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

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Background: Previous studies of racial differences in Alzheimer disease (AD) presentation have not included Native Hawaiians and Pacific Islanders (NHPI).

Objective: 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.

Key Words: Native Hawaiian, Pacific Islander, Alzheimer disease, mild cognitive impairment

(*Cogn Behav Neurol* 2021;34:200–206)

AD = Alzheimer disease. **MCI** = mild cognitive impairment. **MMSE** = Mini-Mental State Examination. **MoCA** = Montreal Cognitive Assessment. **NH** = Native Hawaiian. **NHPI** = Native Hawaiians and Pacific Islanders. **PI** = Pacific Islander.

Medicine has been changing to better recognize the role of social determinants of health in health outcomes of populations. It has become increasingly apparent how race and ethnicity contribute to an individual's overall health outcomes. The recent COVID-19 pandemic has especially highlighted these racial differences, with Black and Latino Americans suffering from 1.9 and 2.3 times the number of COVID-related deaths, respectively, compared with non-Hispanic Whites (Centers for Disease Control and Prevention, 2021b). These racial differences in health outcomes are also prevalent in Hawaii, which has emerged as the state with one of the worst health disparities among COVID patients despite having the second fewest number of total confirmed cases in the nation (Centers for Disease Control and Prevention, 2021a). The Native Hawaiians and Pacific Islanders (NHPI) community in Hawaii has one of the starkest disparities, among which non-Hawaiian Pacific Islanders (PI) are most disproportionately affected. As of May 2021, non-Hawaiian PI comprise 20% of all reported COVID cases despite being only 4% of the state population (State of Hawaii, Department of Health, Disease Outbreak Control Division, COVID-19, 2021). Similar disparities also extend to the field of neurology.

Alzheimer disease (AD), the most common form of dementia, is a neurodegenerative disease that results in the gradual loss of memory and cognitive function over time (Alzheimer's Association, 2019). Differences in disease

Received for publication August 22, 2020; accepted November 16, 2020.
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Supported in part by the John A. Burns School of Medicine Office of the Dean through the Barry and Virginia Weinman Endowment and by the Ola HAWAII (U54MD007601) grant from the National Institutes of Health to S.Y.C. and J.J.C.

The authors declare no conflicts of interest.
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incidence have been observed among racial groups. US studies that have stratified AD by race have shown that African Americans and Latin Americans have a higher incidence and prevalence of AD than Whites (Manly and Mayeux, 2004; Weuve et al, 2018; Zamrini et al, 2004).

Little is known, however, about the incidence and prevalence of AD in NHPI—a rapidly growing racial group that is frequently understudied (Hoeffel et al, 2012). Published studies involving NHPI either have focused solely on inpatient data or have combined NHPI with other minority groups, including American Indians and Alaskan Natives (Panegyres et al, 2014; Sentell et al, 2015). Increasing the representation of NHPI in neurologic literature is critical to understanding the underlying factors that contribute to the observed health disparities among these populations, especially as they relate to social determinants of health.

NHPI also face a unique set of historical, socioeconomic, and policy-related circumstances that predispose them to certain health outcomes. For example, the mortality rates of Compact of Free Association migrants in Hawaii who hail from the Federated States of Micronesia, the Republic of Palau, and the Republic of the Marshall Islands increased relative to that of Whites during the 25-year period in which their eligibility for Medicaid was revoked (Molina et al, 2020). This longstanding federal policy, which affected health care coverage for many PI throughout the United States, was only recently overturned in early 2021, with the restoration of Medicaid eligibility for Compact of Free Association migrants. The impact of unique factors like this on health disparities are masked when NHPI are not studied separately from other minority groups, particularly those that exhibit more positive health outcomes.

Systematic discrimination, a lack of underrepresented groups on research teams, a general distrust of physicians and Western medicine, and negative experiences with medical providers that stem from a lack of cultural competence may be factors that cause NHPI to either avoid engagements with the health care system and direct participation in clinical studies or be excluded by the study itself (Kamaka et al, 2011). This distrust stems as far back as 1778, when Captain James Cooke arrived to the Hawaiian islands, decimating 90% of the Native Hawaiian (NH) population within the next 100 years due to introduced infectious diseases (Kana'iaupuni and Malone, 2006; McCubbin and Marsella, 2009).

There are substantial gaps in the neurology literature regarding racial factors and the risk of developing, or the prevalence of, AD (Babulal et al, 2019). A high prevalence of early onset AD or mild cognitive impairment (MCI) in NHPI may pose health, economic, and social challenges for Hawaii, where one out of four individuals identifies as NHPI (State of Hawaii, Department of Health, 2008). A better understanding of risk factors for the development of AD or MCI in NHPI may allow for more targeted interventions that may slow disease progression.

In patients with AD and MCI at diagnosis, we examined baseline cognition via Mini-Mental State Examination (MMSE; Folstein et al, 1975) score, age, gender, race, marital status, and insurance at presentation among NHPI compared with other racial groups in Hawaii. Due to the higher incidence of risk factors for dementia among NHPI, including hypertension, obesity, and diabetes, we hypothesized that NHPI would present with AD and MCI at younger ages and with different comorbidities that could put them at higher risk for dementia compared with Whites or Asians (Alzheimer's Association, 2019; Mau et al, 2009). The disproportionate prevalence of chronic metabolic diseases like diabetes related to higher obesity rates among NHPI are associated with poor socioeconomic standing, with educational attainment being a strong predictor of adiposity (Brown et al, 2009).

Other barriers to care also facilitate increased risk factors for disease among NHPI. Language barriers are significant among Compact of Free Association migrants, who comprise a substantial portion of the PI population in Hawaii, which leads to poor health literacy and an impaired ability to navigate the health care system due to the lack of translation services by health care providers in languages like Chuukese, Yapese, Kosraean, Pohnpeian, and Marshallese (Riklon et al, 2010). A recent study found that NHPI who have health insurance were still more likely than insured Asians to face cost barriers to care, and that uninsured Asians were more likely than their uninsured NHPI counterparts to receive an annual checkup (Morisako et al, 2017).

METHOD

Participants

We conducted a retrospective review of all patient records at Hawaii Pacific Neuroscience in Honolulu, Hawaii, during the time period from September 2000 to September 2019. We extracted data from patient charts using the 10th revision of the *International Classification of Diseases and Related Health Problems* (World Health Organization, 2016) clinical modification diagnostic codes for unspecified AD (early onset, late onset, unspecified) and MCI. Exclusion criteria included a previous diagnosis of AD or MCI. Variables of interest included age at diagnosis, gender (male/female), race (Asian, White, NHPI, Other), marital status (single/married/widowed/divorced or separated), insurance (private/other), comorbidities, and MMSE or Montreal Cognitive Assessment (MoCA; Nasreddine et al, 2005) score.

Procedure

We categorized patients with multiple self-reported races by their primary self-reported racial identity, similarly to Sentell et al (2015), with priority given in the order of NHPI, Asian, White, and Other. We did this to keep the population counts at 100%; if we had counted all of the patients who identified as more than one race for all of their races, the population counts would have exceeded 100%. Available comorbidities information was categorized into the following groups: hypertension, hyperlipidemia, type II diabetes, cardiovascular, traumatic brain injury, epilepsy, depression, other neurology, other psychiatry, renal, respiratory, hematology/malignancy/

endocrine/reproductive/gastrointestinal, autoimmune/immunology/musculocutaneous/skin/connective tissue, skeletal, cerebrovascular, Down syndrome, headache, sleep disorders, and Parkinson disease.

Because all of the participants had either an MMSE score or a MoCA score, we used the conversion table by Lawton et al (2016) to convert the MoCA scores to MMSE scores so that a fair comparison could be made between the two cognitive exams. Only MMSE/MoCA scores that had been completed within 1 year of diagnosis (before or after diagnosis) were included. MMSE/MoCA examinations provide a quantitative measure of cognition, and previous meta-analytic studies have found that the conversion of MMSE scores to MoCA scores demonstrates reliable agreement (Lawton et al, 2016).

Statistical Analysis

We used the χ^2 test or Fisher exact test to compare racial groups for the categorical variables and the Kruskal-Wallis test to compare racial groups for the continuous variables. Multivariable Tobit regression was fitted for the MMSE/MoCA, adjusting for age, gender, race, marital status, and insurance.

RESULTS

Participants

We reviewed a total of 780 patient records with a diagnosis of AD or MCI at Hawaii Pacific Neuroscience between September 2000 to September 2019 and identified 598 patients with a new diagnosis of AD or MCI. Patient demographics included 224 Asians, 202 Whites, 87 NHPI, and 85 Other (includes 11 Hispanic, 2 American Indian or Alaskan Native, 2 Black, 67 Undisclosed, and 3 who indicated Other). AD was more dominant than MCI across all of the racial groups (Table 1), with the highest percentage among NHPI (70%, $P = 0.019$). In addition, women had a higher proportion than men of AD diagnosis over MCI across all racial groups, with the highest female prevalence among NHPI (67%, $P = 0.028$).

Among the mean ages at diagnosis, the NHPI were diagnosed at the earliest ages (73.2 ± 12.5 years, $P = 0.024$). Early onset AD/MCI (diagnosis <65 years) was more prevalent among the NHPI (21%, $P = 0.02$) compared with the other racial groups. Hypertension, hyperlipidemia, and type II diabetes were found to be higher among the NHPI (hypertension 74%, $P = 0.012$; hyperlipidemia 70%, $P = 0.050$; type II diabetes 28%, $P = 0.002$), although hyperlipidemia showed a borderline trend toward statistical significance, with a P value of 0.050. No statistically significant differences were found among the racial groups with respect to marital status, insurance, or number of comorbidities.

Three-hundred and fifteen patients had completed either the MMSE or the MoCA. Of these, 176 had completed the MMSE, and 139 had completed the MoCA. All of the MoCA scores were converted to MMSE scores for the purpose of making a fair comparison across the cognitive exams. Based on the Kruskal-Wallis test, there were significant variations ($P < 0.001$) in the test scores by racial group: The mean score was highest among Whites (24.11) and lowest among NHPI (20.08), Asians had a mean test score of 22.79, and Other racial groups had a mean test score of 22.88 (Figure 1 and Table 2).

After adjusting for age, gender, race, marital status, and insurance, the MMSE/MoCA test scores were still significantly associated with race (the predicted test score for Whites was 1.60 points higher [95% CI: 0.22, 2.98] than that predicted for Asians, and the predicted test score for NHPI was 2.59 points lower [95% CI: –4.26, –0.93] than that predicted for Asians) and age (for each year increase in age, the predicted test score decreased by 0.10 point [95% CI: –0.17, –0.03]) (Table 3).

DISCUSSION

We proved our hypothesis that NHPI would present with AD and MCI at younger ages and with different comorbidities that could put them at higher risk of dementia compared with Whites or Asians. This finding is supported by a previous inpatient study that showed that NH had higher dementia rates at earlier ages than other racial groups (Sentell et al, 2015). Specifically, in that study, 13.3% of the NH with dementia were <70 years old, compared with 8.4% Whites, 6.6% Filipinos, 3.0% Chinese, and 3.0% Japanese.

Racial disparities in AD and MCI may be a result of biological and modifiable factors. For example, a known genetic contributor to AD is the presence of the *APOE4* allele (Liu et al, 2013). Previous studies examining Oceania populations, which include NHPI, found higher frequencies of both *APOE2* (protective against AD) and *APOE4* (increased risk of AD) (Singh et al, 2006). Drug metabolism of AD medications and preventative drugs for AD, such as medications that can reduce cardiovascular risk factors, can also vary between racial groups (Cacabelos, 2008; Takahashi et al, 2003). For example, *CYP2C9* is an isoform of cytochrome *P450* that is important in the metabolism of medications with narrow therapeutic windows like warfarin and glipizide; polymorphisms in *CYP2C9* alleles have been found to differ between White and Asian populations (Goldstein, 2001).

Our research also supports the current knowledge that NHPI are often disproportionately affected by chronic diseases, including diabetes, obesity, and cardiovascular disease, which can often lead to a higher risk of AD and MCI (Luchsinger and Mayeux, 2004; Mau et al, 2009). This finding is likely attributed in part to modifiable behaviors such as physical inactivity, unhealthy dietary patterns, smoking, alcohol consumption, and barriers to accessing medical care, among other factors that are related to the lifestyle limitations that are imposed by challenging socioeconomic conditions.

A meta-analysis by Cooper et al (2010) suggested that minorities seek care later in the disease process compared with nonminorities, which may lead to more impairment at presentation. However, in our study, not only were the NHPI more likely to develop AD and MCI at younger ages, but they also had poorer cognitive scores upon presentation. This finding suggests that cognitive decline in NHPI may begin earlier than it does in other

TABLE 1. Patient Characteristics and Bivariate Analysis by Race

Characteristic	Overall	Asian	White	Native Hawaiians and Pacific Islanders	Other	*P*†
Sample size	598	224 (37.46%)	202 (33.78%)	87 (14.55%)	85 (14.21%)	
Diagnosis						0.019*
Alzheimer disease	363 (60.70%)	141 (62.95%)	106 (52.48%)	61 (70.11%)	55 (64.71%)	
MCI	235 (39.30%)	83 (37.05%)	96 (47.52%)	26 (29.89%)	30 (35.29%)	
Age at diagnosis						
Continuous	75.69 (11.82)	77.15 (11.21)	75.18 (12.14)	73.18 (12.51)	75.60 (11.58)	0.024*
Categorical						0.023*
< 65	78 (13.04%)	20 (8.93%)	25 (12.38%)	18 (20.69%)	15 (17.65%)	
≥65– < 80	273 (45.65%)	99 (44.20%)	101 (50.00%)	41 (47.13%)	32 (37.65%)	
≥80	247 (41.30%)	105 (46.88%)	76 (37.62%)	28 (32.18%)	38 (44.71%)	
Gender						0.028*
Female	359 (60.03%)	145 (64.73%)	105 (51.98%)	58 (66.67%)	51 (60.00%)	
Male	239 (39.97%)	79 (35.27%)	97 (48.02%)	29 (33.33%)	34 (40.00%)	
Marital status						0.085
Single	60 (10.43%)	17 (7.66%)	19 (9.69%)	10 (12.20%)	14 (18.67%)	
Married	303 (52.70%)	120 (54.05%)	111 (56.63%)	35 (42.68%)	37 (49.33%)	
Widowed	150 (26.09%)	64 (28.83%)	41 (20.92%)	27 (32.93%)	18 (24.00%)	
Divorced/separated	62 (10.78%)	21 (9.46%)	25 (12.76%)	10 (12.20%)	6 (8.00%)	
Insurance						0.13
Private	301 (50.50%)	106 (47.32%)	115 (56.93%)	43 (50.00%)	37 (44.05%)	
Other (Public/none)	295 (49.50%)	118 (52.68%)	87 (43.07%)	43 (50.00%)	47 (55.95%)	
Comorbidities						
Number of comorbidities	4.14 (1.96)	4.16 (2.10)	4.02 (1.79)	4.50 (2.04)	4.00 (1.88)	0.43
Hypertension	367 (62.20%)	145 (65.32%)	110 (55.28%)	64 (74.42%)	48 (57.83%)	0.012*
Hyperlipidemia	348 (58.98%)	136 (61.26%)	109 (54.77%)	60 (69.77%)	43 (51.81%)	0.050*
Type II diabetes	110 (18.64%)	49 (22.07%)	21 (10.55%)	24 (27.91%)	16 (19.28%)	0.0017**
Epilepsy	24 (4.07%)	7 (3.15%)	6 (3.02%)	2 (2.33%)	9 (10.84%)	0.026*
Skeletal	177 (30%)	78 (35.14%)	62 (31.16%)	17 (19.77%)	20 (24.1%)	0.036*
Cerebrovascular	222 (37.63%)	97 (43.69%)	61 (30.65%)	34 (39.53%)	30 (36.14%)	0.050*

Values are provided as either M ± SD or n (%). Percentages are column percentages (except for the *Sample Size* row) and exclude missing data. Not all numbers total to 598 because some patient data were unavailable.

*Significant at $P < 0.05$.

**Significant at $P < 0.01$.

†*P* values are based on the χ^2 test or Fisher exact test for the categorical variables and on the Kruskal–Wallis test for the continuous variables (continuous age and number of comorbidities).

racial groups, and progression is more severe and rapid. It is possible that lower educational attainment among the NHPI could account for the earlier manifestation of dementia symptoms, explaining the difference in MMSE/MoCA scores upon presentation. Although NH comprise ~¼ of Hawaii's population, they make up a significantly smaller proportion of university graduates (Makuakane-Drechsel and Hagedorn, 2000; University of Hawaii at Mānoa, Office of Student Equity, Excellence & Diversity, 2016). Higher educational attainment may exhibit a protective effect that delays the progression of dementia by increasing one's cognitive reserves (Rawlings et al, 2019). However, we did not collect educational attainment data, thus limiting our ability to assess the relationship between education level at the age of onset and MMSE/MoCA scores on presentation.

In 2019, the total health care cost for individuals with AD and other dementias—not accounting for out-of-pocket costs such as unpaid care—was estimated to be $290 billion nationwide. Medicare and Medicaid are expected to fund 67% of the total health care for these individuals (Alzheimer's Association, 2019). The high prevalence of early onset AD and MCI in NHPI may translate to a high financial burden on Hawaii, where one out of four individuals in Hawaii identifies as NHPI (State of Hawaii, Department of Health, 2008), and NHPI represent one of the fastest growing racial groups in the United States, with the population having grown by 61% within the 2000–2019 period (Budiman and Ruiz, 2021).

Study Limitations

There are several limitations to this study. First, patients who listed multiple self-reported races were assigned one race via the Hawaii ethnicity coding guide by the researchers. Because NHPI were not specified further into *full* or *part,* it is unclear if there are disparities between the two groups. Furthermore, NH and PI are two distinct groups of people, and due to their differences in

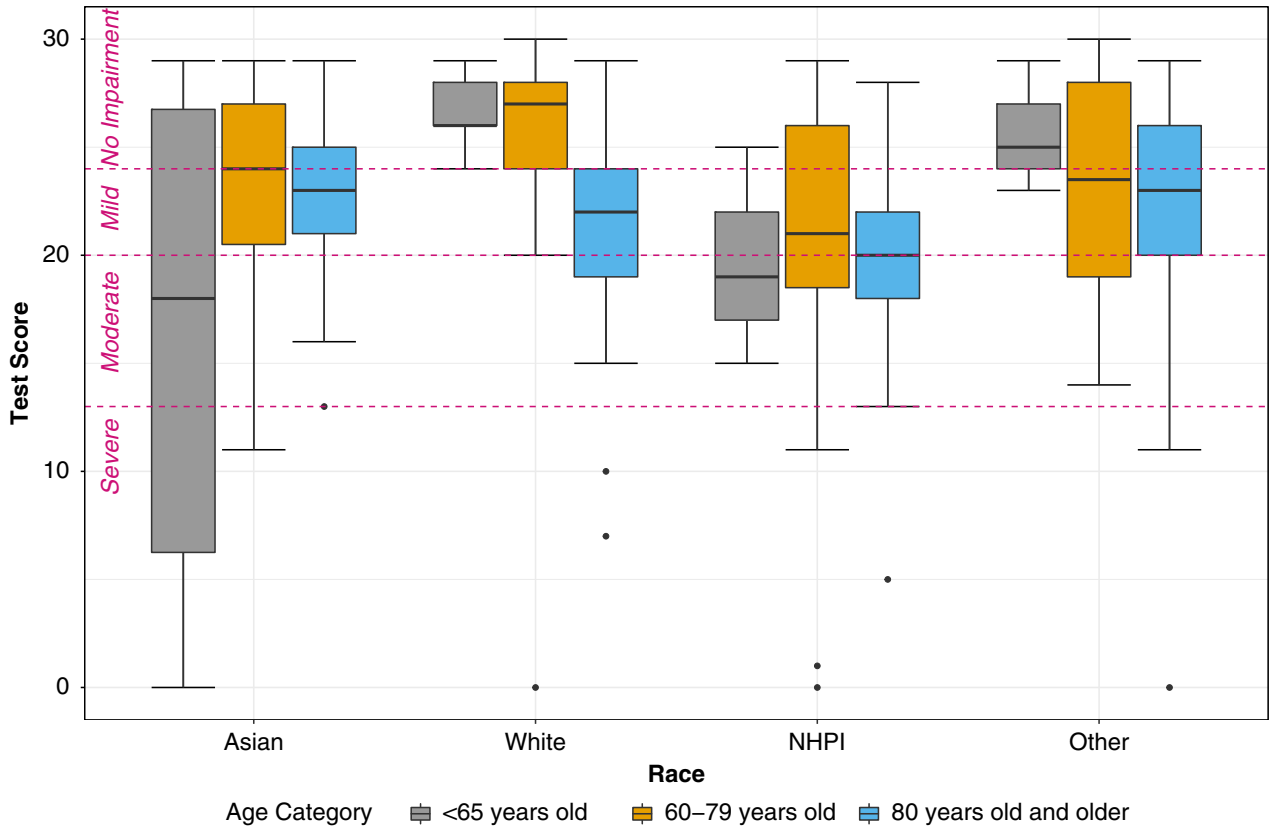

FIGURE 1. Mini-Mental State Examination scores and Montreal Cognitive Assessment scores converted to Mini-Mental State Examination scores by age and racial group. **NHPI** = Native Hawaiians and Pacific Islanders.

lifestyle and assimilation to Western culture, they could have differences in AD/MCI presentation that the current study did not assess. Second, because this study was a single-center study, the sample may not be generalizable to the population. Third, *APOE* data were not available, which limits one's understanding of potential reasons why differences may exist between racial groups. Fourth, because this study did not examine the exact neuropsychological measures that are indicative of the decline in cognitive function associated with AD and MCI, it lacks resolution in determining the precise cognitive disparities among racial groups. Last, we did not include comorbidities as covariates on the regression model because information on comorbidities was not recorded consistently. As a result, our study summarized only the general effects of the demographic and sociological characteristics on the MMSE/MoCA scores.

TABLE 2. Test Score by Racial Group

Group	n (%)	Test Score
Asian	130 (41.27%)	22.79 (4.63)*
White	92 (29.21%)	24.11 (4.95)*
Native Hawaiians and Pacific Islanders	51 (16.19%)	20.08 (6.31)*
Other	42 (13.33%)	22.88 (6.02)*

Values are provided as either M ± SD or n (%). Percentages are column percentages and exclude missing data. Not all numbers total to 598 because some patient data were unavailable.
*Significant at $P < 0.0001$ for test score among racial groups, based on the Kruskal–Wallis test.

TABLE 3. Multivariable Tobit Regression Results

Predictor	Estimate	95% CI	*P*
Race (reference: Asian)			
White	1.60	0.22, 2.98	0.024*
NHPI	–2.59	–4.26, –0.93	0.0023**
Other	–0.13	–2.01, 1.75	0.90
Male (reference: female)	0.34	–0.92, 1.60	0.60
Age	–0.10	–0.17, –0.03	0.0078**
Public or no insurance (reference: private)	0.75	–0.40, 1.90	0.21
Marital status (reference: single)			
Married	1.54	–0.53, 3.61	0.15
Widowed	1.82	–0.51, 4.15	0.13
Divorced or separated	1.99	–0.62, 4.61	0.14

*Significant at $P < 0.05$.
**Significant at $P < 0.01$.
NHPI = Native Hawaiians and Pacific Islanders.

CONCLUSION

Future research could include data on the long-term health outcomes of NHPI compared with other racial groups. Previous studies have found that although Whites have a higher mortality rate from AD than African Americans and Hispanics, they have a lower prevalence and incidence rate (Gillum and Obisesan, 2011; Mehta et al, 2008).

Another variable of interest is subjective health measures. Other minority racial groups, Native Americans specifically, have been shown to demonstrate the phenomenon of *tolerated illness*, which is a discordance in subjective and objective health measures among chronically ill patients (Moss, 2005). These groups often exhibit tight family structures and reverence for elders. Thus, although NHPI may have multiple risk factors for AD and MCI in addition to lower MMSE/MoCA scores upon presentation, they may subjectively feel as if they are in better health than other racial groups. Additionally, collecting symptoms at presentation could possibly reveal atypical presentations of AD and MCI among NHPI. A previous study found that, compared with Whites with dementia, African Americans with dementia were at an increased risk of being more talkative, experiencing more hallucinations, expressing unreasonable anger, and wandering (Sink et al, 2004).

This study offers insight into the presentation of AD and MCI among NHPI and builds on the limited data that currently exist regarding NHPI. This research should encourage further investigation into the contributing factors behind earlier onset of AD and MCI in NHPI and possibly influence clinical care and policy with regard to screening for the disease.

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