

Prevalence and Risk Factors of Self-reported Vision Impairment among Native Hawaiians and Pacific Islanders in the United States

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Abstract

Racial disparities in vision impairment have been reported among Black, Hispanic, and White Americans. However, there is a paucity of research on vision impairment among Native Hawaiians and Pacific Islanders (NHPIs). The objective of this study was to determine the prevalence of, and risk factors for, self-reported visual impairment in NHPI adults in the United States (US). Data from the NHPI and 2014 National Health Interview Surveys were analyzed using sample weights and variance estimates. Prevalence was calculated for vision impairment and blindness for the NHPI and overall US populations. Sociodemographic and clinical risk factors of vision impairment were explored using descriptive statistics, χ^2 tests, and simple and multiple logistic regression. In total, 2 586 NHPIs and 36 673 individuals in the US were included. The prevalence of vision impairment was 8.8% among NHPIs and 9.1% for the overall US population, and the prevalence of blindness was 0.72% for NHPIs and 0.35% for the overall population. Independent risk factors associated with vision impairment were having a Charlson Comorbidity Index over 1 [OR: 2.89, 95% CI: (1.42–5.88)] and having a family income below \$35 000 [OR: 2.03, 95% CI: (1.06–3.89)]. In summary, the rate of blindness is higher among NHPIs than the overall US population, especially for older and unemployed individuals with more comorbidities. Higher comorbidity burden, lower family income, and recent eye care were risk factors for vision impairment. More research is necessary to develop targeted and culturally sensitive interventions to promote NHPI eye health.

Keywords

Vision loss, epidemiology, Native Hawaiians and Pacific Islanders, National Health Interview Survey

Abbreviations

CDC = Centers for Disease Control and Prevention

CCI = Charlson Comorbidity Index

NHPIs = Native Hawaiians and Pacific Islanders

Introduction

Racial disparities in vision impairment have been identified among Black, Hispanic, and White Americans based on large, publicly accessible databases.¹⁻² Differences in income, education, and insurance have been proposed as explanatory factors.¹⁻² Comorbidities associated with vision impairment include diabetes, hypertension, arthritis, hyperthyroidism, neurodegenerative disorders, hematologic cancers, and other systemic infections.³ However, there is limited information on vision impairment among Native Hawaiians and Pacific Islanders (NHPIs). Based on a digitized search of the PubMed literature databases from inception to January 7, 2023, the only published study result on vision impairment among NHPIs in the United States (US)

was a survey of 124 adults on Ta'u Island, American Samoa, which found a prevalence of 10.5%.⁴

Although NHPIs represent 0.4 percent (1.4 million) of the US population, they have historically been aggregated with Native Americans or Asian Americans,⁵ leading to their underrepresentation in health research.⁶ A recent study using the NHPI National Health Interview Survey (NHIS) showed that NHPIs have a lower rate of eye care utilization than the overall US population, raising concerns about potential disparities in vision impairment.⁷ Predictors of eye care utilization among NHPIs were higher family income, older age, and vision impairment.⁷

To address the paucity of public health data for NHPIs, the US Centers for Disease Control and Prevention (CDC) National Center for Health Statistics conducted the overall NHIS and the NHPI NHIS in 2014 using trained interviewers.⁸ Using the NHIS data, this study compared the prevalence of self-reported vision impairment among NHPI and overall US populations and investigated socioeconomic and health risk factors for vision impairment in NHPI adults.

Methods

The Rhode Island Hospital Institutional Review Board reviewed this study and determined that this research did not involve human subjects.

The CDC defines an NHPI individual as having origins in any of the original inhabitants of Hawai'i, Guam, Samoa, or other Pacific Islands.⁸ Participants were classified as visually impaired if they answered yes to the question: "Do you have any trouble seeing, even when wearing glasses or contact lenses?". Nonrespondents were excluded from the analysis. Blindness was based on the response to the question, "Are you blind or unable to see at all?".

The NHIS is a large-scale household interview survey collecting demographic and health information that has been conducted each year since 1957.^{8,9} The NHIS involves a statistically representative sample, randomly selected via simple random sampling from households in all 50 states and the District of Columbia but did not include other US territories or residents of institutional group quarters such as university dormitories.^{8,9} The 2014 NHPI NHIS was the first and only NHIS focused exclusively on the NHPI population.^{8,9}

In this study, the authors calculated Charlson Comorbidity Index (CCI) as a measure of health status, ranging from a minimum score of 0 to 17 (indicating a more severe level of comorbidities) based on the presence of myocardial infarction, cerebrovascular disease, chronic pulmonary disease, ulcer disease, cancer, diabetes, renal disease, liver disease, connective tissue disease, and dementia, using methodologies from previous studies of NHIS data.^{10,11} The CCI is a commonly used tool for summarizing comorbid disease statuses in public health research, substituting for individual comorbidity measures.^{12,13}

Sample adult record weights, strata, and cluster information provided in CDC data were used to produce estimates representative of the NHPI and overall US populations. Weighted percentages were used and, therefore, may not precisely reflect the survey sample. Descriptive statistics were used to characterize both populations. Prevalence was calculated for vision impairment and blindness of the NHPI and overall US populations.^{8,9} Characteristics of NHPIs with and without vision impairment were compared using descriptive statistics and Rao-Scott χ^2 tests. Simple logistic regression was used to identify factors associated with vision impairment in NHPIs, including age, sex, race, ethnicity, employment, marital status, family income, CCI, eye care utilization, functional limitations, health insurance, routine care, and delayed medical care. Following sensitivity analysis to identify collinear variables, odds ratios were calculated using multiple logistic regression based on significant factors in simple regression and adjusting for prior eye care utilization, which has been predictive of vision impairment in previous studies.⁷ All analyses were conducted with $\alpha=0.05$ in Stata SE 17 (StataCorp, College Station, TX); relationships with $P<.05$ were considered statistically significant.

Results

Nearly all respondents completed the question about vision impairment for the NHPI NHIS (99.9%; 2 586/2 590) and overall NHIS (99.9%; 36 673/36 697). Initial estimates indicated that 10.0% (259/2 586) and 10.0% (3 707/36 673) of the NHPI and overall samples, respectively, had vision impairment. After weighting, 8.8% and 9.1% of the NHPI and overall US population, respectively, had vision impairment (**Table 1**). The mean ages of the NHPI and overall US study populations were 40.4 (SD: 15.7) and 47.0 (SD: 18.0) years, respectively. Both populations were mostly female, married, and members of families earning less than \$75 000.

Approximately 8.2% of NHPIs with vision loss reported blindness compared with 3.9% in the overall US population (data not shown). NHPIs with vision impairment were significantly more likely than those without impairment to be older or unemployed, to have a higher CCI and a functional limitation, and to have visited an eye doctor in the past year and delayed medical care due to cost or other reasons (**Table 2**).

In simple logistic regression, age, employment status, family income, CCI, recent eye care, functional limitations, and delayed medical care were identified as correlates of vision impairment in NHPIs (**Table 3**). After sensitivity analysis, multiple regression analysis identified 2 independent risk factors for vision impairment in NHPIs: a CCI over 1 (Odds Ratio [OR]: 2.89, 95% Confidence Interval [CI]: 1.42–5.88) and family income below \$35 000 (OR: 2.03, 95% CI: 1.06–3.89).

Discussion

This study investigated the epidemiology of self-reported vision impairment and blindness among NHPI adults using the first national survey designed to assess the health of NHPIs in the US. Significant disparities in blindness were identified between the NHPI and overall US populations.

The prevalence of vision impairment was similar for the NHPI and overall US population. However, the prevalence of blindness in NHPIs was nearly twice that of the overall US population. This finding may be related in part to the lower rates of eye care utilization in the NHPI population.⁷ In the present study, however, lack of recent eye care utilization did not fully explain the association of low family income with vision impairment; lower family income may be linked to longer-term lack of eye care among NHPIs, possibly due to high costs or other barriers to access.⁷

This study's findings align with previous research on self-reported and measured vision impairment. The World Health Organization Study on Global Aging and Adult Health similarly identified comorbidities (a variable constructed by study authors indicating self-reported arthritis, stroke, angina, diabetes, chronic lung disease, asthma, depression, and hypertension) and low household wealth as risk factors for self-reported vision impairment in nationally representative samples of 6 developing countries (China, Ghana, India, Mexico, Russia, and South Africa).¹⁴ Additionally, receiving eye care was associated with impaired vision in previous studies.¹⁵⁻¹⁷ Based on surveys of older Americans, the most common reason for not visiting an eye doctor was that there was no reason to go (i.e., they did not have vision loss).¹⁸ This may explain why people who reported vision loss were more likely to see an eye doctor in the past year in this study.

Epidemiological studies of vision impairment of Pacific Islanders outside the US have found different rates of vision impairment and blindness. The Global Burden of Disease, Injuries, and Risk Factors Vision Loss Project estimated that the age-standardized prevalence of measured moderate-to-severe vision impairment in Southeast Asia and Oceania was approximately 4.93% in 2020.¹⁹ However, the age standardization was based on demographics of the global population, which is younger than the US population.^{20,21} Prevalence of blindness varied from 0.47%

Table 1. Prevalence of Vision Impairment Among NHPI Adults in the US Compared with Overall US Adult Population		
Population	NHPI ^a , weighted % ^c (N=2586)	Overall ^b , weighted % ^c (N=36 673)
Total vision impairment	8.8	9.1
Blindness	0.7	0.4
Age (years)		
≤30	7.1	5.4
31-50	6.3	7.6
51-64	12.6	11.2
≥65	18	13.5
Sex		
Male	8.7	7.8
Female	8.8	10.2
Race		
NHPI only	7.6	N/A
Multiracial	10.2	9.8
AIAN only	N/A	17.1
Asian only	N/A	5.3
Black only	N/A	11.1
White only	N/A	8.9
Ethnicity		
Not Hispanic	8.9	9.2
Hispanic	7.7	8.1
Employment Status		
Unemployed	11.8	12.9
Employed	7.3	6.7
Marital Status		
Married	7.7	8.4
Unmarried	9.9	9.8

Family Income		
≤\$34,999	12.9	12.6
\$35,000-\$74,999	8.4	8.9
\$75,000-\$99,999	6.8	7
≥\$100,000	7.2	6.4
Charlson Comorbidity Index		
0	4.9	4.3
1	7.9	8.7
≥2	15.7	14.2
Eye Doctor Visit in Past 12 Months		
Yes	14.7	11.9
No	7.6	7.4
Functional Limitations		
Yes	17	17.9
No	5.5	4.6
Health Insurance in Past 3 Years		
Yes	8.1	8.9
No	16.3	14.5
Usual Place of Routine Care		
No routine care	5.9	8.7
Clinic or hospital	9	9.4
Delayed Medical Care for Reasons Other than Cost		
No	7.4	8
Yes	19.7	19.6
Delayed Medical Care Due to Cost		
No	6.6	7
Yes	18.7	19.5

AIAN, American Indian and Alaska Native; NHPI, Native Hawaiian and Pacific Islander.

^a Data was obtained from the NHPI National Health Interview Survey.⁸

^b Data was obtained from the overall National Health Interview Survey.⁸

^c Proportions were calculated using sample weights and therefore do not precisely reflect sample sizes.

Table 2. Baseline Characteristics of NHPI Adults in the US with and without Vision Impairment ^a			
NHPI Population	Vision impairment, weighted %	No vision impairment, weighted %	<i>P</i> -value ^b
Age (years)			
≤30	26.5	33.2	.004
31-50	28.8	41.1	
51-64	26.4	17.7	
≥65	18.3	8	
Sex			
Male	48.2	49.4	.95
Female	51.8	50.6	
Race			
NHPI only	47.3	55.3	.197
Multiracial	52.7	44.7	
Ethnicity			
Not Hispanic	93.3	92.3	.61
Hispanic	6.7	7.7	
Employment Status			
Unemployed	43.6	31.4	.014
Employed	56.4	68.6	
Marital Status			
Married	44.1	51	.22
Unmarried	55.9	49	
Family Income			
≤\$34,999	35.9	23.9	.091
\$35,000-\$74,999	31.3	33.7	
\$75,000-\$99,999	10	13.5	
≥\$100,000	22.8	28.9	

Charlson Comorbidity Index			
0	27.1	50.5	<.001
1	19.5	22	
≥2	53.5	27.6	
Eye Doctor Visit in Past 12 Months			
Yes	44.4	29.2	.006
No	55.6	70.8	
Functional Limitations			
Yes	55.7	26.2	<.001
No	44.3	73.8	
Health Insurance in Past 3 Years			
Yes	37.9	57.3	.198
No	62.1	42.7	
Usual Place of Routine Care			
No routine care	48.2	59.4	.29
Clinic or hospital	51.8	40.6	
Delayed Medical Care for Reasons Other than Cost			
Yes	25.2	9.9	<.001
No	74.8	90.1	
Delayed Medical Care Due to Cost			
Yes	38.4	16.1	<.001
No	61.6	83.9	

NHPI, Native Hawaiian and Pacific Islander; US, United States.

^a Data was obtained from the NHPI National Health Interview Survey.⁸

^b *P*-values were calculated using Rao-Scott χ^2 tests. All statistically significant relationships (defined as $P \leq .05$) are bolded. Proportions were calculated using sample weights and therefore do not precisely reflect sample sizes. *P*-values compared respondents with and without vision impairment.

Table 3. Characteristics Associated with Vision Impairment in NHPIs in the US in Simple and Multiple Logistic Regression				
Characteristics	Simple odds ratio (95% CI)	<i>P</i> -value	Multiple adjusted odds ratio ^a (95% CI)	<i>P</i> -value
Age (years)				
18-30	1 [reference]		Omitted ^b	
31-50	0.88 (0.44–1.75)	.7		
51-64	1.87 (0.83–4.22)	.126		
≥65	2.86 (1.56–5.26)	.001		
Sex				
Male	1 [reference]			
Female	1.02 (0.61–1.70)	.95		
Race				
NHPI only	1 [reference]			
Multiracial	1.38 (0.84–2.28)	.198		

Table 3. Characteristics Associated with Vision Impairment in NHPs in the US in Simple and Multiple Logistic Regression (Con't)				
Characteristics	Simple odds ratio (95% CI)	P-value	Multiple adjusted odds ratio ^a (95% CI)	P-value
Ethnicity				
Not Hispanic	1 [reference]			
Hispanic	0.86 (0.48–1.56)	.61		
Employment Status				
Unemployed	1 [reference]		1 [reference]	
Employed	0.59 (0.39–0.89)	.014	0.77 (0.47–1.27)	.29
Marital Status				
Married	1 [reference]			
Unmarried	1.32 (0.83–2.09)	.23		
Family Income				
<\$34,999	1.91 (1.09–3.38)	.026	2.03 (1.06–3.89)	.035
\$35,000–\$74,999	1.17 (0.62–2.24)	.61	1.26 (0.62–2.57)	.5
\$75,000–\$99,999	0.93 (0.32–2.72)	.89	0.94 (0.32–2.77)	.9
≥\$100,000	1 [reference]		1 [reference]	
Charlson Comorbidity Index				
0	1 [reference]		1 [reference]	
1	1.65 (0.84–3.26)	.141	1.58 (0.72–3.49)	.25
≥2	3.62 (2.01–6.53)	<.001	2.89 (1.42–5.87)	.005
Eye Doctor Visit in Past 12 Months				
Yes	1 [reference]		1.81 (1.03–3.18)	.04
No	0.52 (0.33–0.82)	.007	1 [reference]	
Functional Limitations				
Yes	1 [reference]		Omitted ^b	
No	0.28 (0.18–0.43)	<.001		
Health Insurance in Past 3 Years				
Yes	1 [reference]			
No	0.46 (0.13–1.58)	.21		
Usual Place of Routine Care				
No routine care	1 [reference]			
Clinic or hospital	1.57 (0.66–3.73)	.29		
Delayed Medical Care for Reasons Other than Cost				
No	1 [reference]		Omitted ^b	
Yes	0.33 (0.21–0.51)	<.001		
Delayed Medical Care Due to Cost				
No	1 [reference]		Omitted ^b	
Yes	0.31 (0.20–0.47)	<.001		

NH, Native Hawaiian; PI, Pacific Islander. All statistically significant relationships (defined as $P \leq 0.05$) are bolded.

^a Adjusted for employment status, family income, comorbidities, and eye care utilization.

^b Omitted due to collinearity in sensitivity analysis. Age and functional limitations were collinear with Charlson Comorbidity Index; delaying care due to cost or other reasons were collinear with family income.

to 0.63% in the Pacific region, which was higher than that in the overall US population but lower than that in the US NHPI population.¹⁹

This study has several limitations. First, all data were self-reported and, therefore, subject to recall and response bias. However, all NHIS interviewers were extensively trained, and the survey had been prepared and tested for both populations, which limited misunderstanding of terminology.¹³ Second, the CCI was calculated based on self-reported NHIS data rather than hospital administrative data, although this methodology was previously validated.^{9,10} The CCI has been frequently used in clinical prognosis and comorbidity adjustment in analyses due to its mathematical and clinical validity.²² Although the CCI includes diabetes, its coverage of 19 pre-defined comorbid conditions may neglect a specific focus on diabetes, which is more common among NHPIs.²³ Third, the NHPI NHIS contains data that is nearly 10 years old, although this remains the only national source of NHPI-specific health data. Finally, the NHIS was subject to the inherent limitations of cross-sectional study design, but population surveys are essential for public health surveillance.

In sum, major disparities exist in self-reported blindness between the NHPI and overall US populations, possibly due to a lower rate of seeing an eye doctor and receiving treatment among NHPIs.⁷ Consequently, improving eye care utilization among NHPIs, particularly among lower-income NHPIs, may help mitigate the impact of these disparities. Culturally sensitive interventions for health education for NHPIs may be delivered in-person, by mail, or by video; cultural traditions such as storytelling and group discussions should be integrated, and lay community members should be recruited.²⁴ Future studies are needed to develop targeted interventions to optimize NHPI eye health.

Conflict of Interest

None of the authors identify a conflict of interest.

Disclaimer

The views expressed here are those of the authors and do not necessarily reflect the position or policy of the US Department of Veterans Affairs or the US government.

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References

1. Zhang X, Cotch MF, Ryskulova A, et al. Vision health disparities in the United States by race/ethnicity, education, and economic status: findings from two nationally representative surveys. *Am J Ophthalmol*. 2012;154:S53-62.e51.
2. Chou C-F, Barker LE, Crews JE, et al. Disparities in eye care utilization among the United States adults with visual impairment: findings from the behavioral risk factor surveillance system 2006-2009. *Am J Ophthalmol*. 2012;154:S45-52.e41.
3. Pinazo-Durán MD, Arévalo JF, García-Medina JJ, Zanón-Moreno V, Gallego-Pinazo R, Nucci C. Ocular Comorbidities and the relationship between eye diseases and systemic disorders. *Biomed Res Int*. 2016;2016:9519350. doi: 10.1155/2016/9519350. Epub 2016 Mar 29. PMID: 27119086; PMCID: PMC4828520.
4. Barnes SS, Utu P-JM, Sumida L, O'Carroll DC, Jenkins TL, Corboy J. Survey on visual impairment and refractive errors on Ta'u Island, American Samoa. *J Ophthalmic Vis Res*. 2011;6(1):32-35.
5. Woodward MA, Hughes K, Ballouz D, Hirth RA, Erickson J, Newman-Casey PA. Assessing eye health and eye care needs among North American Native Individuals. *JAMA Ophthalmol*. 2022 Feb 1;140(2):134-142. doi: 10.1001/jamaophthalmol.2021.5507. PMID: 34940785; PMCID: PMC8855236.
6. Doãn LN, Takata Y, Sakuma K-LK, Irvin VL. Trends in clinical research including Asian American, Native Hawaiian, and Pacific Islander participants funded by the US National Institutes of Health, 1992 to 2018. *JAMA Netw Open*. 2019;2(7):e197432.
7. Lin JC, Ghauri SY, Scott IU, Greenberg PB. Eye health care utilization among Native Hawaiian and Pacific Islander adults in the United States. *Ophthalmic Epidemiol*. 2022;1-5.
8. National Center for Health Statistics. 2014 Native Hawaiian and Pacific Islander National Health Interview Survey (NHPI NHIS) public use data release: Survey description. Centers for Disease Control and Prevention. Published 2017. Accessed December 5, 2021. <https://www.cdc.gov/nchs/nhis/nhpi.html>
9. National Center for Health Statistics. 2014 National Health Interview Survey (NHIS) National Health Interview Survey (NHPI NHIS) public use data release: Survey description. Centers for Disease Control and Prevention. Published 2015. Accessed January 14, 2023. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2014/srnydesc.pdf
10. Amante DJ, Hogan TP, Pagoto SL, English TM, Lapane KL. Access to Care and use of the internet to search for health information: Results from the US National Health Interview Survey. *J Med Internet Res*. 2015;17(4):e106.
11. Meissner HI, Tiro JA, Haggstrom D, Lu-Yao G, Breen N. Does patient health and hysterectomy status influence cervical cancer screening in older women? *J Gen Intern Med*. 2008;23(11):1822-1828.
12. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson Comorbidity Index predicted in-hospital mortality. *J Clin Epidemiol*. 2004;57(12):1288-1294.
13. D'Hoore W, Bouckaert A, Tilquin C. Practical considerations on the use of the Charlson comorbidity index with administrative data bases. *J Clin Epidemiol*. 1996 Dec;49(12):1429-33.
14. Ehrlich JR, Stagg BC, Andrews C, Kumagai A, Musch DC. Vision impairment and receipt of eye care among older adults in low- and middle-income countries. *JAMA Ophthalmol*. 2019;137(2):146-158.
15. Varma R, Torres M, McKean-Cowdin R, et al. Prevalence and risk factors for refractive error in adult Chinese Americans: The Chinese American Eye Study. *Am J Ophthalmol*. 2017;175(201-12).
16. McCarty CA, Taylor HR. Myopia and vision 2020. *Am J Ophthalmol*. 2000;129(4):525-527.
17. Tarczy-Hornoch K, Ying-Lai M, Varma R, Los Angeles Latino Eye Study Group. Myopic refractive error in adult Latinos: the Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci*. 2006;47(5):1845-1852.
18. McGwin G, Khoury R, Cross J, Owsley C. Vision impairment and eye care utilization among Americans 50 and older. *Curr Eye Res*. 2010;35(6):451-458.
19. GBD 2019 Blindness and Vision Impairment Collaborators; Vision Loss Expert Group of the Global Burden of Disease Study. Trends in prevalence of blindness and distance and near vision impairment over 30 years: an analysis for the Global Burden of Disease Study. *Lancet Glob Health*. 2021;9(2):e130-e143.
20. Ortman JM, Velkoff VA, Hogan H. An Aging Nation: The Older Population in the United States. U.S. Census Bureau. Published 2014. Accessed May 22, 2021. <https://www.census.gov/prod/2014pubs/p25-1140.pdf>.
21. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJ, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. World Health Organization. Published 2001. Accessed May 22, 2021. <https://www.who.int/healthinfo/paper31.pdf>
22. Austin SR, Wong YN, Uzzo RG, Beck JR, Eggleston BL. Why summary comorbidity measures such as the Charlson Comorbidity Index and Elixhauser Score work. *Med Care*. 2015 Sep;53(9):e65-72. doi: 10.1097/MLR.0b013e318297429c.
23. King GL, McNeely MJ, Thorpe LE, Mau ML, Ko J, Liu LL, Sun A, Hsu WC, Chow EA. Understanding and addressing unique needs of diabetes in Asian Americans, Native Hawaiians, and Pacific Islanders. *Diabetes Care*. 2012 May;35(5):1181-8. doi: 10.2337/dc12-0210.
24. Kaholokula JK, Ing CT, Look MA, Delafield R, Sinclair K. Culturally responsive approaches to health promotion for Native Hawaiians and Pacific Islanders. *Ann Hum Biol*. 2018 May;45(3):249-263. doi: 10.1080/03014460.2018.1465593.