma, migraines, and chronic pain. Relative to females, male PNES patients exhibited increased odds of military insurance, diabetes mellitus type 2, and hypertension. Relative to Whites, the NHPI and Asian PNES patients presented increased odds of asthma, migraines, chronic pain, gastroesophageal reflux disease, and thyroid disease. Per multivariable logistic regression, anxiety was the only consistent predictor of PNES across all sex and race strata.

**Conclusion:** Predictors of PNES's vary amongst the strata of race and sex. Lower socioeconomic status, along with several psychiatric and medical comorbidities, could increase a clinician's suspicion for earlier medical workup and diagnosis of PNES.

### RESEARC CATEGORY: NEUROLOGY, NEURODEGENERATIVE & GENOTYPIC DEMOGRAPHICS



### **PubMed Full Length Publication:**

Smith M, Van N, Roberts A, Hosaka KRJ, Choi SY, Viereck J, Carrazana E, Borman P, Chen JJ, Liow KK. <u>Disparities in Alzheimer Disease and Mild Cognitive Impairment Among Native Hawaiians and Pacific Islanders.</u> Cogn Behav Neurol. 2021 Sep 2;34(3):200-206. doi: 10.1097/WNN.0000000000000279.

PubMed PMID: 34473671.

# Disparities in Alzheimer Disease and Mild Cognitive Impairment Among Native Hawaiians and Pacific Islanders



<u>Maiya Smith</u> <sup>1</sup>, <u>Nicholas Van</u> <sup>2</sup>, <u>Alyssa Roberts</u> <sup>2</sup>, <u>Kalei R J Hosaka</u> <sup>1</sup>, <u>So Yung Choi</u> <sup>3</sup>, <u>Jason</u> Viereck <sup>1</sup> <sup>4</sup> <sup>5</sup>, Enrique Carrazana <sup>1</sup> <sup>6</sup>, Pat Borman <sup>7</sup> <sup>5</sup>, John J Chen <sup>3</sup>, Kore Kai Liow <sup>1</sup> <sup>4</sup> <sup>5</sup>

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**Background:** Previous studies of racial differences in Alzheimer disease (AD) presentation have not included Native Hawaiians and Pacific Islanders (NHPI). To explore the presentation of AD and mild cognitive impairment (MCI) in NHPI.

**Method:** We conducted a retrospective review of patient records from Hawaii with a diagnosis of unspecified AD or MCI from September 2000 to September 2019. Variables of interest included age at diagnosis, gender, race, marital status, insurance, comorbidities, and scores on the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA).

**Results:** We reviewed the medical records of 598 patients, including 224 Asians, 202 Whites, 87 NHPI, and 85 Other. AD was more dominant than MCI across all of the groups, with the highest percentage in NHPI. Among the mean ages of diagnosis, NHPI were the youngest. Across all groups, a higher proportion of women than men had AD, with the highest female prevalence among NHPI. Hypertension, hyperlipidemia, and type II diabetes were highest among NHPI compared with the other groups. Of individuals with MMSE/MoCA scores, there were significant variations in scores by racial group. The mean MMSE/MoCA score was highest among Whites and lowest among NHPI.

**Conclusion:** Compared with other racial groups, NHPI have a higher proportion of AD than MCI at diagnosis, are diagnosed at a younger age, have a higher female prevalence, have more comorbidities that may contribute to AD/MCI onset, and present with lower MMSE scores.

### nature





Scientific Reports is the 5th Most-Cited Journal in the World with 5-Year Impact Factor (2021) of 5.516

Demographic Recruitment Bias of Adults in United States Randomized Clinical Trials by Disease Categories Between 2008 to 2019: A Systematic Review and Meta-Analysis. Sci Rep. 2023 Jan 2;13(1):42.

Buffenstein I, Kaneakua B, Taylor E, Matsunaga M, Choi SY, Carrazana E, Viereck J, Liow KK, Ghaffari-Rafi A. John A. Burns School of Medicine: Center for Neuroscience Diversity, Hawaii Pacific Neuroscience

**Objectives:** To promote health equity within the United States (US), randomized clinical trials should strive for unbiased representation. Thus, there is impetus to identify demographic disparities overall and by disease category in US clinical trial recruitment, by trial phase, level of masking, and multi-center status, relative to national demographics.

**Methods:** A systematic review and meta-analysis were conducted using MEDLINE, Embase, CENTRAL, and ClinicalTrials.gov, between 01/01/2008 to 12/30/2019. Clinical trials (N = 5,388) were identified based on the following inclusion criteria: study type, location, phase, and participant age. Each clinical trial was independently screened by two researchers. Data was pooled using a random-effects model. Median proportions for gender, race, and ethnicity of each trial were compared to the 2010 US Census proportions, matched by age. A second analysis was performed comparing gender, race, and ethnicity proportions by trial phase, multi-institutional status, quality, masking, and study start year.

**Results:** 2977 trials met inclusion criteria (participants, n = 607,181) for data extraction. 36% of trials reported ethnicity and 53% reported race. Three trials (0.10%) included transgender participants (n = 5). Compared with 2010 US Census data, females (48.3%, 95% CI 47.2-49.3, p < 0.0001), Hispanics (11.6%, 95% CI 10.8-12.4, p < 0.0001), American Indians and Alaskan Natives (AIAN, 0.19%, 95% CI 0.15-0.23, p < 0.0001), Asians (1.27%, 95% CI 1.13-1.42, p < 0.0001), Whites (77.6%, 95% CI 76.4-78.8, p < 0.0001), and multiracial participants (0.25%, 95% CI 0.21-0.31, p < 0.0001) were under-represented, while Native Hawaiians and Pacific Islanders (0.76%, 95% CI 0.71-0.82, p < 0.0001) and Blacks (17.0%, 95% CI 15.9-18.1, p < 0.0001) were over-represented. Inequitable representation was mirrored in analysis by phase, institutional status, quality assessment, and level of masking. Between 2008 to 2019 representation improved for only females and Hispanics. Analysis stratified by 44 disease categories (i.e., psychiatric, obstetric, neurological, etc.) exhibited significant yet varied disparities, with Asians, AIAN, and multiracial individuals the most under-represented. **Conclusions:** These results demonstrate disparities in US randomized clinical trial recruitment between 2008 to 2019, with the reporting of demographic data and representation of most minorities not having improved over time.

### **PubMed Full Length Publication:**

Identification Of Associations and Distinguishing Moyamoya Disease from Ischemic Strokes Of Other Etiologies: A Retrospective Case-Control Study

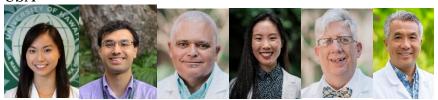
Annals of Medicine and Surgery, Volume 78, June 2022,103771, ISSN 2049-0801

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### Introduction

Better characterizing moyamoya disease (MMD) from ischemic strokes of other etiologies may facilitate earlier diagnosis by raising suspicion for a diagnostic work-up.

### Methods

To identify associated variables, MMD cases (n = 12) were compared against three sets of controls: age-, sex-, and race-matched controls of patients with general neurological disorders (n = 48), unmatched general controls (n = 48), and unmatched non-MMD ischemic stroke controls (n = 48).

### Results

MMD patients were 32 years (p < 0.0001) younger than ischemic stroke controls. Relative to non-MMD ischemic strokes, MMD patients had greater odds of presenting with visual field defects (OR: 9.13, p = 0.09) or dizziness (OR: 9.13, p = 0.09), as well as being female (OR: 8.04, p = 0.008), Asian (OR: 3.68, p = 0.087), employed (OR: 6.96, p = 0.02), having migraines (OR: 21.61, p = 0.005), epilepsy (OR: 6.69, p = 0.01), insomnia (OR: 8.90, p = 0.099), and a lower Charlson Comorbidity Index (CCI; p = 0.002). Patients with MMD, compared to non-MMD ischemic strokes, also had a 4.67 kg/ greater body mass index (BMI) and larger odds (OR relative to normal BMI: 21.00, p = 0.03) of being from obesity class III (>40 kg/), yet reduced odds of coronary artery disease (OR: 0.13, p = 0.02). Relative to general controls, MMD patients had greater odds of diabetes mellitus type 2 (OR: 10.07, p = 0.006) and hypertension (OR: 7.28, p = 0.004).

### Conclusion

MMD not only has a unique clinical presentation from other ischemic strokes, but also unique comorbidities, which may facilitate earlier work-up and treatment.

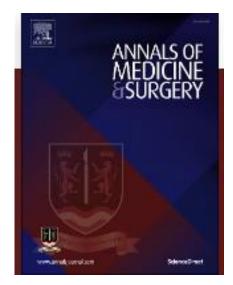
Moyamoya patients are 32 years younger than ischemic strokes of other etiologies.

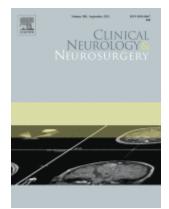
Moyamoya patients are 4.67 kg/ heavier than those with ischemic strokes.

Moyamoya patients are at greater odds of type 2 diabetes mellitus and hypertension.

Moyamoya patients are at reduced odds of coronary artery disease.

Moyamoya patients present more often with visual field deficits or dizziness.





Characterizing idiopathic intracranial hypertension socioeconomic disparities and clinical risk factors: A retrospective case-control study, Clinical Neurology and Neurosurgery, Volume 208,2021,106894,ISSN 0303-8467

Frances Tiffany Cava Morden, Charissa Tan, Enrique Carrazana, Jason Viereck,

Kore Kai Liow, Arash Ghaffari-Rafi



### Introduction

Against the backdrop of the diverse minority-majority state of Hawaii, this study seeks to better characterize associations between idiopathic intracranial hypertension (IIH) with sociodemographic variables and medical comorbidities.

### **Methods**

A retrospective case-control study was conducted by utilizing 54 IIH patients and 216 age-, sex-, and race-matched controls, 216 unmatched controls, and 63 age-, sex-, and race-matched migraine patients.

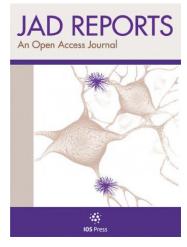
### Results

Relative to controls, IIH were 25 years younger (p < 0.0001) and 10.18 kg/m2 heavier (p < 0.0001), as well as exhibited greater odds of the following variables (p < 0.05): female (odds ratio [OR]: 8.87), the lowest income quartile (OR: 2.33), Native Hawaiian or other Pacific Islander (NHPI; OR: 2.23), Native American or Alaskan Native (OR: 16.50), obesity class 2 (35.0–39.9 kg/m2; OR: 4.10), obesity class 3 (>40 kg/m2; OR: 6.10), recent weight gain (OR: 11.66), current smoker (OR: 2.48), hypertensive (OR: 3.08), and peripheral vascular disease (OR: 16.42). Odds of IIH were reduced (p < 0.05) for patients who were Asian (OR: 0.27) or students (OR: 0.30;). Unique from Whites, NHPI IIH patients exhibited greater odds (p < 0.05) for being from lower socioeconomic status and currently smoking, as well as potential association with seizures (p = 0.08). Compared to migraines, IIH headaches were at increased odds of occurring (p < 0.05) occipitally, for greater than 15 days per month, aggravated by postural changes, and comorbid with dizziness and tinnitus.

### Conclusions

These results not only better characterize IIH, but also highlight socioeconomic and racial disparities in diagnosis

https://doi.org/10.1016/j.clineuro.2021.106894



### Racial/Ethnic Disparities in the Alzheimer's Disease Link with Cardio and Cerebrovascular diseases, based on Hawaii Medicare Data



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(Accepted for Publication Journal of Alzheimer's Disease Reports 2023 December Issue)

**Background:** There is an expanding body of literature implicating heart disease and stroke as risk factors for Alzheimer's disease (AD). Hawaii is one of the six majority-minority states in the US and has significant racial health disparities. Native-Hawaiians/Pacific-Islander (NHPI) population is well-known as a high-risk group for a variety of disease conditions.

**Objective:** We explored the association of cardiovascular disease with AD development based on the Hawaii Medicare data, focusing on racial disparities. Methods: We utilized nine years of Hawaii Medicare data to identify subjects who developed heart failure (HF), ischemic heart disease (IHD), atrial fibrillation (AF), acute myocardial infarction (AMI), stroke, and progressed to AD, using multistate models. Propensity score-matched controls without cardiovascular disease were identified to compare the risk of AD after heart disease and stroke. Racial/Ethnic differences in progression to AD were evaluated, accounting for other risk factors.

**Results:** We found increased risks of AD for AF, HF, IHD, and stroke. Socioeconomic (SE) status was found to be critical to AD risk. Among the low SE group, increased AD risks were found in NHPIs compared to Asians for all conditions selected and compared to whites for HF, IHD, and stroke. Interestingly, these observations were found reversed in the higher SE group, showing reduced AD risks for NHPIs compared to whites for AF, HF, and IHD, and to Asians for HF and IHD.

**Conclusion:** NHPIs with poor SE status seems to be mostly disadvantaged by the heart/stroke and AD association compared to corresponding whites and Asians.

# Cognitive and Behavioral Neurology The same of the Control of the

# Barriers To Alzheimer's Disease Clinical Trial Participation in Hawaii's Minority-Majority Population



Anson Y Lee, Julia R Jahansooz, Darrell Guittu, Rexton Suzuki, Lauren Pak, Kyle M Ishikawa, Connor Goo, John J Chen, Enrique Carrazana, Jason Viereck, Kore K Liow (Accepted for Publication Cognitive and Behavioral Neurology December 2023 Issue)

**Background:** Alzheimer's disease (AD) is the most common neurodegenerative disorder in the United States and disproportionately burdens minority populations. Yet, clinical AD trials regularly face a shortage of eligible participants numbering in the thousands and this number is set to increase in the next several years. As such, recruitment barriers have been noted as the primary factor negatively impacting AD clinical research progress. While research has been conducted to assess the primary reasons for the lack of clinical trial participation in minority groups, amongst minority populations, Asians and Native Hawaiians are the most understudied. This study explores the barriers to AD clinical trial participation in patients diagnosed with AD or mild cognitive impairment (MCI) in Hawai'i, the state with the largest relative population of Asian and NHPI in U.S. **Objectives:** Understanding barriers to Alzheimer's Disease (AD) clinical trial participation in underrepresented Asian and Native Hawaiian (NH) patients diagnosed with AD or mild cognitive impairment (MCI) in Hawaii. **Methods:** Patients and caregivers completed a 15-question telephone survey that assessed demographics, barriers, and improvement methods. Descriptive statistics were performed using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Incomplete surveys were included for analysis.

**Results:** Forty-nine patients responded (29 AD, 20 MCI). The mean patient age was 77 years, 51% were male, and the mean MMSE score was 23.2. Compared to the clinic population (20.0% Asian, 30.7% NH, 39.7% White), 5.6% Asian, 22% NH, and 32% White patients were in an active trial. More NH and White patients participated in trials than Asian patients. The decision to participate in trials to help others significantly differed by race (91% White, 80% NH, 29% Asian; p=0.023), with other reasons being statistically insignificant. Asian (30%) and NH (80%) patients reported the main barrier to participation was a lack of information about trials, with psychosocial conflicts and financial burdens as the least important barrier. Additional trial information given to family members (64% Asian, 88% NH, 62% White) and patients (64% Asian, 88% NH, 46% White) were listed as the most popular trial improvements.

Conclusions: Asian and NH patients were less likely to participate in AD trials compared to White patients. A deficiency in information was the primary barrier amongst minority patients. To overcome this barrier, increased outreach and education to patients and their families should be pursued. The results of this study reflect that Asian and NH patients feel they are often lacking information and face logistical obstacles when it comes to AD clinical trial participation. Interestingly, White patients shared comparable barriers indicating that all three groups had similar impediments to involvement potentially indicating problems with how trials are run across all three races. The top two trial improvement methods were consistent across Asian and NH populations (additional information provided to family members and patients), but White patients were equally concerned with financial burdens, transportation logistics, and information provided to family members when considering their second most important trial change. A primary limitation to this study was the small sample size of completed responses, and as such, future research should investigate these barriers in a larger cohort spanning a wider range of time to better generalize results and provide a more complete dataset.



### American Academy of Neurology (AAN) 2023 Annual Meeting, April 2023, Boston, MA



# Impact of Return-to-Exercise on Traumatic Brain Injury Recovery in a Community Setting

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### **Objective:**

To investigate the relationship between exercise modalities, intensities, and patterns following TBI and recovery, and to identify health inequities and barriers to recovery that may negatively impact recovery.

### **Background:**

Recommendations on return-to-exercise post-traumatic brain injury (TBI) remain controversial. This study surveyed Hawaii's diverse population to identify trends in exercise and recovery for TBI patients to shape recommendations on return-to-exercise. This study also aimed to identify health inequities and factors contributing to different outcomes, allowing inequities to be addressed.

### **Design/Methods:**

Retrospective review of 100 patients diagnosed with TBI between January 2020 and January 2022 was performed. Variables collected include demographics, etiologies, and symptoms at diagnosis. Self-generated phone surveys were completed to evaluate exercise patterns post-TBI and barriers to recovery. Statistical analysis was performed using RStudio.

### **Results:**

Patients who recovered within two years displayed similar exercise patterns to patients who took longer than two years. Exercise frequency, intensity, and duration did not differ significantly (p=0.75, p=0.51, p=0.80, respectively). Hiking/walking for exercise was more common in the long recovery group (p=0.018), likely reflecting advanced age compared to the short recovery group (50 vs. 39 years old, p=0.003). Otherwise, exercise modalities did not differ significantly. Additionally, no correlation exists between exercise intensity and symptom change (p=0.920), suggesting patients exhibit exercise patterns suitable for their specific condition. Finally, when comparing TBI recovery resources accessed across races or insurance types, Caucasian patients and individuals with private insurance utilized the most resources (p=0.032).

### **Conclusions:**

Return-to-exercise does not appear to be a predictor for TBI recovery. If encouraged to exercise post-TBI, patients will self-regulate a regimen not likely exacerbating their symptoms or recovery time, thus it may be suitable to recommend return-to-exercise as tolerated. The study also found worrying inequitable trends in TBI recovery resources accessed, and these disparities should be further investigated to rectify this issue.

Other Recent Brain Research, Innovation, Translation Labs (BRITL) Publications



# American Academy of Neurology (AAN) 2022 Annual Meeting Neuro Trauma Poster Presentation April 2022, Seattle, WA, USA



# Influence of Ethnoracial and Sociodemographic Variables on Incidence and Management of Traumatic Brain Injury Patients in Hawaii

Kayti Luu<sup>1,2</sup>, Michelle Pang<sup>1,2</sup>, Rachel Gorenflo<sup>1,2</sup>, Frances Morden<sup>1,2</sup>, Ariel Ma<sup>2,3</sup>, Nicholas Sims<sup>2,4</sup>, Lauren Fujii<sup>2,5</sup>, Kent Yamamoto<sup>2</sup>, Enrique Carrazana<sup>1,2</sup>, Jason Viereck<sup>1,2</sup>, Kore Liow<sup>1,2</sup>

<sup>1</sup>John A. Burns School of Medicine, University of Hawai'i at Manoa, <sup>2</sup>Concussion and Traumatic Brain Injury Center, Hawaii Pacific Neuroscience, <sup>3</sup>Rice University, <sup>4</sup>University of California, Berkeley, <sup>5</sup>Santa Clara University

### Objective:

Investigate potential sociodemographic disparities and medical comorbidities associated with the diagnosis and management of traumatic brain injury (TBI) in a minority-majority state.

### Background:

Previous studies have identified a relationship between TBI and sociodemographic variables, such as race and insurance status. However, few studies have investigated these variables in a minority-majority population in the United States.

### Design/Methods:

A retrospective case-control study was conducted on TBI patients seen at a traumatic brain injury center within the last 2 years. We identified 412 patients with TBI. 412 unmatched controls were randomly selected from the institution's patient pool. Injury characteristics, sociodemographic information, and psychological and biological variables were collected.

### Results:

Patients diagnosed with TBI had higher odds of being younger (p<0.0001), male (p<0.0001), Native Hawaiian or other Pacific Islander (NHPI; p=0.049), and having a lower median household income (p=0.032). NHPI patients with TBI were 2.87 times more likely to have Medicaid insurance (95% CI: 1.70-4.85; p<0.0001). Asian patients with TBI were 6.36 times (95% CI: 3.22-13.17; p<0.0001) less likely to have depression at diagnosis compared to other races. In contrast, other underrepresented minorities (OUM) reported depression 6.62 times more (95% CI: 1.18-16.89; p=0.022). Hispanics reported sleep disturbance 18.23 times more (95% CI: 1.76-909.14; p=0.0049). Caucasian patients with TBI underwent diagnostic imaging 1.99 times more than other races (95% CI: 1.23-3.23; p=0.0042).

### **Conclusions:**

Patients with TBI were more likely to be young, male, NHPI, and have a lower median income, which suggests a potential socioeconomic disparity. In addition, differing rates of Medicaid insurance, sleep disturbances, depression, and diagnostic imaging amongst ethnoracial groups indicates the need for a biopsychosocial approach to management.



### American Academy of Neurology (AAN) 2022 Annual Meeting April 2022, Seattle, WA, USA

**Employability, Work Difficulties and Factors Impacting Chronic Migraine Patients of Hawaii: Results of a Quality Improvement Survey** 



Michelle Stafford, Tracy Van, Rachel Gorenflo, Frances Morden, Kara Ushijima, Ashley Ung, Emma Inouye, Uiyeol Yoon, Dr. Vimala Vajjala, Dr. Enrique Carrazana, Dr. Kore Liow

Chronic intractable migraines have a significant impact on patients' daily lives. Many tools measure migraine impact on daily functioning, but triggers and work-related difficulties are often inadequately addressed. The Headache Impact Test (HIT-6) and HEADWORK questionnaire capture a variety of difficulties and factors that may impact patients with migraine at work and home.

<u>Objective</u>: Investigate the relationship between work-related difficulties and key factors that negatively impact employability and quality of life (QoL) for patients with intractable vs. non-intractable chronic migraines.

Methods: A single-centered, retrospective chart review was conducted to identify patients diagnosed with migraine and seen in the clinic between April 2021 through June 2021. Patient demographics, past medical history, and medication trials for abortive and preventative migraine treatments were collected. Phone surveys were performed using the HIT-6 and HEADWORK questionnaire. Employed patients were categorized using the Standard Occupational Classification system for statistical analysis. Nonparametric bivariate analyses with an alpha < 0.05 were utilized.

Results: Of 654 patients recruited for phone calls, 182 (28%) completed the survey and were further analyzed. 64.8% were diagnosed with intractable migraines and 35.2% with non-intractable migraines. Using non-intractable migraine patients as the reference group, patients with intractable migraines had an odds ratio of 0.51 for being employed and were 3.70 times as likely to encounter difficulties dealing with work problems. There was no statistically significant difference in other work-related difficulties, such as paying attention to tasks, solving organizational problems, and reading and writing. Patients with intractable migraines also had one more factor affecting work (e.g., noise, smell, brightness, extended working hours, negative attitudes of colleagues, air conditioning) than their counterparts.

56.3% of patients have tried five or more medications to control their migraines with 37.5% of these patients having a positive HIT6 score and 70% having intractable migraines.

<u>Conclusions:</u> The findings suggest that intractable migraine patients are less likely to be employed, but when they are, there are greater challenges faced during work, highlighting the incapacitating nature of this condition. Higher HIT-6 scores and evidence of polypharmacy in intractable migraine patients is another measure corresponding to decreased QoL. The multifactorial management of these patients with potentially debilitating migraines may necessitate a biopsychosocial approach for improved quality of care and life.

### Association of Academic Physiatrists February 1 – 5, 2022, New Orleans, Louisiana





# Sociodemographic Disparities of Patients with Lumbar Radiculopathy: A Single-Centered Retrospective Study

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### **Objectives**

Investigate sociodemographic disparities and differences in pain reporting amongst patients with chronic pain due to lumbar radiculopathy (LR) in a diverse minority-majority state.

### Design

A single-centered, retrospective study was conducted to identify patients with LR who underwent both electromyography (EMG) to confirm LR and lumbar magnetic resonance imaging (MRI); had a chief complaint of low back pain (LBP), numbness, tingling, or weakness; and received the ICD-10 code for LR. We identified 108 patients who met inclusion criteria. Nonparametric bivariate analyses with an alpha < 0.05 were utilized.

### Results

Asian LR patients were 8.00 years older than other LR patients (p=0.017). LR patients of other underrepresented minorities (OUM; including Black, Hispanic, and Native American) were 23.00 years younger than other LR patients (p=0.0012). Native Hawaiian and other Pacific Islander (NHPI) LR patients were 3.85 times more likely to be employed (95%CI: 1.13-15.50; p=0.030), while Asians were 4.36 times more likely to be retired (95%CI: 1.43-13.92; p=0.0066). OUM LR patients were at increased odds of reporting pain consistent with the severity of neuroforaminal stenosis identified on MRI (OR=14.59; 95%CI: 1.30-768.33; p=0.012). Both OUM (OR=7.42; 95%CI: 1.12-83.13; p=0.017) and Medicaid LR patients (OR=3.98; 95%CI: 1.40-11.66; p=0.0063) had increased odds of having no findings on MRI or EMG. Medicare LR patients were 3.73 times more likely to have moderate stenosis on MRI (95%CI: 1.31-10.85; p=0.0094).

### **Conclusions**

The results suggest that Asian LR patients were significantly older and more likely to be retired. Conversely, NHPI LR patients were at increased odds of being employed and OUM LR patients were younger at diagnosis, suggesting that these minority groups tended to present at working age. Additionally, OUM were more likely to accurately endorse lumbar pain of the same severity as reported in imaging. Overall, minority LR patients have diverse experiences of pain and require a biopsychosocial approach to pain management.

### Association of Academic Physiatrists February 1 – 5, 2022, New Orleans, Louisiana





### Sociodemographic and Biological Differences Between Traumatic Brain Injury Patients Of Different Ethnoracial Groups

Michelle Pang<sup>1,2</sup>, Kayti Luu<sup>1,2</sup>, Rachel Gorenflo<sup>1,2</sup>, Frances Morden<sup>1,2</sup>, Ariel Ma<sup>1,3</sup>, Nicholas Sims<sup>1,4</sup>, Lauren Fujii<sup>1,5</sup>, Kent Yamamoto, MD<sup>1</sup>, Enrique Carrazana, MD<sup>1,2</sup>, Jason Viereck, MD, PhD<sup>1</sup>, , Kore Kai Liow, MD, FACP, FAAN<sup>1,2</sup>

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### Introduction

Traumatic Brain Injury (TBI) is a significant public health concern. This study aimed to examine the intersection of race, sex, socioeconomic, psychiatric, and biological variables for TBI patients in a diverse minority-majority state.

### **Methods**

Retrospective chart review was conducted on TBI patients seen at a multidisciplinary neurological institution from 1/1/19 to 6/23/21. Patients were excluded for insufficient information in the electronic health record. 412 unmatched controls were randomly selected from the institution's patient pool. Variables collected include sociodemographic information, characteristics of the injury, in addition to psychological and biological variables.

### **Results**

Of the 412 patients included, 56% were male and 44% were female (p=0.00013). 32.0% of patients were white, 23.3% were Native Hawaiian or Other Pacific Islander (NHPI), 20.9% were Asian, 3.6% were Hispanic, 3.6% were other underrepresented minorities (OUM; included Black and Native American/Alaska Native), and 16.5% did not report their race. Caucasian patients with TBI underwent diagnostic imaging 1.99 times more than other races (95% CI 1.23-3.23; p=0.0042). Asian patients had an odds of 2.17 (95% CI 1.26-3.77; p=0.0041) for being employed and 2.32 (95% CI 1.36-4.02; p=0.0015) for having private insurance. NHPI had an odds of 0.53 (95% CI 0.32-0.88; p=0.014) for having private insurance and an odds of 4.22 (95% CI 1.18-16.89; p=0.019) for exhibiting Class III obesity. Hispanics reported sleep disturbance 18.23 times more (95% CI 1.76-909.14; p=0.0049) and OUM reported depression 6.62 times (95% CI 1.18-16.89; p=0.022) when compared to other races.

### Conclusion

These results suggest that Caucasian patients with TBI were more likely to undergo imaging studies. Asians were at an increased odds of having private insurance, while NHPI were at decreased odds, suggesting a potential disparity in diagnosing TBI. Hispanics had significantly higher rates of sleep disturbances, while OUM had higher rates of depression, which indicate the need for a biopsychosocial approach to TBI management.



# Chronic Migraine and Comorbidity Characterization: A Focus on Native Hawaiians and Other Pacific Islanders

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### **Objectives:**

Migraines are the second leading cause of disability worldwide. However, there is a paucity of research focused on the clinical presentation of chronic migraines (CM) in Native Hawaiian and other Pacific Islanders (NHOPI). This study aims to identify possible differences in the clinical presentation of CM in NHOPI in contrast to other Ethnocultural racial groups in Hawaii.

### Methods:

A retrospective case-control study was conducted to examine the relationship between demographics, comorbidities, and chronic migraines. Data from a single neurological care center in Hawaii were used to identify adults aged ≥18 years diagnosed with CM between 2018-2023. Adults with CM were matched for age and sex to 3 controls (patients with radiculopathy who did not present with CM).

### **Results:**

Overall, 309 CM patients and 964 matched controls were identified for analysis. NHOPI populations accounted for 24.9% of CM and 25% of radiculopathy patients. NHOPIs, on average, were diagnosed with CM or radiculopathy 2-3 years earlier (p=0.07) and had a higher average BMI than their White counterparts (p<0.01). Among NHOPIs, CM cases were more likely to have public insurance coverage (p=0.04), hyperlipidemia (p<0.01), diabetes (p=0.02), and insomnia (p=0.01). They were also more likely to be on more medications than White patients (p<0.001).

### Conclusion:

NHOPI CM patients were more likely to be diagnosed earlier than White patients and had higher BMIs, as well as higher rates of hyperlipidemia, insomnia, diabetes, and polypharmacy. These findings have important implications for understanding underlying comorbidities among NHOPI CM patients and developing targeted interventions.



# Investigating Young Atypical Stroke Risk Factors and Etiologies in Native Hawaiian and Pacific Islander Populations

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Introduction: Ischemic and hemorrhagic strokes in patients ≤45 years old are uncommon and represent only 10%-15% of all stroke patients. Native Hawaiian/Pacific Islander (NHPI) populations in particular have a 30% higher occurrence of younger atypical stroke patients than non-Hispanic Whites, but a thorough analysis of differences in risk factors and etiologies has not been conducted. Hence, this study aimed to characterize distinctions in atypical stroke patient profiles among the NHPI population.

Methods: This retrospective study was a single-center analysis of all atypical stroke patients ≤45 years old from 2009-23. Patient charts were reviewed for demographics, risk factors, and stroke etiology. Descriptive statistics were performed using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.

**Results:** Of the 66 patients included, 25 were identified as NHPI. The mean patient age at the time of stroke was 38 years for both NHPI and non-NHPI cohorts. NHPI patients had higher rates of hypertension (p=0.022) and a positive family history of stroke (p=0.045). However, all other variables were insignificant between the two patient groups including known risk factors for stroke such as coronary artery disease (p>0.999), hyperlipidemia (p=.792), arrhythmias (p=0.396), and diabetes (p=0.724).

**Conclusion:** NHPI atypical stroke patients were significantly associated with higher rates of hypertension and a positive family history of stroke compared with non-NHPIs. This study identified key differences in atypical stroke risk among NHPIs that should be further investigated to guide preventative health guidelines.



### Barriers To Alzheimer's Disease Clinical Trial Participation in Hawaii's Minority-Majority Population



Anson Y Lee, Julia R Jahansooz, Darrell Guittu, Rexton Suzuki, Lauren Pak, Kyle M Ishikawa, Connor Goo, John J Chen, Enrique Carrazana, Jason Viereck, Kore K Liow

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**Background:** Alzheimer's disease (AD) is the most common neurodegenerative disorder in the United States and disproportionately burdens minority populations. Yet, clinical AD trials regularly face a shortage of eligible participants numbering in the thousands and this number is set to increase in the next several years. As such, recruitment barriers have been noted as the primary factor negatively impacting AD clinical research progress. While research has been conducted to assess the primary reasons for the lack of clinical trial participation in minority groups, amongst minority populations, Asians and Native Hawaiians are the most understudied. This study explores the barriers to AD clinical trial participation in patients diagnosed with AD or mild cognitive impairment (MCI) in Hawai'i, the state with the largest relative population of Asian and NHPI in U.S.

**Objectives:** Understanding barriers to Alzheimer's Disease (AD) clinical trial participation in underrepresented Asian and Native Hawaiian (NH) patients diagnosed with AD or mild cognitive impairment (MCI) in Hawaii.

**Methods:** Patients and caregivers completed a 15-question telephone survey that assessed demographics, barriers, and improvement methods. Descriptive statistics were performed using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Incomplete surveys were included for analysis.

**Results:** Forty-nine patients responded (29 AD, 20 MCI). The mean patient age was 77 years, 51% were male, and the mean MMSE score was 23.2. Compared to the clinic population (20.0% Asian, 30.7% NH, 39.7% White), 5.6% Asian, 22% NH, and 32% White patients were in an active trial. More NH and White patients participated in trials than Asian patients. The decision to participate in trials to help others significantly differed by race (91% White, 80% NH, 29% Asian; p=0.023), with other reasons being statistically insignificant. Asian (30%) and NH (80%) patients reported the main barrier to participation was a lack of information about trials, with psychosocial conflicts and financial burdens as the least important barrier. Additional trial information given to family members (64% Asian, 88% NH, 62% White) and patients (64% Asian, 88% NH, 46% White) were listed as the most popular trial improvements.

Conclusions: Asian and NH patients were less likely to participate in AD trials compared to White patients. A deficiency in information was the primary barrier amongst minority patients. To overcome this barrier, increased outreach and education to patients and their families should be pursued. The results of this study reflect that Asian and NH patients feel they are often lacking information and face logistical obstacles when it comes to AD clinical trial participation. Interestingly, White patients shared comparable barriers indicating that all three groups had similar impediments to involvement potentially indicating problems with how trials are run across all three races. The top two trial improvement methods were consistent across Asian and NH populations (additional information provided to family members and patients), but White patients were equally concerned with financial burdens, transportation logistics, and information provided to family members when considering their second most important trial change. A primary limitation to this study was the small sample size of completed responses, and as such, future research should investigate these barriers in a larger cohort spanning a wider range of time to better generalize results and provide a more complete dataset.











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Jong-Mi Lee, NP

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### Introduction

Multiple sclerosis (MS) is a presumed autoimmune disorder of the central nervous system (CNS) characterized by inflammatory demyelination and neurodegeneration. It affects approximately 1 million people across the United States and an estimated 2.8 million people worldwide.¹ Symptoms of MS, a disease typically diagnosed between ages 20 and 50 years, vary tremendously and may comprise diffuse symptoms such as depression, pain, cognitive difficulties, and fatigue, as well as focal symptoms such as motor and sensory deficits, visual disorders, spasticity, bladder and bowel dysfunction, and dysphagia. Diagnosis at a young age makes MS a long-term disease that impacts patients, the health care system, and society for decades. Patients diagnosed at a younger age hit disability milestones earlier and therefore could be considered to have a poorer prognosis.

Although the cause of MS is unknown, it is a heterogeneous disease thought to result from complex interactions among genetic predisposition, sex, and the environment. Race is another important factor, but due to the complexity of the disease and its overlap with some of the aforementioned characteristics, there is uncertainty around the role of race in MS. What is clear is that around the world, the variability in the prevalence of MS, and the differences in presentation, depict MS as a complicated disease that requires inclusion of diverse groups in study populations in clinical trials. For

example, Balo's disease, a rare and progressive variant of MS, has a greater prevalence in the Philippines than in other Asian regions.<sup>2</sup> In many Asian countries, and China, corticospinal involvement is the predominant presentation.

A complex task is to ensure that when marginalized groups are included, they represent the full spectrum of the population targeted to receive the therapy. The ultimate goal of this process is to learn how to prescribe drug therapies safely for the patient groups who will be receiving them.

MS has been reported in most ethnic/racial groups, but it tends to be more common in Whites of northern European ancestry. Minority populations in the United States, such as Asian Americans and Hispanic Americans, have a higher incidence of MS compared with their ancestral countries of origin. However, minority populations are often underrepresented in clinical trials not only in the United States, but worldwide.<sup>3-5</sup> It is therefore difficult to assess treatment response in minority populations, even in subgroup analyses, because of the small numbers of patients.

The growing arsenal of disease-modifying therapies (DMTs) offers opportunities to reduce disability and extend survival for persons with MS. Thus, there is a continued, compelling need for high-quality epidemiologic data worldwide to improve our understanding of disease risk, support health policies aimed at meeting the diverse needs of people with MS, and encourage advocacy efforts.

High-quality epidemiologic data has the potential to improve personalized medicine. This occurs through earlier diagnosis, more effective prevention programs, and a higher precision in the treatment of disease in diverse populations.<sup>6</sup> An epidemiologic perspective applies principles of population screening to preventive medicine and uses evidencebased practices to personalize medicine.

### Update: Worldwide Trends in MS Prevalence

The estimated prevalence of MS has increased worldwide, with the number of affected patients rising from 2.1 million in 2008<sup>7</sup> to 2.8 million in 2020 (Figure). The 2020 global prevalence is 35.9 (95% CI, 35.87, 35.95) per 100,000 people, compared with a global prevalence of 29.26 (29.21, 29.30) per 100,000 in 2013.1

However, the increase has not been uniform around the globe. Although Asia was considered a low-risk zone for MS in the past, the epidemiologic status of MS in Asia has changed in recent decades, with studies showing an increased prevalence in many countries in Asia.8-10 It is important to note that within Asia, where half of the world's population resides, there is vast geographic, ethnic, and

cultural diversity; therefore, the Asian population cannot be grouped into one large ethnicity.<sup>10</sup>

Racial-ethnic differences in MS underscore the complex interaction between genetic, biologic, and environmental factors in the etiology of this disease. More studies are needed to understand differences in MS prevalence among diverse racial-ethnic groups across geographic regions and within populations residing in the same geographic region.

### **How MS Differs in Asian Populations**

The presentation and progression of MS in the Asia-Pacific region may differ from presentation and progression in Europe and North America. Unfortunately, data collection systems and registries for neurologic diseases that are necessary for understanding the burden of the disease (eg, accumulation of disability, impact of DMTs, safety risks, financial impact, effects on quality of life) are limited in the region.<sup>10</sup> Nationalized health care systems in some Asian countries are able to track disease prevalence<sup>11</sup>; some report into networks like MSBase. However, it may be the access to health care within the country that limits accurate data collection. Furthermore, because the Asian population covers a vast geography, and

> there is substantial diversity as a result of the numerous countries of origin, collection of data from one region within Asia may not be reflective of other regions. However, even with recognizing this, some similarities and commonalities across Asian regions may exist.

# Distribution of MS Cases Around the World Number of people with MS, Prevalence per 100,000 peop Unknown 0-25 26-50 51 - 100 101 - 200 > 200

Atlas of MS, 3rd ed.30 Reprinted with permission of MSIF (Multiple Sclerosis International Foundation)

### Differences in Presentation

In studies of Asian populations, many differences in presentation have been reported versus MS in White populations. 10-15 In general, MS in Asians is characterized by a more rapid progression, limited familial occurrence, more frequent attacks, more severe involvement of the visual system at onset as well as during the entire clinical course, and more common opticospinal

### **AFFILIATIONS AND DISCLOSURES:**

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involvement (Table). This opticospinal involvement is sometimes misdiagnosed as neuromyelitis optica (NMO),12 which is more common in Japanese and Chinese populations. 16

### Cerebrospinal Fluid (CSF) Findings

The hallmark of MS-specific changes in CSF is the detection of oligoclonal bands, which are seen in the vast majority of Western MS patients (at least 90%). In contrast, the frequency of oligoclonal bands in Japanese patients with MS is reported to be much lower (~50%). 17 These findings have been documented in a few other Asian populations, 18-20 but more data is needed in this large and diverse region.

### **MRI Findings**

In Asian patients with "Western-type" MS, MRI findings are largely similar to those of Western patients in terms of lesion distribution and appearance; however, there are significant differences in patients with opticospinal MS. These patients have fewer lesions on brain MRI. The spinal MRI shows larger and more extensive spinal cord lesions. 12,21

### Genetic Differences

Changes in the HLA-DRB1 gene and the IL-7R gene are the strongest genetic risk factors for developing MS. "Westerntype" MS is associated with HLA-DRB1\*1501, whereas opticospinal MS is associated with HLA-DPB1\*0501.

However, variations in dozens of other genes are thought to be involved in MS risk. It is extremely difficult to compare genetic characteristics of MS in Western and Asian populations since the Asian subcontinent comprises such racially and geographically diverse populations.<sup>15</sup> Recent studies call into question the strength of the genetic component as a differentiating factor between MS in Western populations and that in Asian populations. For example, Pandit and colleagues<sup>22</sup> suggest that many, if not all, of the MS risk variants identified in populations of European ancestry are likely also risk variants in the Indian population.

### Impact of Environment

Geographic gradient. MS is known to occur more frequently in areas that are farther from the equator; some of the highest prevalence rates are in Canada, the United States, and the Scandinavian countries (Figure). Epidemiologists continue to examine variations in geography, demographics (age, gender, and ethnic background), genetics, infectious causes, and migration patterns in an effort to understand why.

Migrant studies support the important influence of environmental factors in the risk of MS. In a systematic review of such studies, two consistent patterns were apparent: migrants moving from a region of high MS risk to one of lower risk had a lower-than-expected MS prevalence, particularly when migration occurred before age 15 years;

### In Asian populations, MS is more often characterized by<sup>14</sup>:

Selective clinical involvement of both the optic nerve and the spinal cord

A higher cell count and total protein concentration in the CSF

A higher frequency of gadolinium-enhanced lesions on spinal cord MRIs

Fewer lesions on the T2-weighted as well as gadolinium-enhanced TI-weighted brain MRIs

and migrants moving from an area of lower risk to one of higher risk tended to retain the lower MS risk of their country of origin, with no clear age-at-migration effect.<sup>23</sup>

### A Call to Action

Despite mandates from the National Institute of Minority Health and Health Disparities (within the National Institutes of Health [NIH]) to include more minorities in clinical trials, the participation of members of minority populations, especially Asian, Native Hawaiian, and Pacific Islander populations is disproportionately low in clinical trials funded by the NIH.24 This underrepresentation hinders the ability to identify differences in treatment response and supports the need for epidemiologic studies to incorporate cultural, environmental, or physiologic factors unique to that population.

Because MS differs both in incidence and clinical expression, prospective cohort studies that incorporate race/ ethnicity need to be conducted if we are to better understand MS and establish the best standard of care specific to each

### Is it MS or NMO?

While MS is a demyelinating disease of the CNS, NMO is an inflammatory disease of the CNS that selectively affects the optic nerves and spinal cord. MS in Asian populations is often characterized by the selective and severe involvement of the optic nerves and spinal cord. This form, termed 'opticospinal MS', has features similar to those of the relapsing form of NMO in Western populations.

A summary of differential diagnosis is<sup>29</sup>:

- On spinal MRI, NMO is strongly suggested by acute continuous longitudinal lesions covering three or more vertebral levels, while MS is suggested by patchy lesions that are rarely continuous over more than one vertebral segment
- In NMO, spinal cord lesions tend to be centrally located, rarely extending to the surface of the cord; whereas in MS, such lesions are usually located peripherally
- Chronic cord lesions in NMO often change over time, becoming patchier in appearance, making these distinguishing criteria less applicable to older lesions

### The 2017 McDonald Criteria for Diagnosis of MS: **Need for Validation in Diverse Groups**

MS can be difficult to diagnose because there is no single test that can determine the presence of the condition. The process of diagnosis involves obtaining evidence from a clinical examination, medical history, lab tests, and MRI imaging of the brain and, sometimes, the spinal cord. These tests are intended to rule out other possible causes of a person's neurologic symptoms and to gather data consistent with MS. A key principle for diagnosing MS has been to uncover evidence that demonstrates lesions in the CNS showing "dissemination in space" (suggestions of damage in more than one place in the CNS) and "dissemination in time" (suggestions that damage has occurred more than once).

The 2017 revision of the McDonald criteria for diagnosing MS was designed, in part, to allow earlier diagnosis of MS.<sup>27</sup> As such, it allowed an alternative to dissemination in time. In patients who present with a typical clinically isolated syndrome and clinical or MRI demonstration of dissemination in space, the presence of CSF-specific oligoclonal bands confirms a diagnosis of MS.27

However, 40% to 55% of Asian persons with MS are negative for oligoclonal bands. 17,28 The 2017 criteria are derived mainly from Western European/White populations. The authors note that the criteria require validation in diverse populations, in this case, persons of Asian ethnicity.<sup>27</sup>

patient's needs. The increased recruitment and inclusion of ethnic minority patients in MS research are essential.<sup>25</sup>

Robers and colleagues<sup>26</sup> conducted a systematic literature review of studies of DMTs for people with MS of varied racial and ethnic backgrounds published as of December 2019. Of 275 search results, 32 articles met the inclusion criteria; only 4 were randomized controlled trials (RCTs). Among studies that included Asian patients, the investigators found studies supporting the efficacy of interferons, fingolimod, teriflunomide, dimethyl fumarate, natalizumab, and alemtuzumab in Asian populations. Additionally, studies evaluating efficacy in Asian versus White patients have revealed no differences, suggesting that DMT choice need not differ in Asian patients. However, the studies included in this literature review were small<sup>26</sup>; more larger studies are needed. Future RCTs should strive to increase minority representation and planned analyses that incorporate race and ethnicity.

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# Characterizing Small Vessel Disease in Native Hawaiian and Other Pacific Islanders with Dementia: A Retrospective Pilot Study

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### **Background**

Small vessel disease (SVD), a major cause of age-related cognitive decline, affects small cerebral blood vessels, leading to cerebral hypoperfusion. Native Hawaiians and other Pacific Islanders (NHOPI) are reported to have higher rates of vascular risk factors of SVD, such as hypertension. This study aims to characterize the prevalence of severity of SVD in NHOPI dementia patients compared to their Caucasian and Asian counterparts.

### Methods

This retrospective chart review analyzed data from dementia patients ≥ 18 years old with a brain MRI and MMSE score between 23-27. Each NHOPI patient was matched with a Caucasian and Asian patient based on age, sex, and MMSE score. Patient charts were reviewed for demographics, comorbidities, medications, and SVD MRI findings at time of presentation of memory concerns.

### Results

Overall, 108 patients were included, with 36 patients in each racial group, a mean patient age of 72.1 years, and 72 (66.7%) females. NHOPI patients had a higher BMI (p<0.001) and higher rates of hypertension (p=0.024), diabetes mellitus (p=0.020), and coronary artery disease (p=0.026). NHOPI had higher rates of reporting attention deficits as a symptom of dementia (p=0.015). However, no significant differences in prevalence or severity of white matter lesions, subcortical infarcts, or brain atrophy.

### **Conclusions**

NHOPI patients were significantly associated with higher rates of vascular risk factors and showed differences in presentation of dementia. Further investigation is needed to identify potential preventative targets and improve risk predictions for individuals with SVD.

# Exploring Radiculopathy in Underserved Communities: A Focus on AANHPI Populations and Risk Factors

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### **Background/Objectives**

Radiculopathy (RP) is a debilitating nerve compression condition. This study aims to address the paucity of research on RP in Asian American, Native Hawaiian, and Pacific Islander (AANHPI) populations and to identify differences in clinical presentation, comorbidities, and treatment of AANHPI compared to other ethnocultural groups in Hawaii.

### Methods

This retrospective cohort study utilizes data from a single neurological center in Hawaii. Adults aged ≥18 years diagnosed with RP between 2016-2023 were identified using ICD10 codes. Patients without electromyography, magnetic renaissance imaging, or insufficient demographical data were excluded. Statistical analysis was completed on R, with p<0.05 considered statistically significant.

### Results

Data from 1287 out of 1,764 patients are included in the analysis, with 477 excluded. The cohort consisted of 28% Asians and 20% NHPIs. NHPIs had the youngest age of diagnosis, while Asians had the highest age of diagnosis (p<0.001). AANHPI populations were more likely to have public insurance (p<0.001). NHPIs had the highest rates of obesity (p<0.001), while Asians had the lowest (p<0.001). AANHPIs were more likely to have more than two medical comorbidities (p<0.001) and higher rates of hypertension (p<0.001), hyperlipidemia (p<0.001), hypercholesterolemia (p<0.001), and diabetes (p<0.001). AANHPIs were mainly treated with medications and were less likely to have received physical therapy, steroid injections, or surgery (p=0.042)

### **Conclusions**

AANHPI patients are more likely to be publicly insured, have multiple comorbidities, and are less likely to receive specialized treatments. NHPI are diagnosed earlier and have higher rates of obesity. These findings are important for addressing underlying comorbidities and treatment disparities amongst AANHPI patients.

# Use of Optimal Treatment Modalities for Spasticity and Stiffness in Post-Stroke and Cerebral Palsy Patients in Native Hawaiian Pacific Islanders and Underserved Populations in Hawaii

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### Introduction

Spasticity is a common sequela of Stroke and Cerebral Palsy which can lead to a lower quality of life for patients. Stroke is the most common cause of chronic disability in Hawai'i and is more prevalent in Native Hawaiian and Pacific Islander (NHPI) populations. This study aims to quantify any disparities in treatment decisions for spasticity based on socioeconomic factors in NHPI in Hawaii.

### Methods

A retrospective single-center chart review was performed at HPN to collect demographic information of patients diagnosed with Post-Stroke Spasticity or Cerebral Palsy who did and did not receive injection treatments. The study recorded 53 males and 56 females (ages 7-101) using ICD-10 codes from the inception of HPN to 2023. Statistical Analysis was performed using a Wilcoxon rank sum test, Pearson's Chi-squared test, and Fisher's exact test.

### Results

Of the 109 patients observed, 48% received injection treatments for spasticity. There were no significant differences between patients who did and did not receive injection treatments based on demographic factors like sex (p = 0.6), race (p = 0.3), insurance types (p > 0.9), or residential area (p = 0.7).

### Conclusions

Our research found limited evidence to show the disparities between patients who received injections based on race and socioeconomic factors. Our data set shows that efforts to eliminate racial/ethnic disparities are effective at improving access to healthcare. The small sample size and single-center study are the limitations that might influence the statistical significance of the results.

# Analyzing the Accuracy of Electromyography Findings when Magnetic Resonance Imaging is Positive for Brachial Plexopathy

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### Introduction

Magnetic resonance imaging (MRI) and electromyography (EMG) are commonly used to diagnose brachial plexopathies. However, there is limited research on the correlation of EMG and MRI findings for brachial plexus injuries in adults.

### **Objective**

To investigate the concordance of MRI and EMG findings in adult patients diagnosed with brachial plexopathy.

### Methods

This retrospective chart review involved adult patients (≥18 years) at Hawaii Pacific Neuroscience (HPN) with the diagnosis code G54.0 or S14.3XXA for brachial plexus injuries from database conception to June 17, 2023. Data collected from patients included demographics, risk factors, physical exam findings, symptoms, MRI findings, and EMG findings. Statistical analyses were performed using version 4.2.0 of R software (R Core Team, 2022).

### Results

Among the 64 patients, the overall percentage agreement between the EMG findings and MRI impressions was 75.0%. Sex and BMI were found to be significantly associated with EMG findings. 89.3% (n=25) of females had a negative EMG finding while 41.7% (n=15) of males had a positive EMG finding (p=0.006). BMI was also higher among patients with a positive EMG finding at an average of 29 compared to patients with a negative EMG finding with an average BMI of 26 (p=0.042).

### Conclusions

This study supports current literature demonstrating statistical significance in the concordance between EMG and MRI findings for diagnosing adult brachial plexopathies. This study also highlights the importance of considering sex and BMI in the diagnosis of adult brachial plexus injuries.

# Investigating The Relationship of Smoking, Sociodemographic factors, and Medical Comorbidities Among Chronic Pain Patients in Hawaii

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### Introduction

Chronic pain is a debilitating condition that can negatively impact cognitive performance, psychosocial well-being, and overall quality of life. The relationship between chronic pain and smoking has been well established, but understanding how other factors can influence chronic pain could provide insight for physicians recommending treatment options.

### Methods

A retrospective chart review was conducted on 175 patient records diagnosed with G89.4 (chronic pain syndrome) with pain for more than 12 weeks. Patients were grouped by smoking status. Other variables such as sociodemographic factors, medical comorbidities, and numerical pain rating scale were collected.

### Results

When compared between groups, 57% of current and former smokers had continued opioid use compared to 41% of non-smokers. Former or current smokers had a higher proportion of private insurance users and non-smokers had a higher proportion of public and other insurance users. Of the collected medical comorbidities, spine pain related diagnoses were more common in former smokers (56.3%) compared to current smokers (37.9%) and non-smokers (25.7%). Lastly, all NHPI patients (n=25) had at least one or more medical comorbidity.

### **Conclusions**

Chronic pain may require complex treatment that should consider a plethora of various factors. Pain ratings did not differ depending on smoking status, but those with a smoking history tended to remain opioid-dependent. Furthermore, spine pain may be a significant comorbid condition in smokers and NHPI patients may commonly present with comorbidities. The effect of insurance type should be studied further in smokers with chronic pain.

### Factors Associated with Risk for Depression in People with Epilepsy

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### Background

Depression is highly prevalent in individuals with epilepsy, affecting 32% of patients. Screening for depression is commonly done using the PHQ-2 and PHQ-9 self-report questionnaires in outpatient settings. Research on depression risk factors using these tools within neurology clinics remains limited. No studies have explored this in Native Hawaiian and Pacific Islander (NHPI) communities. This study aimed to identify factors associated with elevated PHQ-9 scores in epilepsy patients to enhance depression management.

### Methods

The research conducted a retrospective chart review of 126 epilepsy patients (62 PHQ-2 negative, 64 PHQ-9 positive) from a private neurology clinic. Eligible adults with epilepsy diagnoses and PHQ-2/PHQ-9 records were included. The PHQ9-positive patients comprised the test group (score ≥9), while PHQ2-negative patients acted as controls. Analysis encompassed demographic data, clinical history, and treatment records. Additional assessments were performed for positive PHQ9 patients and NHPI subgroups.

### Results

Results revealed a significant correlation between positive PHQ9 scores and substance use, with nicotine alone predicting a positive PHQ9 score. Patients with positive PHQ9 scores were also more likely to have at least one additional health comorbidity or a diagnosis of anxiety. In the NHPI subgroup, positive PHQ9 scores showed significant correlation with asthma, hypertension, and obesity.

### Conclusions

This study provides valuable insights into depression screening within epilepsy and establishes the link between epilepsy and depression in NHPI communities. These findings suggest the clinical utility of conducting PHQ-9 assessments even when PHQ-2 results are negative, using identified risk factors as screening indicators.

# Factors Associated with Depression Risk in Post-Concussive Syndrome Patients in Hawaii

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### **Background and Aims**

Post-Concussion Syndrome (PCS) describes symptoms which persist beyond the typical recovery time frame for mild traumatic brain injury (mTBI). Although there is a confirmed correlation between mTBI and depression risk, there is a paucity of literature investigating risk factors for depression in the context of PCS (DPCS). This study aims to assess patient demographics, concussion etiologies, clinical course, substance use, and medication use associated with DPCS risk.

### **Methods**

This single-center, retrospective study included patients diagnosed with PCS between January 2020 and January 2023. Data comprised demographics, concussion etiology, loss of consciousness (LOC) following injury, PCS symptoms, PHQ-2/PHQ-9 surveys, substance use pre- and post-PCS diagnosis, and CNS-active medications pre- and post-PCS diagnosis. P-values were calculated using Fisher's exact tests and Wilcoxon rank sum tests.

### Results

Of the initial 297 patients, 82% received depression screening, and 31% were at risk of DPCS based on PHQ-2 scores. Patients who experienced LOC of unspecified duration were at higher risk of developing DPCS (p=0.037). Patients presenting with symptoms of confusion, insomnia, or memory loss at PCS diagnosis had increased DPCS risk (p=0.014, p=0.035, p=0.003). Tobacco use pre-TBI (p=0.039) and marijuana use pre- (p=0.003) and post-TBI (p=0.009) were associated with increased risk of DPCS. Elevated DPCS risk was also seen in patients who used SSRIs (p=0.005), SNRIs (p=0.010), atypical antidepressants (p=0.040), or mood stabilizers (0.022) pre-TBI or atypical antidepressants (p=0.005) post-TBI.

### Conclusions

This study highlights several risk factors for DPCS which may inform improved PCS patient management and emphasizes the need to develop standardized screening protocols for DPCS.

# Prevalent Onset Symptoms of Multiple Sclerosis in Native Hawaiian/Pacific Islander, Asian American and Caucasian Patients in Hawaii

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### Introduction

Multiple sclerosis (MS) is a chronic degenerative disease of the CNS characterized by demyelination and axonal degeneration in the brain and spinal cord, which are caused by an immune-mediated inflammatory process. Onset symptoms of MS differ from one patient to another, making MS a challenging condition to diagnose. This research will improve overall understanding of how MS presents in our local population in Hawaii.

### **Objective**

Examine the baseline characteristics and onset symptoms of Asian American, Native Hawaiian/Pacific Islander (NHPI), and Caucasian patients with MS in Hawaii.

### Methods

We conducted a retrospective chart review of patient records using hospital data from Hawaii Pacific Neuroscience (HPN) with a diagnosis of MS from June 1st 2018 to June 26th 2023. Patient charts were reviewed for demographics, onset MS characteristics, and medical comorbidities. Differences across the race/ethnicity groups were examined by analysis of variance or Kruskal-Wallis rank sum test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. A p-value less than 0.05 was considered statistical significance.

### Results

NHPI are more likely to experience vision loss (p=0.025), comorbid seizures (p=0.014) and headaches/migraines (p=0.021) compared to White and Asian groups. NHPI represented the youngest group diagnosed with MS (43 years old; p=0.038); no significant findings for NHPI at age of diagnosis (p=0.5).

### Conclusions

There was very little NHPI and Asian representation to effectively compare with Caucasian patients which likely affected the external validity of the study. More research should be done to study how MS affects NHPI patients.

# Native Hawaiian and Pacific Islanders Risk Factors for Peripheral Neuropathy: An Ethnographic Study

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### Introduction

This study explored the prevalence and characteristics of peripheral neuropathy, focusing on Native Hawaiian and Pacific Islander (NHPI) patients. The higher prevalence of diabetes and unique lifestyle factors in NHPI communities may contribute to an increased risk of neuropathy, highlighting the need for targeted research in this underrepresented population.

### **Methods**

A retrospective review of 298 patients from a single-center neurology clinic was conducted. Race was categorized into four groups. Pearson's Chi-squared tests, Fisher's exact tests, and Kruskal-Wallis rank sum test were used to analyze associations between race, age, pre-existing conditions, and neuropathy symptoms.

### Results

Findings revealed a higher prevalence of neuropathy testing among NHPI patients under 35. Significant associations were found between race, age, conditions like Type 2 Diabetes, obesity, hypertension, and sensory symptoms of neuropathy. No significant differences were found in motor and autonomic symptoms between NHPI and White groups.

### Conclusions

The study emphasizes the need for targeted screening and early management, particularly for younger NHPI patients. Limitations include potential selection bias and broad racial categorization. Insights may lead to more equitable care for at-risk populations, with future research needed to explore underlying mechanisms and develop personalized approaches.

# Progression of Parkinson's Disease in Asian and Native Hawaiian and Pacific Islander Patients

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### Background

Parkinson's disease (PD) is a neurodegenerative disorder caused by dopaminergic cell death in the basal ganglia of the brain. The incidence of PD increases with age, and patients often experience a wide range of symptoms as the disease progresses. A detailed characterization of PD presentation and progression in Asian and Native Hawaiian and Pacific Islander populations (NHPI) has not been well documented.

### Methods

This retrospective chart review analyzed data from Hawaii Pacific Neuroscience between 2017-2022. ICD-10 codes were used to identify PD patients. Recorded data included demographics, date of diagnosis, Parkinson's medications and dosing at time of diagnosis, and current Parkinson's medications and dosing. Severity of PD was measured by medication dosage amount and frequency using the Levodopa Equivalent Daily Dosage (LEDD). Fisher's exact test, Kruskal-Wallis rank sum test, and Spearman's correlation coefficient were used as appropriate.

### Results

NHPI are diagnosed with PD at a younger age compared to other groups (p=0.040). Additionally, there is a positive correlation between time from PD diagnosis and LEDD score among Asians (p=0.00023) and NHPI (p=9e-04), indicating that PD severity in Asians and NHPI increased the longer the duration of their PD. This contrasts with Whites, whose LEDD score did not increase significantly, even over a longer disease duration.

### **Conclusions**

NHPI were found to be diagnosed with PD at a younger age and experience more severe progression of PD. Further understanding these ethnicity-specific differences is crucial for physicians to manage patient expectations about the progression of their disease.

# The Safety and Efficacy of Dual and Sequential Calcitonin Gene-Related Peptide Therapies for Migraine Treatment

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### Introduction

Although singular regimens of calcitonin gene-related peptides (CGRP) are shown to be effective in treating migraines, a considerable number of patients continue to experience suboptimal outcomes. Adding a second CGRP inhibitor could provide increased relief; however, limited research is available to support this practice.

### **Objective**

To assess the safety and efficacy of dual and sequential CGRP therapies.

### Methods

This retrospective chart review analyzed 88 patients diagnosed with episodic or chronic migraine at Hawai'i Headache & Facial Pain Center. Between May 2018 and July 2023, 67 patients received two CGRP medications simultaneously (dual group), and 21 patients transitioned to a second CGRP after discontinuing the first due to adverse events or inefficiency (sequential group). Variables, including age of onset, current age, sex, race, ethnicity, baseline symptoms, and adverse events, were collected. Pre-treatment monthly headache frequency and severity were compared to post-treatment results evaluated for 1 to 8 months.

### Results

In the dual-CGRP group, 51% of patients experienced a 14% average reduction in headache severity ( $p = 4.4 \times 10^{-6}$ ), while 57% showed an average reduction of 5 days in headache frequency ( $p = 1.4 \times 10^{-6}$ ). Among the sequential CGRP group, 57% of patients had a 10.7% average reduction in headache severity (p = 0.0033), but the change in headache frequency was not significant. No significant adverse events were reported from both groups.

### Conclusions

These findings support the benefits related to individual CGRP medication regimens and suggest that dual-CGRP therapies may further improve treatment outcomes.

# Identifying Racial Differences in Clinical Presentation of Obstructive Sleep Apnea in Native Hawaiian and Pacific Islander Patients

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### Introduction

Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder in the United States. Disparities in the severity of OSA have been identified in other minority racial groups, but there has been little study of OSA in the Native Hawaiian and Pacific Islander (NHPI) population.

### **Objective**

To compare the clinical presentation of OSA between NHPIs and Whites.

### **Methods**

A retrospective chart review was conducted on all patients diagnosed with OSA via polysomnography between 1/1/13 to 6/1/23 at a single outpatient sleep medicine center. Pearson's Chi-squared and Fisher's exact tests were used to identify associations between apnea-hypopnea index (AHI) severity and clinical characteristics such as BMI. Logistic regression models were utilized to estimate associations between AHI severity and race.

### Results

Overall, 91 NHPI and 129 White patients were included for analysis. In NHPIs, 76.2% were obese, compared to 48.8% of Whites (p<0.001). Among NHPIs, 74.6% had moderate or severe OSA based on AHI scores, compared to 47.3% of Whites (p<0.001). The odds of NHPIs being diagnosed with moderate or severe OSA were two times greater than Whites (adjusted odds ratio = 2.84 [95% CI: 1.20, 7.03]).

### Conclusion

To our knowledge, this is the first study to compare the severity of OSA in NHPIs with another racial group. With NHPIs 2.84 times more likely to be diagnosed with moderate or severe OSA than Whites, there is a need for further research on interventions and prevention.

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