ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuro-oncology

Editor
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI® Open Access

Original Article

Differences in tumor size, clinical, demographic, and socioeconomic profiles of central nervous system tumors among a racially diverse cohort: A retrospective case–control study

Kyung Moo Kim[1,2], Rachel Jane Lew[1], Tate Justin Higashihara[1], Shaina Yamashita[1], Michelle Pang, Michelle Stafford[1], Connor Goo[1], Kimberly Bergenholtz Teehera[1], Kayti Luu[1], Richard Ho[1], Enrique Carrazana[1], Jason Viereck[1,3], Kore Kai Liow[1,3], Arash Ghaffari-Rafi[1,4]

[1]Department of Medicine, University of Hawai'i at Mānoa, John A. Burns School of Medicine, [2]East-West Center, [3]Hawai'i Pacific Neuroscience, Brain Research, Innovation and Translation Lab, Honolulu, Hawaii, [4]Department of Neurological Surgery, University of California, Davis School of Medicine, Sacramento, California, USA.

E-mail: Kyung Moo Kim - kkim29@hawaii.edu; Rachel Jane Lew - rjlew@hawaii.edu; Tate Justin Higashihara - tatejh@hawaii.edu; Shaina Yamashita - sbyama@hawaii.edu; Michelle Pang - mylp@hawaii.edu; Michelle Stafford - mvs808@hawaii.edu; Connor Goo - cgoo24@hawaii.edu; Kimberly Bergenholtz Teehera - kteehera@hawaii.edu; Kayti Luu - kaytiluu@hawaii.edu; Richard Ho - rho4@hawaii.edu; Enrique Carrazana - ecarrazana@aol.com; Jason Viereck - jviereck@hawaiineuroscience.com; Kore Kai Liow - kliow@hawaiineuroscience.com; *Arash Ghaffari-Rafi - arashgr@hawaii.edu

***Corresponding author:**
Arash Ghaffari-Rafi,
Department of Neurological Surgery, School of Medicine, University of California, Davis 4860 Y Street Suite 3740 Sacramento, CA, 95817, USA.

aghaffarirafi@ucdavis.edu

Received: 15 March 2024
Accepted: 15 July 2024
Published: 13 December 2024

DOI
10.25259/SNI_190_2024

Quick Response Code:

Supplementary material:
https://doi.org/10.25259/SNI_190_2024

ABSTRACT

Background: One avenue to improve outcomes among brain tumor patients involves the mitigation of healthcare disparities. Investigating clinical differences among brain tumors across socioeconomic and demographic strata, such can aid in healthcare disparity identification and, by extension, outcome improvement.

Methods: Utilizing a racially diverse population from Hawaii, 323 cases of brain tumors (meningiomas, gliomas, schwannomas, pituitary adenomas, and metastases) were matched by age, sex, and race to 651 controls to investigate the associations between tumor type and various demographic, socioeconomic, and medical comorbidities. Tumor size at the time of diagnosis was also compared across demographic groups.

Results: At the time of diagnosis for benign meningiomas, Native Hawaiians and Pacific Islanders (NHPI; $P < 0.05$), Asians, and Hispanics exhibited nearly two-fold larger tumor volumes than Whites. For gliomas, NHPI similarly presented with larger tumor volumes relative to Whites ($P = 0.04$) and Asians ($P = 0.02$), while for vestibular schwannomas, NHPI had larger tumor sizes compared to Asians ($P < 0.05$). Benign meningiomas demonstrated greater odds of diagnosis ($P < 0.05$) among Native American or Alaskan Natives, patients comorbid with obesity class I, hypertension, or with a positive Alcohol Use Disorders Identification Test-Consumption (AUDIT-C). Malignant meningiomas demonstrated greater odds ($P < 0.05$) among patients from higher median household income and urban geography. Gliomas overall exhibited increased odds ($P < 0.05$) of diagnosis among Whites and reduced odds among Asians, with greater comorbidity with obesity class III; for glioblastoma specifically, there were reduced odds of asthma diagnosis. Patients with vestibular schwannomas were at increased odds ($P < 0.05$) of being from the highest income quartile and having a positive AUDIT-C, yet reduced odds of psychiatric disorders. Pituitary adenomas exhibited reduced odds of diagnosis among Whites, yet greater odds among NHPI, military personnel, obesity class I, and psychiatric disorders. Intracranial metastases were more common in patients with pre-obesity, asthma, a positive AUDIT-C, and living in more affluent regions. Benign meningiomas are most often presented with seizures, while malignant meningiomas have the addition of cognitive difficulty. Gliomas often present with seizures, cognitive difficulty, dizziness/nausea/vomiting (DNV), vestibular schwannomas with DNV, and metastases with seizures.

Conclusion: Brain tumors exhibit unique sociodemographic disparities and clinical comorbidities, which may have implications for diagnosis, treatment, and healthcare policy.

Keywords: Central nervous system, Disparities, Risk factors, Socioeconomic, Tumors

INTRODUCTION

Brain tumors impose a significant morbidity and mortality burden globally.[2,32] In the United States, the incidence of brain tumors is 23.79/100,000, with a median survival of 8 months to 20 years, depending on pathology.[38,67] Despite advances in treatment and therapies, survival rates and prognosis have not made commensurate improvements.[2] Besides conducting molecular and clinical studies, another avenue to improve outcomes involves the mitigation of healthcare disparities. Investigating epidemiologic differences between brain tumors provides a conduit to identify healthcare disparities and improve outcomes for disadvantaged populations. Establishing a comprehensive risk stratification profile among subsets of the population will not only help characterize modifiable risk factors of a disease but also identify population subsets who face barriers to treatment. To elucidate socioeconomic, demographic, and psychobiologic risk factors associated with brain tumors (i.e., gliomas, meningiomas, vestibular schwannomas, pituitary adenomas, and intracranial metastases), we conducted a retrospective case–control study within the diverse state of Hawai'i, where minorities are the plurality.

MATERIALS AND METHODS

Design and setting

The electronic medical records of a neuroscience clinic in Honolulu, Hawaii (i.e., Hawaii Pacific Neuroscience) were retrospectively searched from January 1, 2009, to January 1, 2021. The following International Classification of Diseases 9th or 10th editions and Clinical Modification codes (ICD-9-CM or ICD-10-CM) for patients with benign intracranial tumors were used for 2015-2021: ICD-9-CM (225.0, 225.1, 225.2, 225.3, 225.4, 225.8, and 225.9) for 2009–2014, and ICD-10-CM (D32.0, D32.1, D32.9, D33.0, D33.1, D33.2, D33.3, D33.4, D33.7, D33.9, V12.41, and Z86.011). For malignant and miscellaneous intracranial tumors, the respective codes were applied: ICD-9-CM (191.0, 191.1, 191.2, 191.3, 191.4, 191.5, 191.6, 191.7, 191.8, 191.9, 192.0, 192.1, 192.2, 192.8, and 192.9) for 2009-2014 and ICD-10-CM (D42.0, D42.1, D42.9, V10.85, and Z85.841) for 2015–2021. The Institutional Review Board approval was obtained before the study from the University of Hawaiʻi Office of Research Compliance (protocol number: 2020-01010).

Predictor and outcome variables

For cases, the data for the following variables were collected: age at diagnosis, sex, presenting symptom, history of head trauma, history of stroke, presence of gait disturbances, seizures, cognitive difficulties, dizziness, nausea or vomiting (DNV), sleep disturbances, and self-identified race (White, Black, Hispanic/Latino, Asian, Native Hawaiian or Pacific Islander [NHPI], and Native American or Alaskan Natives [NAAN]). Tumor type and dimensions were attained from pathology and imaging reports. Tumor volume and area were calculated using the established formula for a spheroid:

$$V = \frac{4}{3} r_1 r_2 r_3 \quad A = r^2$$ [42,62,80]

V = volume, r = radius (half the diameter) along the longest dimension of the tumor along the axial (r_1), coronal (r_2), and sagittal (r_3) planes.

A = area, r = radius (half the diameter) along the longest dimension of the tumor along either the axial, coronal, or sagittal plane.

The insurance and zone improvement plan code of the patient's residence was collected as a proxy measure for median household income, in addition to the percentage or residence in a municipality below the poverty level (for all ages, 18–64 years, and 65 years and over). Such data were acquired from the United States Census Bureau, 2015–2019 American Community Survey 5-Year Estimates (http://www.census.gov). Insurance was classified as Medicare, Medicaid, private insurance, or military insurance, consistent with the criteria of the Agency of Health-care Research and Quality (Rockville, MD) for the Health-care Cost and Utilization Project (http://www.hcup-us.ahrq.gov).

The presence of the following cardiovascular risk factors was collected: type II diabetes mellitus, hypertension, atrial fibrillation/flutter, congestive heart failure (CHF), coronary artery disease or previous myocardial infarction, prosthetic valve replacement, and peripheral vascular disease. Associations between intracranial tumors and the following were also explored: autoimmune pathology, thyroid disorders, glaucoma, body mass index (BMI), obstructive sleep apnea, asthma or chronic obstructive pulmonary disease (COPD), and gastrointestinal diseases.

Social history elements collected included marital status and family histories of intracranial tumors, neurological disorders, stroke, and cancer. Self-reported smoking status (current, former, and never) was also collected. The smoking classification was based on the United States Centers for Disease Control and Prevention (CDC), National Health Interview Survey, and Adult Tobacco Use (https://www.cdc.gov/nchs/surveys.htm).

The collection of psychiatric risk factors included a history of depression and the extent of alcohol use. Depression was measured by the Patient Health Questionnaire-2 (PHQ-2) and Patient Health Questionnaire-9 (PHQ-9). The PHQ-2 and PHQ-9 are validated two-question and nine-question modules that detect and assess depression.[47,50,51] For PHQ-2, a score of 3 or greater was classified as positive, while a score of 2 or lower was classified as negative. For PHQ-9, raw scores were utilized. Alcohol consumption habit was collected using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), a modified version of the ten question AUDIT developed by the World Health Organization (WHO).[10,19,49,72]. AUDIT-C cutoff scores of ≥3 for women and ≥ 4 for men were classified as positive.[72] Collected data also included prior diagnoses of psychiatric disorders other than depression, consistent with criteria from the Diagnostic and Statistical Manual of Mental Disorders 4th or 5th Edition.

Controls

Two to four controls were collected per case (n = 323) to maximize statistical power.[39] Using a random number generator, two sets of controls were collected from the clinic's total patient pool from January 1, 2019, to January 1, 2021. The first set of controls consisted of 1292 patients to examine differences between the clinic's general patient population and cases with respect to age, sex, and race. The second set of controls (n = 651) was matched to age, sex, and race to examine all other variables.

Statistical analysis

The normality of data was assessed through quantile-quantile plots and histograms to determine parametric or non-parametric analysis. For categorical variables, either Pearson's Chi-squared test or Fisher's exact test of independence was chosen, while for non-parametric continuous variables, the independent Wilcoxon rank-sum test was used.[56,93] Univariate and multivariate logistic regression with Firth's correction was used to identify variables independently predictive of central nervous system tumors. To determine significance, all tests used an alpha level of 0.05 and were two-tailed. All calculations were performed using R Statistical Software (R Foundation for Statistical Computing, Vienna, Austria).[81]

RESULTS

All tumors

Cases of all intracranial tumors (n = 323) were compared to unmatched controls (n = 1292) [Tables 1a-c]. Females had significantly higher odds of tumor diagnosis than males (1.44, 95% confidence interval [CI]: 1.08, 1.92; P = 0.013). Meanwhile, Hispanics/Latinos had significantly decreased odds of having a brain tumor (0.46, 95% CI: 0.20, 0.97; P = 0.046), while NAAN had significantly increased odds (8.22, 95% CI: 0.91, 389.61; P = 0.032).

Meningiomas

Of the analyzed meningiomas (n = 159), 81.1% were benign (n = 129) and 18.9% were malignant (n = 30) [Table 1a]. The median age of diagnosis was 61 years overall: 61 years for benign meningiomas and 66.5 years for malignant (P > 0.05). While there was a female predisposition for benign meningiomas (1.81, 95% CI: 1.17, 2.86; P = 0.01), this was not the case for malignant meningiomas (P > 0.05). Regarding race/ethnicity, NAAN exhibited a 12.26 (95% CI: 1.26, 118.87, P = 0.03) fold increased odds of benign meningioma diagnosis relative to other groups.

Socioeconomic variables

For benign meningiomas, patients had a 2.55 fold increased odds of having Medicare (95% CI: 1.68, 3.87; P < 0.001) and 0.47 fold decreased odds of having private insurance (95% CI: 0.30, 0.73; P < 0.001). Among malignant meningiomas, patients were at reduced odds of being from the first quartile (0.15, 95% CI: 0.0034, 0.99; P = 0.048). Meanwhile, geographically, malignant meningioma patients were at 6.36 fold greater odds of being from an urban location (95% CI: 1.81, 34.55; P = 0.001) and reduced odds of living in a suburban region (0.17, 95% CI: 0.031, 0.59; P = 0.002).

Presenting symptoms

For both benign (2.54, 95% CI: 1.47, 4.71; P < 0.001) and malignant meningiomas (6.80, 95% CI: 2.42, 19.59; P < 0.001), seizures were the most likely presentation; however, malignant meningioma patients were also more likely to present with cognitive difficulties (3.38, 95% CI: 1.23, 9.57; P = 0.014).

Medical comorbidities

In general, meningioma patients were found to have 1.86 times greater odds of a positive alcohol use screen (95% CI: 1.02, 3.29; P = 0.04). Benign meningiomas were specifically found to have increased odds of hypertension (1.54, 95% CI: 1.03, 2.31; P = 0.04), personal history of prior neoplasm (95% CI: 1.08, 2.97; P = 0.02), and family history of brain tumors (4.25, 95% CI: 1.63, 11.10; P < 0.001). Moreover, malignant meningioma patients not only had an increased odds of a history of prior neoplasm (5.15, 95% CI: 1.91, 14.08; P < 0.001) but also an 8.33 fold greater odds of head trauma history (95% CI: 1.32, 346.60; P = 0.03).

Multivariable analysis

Multivariable regression modeling was conducted to determine the best predictors of meningioma diagnosis. For benign meningiomas, variables that significantly increased the odds of diagnosis included: presentation with DNV (2.52, 95% CI: 1.25, 5.08; P = 0.01) or seizures (4.36, 95% CI: 1.78, 10.65; P = 0.001), presence of obesity class I (2.87, 95% CI: 1.08, 7.67; P = 0.04), CHF (6.64, 95% CI: 1.39, 31.73; P = 0.02), glaucomatous disease

Table 1a: Sociodemographic characteristics and medical comorbidities of all patients with intracranial tumors and patients with meningiomas alone: Crude odds ratios.

	All Tumors		All Meningiomas		Benign Meningiomas		Malignant Meningiomas	
	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)
Age								
Cases	60.00 (46.00, 71.00)	1.00 (−2.00, 4.00), *P*=0.52	61.00 (49.00, 73.00)	1.00 (−2.00, 5.00), *P*=0.54	61.00 (50.00, 71.00)	0.00 (−4.00, 4.00) *P*=0.93	66.50 (49.00, 76.00)	2.00 (−7.00, 10.00), *P*=0.72
Controls	61.00 (44.00, 74.00)		61.00 (44.00, 74.00)		62.00 (45.00, 74.00)		63.00 (44.50, 77.25	
Median household income								
Cases	102242 (81727, 110939)	0.00 (0.00, 0.00), *P*=0.49	102242 (81727, 110939)	0.00 (0.00, 0.00), *P*=0.97	102228 (79398, 106693)	0.00 (0.00, 3390), *P*=0.20	102242 (102242, 110939)	6920 (5.28 10–5, 9210), *P*=0.02
Controls	102242 (81727, 106006)		102242 (81727, 110939)		102242 (81727, 110939)		102242 (83358, 110939)	
Overall poverty level in municipality								
Cases	0.056 (0.049, 0.096)	0.00 (0.00, 0.00), *P*=0.77	0.056 (0.049, 0.096)	0.00 (0.00, 0.00), *P*=0.85	0.056 (0.049, 0.10)	0.00 (0.00, 0.0051), *P*=0.35	0.056 (0.049, 0.056)	0.00 (0.00, 0.01), *P*=0.16
Controls	0.056 (0.049, 0.096)		0.056 (0.049, 0.091)		0.056 (0.049, 0.090)		0.056 (0.049, 0.096)	
Poverty level for ages 18–64								
Cases	0.059 (0.049, 0.089)	0.00 (0.00, 0.00), *P*=0.72	0.059 (0.049, 0.086)	0.00 (0.00, 0.00), *P*=0.73	0.059 (0.049, 0.089)	0.00 (0.00, 0.004), *P*=0.41	0.059 (0.049, 0.059)	0.00 (0.00, 0.010), *P*=0.44
Controls	0.059 (0.049, 0.089)		0.059 (0.049, 0.089)		0.059 (0.049, 0.089)		0.059 (0.049, 0.089)	
Poverty level for ages 65 and older								
Cases	0.043 (0.039, 0.079)	0.00 (0.00, 0.0011), *P*=0.02	0.043 (0.039, 0.079)	0.00 (0.00, 0.001), *P*=0.27	0.043 (0.039, 0.083)	0.00 (0.00, 0.001), *P*=0.81	0.043 (0.039, 0.043)	0.004 (4.33 10–5, 0.01), *P*=0.005
Controls	0.043 (0.042, 0.079)		0.043 (0.039, 0.079)		0.043 (0.039, 0.079)		0.043 (0.039, 0.082)	
Geographic origin population size								
Cases	51511 (40857, 51601)	0.00 (0.00, 90.00), *P*=0.12	51511 (39017, 51601)	0.00 (0.00, 0.00), *P*=0.73	51511 (30850, 51601)	0.00 (0.00, 90.00), *P*=0.55	51556 (51511, 51601)	90.00 (0.00, 4640), *P*=0.07
Controls	51511 (31445, 51601)		51511 (31445, 51601)		51511 (38000, 51601)		51511 (24521, 51601)	
	Odds Ratio (95% CI)	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**
Sex								
Female	1.44 (1.08, 1.92)	*P*=0.01	1.98 (1.33, 2.98)	*P*<0.001	1.81 (1.17, 2.86)	*P*=0.01	2.39 (0.86, 7.69)	*P*=0.11
Male	0.70 (0.52, 0.93)		0.51 (0.34, 0.75)		0.55 (0.35, 0.85)		0.42 (0.13, 1.16)	
Race								
White	1.02 (0.76, 1.37)	*P*=0.94	0.97 (0.66, 1.41)	*P*=0.92	1.08 (0.72, 1.63)	*P*=0.76	0.40 (0.14, 1.02)	*P*=0.06
Asian	0.95 (0.69, 1.30)	*P*=0.79	1.01 (0.67, 1.51)	*P*=1.00	0.97 (0.62, 1.51)	*P*=0.98	1.38 (0.52, 3.53)	*P*=0.61
NHPI	1.17 (0.83, 1.67)	*P*=0.39	1.071 (0.67, 1.68)	*P*=0.84	0.99 (0.59, 1.63)	*P*=1.00	1.79 (0.60, 4.95)	*P*=0.33
Hispanic	0.46 (0.20, 0.97)	*P*=0.046	0.76 (0.30, 1.73)	*P*=0.63	0.69 (0.23, 1.72)	*P*=0.54	1.40 (0.13, 8.43)	*P*=0.65
Black	0.93 (0.20, 3.68)	*P*=1.00	0.47 (0.010, 3.68)	*P*=0.69	0.28 (0.0066, 1.87)	*P*=0.33	8.48 (0.43, 505.94)	*P*=0.10
NAAN	8.24 (0.96, 70.84)	*P*=0.06	10.05 (1.04, 97.26)	*P*=0.04	12.26 (1.26, 118.87)	*P*=0.03	2.05 (0.034, 39.93)	*P*=0.48
Marital status								
Divorced/Separated	0.77 (0.52, 1.13)	*P*=0.20	0.78 (0.45, 1.32)	*P*=0.41	0.58 (0.29, 1.07)	*P*=0.10	2.30 (0.70, 6.93)	*P*=0.17
Married	1.12 (0.87, 1.46)	*P*=0.39	0.93 (0.64, 1.35)	*P*=0.77	1.01 (0.67, 1.53)	*P*=1.00	0.65 (0.26, 1.60)	*P*=0.41
Single	0.85 (0.63, 1.14)	*P*=0.30	1.24 (0.79, 1.90)	*P*=0.37	1.36 (0.84, 2.18)	*P*=0.22	0.780 (0.21, 2.38)	*P*=0.84
Widowed	1.51 (0.96, 2.34)	*P*=0.07	1.14 (0.58, 2.13)	*P*=0.78	1.12 (0.50, 2.31)	*P*=0.90	1.25 (0.28, 4.46)	*P*=0.75
Insurance type								
Medicaid	0.99 (0.72, 1.34)	*P*=1.00	0.86 (0.53, 1.37)	*P*=0.59	0.89 (0.52, 1.49)	*P*=0.74	0.71 (0.14, 2.38)	*P*=0.79
Medicare	1.77 (1.37, 2.30)	*P*<0.001	2.39 (1.65, 3.47)	*P*<0.001	2.55 (1.68, 3.87)	*P*<0.001	1.84 (0.75, 4.64)	*P*=0.20
Military	0.86 (0.49, 1.46)	*P*=0.66	0.79 (0.35, 1.63)	*P*=0.62	0.68 (0.25, 1.59)	*P*=0.47	1.27 (0.21, 5.40)	*P*=0.72
Private	0.59 (0.45, 0.78)	*P*<0.001	0.48 (0.31, 0.71)	*P*<0.001	0.47 (0.30, 0.73)	*P*<0.001	0.49 (0.13, 1.45)	*P*=0.25
Income quartiles								
Q1	1.05 (0.77, 1.42)	*P*=0.80	1.018 (0.64, 1.59)	*P*=1.00	1.25 (0.77, 2.01)	*P*=0.38	0.15 (0.0034, 0.99)	*P*=0.048
Q2	0.82 (0.59, 1.13)	*P*=0.24	1.30 (0.79, 2.091)	*P*=0.31	1.00 (0.60, 1.63)	*P*=1.00	0.37 (0.066, 1.33)	*P*=0.17
Q3	0.94 (0.71, 1.24)	*P*=0.72	1.15 (0.77, 1.71)	*P*=0.54	1.00 (0.63, 1.57)	*P*=1.00	1.99 (0.78, 4.97)	*P*=0.16
Q4	1.19 (0.90, 1.57)	*P*=0.22	0.97 (0.65, 1.44)	*P*=0.96	0.82 (0.51, 1.29)	*P*=0.43	1.81 (0.74, 4.42)	*P*=0.22
Geographic origin								
Urban	1.28 (0.99, 1.66)	*P*=0.066	1.18 (0.81, 1.73)	*P*=0.42	0.90 (0.59, 1.36)	*P*=0.65	6.36 (1.81, 34.55)	*P*=0.0011
Suburban	0.79 (0.61, 1.03)	*P*=0.081	0.83 (0.57, 1.21)	*P*=0.36	1.07 (0.71, 1.62)	*P*=0.81	0.17 (0.031, 0.59)	*P*=0.0021
Rural	0.67 (0.072, 3.03)	*P*=1.00	1.62 (0.15, 10.00)	*P*=0.63	2.71 (0.22, 23.91)	*P*=0.26	0.98 (0.020, 10.17)	*P*=1.00
Presenting symptoms								
Headache								
Yes	1.06 (0.81, 1.39)	*P*=0.72	1.0056 (0.69, 1.47)	*P*=1.00	1.04 (0.68, 1.56)	*P*=0.94	0.93 (0.32, 2.71)	*P*=1.00
No	0.94 (0.72, 1.24)		0.99 (0.68, 1.45)		0.97 (0.64, 1.46)		1.07 (0.37, 3.12)	
DNV								
Yes	1.08 (0.82, 1.43)	*P*=0.62	1.35 (0.91, 1.98)	*P*=0.13	1.41 (0.92, 2.14)	*P*=0.12	1.18 (0.40, 3.42)	*P*=0.92
No	0.92 (0.70, 1.22)		0.74 (0.51, 1.093)		0.71 (0.47, 1.08)		0.85 (0.29, 2.51)	
Cognitive Difficulty								
Yes	1.53 (1.14, 2.04)	*P*=0.004	1.32 (0.88, 1.97)	*P*=0.19	1.08 (0.68, 1.71)	*P*=0.80	3.38 (1.23, 9.57)	*P*=0.014
No	0.65 (0.49, 0.88)		0.76 (0.51, 1.14)		0.92 (0.59, 1.48)		0.30 (0.10, 0.81)	
Gait/Coordination Disorder								
Yes	1.16 (0.88, 1.52)	*P*=0.31	1.13 (0.77, 1.65)	*P*=0.56	1.14 (0.75, 1.72)	*P*=0.58	1.04 (0.35, 2.88)	*P*=1.00
No	0.86 (0.66, 1.14)		0.88 (0.60, 1.29)		0.88 (0.58, 1.33)		0.96 (0.35, 2.85)	
Seizures/Epilepsy								
Yes	3.04 (2.20, 4.19)	*P*<0.001	3.24 (1.98, 5.26)	*P*<0.001	2.65 (1.46, 4.71)	*P*<0.001	6.80 (2.42, 19.59)	*P*<0.001
No	0.33 (0.24, 0.45)		0.31 (0.19, 0.50)		0.38 (0.21, 0.68)		0.15 (0.051, 0.41)	
Sleep Disturbances								
Yes	0.77 (0.59, 1.01)	*P*=0.06	0.77 (0.52, 1.13)	*P*=0.19	0.67 (0.43, 1.03)	*P*=0.07	1.34 (0.48, 3.58)	*P*=0.69
No	1.30 (0.99, 1.71)		1.31 (0.89, 1.94)		1.49 (0.97, 2.30)		0.75 (0.28, 2.07)	
Medical comorbidities								
	Median (IQR)	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**
BMI (kg/m^2)								
Cases	26.84 (22.72, 30.93)	0.35 (−0.44, 1.12), *P*=0.39	27.22 (22.92, 30.93)	−0.55 (−1.62, 0.54), *P*=0.33	27.29 (23.88, 30.90)	0.82 (−0.34, 1.98), *P*=0.17	25.66 (20.33, 30.25)	1.13 (−1.87, 3.95), *P*=0.42
Controls	26.27 (22.85, 31.07)		26.09 (22.93, 30.68)		26.04 (22.82, 30.80)		26.11 (23.24, 29.55)	
	Odds ratio (95% CI)	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds ratio (95% CI)**	**Chi-square/Fisher Exact Test**
Weight class								
Underweight	0.75 (0.28, 1.71)	*P*=0.62	0.77 (0.19, 2.32)	*P*=0.80	0.20 (0.005, 1.27)	*P*=0.10	8.85 (1.39, 56.34)	*P*=0.01
Normal	0.83 (0.62, 1.10)	*P*=0.21	0.75 (0.49, 1.12)	*P*=0.17	0.76 (0.48, 1.18)	*P*=0.24	0.71 (0.23, 1.98)	*P*=0.63
Preobesity	1.31 (0.98, 1.73)	*P*=0.06	1.33 (0.89, 1.98)	*P*=0.17	1.49 (0.96, 2.31)	*P*=0.08	0.78 (0.25, 2.21)	*P*=0.80
Obesity Class 1	1.17 (0.80, 1.68)	*P*=0.44	1.25 (0.74, 2.066)	*P*=0.44	1.16 (0.64, 2.02)	*P*=0.70	1.80 (0.46, 6.02)	*P*=0.47
Obesity Class 2	0.63 (0.33, 1.10)	*P*=0.13	0.66 (0.26, 1.44)	*P*=0.37	0.80 (0.31, 1.77)	*P*=0.70	0.24 (0.0057, 1.58)	*P*=0.22
Obesity Class 3	1.01 (0.54, 1.78)	*P*=1.00	1.13 (0.44, 2.58)	*P*=0.93	1.05 (0.38, 2.54)	*P*=1.00	1.76 (0.032, 23.15)	*P*=0.51
Type 2 diabetes mellitus								
Yes	1.12 (0.78, 1.58)	*P*=0.57	1.14 (0.70, 1.83)	*P*=0.65	1.21 (0.71, 2.02)	*P*=0.53	0.85 (0.19, 2.89)	*P*=1.00
No	0.89 (0.63, 1.28)		0.87 (0.55, 1.43)		0.83 (0.49, 1.42)		1.17 (0.35, 5.17)	
Hypertension								
Yes	1.41 (1.09, 1.82)	*P*=0.008	1.54 (1.07, 2.22)	*P*=0.02	1.54 (1.03, 2.31)	*P*=0.04	1.55 (0.63, 3.81)	*P*=0.39
No	0.71 (0.55, 0.92)		0.65 (0.45, 0.93)		0.70 (0.43, 0.98)		0.65 (0.26, 1.58)	
Coronary artery disease/prior myocardial infarction								
Yes	0.95 (0.57, 1.55)	*P*=0.94	0.90 (0.41, 1.80)	*P*=0.88	1.12 (0.48, 2.39)	*P*=0.91	0.30 (0.007, 2.13)	*P*=0.31
No	1.05 (0.65, 1.76)		1.12 (0.55, 2.44)		0.89 (0.42, 2.08)		3.38 (0.47, 149.57)	
PVD								
Yes	1.96 (0.77, 4.60)	*P*=0.15	2.030 (0.32, 9.63)	*P*=0.39	1.61 (0.15, 9.96)	*P*=0.63	4.19 (0.052, 335.37)	*P*=0.35
No	0.51 (0.22, 1.29)		0.49 (0.10, 3.077)		0.62 (0.10, 6.60)		0.24 (0.0030, 19.12)	
Stroke								
Yes	1.31 (0.90, 1.89)	*P*=0.16	1.60 (0.95, 2.64)	*P*=0.07	1.73 (0.95, 3.07)	*P*=0.07	1.24 (0.37, 3.66)	*P*=0.89
No	0.76 (0.53, 1.11)		0.63 (0.38, 1.055)		0.58 (0.33, 1.05)		0.81 (0.27, 2.73)	
Atrial fibrillation/atrial flutter								
Yes	1.16 (0.63, 2.06)	*P*=0.69	1.36 (0.58, 2.95)	*P*=0.53	1.98 (0.81, 4.53)	*P*=0.13	0.21 (0.005, 1.41)	*P*=0.14
No	0.86 (0.49, 1.59)		0.73 (0.34, 1.72)		0.51 (0.22, 1.24)		4.69 (0.71, 199.11)	
CHF								
Yes	1.34 (0.60, 2.74)	*P*=0.53	1.95 (0.72, 4.89)	*P*=0.19	2.23 (0.74, 6.18)	*P*=0.15	1.04 (0.020, 11.01)	*P*=1.00
No	0.75 (0.37, 1.66)		0.51 (0.20, 1.40)		0.45 (0.16, 1.35)		0.97 (0.091, 49.23)	
CVR								
Yes	1.76 (0.29, 7.75)	*P*=0.67	0.40 (0.0092, 2.83)	*P*=0.70	0.66 (0.014, 5.50)	*P*=1.00	1.02 (0.020, 10.53)	*P*=1.00
No	0.57 (0.13, 3.43)		2.50 (0.35, 108.96)		1.51 (0.18, 69.65)		0.98 (0.095, 49.24)	
History of head trauma								
Yes	0.56 (0.35, 0.85)	*P*=0.007	0.66 (0.33, 1.21)	*P*=0.21	0.82 (0.41, 1.54)	*P*=0.62	0.12 (0.003, 0.75)	*P*=0.03
No	1.80 (1.18, 2.83)		0.66 (0.33, 1.21)		1.22 (0.65, 2.44)		8.33 (1.32, 346.60)	
History of cancer								
Yes	2.79 (2.08, 3.75)	*P*<0.001	2.26 (1.45, 3.49)	*P*<0.001	1.81 (1.08, 2.97)	*P*=0.020	5.15 (1.91, 14.08)	*P*<0.001
No	0.36 (0.27, 0.48)		0.44 (0.29, 0.69)		0.55 (0.34, 0.93)		0.19 (0.071, 0.52)	
Obstructive sleep apnea								
Yes	1.04 (0.63, 1.64)	*P*=0.97	0.87 (0.38, 1.79)	*P*=0.82	0.72 (0.27, 1.69)	*P*=0.56	1.61 (0.26, 7.32)	*P*=0.45
No	0.97 (0.61, 1.58)		1.15 (0.56, 2.63)		1.38 (0.59, 3.77)		0.62 (0.17, 3.88)	
Asthma/chronic obstructive pulmonary disease								
Yes	0.81 (0.55, 1.17)	*P*=0.29	0.65 (0.36, 1.12)	*P*=0.14	0.60 (0.31, 1.09)	*P*=0.11	1.04 (0.18, 4.25)	*P*=1.00
No	1.23 (0.85, 1.81)		1.54 (0.89, 2.79)		1.67 (0.92, 3.23)		0.96 (0.24, 5.70)	
GERD								
Yes	0.48 (0.26, 0.83)	*P*=0.01	0.56 (0.25, 1.14)	*P*=0.13	0.60 (0.24, 1.33)	*P*=0.26	0.45 (0.048, 2.09)	*P*=0.37
No	2.08 (1.21, 3.81)		1.77 (0.88, 3.95)		1.66 (0.75, 4.15)		2.22 (0.48, 20.98)	
Diverticular disease								
Yes	2.10 (1.03, 4.08)	*P*=0.031	2.34 (0.89, 5.75)	*P*=0.073	2.55 (0.90, 6.82)	*P*=0.067	1.39 (0.026, 18.06)	*P*=0.58
No	0.48 (0.25, 0.97)		0.43 (0.17, 1.12)		0.39 (0.15, 1.12)		0.72 (0.055, 39.02)	
Autoimmune disease								
Yes	0.97 (0.52, 1.72)	*P*=1.00	1.24 (0.53, 2.65)	*P*=0.70	1.42 (0.57, 3.24)	*P*=0.50	0.58 (0.012, 4.81)	*P*=1.00
No	1.03 (0.58, 1.94)		0.80 (0.38, 1.87)		0.70 (0.31, 1.75)		1.73 (0.21, 80.90)	
Thyroid disease								
Yes	1.05 (0.71, 1.53)	*P*=0.85	1.20 (0.70, 2.00)	*P*=0.55	1.44 (0.81, 2.49)	*P*=0.22	0.42 (0.045, 1.94)	*P*=0.37
No	0.95 (0.65, 1.40)		0.83 (0.50, 1.43)		0.69 (0.40, 1.24)		2.37 (0.51, 22.34)	
History of glaucoma								
Yes	1.74 (0.73, 3.82)	*P*=0.21	2.48 (0.73, 7.68)	*P*=0.14	2.76 (0.79, 8.89)	*P*=0.10	2.05 (0.034, 39.93)	*P*=0.48
No	0.57 (0.26, 1.36)		0.40 (0.13, 1.37)		0.36 (0.11, 1.26)		0.49 (0.025, 29.25)	
Neurofibromatosis type 2								
Yes	16.09 (1.59, 790.27)	*P*=0.01						
No	0.06 (0.00, 0.63)							
Social history and psychiatric risk factors								
Smoking status								
Never Smoker	0.91 (0.70, 1.19)	*P*=0.51	1.13 (0.77, 1.67)	*P*=0.58	1.21 (0.79, 1.87)	*P*=0.42	0.83 (0.32, 2.32)	*P*=0.87
Former Smoker	1.19 (0.88, 1.61)	*P*=0.26	0.99 (0.62, 1.54)	*P*=1.00	0.92 (0.55, 1.50)	*P*=0.81	1.41 (0.41, 4.24)	*P*=0.70
Current Smoker	0.93 (0.63, 1.34)	*P*=0.74	0.80 (0.45, 1.38)	*P*=0.49	0.79 (0.41, 1.43)	*P*=0.51	0.87 (0.15, 3.43)	*P*=1.00
Alcohol use screen (AUDIT–C)								
Positive Screen	1.84 (1.24, 2.70)	*P*=0.002	1.86 (1.02, 3.29)	*P*=0.037	2.05 (1.07, 3.80)	*P*=0.024	1.14 (0.11, 6.11)	*P*=1.00
Negative Screen	0.54 (0.37, 0.81)		0.54 (0.30, 0.98)		0.49 (0.26, 0.94)		0.88 (0.16, 8.90)	
Alcohol use disorder								
Yes	0.99 (0.44, 2.03)	*P*=1.00	0.94 (0.17, 3.47)	*P*=1.00	0.72 (0.077, 3.38)	*P*=1.00	2.24 (0.037, 44.44)	*P*=0.46
No	1.01 (0.49, 2.29)		1.07 (0.29, 5.90)		1.38 (0.30, 13.00)		0.45 (0.023, 27.22)	
PHQ–2 screen								
Positive Screen	0.69 (0.36, 1.22)	*P*=0.24	0.94 (0.46, 1.80)	*P*=0.97	0.88 (0.41, 1.75)	*P*=0.84	1.75 (0.032, 23.37)	*P*=0.51
Negative Screen	1.45 (0.82, 2.75)		1.07 (0.56, 2.20)		1.13 (0.57, 2.42)		0.57 (0.043, 31.48)	
	Median (IQR)	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank Sum Test (estimated difference)**
PHQ–9 score								
Cases	12.00 (7.25, 16.00)	1.00 (−2.00, 3.00), *P*=0.66	12.00 (5.00, 19.00)	2.00 (-3.00, 6.00), *P*=0.46	14 (8, 20)	3.00 (-2.00, 8.00), *P*=0.19	3 0.00 (3.00, 3.00)	6.00 (−1.00, 18.00), *P*=0.07
Controls	10.50 (7.00, 16.00)		10.00 (6.00, 16.00)		10.00 (6.75, 16.00)		9.00 (6.00, 16.00)	
	Odds Ratio (95% CI)	**Chi-square/Fisher Exact Test**	**Odds Ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds Ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds Ratio (95% CI)**	**Chi-square/Fisher Exact Test**
Depression								
Yes	0.95 (0.67, 1.32)	*P*=0.80	1.13 (0.66, 1.88)	*P*=0.72	1.49 (0.83, 2.61)	*P*=0.18	0.30 (0.033, 1.36)	*P*=0.17
No	1.06 (0.76, 1.49)		0.89 (0.53, 1.52)		0.67 (0.38, 1.20)		3.30 (0.74, 30.68)	
Psychiatric disorders (Excluding Depression)								
Yes	0.85 (0.61, 1.18)	*P*=0.36	0.97 (0.57, 1.59)	*P*=0.98	0.99 (0.54, 1.74)	*P*=1.00	0.90 (0.24, 2.79)	*P*=1.00
No	1.17 (0.85, 1.64)		1.04 (0.63, 1.76)		1.01 (0.58, 1.85)		1.11 (0.36, 4.14)	
Family history								
Family history of brain tumors								
Yes	3.12 (1.58, 6.05)	*P*<0.001	4.27 (1.72, 10.65)	*P*<0.001	4.25 (1.63, 11.10)	*P*<0.001	4.33 (0.054, 347.39)	*P*=0.34
No	0.32 (0.17, 0.63)		0.23 (0.094, 0.58)		0.24 (0.090, 0.62)		0.23 (0.0029, 18.55)	
Family history of neurological disease								
Yes	0.41 (0.27, 0.61)	*P*<0.001	0.26 (0.12, 0.51)	*P*<0.001	0.17 (0.059, 0.39)	*P*<0.001	1.01 (0.22, 3.52)	*P*=1.00
No	2.44 (1.64, 3.76)		3.89 (1.98, 8.53)		5.93 (2.55, 16.91)		0.99 (0.28, 4.46)	
Family history of stroke								
Yes	1.20 (0.83, 1.71)	*P*=0.35	0.97 (0.53, 1.68)	*P*=1.00	0.88 (0.44, 1.66)	*P*=0.80	1.37 (0.36, 4.46)	*P*=0.79
No	0.83 (0.58, 1.21)		1.04 (0.60, 1.87)		1.14 (0.60, 2.28)		0.73 (0.22, 2.82)	
Family history of cancer								
Yes	1.03 (0.79, 1.34)	*P*=0.88	0.75 (0.52, 1.09)	*P*=0.13	0.85 (0.56, 1.27)	*P*=0.46	0.41 (0.14, 1.09)	*P*=0.08
No	0.97 (0.75, 1.26)		1.33 (0.92, 1.94)		1.18 (0.79, 1.78)		2.45 (0.92, 7.07)	

IQR: Interquartile range, CI: Confidence interval, PHQ: Patient health questionnaire, AUDIT-C: Alcohol Use disorders identification test-consumption, DNV: Dizziness, nausea, or vomiting, BMI: Body mass index, Afib: Atrial fibrillation or flutter, CHF: Congestive heart failre, PVD: Peripheral vascular disease, CVR: Cardiac valve replacement, OSA: Obstructive sleep apnea, GERD: Gastroesophageal reflux disease, AUDIT-C: Alcohol use disorders identification test-consumption, NAAN: Native american or alaskan native, PHQ: Patient health questionnaire, COPD: Chronic obstructive pulmonary disease.

Table 1b: Sociodemographic characteristics and medical comorbidities of patients with gliomas: Crude odds ratios.

	Gliomas (Grades I–IV)		Gliomas (Grades I–III)		Gliomas (Grade IV)	
	Median (IQR)	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**
Age						
Cases	57.0 (38.0, 67.5)	7.00 ($2.22\ 10^{-5}$, 14.00),	47.50 (31.50, 62.00)	12.00 (2.00, 22.00),	59.00 (50.00, 70.50)	3.00 (–8.00, 13.00),
Controls	61.00 (49.00, 76.00)	*P*=0.04	60.50 (49.75, 74.00)	*P*=0.02	62.00 (49.00, 76.25)	*P*=0.61
Median household income						
Cases	96297 (70468, 102242)	14.0 (0.00, 8697),	96297 (81208, 102242)	1050.40 (–3044.00,	102242 (64502, 102242)	0.00 (–1719.00, 9719.00),
Controls	102242 (79818, 105190)	*P*=0.28	102242 (86950, 105278)	8697.00), *P*=0.37	102242 (78948, 102972)	*P*=0.53
Overall poverty level in municipality						
Cases	0.056 (0.049, 0.099)	0.00 (–0.01, 0.0070),	0.056 (0.046, 0.067)	0.003 (–0.003, 0.017),	0.056 (0.056, 0.11)	0.00 (–0.01, 0.014),
Controls	0.056 (0.049, 0.091)	*P*=0.71	0.056 (0.049, 0.087)	*P*=0.34	0.056 (0.049, 0.10)	*P*=0.62
Poverty level for ages 18–64						
Cases	0.059 (0.049, 0.092)	0.00 (–0.01, 0.0070),	0.056 (0.045, 0.066)	0.01 (–0.001, 0.015),	0.059 (0.059, 0.104)	0.00 (–0.01, 0.021),
Controls	0.059 (0.049, 0.091)	*P*=0.68	0.059 (0.049, 0.092)	*P*=0.21	0.059 (0.049, 0.091)	*P*=0.42
Poverty level for ages 65 and older						
Cases	0.043 (0.043, 0.082)	0.00 (–0.004, 0.001),	0.043 (0.043, 0.072)	0.036 (–0.01, 0.004),	0.043 (0.043, 0.092)	0.00 (–0.004, 0.005),
Controls	0.043 (0.042, 0.068)	*P*=0.52	0.043 (0.042, 0.057)	*P*=0.76	0.043 (0.041, 0.072)	*P*=0.52
Geographic origin population size						
Cases	51511 (27449, 51601)	0.00 (–1974.00, 90.00),	51511 (40143, 51946)	1470 (–90.00,	51511 (25354, 51556)	0.00 (–90.00, 3535.00),
Controls	51511 (29066, 51601)	*P*=0.70	49834 (18580, 51511)	14913.00), *P*=0.25	51511 (43488, 51601)	*P*=0.45
	Odds ratio (95% CI)	**Chi-square/Fisher Exact Test**	**Odds Ratio (95% CI)**	**Chi-square/Fisher Exact Test**	**Odds Ratio (95% CI)**	**Chi-square/Fisher Exact Test**
Sex						
Female	1.24 (0.57, 2.79)	*P*=0.69	1.59 (0.52, 5.23)	*P*=0.51	0.95 (0.30, 3.19)	*P*=1.00
Male	0.81 (0.36, 1.76)		0.63 (0.19, 1.91)		1.06 (0.31, 3.34)	
Race						
White	3.02 (1.35, 7.07)	*P*=0.01	1.57 (0.52, 4.94)	*P*=0.52	6.59 (1.83, 30.31)	*P*=0.001
Asian	0.35 (0.13, 0.96)	*P*=0.04	0.53 (0.091, 2.13)	*P*=0.55	0.23 (0.024, 1.10)	*P*=0.050
NHPI	1.08 (0.36, 2.85)	*P*=1.00	1.88 (0.45, 6.88)	*P*=0.46	0.51 (0.052, 2.58)	*P*=0.51
Marital status						
Divorced/ Separated	0.50 (0.053, 2.28)	*P*=0.53	1.06 (0.10, 6.01)	*P*=1.00	0.23 (0.01, 1.58)	*P*=0.20
Married	1.27 (0.58, 2.80)	*P*=0.64	3.77 (1.25, 12.31)	*P*=0.01	0.76 (0.23, 2.41)	*P*=0.79
Single	0.80 (0.34, 1.79)	*P*=0.69	0.36 (0.081, 1.28)	*P*=0.12	1.66 (0.50, 5.37)	*P*=0.49
Widowed	2.17 (0.33, 10.77)	*P*=0.38	2.15 (0.035, 43.36)	*P*=0.48	2.17 (0.18, 16.69)	*P*=0.33
Insurance type						
Medicaid	0.60 (0.19, 1.60)	*P*=0.39	0.41 (0.071, 1.64)	*P*=0.26	0.97 (0.16, 4.23)	*P*=1.00
Medicare	2.24 (0.94, 5.21)	*P*=0.07	2.96 (0.67, 12.06)	*P*=0.16	1.95 (0.59, 6.25)	*P*=0.32
Military	0.64 (0.067, 3.07)	*P*=0.74	0.65 (0.013, 5.89)	*P*=1.00	0.63 (0.013, 5.75)	*P*=1.00
Private	0.84 (0.39, 1.79)	*P*=0.74	1.10 (0.37, 3.38)	*P*=1.00	0.62 (0.18, 1.93)	*P*=0.51

Table 1b: (*Continued*).

	Odds ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Income quartiles						
Q1	1.41 (0.57, 3.29)	*P*=0.52	1.08 (0.23, 4.07)	*P*=1.00	1.74 (0.50, 5.66)	*P*=0.45
Q2	0.80 (0.25, 2.18)	*P*=0.82	1.00 (0.21, 3.72)	*P*=1.00	0.57 (0.06, 2.93)	*P*=0.73
Q3	1.46 (0.67, 3.15)	*P*=0.39	1.85 (0.61, 5.62)	*P*=0.33	1.12 (0.33, 3.54)	*P*=1.00
Q4	0.44 (0.13, 1.25)	*P*=0.16	0.32 (0.033, 1.51)	*P*=0.15	0.61 (0.10, 2.49)	*P*=0.55
Geographic origin						
Urban	1.00 (0.47, 2.18)	*P*=1.00	1.35 (0.45, 4.12)	*P*=0.73	0.72 (0.23, 2.33)	*P*=0.71
Suburban	1.03 (0.47, 2.20)	*P*=1.00	0.74 (0.24, 2.22)	*P*=0.73	1.48 (0.45, 4.64)	*P*=0.63
Rural	1.98 (0.03, 38.50)	*P*=0.49			1.97 (0.03, 38.65)	*P*=0.50
Presenting symptoms						
Headache						
Yes	0.75 (0.32, 1.74)	*P*=0.60	0.49 (0.14, 1.58)	*P*=0.29	1.25 (0.34, 4.69)	*P*=0.92
No	1.33 (0.57, 3.16)		2.04 (0.63, 7.30)		0.80 (0.21, 2.98)	
DNV						
Yes	0.10 (0.01, 0.41)	*P*<0.001	0.082 (0.002, 0.58)	*P*=0.002	0.12 (0.0028, 0.92)	*P*=0.03
No	10.13 (2.41, 90.73)		12.22 (1.73, 535.11)		8.02 (1.09, 358.91)	
Cognitive difficulty						
Yes	5.80 (2.39, 14.52)	*P*<0.001	7.72 (2.21, 29.88)	*P*<0.001	4.06 (1.03, 16.18)	*P*=0.04
No	0.17 (0.07, 0.42)		0.13 (0.033, 0.45)		0.25 (0.062, 0.97)	
Gait/coordination disorder						
Yes	1.57 (0.66, 3.73)	*P*=0.35	1.61 (0.45, 5.48)	*P*=0.56	1.54 (0.41, 5.77)	*P*=0.65
No	0.64 (0.27, 1.52)		0.62 (0.18, 2.20)		0.65 (0.17, 2.41)	
Seizures/Epilepsy						
Yes	10.46 (4.25, 27.03)	*P*<0.001	16.02 (4.23, 71.56)	*P*<0.001	6.66 (1.82, 25.82)	*P*=0.002
No	0.10 (0.04, 0.24)		0.06 (0.01, 0.24)		0.15 (0.039, 0.55)	
Sleep disturbances						
Yes	0.38 (0.12, 1.04)	*P*=0.07	0.35 (0.059, 1.39)	*P*=0.16	0.44 (0.069, 1.98)	*P*=0.34
No	2.62 (0.96, 8.37)		2.89 (0.72, 16.97)		2.29 (0.51, 14.41)	
Medical comorbidities						
	Median (IQR)	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**
BMI (kg/m^2)						
Cases	26.47 (22.30, 30.75)	0.12 (−2.31, 2.49), *P*=0.92	26.67 (22.93, 29.86)	0.83 (−1.91, 3.60), *P*=0.59	24.75 (21.64, 31.73)	0.86 (−3.49, 5.33), *P*=0.66)
Controls	26.58 (22.52, 29.71)		26.34 (21.96, 28.72)		26.90 (23.03, 31.30)	

Table 1b: (*Continued*).

	Odds ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Weight class						
Underweight	0.91 (0.02, 7.77)	*P*=1.00			1.17 (0.02, 10.41)	*P*=1.00
Normal	1.48 (0.58, 3.66)	*P*=0.48	1.01 (0.29, 3.29)	*P*=1.00	2.45 (0.51, 11.87)	*P*=0.32
Preobesity	0.70 (0.25, 1.80)	*P*=0.56	0.83 (0.27, 2.75)	*P*=0.95	0.46 (0.04, 2.53)	*P*=0.48
Obesity Class 1	0.63 (0.11, 2.33)	*P*=0.58	0.43 (0.01, 3.42)	*P*=0.68	0.97 (0.09, 5.60)	*P*=1.00
Obesity Class 2	0.54 (0.01, 3.95)	*P*=1.00	2.25 (0.04, 44.43)	*P*=0.46	0.86 (0.02, 7.05)	*P*=1.00
Obesity Class 3	3.08 (0.63, 12.69)	*P*=0.09	3.89 (0.51, 25.84)	*P*=0.11	1.90 (0.04, 22.28)	*P*=0.48
Type 2 diabetes mellitus						
Yes	0.52 (0.10, 1.89)	*P*=0.42	0.31 (0.01, 2.39)	*P*=0.45	0.79 (0.077, 4.23)	*P*=1.00
No	1.91 (0.53, 10.54)		3.20 (0.42, 145.27)		1.27 (0.24, 12.94)	
Hypertension						
Yes	1.30 (0.58, 2.88)	*P*=0.61	1.19 (0.33, 3.91)	*P*=0.97	1.50 (0.46, 5.17)	*P*=0.63
No	0.77 (0.35, 1.72)		0.84 (0.26, 3.04)		0.67 (0.19, 2.18)	
Coronary artery disease/prior myocardial infarction						
Yes	0.46 (0.010, 3.55)	*P*=0.69	0.67 (0.014, 5.76)	*P*=1.00	0.73 (0.02, 6.72)	*P*=1.00
No	2.15 (0.28, 97.20)		1.50 (0.17, 70.77)		1.37 (0.15, 66.95)	
PVD						
Yes	2.13 (0.04, 41.51)	*P*=0.47			2.19 (0.04, 43.29)	*P*=0.46
No	0.47 (0.02, 27.96)				0.46 (0.02, 27.52)	
Stroke						
Yes	1.78 (0.52, 5.38)	*P*=0.41	3.72 (0.66, 19.66)	*P*=0.08	0.84 (0.081, 4.60)	*P*=1.00
No	0.56 (0.19, 1.92)		0.27 (0.051, 1.52)		1.19 (0.22, 12.28)	
Atrial fibrillation/atrial flutter						
Yes	1.24 (0.12, 6.92)	*P*=0.68	0.67 (0.014, 5.76)	*P*=1.00	2.37 (0.20, 18.37)	*P*=0.30
No	0.81 (0.14, 8.28)		1.50 (0.17, 70.77)		0.42 (0.05, 5.06)	
CHF						
Yes	2.13 (0.04, 41.51)	*P*=0.47			2.19 (0.04, 43.29)	*P*=0.46
No	0.47 (0.02, 27.96)				0.46 (0.02, 27.52)	
History of head trauma						
Yes	0.50 (0.12, 1.57)	*P*=0.34	0.65 (0.11, 2.65)	*P*=0.76	0.30 (0.01, 2.28)	*P*=0.46
No	1.99 (0.64, 8.33)		1.54 (0.38, 9.17)		3.35 (0.44, 152.53)	
History of cancer or neoplasm						
Yes	1.64 (0.53, 4.52)	*P*=0.44	2.78 (0.63, 11.05)	*P*=0.18	0.79 (0.077, 4.23)	*P*=1.00
No	0.61 (0.22, 1.87)		0.36 (0.09, 1.58)		1.27 (0.24, 12.94)	
Obstructive sleep apnea						
Yes	0.61 (0.01, 5.00)	*P*=1.00	2.15 (0.04, 43.36)	*P*=0.48	0.42 (0.01, 3.13)	*P*=0.69
No	1.64 (0.20, 76.17)		0.47 (0.02, 28.73)		2.39 (0.32, 106.88)	
Asthma/chronic obstructive pulmonary disease						
Yes	0.53 (0.096, 1.91)	*P*=0.42	1.68 (0.26, 8.05)	*P*=0.44	0.12 (0.003, 0.78)	*P*=0.01
No	1.90 (0.52, 10.46)		0.60 (0.12, 3.87)		8.30 (1.28, 350.46)	

Table 1b: (*Continued*).

	Odds ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
GERD						
Yes	0.45 (0.05, 2.04)	P=0.38	0.19 (0.004, 1.23)	P=0.08	1.13 (0.11, 6.53)	P=1.00
No	2.21 (0.49, 20.56)		5.40 (0.81, 230.62)		0.88 (0.15, 9.37)	
Diverticular disease						
Yes	0.86 (0.02, 8.07)	P=1.00	1.03 (0.02, 10.76)	P=1.00	1.51 (0.03, 20.30)	P=0.56
No	1.16 (0.12, 56.36)		0.97 (0.09, 49.23)		0.66 (0.05, 36.65)	
Autoimmune disease						
Yes	0.18 (0.00, 1.17)	P=0.10	0.40 (0.01, 2.94)	P=0.70	0.34 (0.01, 2.48)	P=0.47
No	5.45 (0.85, 228.31)		2.52 (0.34, 112.75)		2.90 (0.40, 128.13)	
Thyroid disease						
Yes	0.80 (0.14, 3.02)	P=1.00	0.69 (0.01, 6.24)	P=1.00	0.88 (0.09, 4.81)	P=1.00
No	1.26 (0.33, 7.11)		1.45 (0.16, 70.79)		1.13 (0.21, 11.72)	
Glaucoma						
Yes	0.53 (0.01, 4.05)	P=1.00	2.07 (0.03, 40.73)	P=0.48	0.72 (0.02, 6.21)	P=1.00
No	1.89 (0.25, 85.20)		0.48 (0.03, 29.12)		1.39 (0.16, 66.12)	
Social history and psychiatric risk factors						
Smoking status						
Never smoker	0.78 (0.34, 1.82)	P=0.65	0.61 (0.19, 2.10)	P=0.52	0.97 (0.28, 3.63)	P=1.00
Former smoker	1.51 (0.56, 3.79)	P=0.47	1.25 (0.26, 4.81)	P=0.74	1.83 (0.43, 6.88)	P=0.50
Current smoker	0.88 (0.20, 2.89)	P=1.00	1.94 (0.29, 9.72)	P=0.40	0.33 (0.0071, 2.52)	P=0.45
Alcohol use screen (AUDIT–C)						
Positive screen	1.60 (0.48, 4.70)	P=0.52	2.07 (0.31, 10.44)	P=0.39	1.40 (0.22, 6.56)	P=0.70
Negative screen	0.62 (0.21, 2.09)		0.48 (0.096, 3.23)		0.71 (0.15, 4.59)	
Alcohol use disorder						
Yes	0.27 (0.01, 1.79)	P=0.33	0.53 (0.012, 4.16)	P=1.00	0.55 (0.01, 4.34)	P=1.00
No	3.71 (0.56, 158.43)		1.89 (0.24, 86.35)		1.82 (0.23, 83.61)	
PHQ–2 screen						
Positive screen	0.85 (0.09, 4.20)	P=1.00	0.63 (0.013, 5.65)	P=1.00	1.23 (0.02, 12.45)	P=1.00
Negative screen	1.18 (0.24, 11.48)		1.59 (0.18, 77.39)		0.82 (0.08, 42.04)	
	Median (IQR)	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**	**Median (IQR)**	**Wilcoxon Rank-Sum Test (estimated difference)**
PHQ–9 score						
Cases	9.00 (6.00, 11.25)	0.00 (–5.00, 7.00),	9.00 (5.00, 9.00)	1.00 (–5.00, 7.00),	24.00 (24.00, 24.00)	9.12 (0.00, 17.00),
Controls	9.00 (6.00, 13.00)	P=0.83	9.00 (4.00, 12.00)	P=0.72	12.50 (8.50, 17.75)	P=0.24

Table 1b: (*Continued*).

	Odds ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Depression						
Yes	1.12 (0.42, 2.75)	*P*=0.96	1.17 (0.32, 3.84)	*P*=0.99	1.02 (0.16, 4.48)	*P*=1.00
No	0.89 (0.36, 2.36)		0.85 (0.26, 3.09)		0.98 (0.22, 6.06)	
Psychiatric disorders (Excluding Depression)						
Yes	0.80 (0.27, 2.08)	*P*=0.79	1.02 (0.25, 3.50)	*P*=1.00	0.53 (0.053, 2.69)	*P*=0.51
No	1.25 (0.48, 3.67)		0.98 (0.29, 3.94)		1.90 (0.37, 18.88)	
Family history						
Family history of brain tumors						
Yes	4.59 (0.59, 35.92)	*P*=0.08	9.50 (0.47, 587.07)	*P*=0.09	2.16 (0.04, 44.00)	*P*=0.47
No	0.22 (0.03, 1.70)		0.11 (0.002, 2.14)		0.46 (0.02, 28.64)	
Family history of neurological disease						
Yes	0.29 (0.05, 1.00)	*P*=0.04	0.28 (0.01, 2.09)	*P*=0.29	0.28 (0.03, 1.38)	*P*=0.13
No	3.49 (1.00, 18.87)		3.63 (0.48, 164.72)		3.55 (0.73, 34.61)	
Family history of stroke						
Yes	0.95 (0.22, 3.18)	*P*=1.00	3.15 (0.24, 30.05)	*P*=0.23	0.50 (0.05, 2.56)	*P*=0.51
No	1.05 (0.31, 4.59)		0.32 (0.03, 4.11)		2.00 (0.39, 19.90)	
Family history of cancer						
Yes	1.62 (0.72, 3.79)	*P*=0.28	2.94 (0.87, 11.61)	*P*=0.09	0.90 (0.27, 3.01)	*P*=1.00
No	0.62 (0.26, 1.40)		0.34 (0.09, 1.15)		1.12 (0.33, 3.70)	

IQR: Interquartile range, CI: Confidence interval, PHQ: Patient health questionnaire, AUDIT-C: Alcohol Use Disorders Identification Test-Consumption, DNV: Dizziness, nausea, or vomiting, BMI: Body mass index, Afib: Atrial fibrillation or flutter, CHF: Congestive heart failure, PVD: Peripheral vascular disease, CVR: Cardiac valve replacement, OSA: Obstructive sleep apnea, GERD: Gastroesophageal reflux disease, AUDIT-C: Alcohol Use Disorders Identification Test-Consumption

Table 1c: Sociodemographic characteristics and medical comorbidities of patients with schwannomas, acoustic neuromas, pituitary tumors, and metastatic brain tumors: Crude odds ratios.

	Schwannomas (Entire CNS)		Vestibular Schwannomas		Pituitary Adenomas		Metastases	
	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)
Age								
Cases	51.00 (43.00, 67.25)	6.00 (-3.00, 13.00), *P*=0.17	51.00 (41.50, 69.00)	7.00 (-3.00, 16.00), *P*=0.18	48.00 (36.50, 61.50)	11.00 (-1.00, 20.00), *P*=0.03	72.50 (60.75, 76.50)	12.64 (6.00, 20.00), *P*=0.0001
Controls	56.00 (45.50, 69.75)		60.00 (48.75, 74.25)		60.00 (50.00, 74.25)		57.00 (40.00, 72.00)	
Median household income								
Cases	102242 (84376, 110939)	7701 (0.00, 1.0590), *P*=0.049	98392 (78388, 109524)	5778 (0.00, 11800) *P*=0.15	102242 (81215, 110939)	0.00 (-7701.00, 5778.00), *P*=0.86	102242 (92321, 110939)	14.00 (0.00, 8700), *P*=0.08
Controls	93034 (76654, 102242)		92321 (74170, 102242)		102242 (91938, 110939)		102242 (79653, 110939)	
Overall poverty level in municipality								
Cases	0.056 (0.049, 0.096)	0.00 (-0.008, 0.00), *P*=0.32	0.056 (0.049, 0.11)	0.00 (-0.01, 0.01), *P*=0.63	0.056 (0.049, 0.084)	0.00 (-0.01, 0.01), *P*=0.90	0.06 (0.05, 0.08)	0.00 (-0.07, 0.00), *P*=0.61
Controls	0.056 (0.056, 0.11)		0.064 (0.056, 0.11)		0.056 (0.049, 0.087)		0.06 (0.05, 0.09)	
Poverty level for ages 18–64								
Cases	0.06 (0.05, 0.09)	0.00 (-0.01, 0.01), *P*=0.73	0.06 (0.05, 0.10)	0.00 (-0.01, 0.01), *P*=0.91	0.06 (0.05, 0.09)	0.00 (-0.001, 0.01) *P*=0.49	0.06 (0.05, 0.08)	0.00 (-0.01, 0.00), *P*=0.76
Controls	0.06 (0.05, 0.10)		0.06 (0.05, 0.11)		0.06 (0.05, 0.09)		0.06 (0.05, 0.09)	
Poverty level for ages 65 and older								
Cases	0.04 (0.04, 0.06)	0.00 (1.57 10–5, 0.02), *P*=0.02	0.04 (0.04, 0.08)	0.004 (0.00, 0.02), *P*=0.07	0.04 (0.04, 0.08)	0.00 (-0.003, 0.004), *P*=0.82	0.04 (0.04, 0.04)	0.004 (1.79 10–5, 0.01), *P*=0.01
Controls	0.05 (0.04, 0.09)		0.06 (0.04, 0.10)		0.04 (0.04, 0.06)		0.04 (0.04, 0.07)	
Geographic origin population size								
Cases	51556 (48074, 51601)	90.00 (0.00, 4670), *P*=0.14	51556 (46750, 51601)	90.00 (-90.00, 8023.00), *P*=0.17	51556 (48747, 51601)	0.00 (-90.00, 1677.00), *P*=0.62	51511 (49925, 51601)	0.00 (0.00, 90.00), *P*=0.37
Controls	51511 (28161, 51601)		50741 (25400, 51601)		51511 (41917, 51601)		51511 (31445, 51601)	
	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Sex								
Female	1.71 (0.64, 4.97)	*P*=0.35	1.52 (0.53, 4.63)	*P*=0.53	1.20 (0.42, 3.54)	*P*=0.89	0.55 (0.25, 1.23)	*P*=0.16
Male	0.59 (0.20, 1.57)		0.66 (0.22, 1.88)		0.83 (0.28, 2.36)		1.80 (0.81, 4.042)	
Race								
White	0.59 (0.20, 1.57)	*P*=0.35	0.433 (0.13, 1.30)	*P*=0.16	0.25 (0.06, 0.85)	*P*=0.02	1.03 (0.46, 2.28)	*P*=1.00
Asian	1.24 (0.44, 3.35)	*P*=0.81	1.52 (0.49, 4.48)	*P*=0.56	1.49 (0.45, 4.60)	*P*=0.62	1.23 (0.49, 2.89)	*P*=0.77
NHPI	1.75 (0.54, 5.22)	*P*=0.40	1.81 (0.50, 6.00)	*P*=0.43	3.21 (0.97, 10.35)	*P*=0.048	1.00 (0.33, 2.66)	*P*=1.00
Hispanic	0.18 (0.004, 1.19)	*P*=0.09	0.23 (0.0053, 1.55)	*P*=0.21	0.92 (0.09, 5.02	*P*=1.00	0.24 (0.01, 1.57)	*P*=0.21
Black	8.22 (0.42, 491.45)	*P*=0.10	8.27 (0.42, 495.44)	*P*=0.10			1.34 (0.03, 17.28)	*P*=1.00
NAAN	8.22 (0.42, 491.45)	*P*=0.10	8.27 (0.42, 495.44)	*P*=0.10				
Marital status								
Divorced/Separated	0.53 (0.09, 2.02)	*P*=0.40	0.59 (0.10, 2.35)	*P*=0.56	0.30 (0.0067, 2.28)	*P*=0.46	1.32 (0.30, 4.65)	*P*=0.75
Married	1.48 (0.56, 3.99)	*P*=0.51	1.84 (0.63, 5.53)	*P*=0.31	2.39 (0.84, 7.089)	*P*=0.11	0.83 (0.36, 1.95)	*P*=0.79
Single	0.73 (0.22, 2.13)	*P*=0.70	0.65 (0.17, 2.11)	*P*=0.61	0.36 (0.094, 1.12)	*P*=0.09	0.84 (0.23, 2.51)	*P*=0.94
Widowed	2.84 (0.23, 26.32)	*P*=0.25	1.38 (0.03, 18.24)	*P*=1.00	4.39 (0.55, 35.41)	*P*=0.093	1.35 (0.41, 3.92)	*P*=0.75
Insurance type								
Medicaid	0.95 (0.28, 2.82)	*P*=1.00	1.13 (0.32, 3.56)	*P*=1.00	0.54 (0.14, 1.73)	*P*=0.39	1.83 (0.63, 4.92)	*P*=0.90
Medicare	0.90 (0.27, 2.67)	*P*=1.00	0.75 (0.19, 2.43)	*P*=0.80	1.81 (0.50, 5.98)	*P*=0.43	1.13 (0.50, 2.57)	*P*=0.90
Military	0.40 (0.01, 2.91)	*P*=0.70	0.50 (0.01, 3.92)	*P*=1.00	12.22 (1.82, 138.40)	*P*=0.003	0.50 (0.010, 3.96)	*P*=1.00
Private	1.36 (0.52, 3.61)	*P*=0.63	1.37 (0.47, 3.99)	*P*=0.68	0.45 (0.13, 1.36)	*P*=0.19	0.58 (0.18, 1.57)	*P*=0.36
Income quartiles								
Q1	0.78 (0.23, 2.27)	*P*=0.80	0.90 (0.26, 2.76)	*P*=1.00	1.97 (0.54, 6.57)	*P*=0.35	0.33 (0.060, 1.16)	*P*=0.09
Q2	0.62 (0.17, 1.90)	*P*=0.52	0.70 (0.18, 2.27)	*P*=0.71	0.37 (0.038, 1.74)	*P*=0.24	1.04 (0.35, 2.76)	*P*=1.00
Q3	0.55 (0.16, 1.57)	*P*=0.33	0.46 (0.10, 1.56)	*P*=0.20	0.63 (0.14, 2.20)	*P*=0.58	1.12 (0.44, 2.68)	*P*=0.96
Q4	5.49 (1.67, 18.27)	*P*=0.002	5.29 (1.37, 20.69)	*P*=0.01	1.45 (0.50, 4.15)	*P*=0.59	1.59 (0.69, 3.62)	*P*=1.00
Geographic origin								
Urban	2.22 (0.81, 6.82)	*P*=0.14	2.13 (0.73, 6.80)	*P*=0.20	1.35 (0.46, 4.32)	*P*=0.73	2.06 (0.86, 5.36)	*P*=0.12
Suburban	0.47 (0.15, 1.29)	*P*=0.17	0.49 (0.15, 1.43)	*P*=0.23	0.78 (0.24, 2.29)	*P*=0.80	0.50 (0.19, 1.20)	*P*=0.14
Rural	1.97 (0.03, 38.57)	*P*=0.50	1.97 (0.03, 38.61)	*P*=0.50	1.97 (0.03, 38.61)	*P*=0.50	2.04 (0.03, 39.66)	*P*=0.48
Presenting symptoms								
Headache								
Yes	0.76 (0.23, 2.35)	*P*=0.78	0.69 (0.17, 2.51)	*P*=0.73	2.15 (0.69, 7.57)	*P*=0.23	1.25 (0.46, 3.28)	*P*=0.78
No	1.32 (0.43, 4.34)		1.46 (0.40, 6.01)		0.46 (0.13, 1.46)		0.80 (0.30, 2.17)	
DNV								
Yes	2.28 (0.72, 8.00)	*P*=0.19	2.20 (0.60, 9.07)	*P*=0.29	0.95 (0.29, 2.95)	*P*=1.00	0.85 (0.28, 2.34)	*P*=0.91
No	0.44 (0.13, 1.38)		0.45 (0.11, 1.66)		1.047 (0.34, 3.47)		1.18 (0.43, 3.62)	
Cognitive difficulty								
Yes	0.67 (0.15, 2.35)	*P*=0.58	0.68 (0.11, 2.88)	*P*=0.75	1.73 (0.42, 6.14)	*P*=0.54	1.33 (0.48, 3.50)	*P*=0.68
No	1.50 (0.43, 6.77)		1.47 (0.35, 8.91)		0.58 (0.16, 2.37)		0.75 (0.29, 2.08)	
Gait/coordination disorder								
Yes	0.68 (0.19, 2.15)	*P*=0.65	0.51 (0.11, 1.92)	*P*=0.38	0.78 (0.22, 2.47)	*P*=0.84	1.96 (0.78, 5.15)	*P*=0.17
No	1.46 (0.46, 5.13)		1.98 (0.52, 9.31)		1.28 (0.40, 4.53)		0.51 (0.19, 1.28)	
Seizures/epilepsy								
Yes	0.28 (0.01, 2.05)	*P*=0.30	0.35 (0.01, 2.66)	*P*=0.46	0.62 (0.06, 3.10)	*P*=0.79	3.68 (1.25, 10.50)	*P*=0.01
No	3.53 (0.49, 156.75)		2.87 (0.38, 130.27)		1.62 (0.32, 16.06)		0.27 (0.10, 0.80)	
Sleep disturbances								
Yes	1.23 (0.47, 3.28)	*P*=0.80	1.04 (0.37, 3.01)	*P*=1.00	0.88 (0.30, 2.49)	*P*=0.97	0.68 (0.23, 1.92)	*P*=0.57
No	0.81 (0.30, 2.11)		1.04 (0.37, 3.01)		1.14 (0.40, 3.31)		1.47 (0.52, 4.40)	
Medical comorbidities/conditions								
	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank-Sum Test (estimated difference)
BMI (kg/m²)								
Cases	25.91 (22.07, 29.64)	0.86 (-1.76, 3.69), *P*=0.55	25.91 (22.41, 29.83)	0.75 (-2.21, 3.91), *P*=0.61	29.43 (25.90, 31.73)	3.31 (0.25, 6.02), *P*=0.03	26.54 (22.85, 28.89)	1.04 (-1.57, 4.21), *P*=0.44
Controls	26.88 (22.88, 33.30)		27.10 (22.75, 33.48)		25.46 (21.92, 30.17)		26.77 (23.48, 31.77)	
	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Weight class								
Underweight	1.00 (0.02, 10.70)	*P*=1.00	1.00 (0.02, 10.82)	*P*=1.00	0.37 (0.01, 2.72)	*P*=0.47	1.79 (0.03, 19.40)	*P*=0.49
Normal	1.27 (0.48, 3.32)	*P*=0.75	1.27 (0.43, 3.64)	*P*=0.80	0.33 (0.07, 1.11)	*P*=0.08	0.63 (0.17, 1.96)	*P*=0.54
Preobesity	1.37 (0.48, 3.69)	*P*=0.66	1.24 (0.38, 3.74)	*P*=0.87	1.47 (0.47, 4.35)	*P*=0.61	2.98 (1.04, 9.02)	*P*=0.04
Obesity Class 1	0.91 (0.15, 3.73)	*P*=1.00	1.00 (0.16, 4.25)	*P*=1.00	5.16 (1.33, 20.19)	*P*=0.01	0.30 (0.01, 2.12)	*P*=0.31
Obesity Class 2	0.28 (0.01, 2.06)	*P*=0.30	0.34 (0.01, 2.56)	*P*=0.45	2.09 (0.31, 10.89)	*P*=0.38	0.52 (0.01, 3.86)	*P*=1.00
Obesity Class 3	0.56 (0.012, 4.67)	*P*=1.00	0.65 (0.014, 5.85)	*P*=1.00	0.20 (0.0046, 1.31)	*P*=0.13	0.48 (0.011, 3.32)	*P*=0.70
Type 2 diabetes mellitus								
Yes	1.56 (0.25, 7.17)	*P*=0.46	1.57 (0.25, 7.38)	*P*=0.46	1.08 (0.18, 4.66)	*P*=1.00	0.82 (0.25, 2.28)	*P*=0.87
No	0.64 (0.14, 4.04)		0.64 (0.14, 4.07)		0.93 (0.21, 5.70)		1.22 (0.44, 3.96)	
Hypertension								
Yes	1.93 (0.75, 5.10)	*P*=0.20	1.89 (0.67, 5.49)	*P*=0.27	1.55 (0.54, 4.44)	*P*=0.49	0.75 (0.32, 1.82)	*P*=0.62
No	0.52 (0.20, 1.34)		0.53 (0.18, 1.50)		0.64 (0.22, 1.84)		1.33 (0.55, 3.14)	
Coronary artery disease/prior myocardial infarction								
Yes	1.00 (0.09, 51.19)	*P*=1.00	1.16 (0.11, 6.73)	*P*=1.00	1.63 (0.15, 10.90)	*P*=0.63	0.56 (0.06, 2.63)	*P*=0.74
No	1.00 (0.18, 10.27)		0.87 (0.15, 9.16)		0.61 (0.09, 6.88)		1.78 (0.38, 16.89)	
PVD								
Yes	1.00 (0.02, 10.70)	*P*=1.00	1.35 (0.03, 17.75)	*P*=1.00	4.02 (0.05, 324.19)	*P*=0.36	2.27 (0.20, 16.69)	*P*=0.31
No	1.00 (0.09, 51.19)		0.74 (0.06, 40.74)		0.25 (0.003, 20.073)		0.44 (0.06, 5.08)	
Stroke								
Yes	0.38 (0.01, 2.89)	*P*=0.69	0.42 (0.01, 3.35)	*P*=0.68	0.33 (0.01, 2.53)	*P*=0.45	1.57 (0.55, 4.17)	*P*=0.46
No	2.64 (0.35, 119.91)		2.38 (0.30, 109.74)		3.017 (0.40, 136.89)		0.64 (0.24, 1.83)	
Atrial fibrillation/atrial flutter								
Yes	2.03 (0.03, 40.39)	*P*=0.49	2.03 (0.03, 40.78)	*P*=0.49	0.47 (0.01, 3.69)	*P*=0.69	0.72 (0.07, 3.49)	*P*=1.00
No	0.49 (0.03, 30.07)		0.49 (0.03, 30.17)		2.11 (0.27, 96.17)		1.39, (0.29, 13.47)	
CHF								
Yes	1.97 (0.03, 38.61)	*P*=0.50	1.97 (0.03, 38.61)	*P*=0.50	0.97 (0.02, 10.08)	*P*=1.00	1.22 (0.21, 5.03)	*P*=0.73
No	0.51 (0.03, 30.35)		0.51 (0.03, 30.51)		1.04 (0.10, 52.13)		0.82 (0.20, 4.86)	
CVR								
Yes	4.06 (0.05, 325.55)	*P*=0.36	4.07 (0.05, 327.90)	*P*=0.36	3.92 (0.05, 311.34)	*P*=0.37	9.01 (0.46, 536.51)	*P*=0.09
No	0.25 (0.003, 19.81)		0.25 (0.003, 19.84)		0.25 (0.003, 20.30)		0.11 (0.002, 2.16)	
History of head trauma								
Yes	0.35 (0.04, 1.59)	*P*=0.24	0.32 (0.03, 1.52)	*P*=0.15	0.55 (0.01, 4.71)	*P*=1.00	0.23 (0.01, 1.57)	*P*=0.20
No	2.89 (0.63, 27.26)		3.14 (0.66, 30.17)		1.81 (0.21, 85.60)		4.36 (0.64, 188.85)	
History of cancer								
Yes	1.77 (0.50, 5.62)	*P*=0.44	0.64 (0.064, 3.23)	*P*=0.73	0.99 (0.095, 5.51)	*P*=1.00	281.60 (47.01, 10686.82)	*P*<0.001
No	0.56 (0.18, 2.00)		1.57 (0.31, 15.61)		1.012 (0.18, 10.52)		0.004 (9.36 10–5, 0.02)	
Obstructive sleep apnea								
Yes	1.27 (0.28, 4.66)	*P*=0.75	1.55 (0.32, 6.05)	*P*=0.50	1.53 (0.32, 5.97)	*P*=0.50	0.70 (0.07, 3.40)	*P*=1.00
No	0.79 (0.21, 3.64)		0.65 (0.17, 3.10)		0.65 (0.17, 3.14)		1.43 (0.29, 13.79)	
Asthma/chronic obstructive pulmonary disease								
Yes	0.40 (0.04, 1.87)	*P*=0.36	0.23 (0.01, 1.70)	*P*=0.19	1.53 (0.38, 5.33)	*P*=0.68	3.39 (1.27, 8.85)	*P*=0.01
No	2.50 (0.53, 23.71)		4.28 (0.59, 190.03)		0.65 (0.19, 2.64)		0.29 (0.11, 0.79)	
GERD								
Yes	0.14 (0.003, 0.86)	*P*=0.02	0.14 (0.003, 0.94)	*P*=0.03	0.23 (0.01, 1.53)	*P*=0.21	0.95 (0.09, 4.91)	*P*=1.00
No	7.40 (1.16, 309.94)		6.91 (1.06, 291.75)		4.44 (0.65, 190.89)		1.06 (0.20, 10.53)	
Diverticular disease								
Yes	8.22 (0.42, 491.45)	*P*=0.10	8.27 (0.42, 495.44)	*P*=0.10	4.17 (0.29, 60.87)	*P*=0.18	0.70 (0.01, 6.13)	*P*=1.00
No	0.12 (0.002, 2.38)		0.00 (0.00, 9.75)		0.24 (0.02, 3.49)		1.42 (0.16, 67.42)	
Autoimmune disease								
Yes	0.66 (0.01, 5.79)	*P*=1.00	1.00 (0.02, 10.82)	*P*=1.00	2.01 (0.03, 40.31)	*P*=0.50	1.75 (0.16, 11.30)	*P*=0.62
No	1.53 (0.17, 73.16)		1.00 (0.09, 51.56)		0.50 (0.03, 30.53)		0.57 (0.09, 6.27)	
Thyroid disease								
Yes	0.50 (0.05, 2.38)	*P*=0.52	0.64 (0.06, 3.23)	*P*=0.73	2.18 (0.43, 9.27)	*P*=0.26	0.49 (0.09, 1.78)	*P*=0.42
No	2.01 (0.42, 19.36)		1.57 (0.31, 15.61)		0.46 (0.11, 2.32)		2.04 (0.56, 11.31)	
Glaucoma								
Yes	17.07 (1.64, 853.14)	*P*=0.01	8.27 (0.42, 495.44)	*P*=0.10	1.95 (0.03, 38.25)	*P*=0.50	0.70 (0.01, 6.13)	*P*=1.00
No	0.06 (0.001, 0.61)		0.12 (0.002, 2.37)		0.51 (0.03, 30.86)		1.42 (0.16, 67.42)	
Neurofibromatosis type 2								
Yes	8.22 (0.42, 491.45)	*P*=0.10	8.27 (0.42, 495.44)	*P*=0.10				
No	0.12 (0.00, 2.38)		0.12 (0.00, 2.37)					
Social history and psychiatric risk factors								
Smoking status								
Never smoker	0.82 (0.31, 2.19)	*P*=0.82	1.10 (0.38, 3.37)	*P*=1.00	1.41 (0.48, 4.53)	*P*=0.66	0.21 (0.07, 0.55)	*P*=0.001
Former smoker	1.00 (0.29, 2.98)	*P*=1.00	1.00 (0.26, 3.31)	*P*=1.00	1.07 (0.27, 3.55)	*P*=1.00	1.25 (0.56, 3.10)	*P*=0.03
Current smoker	1.41 (0.36, 4.70)	*P*=0.76	0.84 (0.14, 3.45)	*P*=1.00	0.45 (0.05, 2.20)	*P*=0.52	2.94 (0.90, 8.99)	*P*=0.06
Alcohol use screen (AUDIT–C)								
Positive screen	5.02 (1.34, 19.01)	*P*=0.01	6.08 (1.37, 28.59)	*P*=0.01	1.55 (0.24, 7.29)	*P*=0.69	0.25 (0.01, 1.61)	*P*=0.22
Negative screen	0.20 (0.05, 0.75)		0.16 (0.04, 0.73)		0.64 (0.14, 4.12)		4.02 (0.62, 169.60)	
Alcohol use disorder								
Yes	0.38 (0.01, 2.79)	*P*=0.70	0.48 (0.01, 3.73)	*P*=0.69	0.78 (0.02, 7.55)	*P*=1.00	5.27 (1.24, 22.42)	*P*=0.01
No	2.62 (0.36, 116.08)		2.09 (0.27, 95.02)		1.28 (0.13, 63.39)		0.19 (0.05, 0.81)	
PHQ–2 screen								
Positive screen	0.43 (0.01, 3.31)	*P*=0.69	0.38 (0.01, 2.95)	*P*=0.69	0.80 (0.02, 7.50)	*P*=1.00	0.64 (0.01, 4.60)	*P*=1.00
Negative screen	2.35 (0.30, 106.87)		2.66 (0.34, 121.05)		1.25 (0.13, 62.25)		1.55 (0.22, 68.34)	
	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)	Median (IQR)	Wilcoxon Rank Sum Test (estimated difference)
PHQ–9 score								
Cases					13.00 (9.75, 15.50)	1.00 (-5.00, 7.00), *P*=0.65	13.50 (12.75, 14.25)	2.00 (-8.00, 12.00), *P*=0.64
Controls					11.50 (8.00, 18.25)		11.00 (6.00, 16.00)	
	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test	Odds Ratio (95% CI)	Chi-square/Fisher Exact Test
Depression								
Yes	0.26 (0.03, 1.17)	*P*=0.07	0.13 (0.003, 0.92)	*P*=0.02	2.01 (0.65, 6.01)	*P*=0.25	0.37 (0.07, 1.35)	*P*=0.13
No	3.86 (0.85, 36.07)		7.57 (1.09, 330.14)		0.50 (0.17, 1.53)		2.69 (0.74, 14.91)	
Psychiatric disorders (Excluding Depression)								
Yes	0.20 (0.02, 0.88)	*P*=0.02	0.09 (0.002, 0.64)	*P*=0.01	4.22 (1.29, 16.40)	*P*=0.01	0.31 (0.03, 1.36)	*P*=0.17
No	5.048 (1.13, 46.71)		10.71 (1.57, 462.94)		0.24 (0.061, 0.78)		3.25 (0.73, 30.00)	
Family history								
Family history of brain tumors								
Yes	2.01 (0.03, 40.00)	*P*=0.49	0.97 (0.02, 10.08)	*P*=1.00	1.87 (0.03, 36.82)	*P*=0.51	11.58 (0.58, 704.03)	*P*=0.06
No	0.50 (0.03, 30.36)		1.04 (0.10, 52.13)		0.53 (0.03, 32.10)		0.09 (0.001, 1.73)	
Family history of neurological disease								
Yes	1.38 (0.46, 3.86)	*P*=0.67	1.30 (0.39, 3.92)	*P*=0.81	0.13 (0.003, 0.88)	*P*=0.02	0.22 (0.01, 1.47)	*P*=0.15
No	0.72 (0.26, 2.16)		0.77 (0.26, 2.53)		7.96 (1.13, 348.25)		4.41 (0.68, 185.95)	
Family history of stroke								
Yes	2.77 (0.81, 8.88)	*P*=0.10	1.83 (0.44, 6.56)	*P*=0.48	1.47 (0.30, 5.80)	*P*=0.51	0.95 (0.21, 3.28)	*P*=1.00
No	0.36 (0.11, 1.23)		0.55 (0.15, 2.25)		0.68 (0.17, 3.29)		1.05 (0.30, 4.67)	
Family history of cancer								
Yes	2.16 (0.83, 5.71)	*P*=0.12	3.84 (1.32, 11.92)	*P*=0.01	0.56 (0.18, 1.65)	*P*=0.35	0.87 (0.32, 2.44)	*P*=0.95
No	0.46 (0.18, 1.21)		0.79 (0.27, 2.44)		1.79 (0.61, 5.56)		1.15 (0.41, 3.14)	

IQR: Interquartile range, CI: Confidence interval, PHQ: Patient health questionnaire, AUDIT-C: Alcohol Use Disorders Identification Test-Consumption, DNV: Dizziness, nausea, or vomiting, BMI: Body mass index, Afib: Atrial fibrillation or flutter, CHF: Congestive heart failure, PVD: Peripheral vascular disease, CVR: Cardiac valve replacement, OSA: Obstructive sleep apnea, GERD: Gastroesophageal reflux disease, AUDIT-C: Alcohol Use Disorders Identification Test-Consumption

Table 2: Tumor size at time of diagnosis in relation to patient race.

Median (25% quartile, 75% quartile)		Wilcoxon rank sum test (estimated difference)		
Benign meningiomas: Tumor volume (mm^3)				
		White	**Asian**	**NHPI**
White	2139.42 (807.78, 3482.46)		2563.92 (−404.22, 8662.42), *P*=0.12	3171.18 (3.67, 15286.99), *P*=0.049
Asian	5564.60 (954.60, 23141.50)			541.74 (−5398.83, 7740.88), *P*=0.70
NHPI	5921.90 (1508.00, 19352.20)			
Hispanic	5686.30 (2931.10, 8441.50)	NA	NA	NA
All gliomas: Largest tumor dimension (mm)				
		White	**Asian**	**NHPI**
White	40.00 (28.00, 50.50)		8.00 (95% CI: −14.00, 26.00, *P*=0.29)	22.00 (95% CI: 1.00, 40.00, *P*=0.04)
Asian	25.0 (20.0, 46.0)			31.00 (95% CI: 2.00, 54.00, *P*=0.02)
NHPI	61.00 (52.75, 68.50)			
Vestibular schwannomas: Largest tumor dimension (mm)				
		White	**Asian**	**NHPI**
White	5.00 (4.00, 6.50)		NA	NA
Asian	9.00 (4.00, 14.50)			14.00 (95% CI: 1.00, 26.00, *P*=0.048)
NHPI	20.00 (18.00, 32.00)			

CI: Confidence interval, NHPI: Native Hawaiians and Pacific Islanders, NA: Not applicable.

(9.80, 95% CI: 1.88, 51.06; *P* = 0.007), positive alcohol use screen (5.65, 95% CI: 2.38, 13.39; p < 0.001), history of stroke (3.05, 95% CI: 1.31, 7.08; *P* = 0.009) or neoplasm (2.26, 95% CI: 1.06, 4.81; *P* = 0.035), and family history of brain tumors (9.27, 95% CI: 1.84, 46.61; *P* = 0.007). In a best-fit model for malignant meningiomas, a presentation with seizures (8.25, 95% CI: 2.49, 27.33; *P* < 0.001) and a history of neoplasm (3.94, 95% CI: 1.12, 13.86; *P* = 0.03) were the strongest predictors of diagnosis.

Tumor size

When tumor size was examined using three-dimensional and two-dimensional volumes, NHPI (3171.18 mm^3, 95% CI: 3.67, 15286.99; *P* = 0.049) and Asian (219.00 mm^3, 95% CI: 12.00, 668.00; *P* = 0.033) patients were found to have larger benign meningioma volumes at the time of diagnosis compared to Whites [Table 2].

Gliomas

Of the 39 gliomas comprising the cohort, 51.3% were WHO Grades I–III gliomas (non-glioblastoma multiforme [GBM], *n* = 20) [Table 1b], and 48.7% were WHO Grade IV gliomas (GBM, *n* = 19). The median age of diagnosis for non-GBM patients was 47.5 years (interquartile range [IQR]: 31.5, 62.0), 12 years younger (95% CI: 2.00, 22.00; *P* = 0.02) than that of controls, while the median age for GBM patients was 59.0 years (IQR: 50.0, 70.5), similar to that of controls. No differences in sex were observed. Overall, Asian patients had significantly reduced odds of being diagnosed with glioma (odds ratio [OR]: 0.35, 95% CI: 0.13, 0.96; *P* = 0.035), while for GBM specifically, Whites had a 6.59 fold increased odds of being diagnosed (95% CI: 1.83, 30.31; *P* = 0.001).

Seizures (non-GBM, OR: 16.8, 95% CI: 4.88–57.8, *P* < 0.001; GBM, OR: 6.86, 95% CI: 2.14–22.0, *P* = 0.001) and cognitive difficulties (non-GBM, OR: 7.94, 95% CI: 2.54–24.9, *P* < 0.001; GBM, OR: 4.14, 95% CI: 1.25–13.7, *P* = 0.020) were the most common presenting symptoms for all gliomas. Meanwhile, glioma patients had significantly reduced odds of presenting with DNV (non-GBM, 0.08, 95% CI: 0.01–0.64, *P* = 0.02; GBM, 0.12, 95% CI: 0.02–0.99; *P* = 0.049) or sleep disturbances (0.38, 95% CI: 0.15, 0.99; *P* = 0.048).

Glioma patients were also found to have increased odds of class III obesity (OR: 49.68, 95% CI: 1.59, 1550; *P* = 0.03), as well as a family history of cancer (OR: 22.6, 95% CI: 2.40, 213; *P* = 0.006). In multivariable analysis, the best predictor of glioma diagnosis was cognitive difficulty (non-GBM, OR: 13300, 95% CI: 5.98–2.94×10^7, *P* = 0.02; GBM, OR: 61.7, 95% CI: 2.31–1650, *P* = 0.01).

Tumor size

NHPI patients had significantly larger tumor dimensions compared to White (22.00 mm, 95% CI: 1.00, 40.00, *P* = 0.04) and Asian (31.00 mm, 95% CI: 2.00, 54.00, *P* = 0.02) patients [Table 2].

Schwannomas

In the cohort, 8.0% of the cases (*n* = 26) cases were schwannomas, of which 84.6% were vestibular schwannomas (*n* = 22) [Table 1c]. The median age at diagnosis was 51.0 years old (IQR: 41.5, 69.0).

Table 3: Summary of associated variables stratified by tumor type.

	Benign meningiomas	Malignant meningiomas	Gliomas overall	Grade I–-II gliomas	Grade IV gliomas	Schwannomas overall	Vestibular schwannomas	Pituitary adenomas	Intracranial metastases
Socioeconomic status		Higher household income Living in municipality with lower poverty level for ages 65 and older Reduced odds among lowest income quartile				Higher household income Living in municipality with lower poverty level for ages 65 and older Highest income quartile	Highest income quartile		Living in municipality with lower poverty level for ages 65 and older
Geographic residence		Urban Reduced odds of suburban residence							
Patient sex	Females	No sex predisposition							
Race	Native American or Alaskan native		White Reduced odds among Asian		White			Native Hawaiian or pacific islander Reduced odds among whites	
Insurance type	Medicare Reduced odds of private insurance		Medicare					Military insurance	
Marital status			Married						
Presenting symptoms	Seizures	Seizures Cognitive difficulty	Seizures Cognitive difficulty Dizziness/nausea/vomiting	Seizures Cognitive difficulty Dizziness/nausea/vomiting	Seizures Cognitive difficulty Dizziness/nausea/vomiting		Dizziness/nausea/vomiting		Seizures
Medical comorbidities	Obesity class i Hypertension History of cancer	Underweight Reduced odds of head trauma History of cancer	Obesity class iii		Preobesity Reduced odds of asthma/COPD	Glaucoma	Reduced odds of GERD	Obesity class i Higher BMI Reduced odds of GERD	Preobesity Asthma/COPD History of cancer
Psychiatric and social history	Positive AUDIT-C					Positive AUDIT-C Reduced odds of psychiatric disorders	Positive AUDIT-C Reduced odds of psychiatric disorders Reduced odds of depression	Psychiatric disorders	Alcohol use disorder Former smoker Reduced odds of never smoking
Family history	Family history of brain tumors		Family history of cancer				Family history of cancer		

COPD: Chronic obstructive pulmonary disease, AUDIT-C: Alcohol Use Disorders Identification Test-Consumption, GERD: Gastroesophageal reflux disease, BMI: Body mass index

Patients with schwannomas had significantly increased odds of being in the highest income quartile (5.49, 95% CI: 1.67, 18.27, $P = 0.002$) and from municipalities with a lower proportion of the populace below the poverty line (0.00, 95% CI: 1.57×10^{-5}, 0.02; $P = 0.02$).

Patients with schwannomas had increased odds of glaucoma (17.07, 95% CI: 1.64, 853.14, $P = 0.006$), while vestibular schwannomas specifically had increased odds of having a positive alcohol screen (6.23, 95% CI: 1.69, 22.88, $P = 0.006$) and family history of cancer (3.89, 95% CI: 1.46, 10.36, $P = 0.007$). Patients with vestibular schwannomas also had decreased odds of depression/dysthymic disorder (0.13, 95% CI: 0.02, 1.03, $P = 0.05$) and other psychiatric disorders (0.09, 95% CI: 0.01, 0.72, $P = 0.023$). Meanwhile, vestibular schwannoma patients exhibited decreased odds of gastroesophageal reflux disease (GERD) (0.14, 95% CI: 0.0034, 0.94, $P = 0.03$).

On conducting multivariable analysis, the following variables were identified as the best predictors of vestibular schwannoma diagnosis, including being from the highest income quartile (24.88, 95% CI: 2.14, 289.14; $P = 0.01$), presenting with DNV (5.75, 95% CI: 1.13, 29.23; $P = 0.04$), and having a family history of cancer (14.66, 95% CI: 2.25, 95.30; $P = 0.005$).

Tumor size

NHPI patients exhibited significantly larger tumor size at the time of diagnosis (14.00, 95% CI: 1.00, 26.00, $P = 0.048$) compared to Asians.

Pituitary adenomas

About 6.8% of the cohort ($n = 22$) had pituitary adenomas, with a median age at diagnosis at 48 years (IQR: 36.50, 61.50), 11.0 years younger than controls (95% CI: 1.00, 20.00; $P = 0.03$) and no sex predisposition [Table 1c]. Whites demonstrated a reduced odds of diagnosis (0.25, 95% CI: 0.056, 0.85, $P = 0.02$), while NHPI had a 3.21 fold increased odds (95% CI: 0.97, 10.35, $P = 0.048$). Furthermore, patients with military insurance demonstrated a 12.22 fold increased odds of diagnosis (95% CI: 1.82, 138.40, $P = 0.003$).

Pituitary adenoma patients at diagnosis had a significantly higher median BMI, by 3.31 kg/m^2 (95% CI: 0.25, 6.02; $P = 0.03$), with obesity class I resulting in a 5.16 fold (95% CI: 1.33, 20.19; $P = 0.01$) greater odds of diagnosis. Meanwhile, having a history of psychiatric disorder (excluding depression) increased the odds of a pituitary adenoma diagnosis by 4.22 fold (95% CI: 1.29, 16.40; $P = 0.01$).

Intracranial metastases

In the tumor cohort, there were 36 patients (11.1%) with intracranial metastases [Table 1c]. Median age at diagnosis was 72.5 years (IQR: 60.75, 76.50), 12.64 years older than controls (95% CI: 6.00, 20.00; $P = 0.0001$). Patients with metastases were more likely to come from municipalities with a lower proportion of the population aged 65 and older living below the poverty line (0.004, 95% CI: 1.79×10^{-5}, 0.01; $P = 0.01$). The most common presenting symptom was seizures (3.72, 95% CI: 1.44, 9.64; $P = 0.007$). Patients were also more likely to have asthma or COPD (3.42, 95% CI: 1.42, 8.21; $P = 0.006$), to be former (4.45, 95% CI: 1.67, 11.87; $P = 0.0030$) or current smokers (5.54, 95% CI: 1.75, 17.52; $P = 0.004$), alcohol use disorder (5.27, 95% CI: 1.24, 22.42; $P = 0.025$), and family history of brain tumors (11.90, 95% CI: 1.03, 137.21; $P = 0.05$). The strongest predictors of intracranial metastases from diagnosis from multivariable analysis included the presenting symptom of seizures (5.23, 95% CI: 1.56, 17.50; $P = 0.007$), being a current smoker (12.28, 95% CI: 1.78, 84.51; $P = 0.01$), and having a family history of brain tumors (36.53, 95% CI: 1.90, 730.90; $P = 0.02$).

Tumor size

Although not statistically significant, Asian patients had significantly larger tumor sizes compared to NHPI ($P = 0.05$) [Table 2].

DISCUSSION

Age and sex

Of the 323 tumors in the cohort, 49.2% were meningiomas (39.9% benign and 9.3% malignant), 12.1% gliomas (6.2% Grades I–III and 5.9% Grade IV), 11.1% intracranial metastases, 8.0% schwannomas (6.8% vestibular schwannomas), and 6.8% pituitary adenomas. These trends overall parallel those from the Central Brain Tumor Registry of the United States (CBTRUS), where meningiomas and gliomas were the most common primary intracranial lesions.[64]

The youngest age of diagnosis was among Grades I–III gliomas at 47.5 years (IQR: 31.5, 62.0), followed by pituitary adenomas at 48.0 (36.5, 61.5), vestibular schwannomas at 51.0 (41.5, 69.0), Grade IV gliomas at 59.0 (50.0, 70.5), benign meningiomas at 61.0 (50.0, 71.0), malignant meningiomas at 66.5 (49.0, 76.0), and metastases at 72.5 (60.8, 76.5). Although gliomas, schwannomas, meningiomas, and metastases had similar values to that of national datasets, the age of diagnosis for pituitary adenomas was younger than expected.[35,37,65,73] The discrepancy may reflect Hawaii's smaller Black population, who are suspected to have an older age at diagnosis for pituitary tumors.[55]

Similar to the CBTRUS results, which found a 1.25 fold higher incidence rate of primary central nervous system tumors in females (26.31/100,000; males: 21.09/100,000), females in our Hawaiian cohort had a 1.44-fold higher odds of tumor diagnosis.[65] On tumor stratification, the female predisposition in our cohort was observed only in benign meningiomas; no other tumors exhibited a male or female predilection, in contrast to some cohorts that found an increased risk of high-grade gliomas in males.[36,65,69,79]

Race/ethnicity

Collectively, Hispanic/Latino patients in Hawaii exhibited a significantly lower likelihood of primary intracranial tumor diagnosis than non-Hispanic patients, similar to observations in CBTRUS.[65] While no clear rationale exists for this disparity, some have suggested differences in inherited risk, although given the known socioeconomic barriers (i.e., language, health literacy, acculturation, and income) that Hispanics face, reduced access to healthcare may contribute in part.[30,66]

In contrast to national datasets where NAAN had the lowest incidence rates of meningioma, NAAN in Hawaii had a 12.26 fold greater odds of benign meningioma diagnosis.[37,65,86] When examining non-central nervous system cancers, NAAN typically has among the highest incidence rates; thus, the discrepancy in Hawaii for benign meningiomas may represent the improved access to health care among the indigenous population – compared to other states, Hawaii has historically had lower uninsured rates, with higher rates of cancer screening and preventive care visits.[13,57,71,86]

For pituitary adenomas, NHPI had the highest odds of diagnosis at 3.21 (1.03, 10.35), followed by Asians at 1.49 (0.45, 4.60), Hispanics at 0.92 (0.09, 5.02) and Whites at 0.25 (0.06, 0.85); these trends parallel a previous nationwide study that found the highest incidence among Asians and Pacific Islanders, and the lowest among Whites.[35] Similar to NAAN, while improved access to health care in Hawaii for indigenous populations may contribute to the greater likelihood of NHPI diagnoses, pituitary adenomas are associated with the risk factor of obesity, which is itself prevalent in the NHPI population.[7,88]

Finally, the observation of higher rates of glioma diagnosis among Whites persisted in Hawaii, with the additional finding that Asians had significantly reduced odds of glioma diagnosis.[29,66,74,87] Given that genome-wide association studies have identified several susceptibility loci for glioma, with literature supporting unique genetic pathways for glioma tumorigenesis, the higher odds among Whites and lower odds among Asians may be due in part to genetic predisposition.[22,28,58,78,94]

Socioeconomic variables

Of the tumors investigated, malignant meningiomas, schwannomas, pituitary adenomas, and intracranial metastases exhibited unique socioeconomic associations. Malignant meningiomas, schwannomas, and metastases were all more likely to be diagnosed in patients from households with greater median income, higher income quartiles, or municipalities with less poverty. For meningiomas, prior literature is inconclusive regarding the role of socioeconomic status: one investigation from Sweden found an increased incidence of meningiomas in women with higher socioeconomic status, while a second Swedish investigation found no association.[60,90] Schwannomas have also been associated with higher socioeconomic status in both Denmark and the continental United States.[26,45,77] Overall, the lower odds of intracranial tumors among patients with lower socioeconomic status are likely to result from disparities in healthcare access, in turn contributing to underdiagnosis.[26,52] While geographic origin from an urban environment was significantly associated with greater odds of malignant meningioma diagnosis, a prior study focusing exclusively on spinal meningiomas found a higher incidence among patients from rural communities – suggesting likely different risk factors between cerebral and spinal meningiomas.[36,37]

The increased odds of brain tumors overall among Medicare patients may be due to an older age of diagnosis for brain tumors.[61] Only for pituitary adenomas were there increased odds of diagnosis among those with military insurance. This association may be due to mandatory visual-optical readiness testing of military personnel, which would likely allow for earlier detection of visual field deficits from pituitary adenomas.[18,84]

Furthermore, among gliomas, the odds of diagnosis were significantly higher among married patients, likely yielding from spouses more likely to appreciate cognitive changes in a patient.[48]

Presenting symptoms

In the overall brain tumor cohort, seizures were the most common presenting symptom, a finding consistent with prior studies.[3,5] When stratified by tumor type, seizures were the most common in benign meningiomas, all types of gliomas, and metastases. Cognitive difficulty was more commonly observed among malignant meningiomas and gliomas, likely arising from the infiltrative nature of such tumors.[17,31] The inclusion of cognitive difficulty, with seizures, as a common presenting symptom distinguishing malignant from benign meningiomas, could aid in narrowing the differential before histopathologic diagnosis. Vestibular schwannomas were the only tumor type within our cohort that presented with increased odds of dizziness, nausea, and vomiting; while consistent with the literature, progressive/sudden onset hearing loss was reported as more common, although the proportion of patients presenting with hearing loss as the most common presenting symptom has decreased over time.[33,54,89]

Medical comorbidities

In the entire cohort, brain tumors overall were associated with decreased odds of GERD and increased odds of hypertension, traumatic brain injury, obesity, diverticular disease, and a prior history of cancer. However, after multivariable analysis, only the association with obesity and prior history of cancer remained significant among the general cohort.

On stratification, benign meningiomas exhibited a positive association with hypertension and obesity, findings consistent with another study in a multiethnic cohort, potentially linking metabolic syndrome with an increased risk of meningioma.[59] Yet, the relationship inverted for malignant meningiomas, where patients were more likely to be underweight, likely representing cachexia. Obesity and pre-obesity were also found to be associated with gliomas, pituitary adenomas, and metastases, with clinical observations consistent with data suggesting that adipocyte cytokines may promote tumor growth.[1,4,6,75]

Asthma was associated with reduced odds of glioblastoma diagnosis, a trend paralleling that of pediatric brain tumors, where T-cell mediated disorders result in reduced tumor frequency.[21,41,44,83,91] The protective mechanism of asthma is suspected to be secondary to T-cell decorin-mediated microglial inhibition, which ultimately reduces glioma formation.[21]

The increased odds of glaucoma among schwannomas overall, as well as reduced odds of GERD among vestibular schwannomas and pituitary adenomas, have not been described in the literature. Of note, sensorineural hearing loss has been linked to an increased incidence of glaucoma; however, the etiology of the association remains unelucidated, and a link with schwannomas is unclear.

Psychiatric risk factors and social history

Our cohort did exhibit a correlation between a positive AUDIT-C screen with intracranial tumor diagnosis, contrary to prior studies that found no association between alcohol consumption and brain tumor risk.[9,11,25,34,76] A link with positive AUDIT-C was found in benign meningiomas and vestibular schwannomas, with alcohol use disorder being more likely in those with intracranial metastases. Although alcohol use has been linked to other cancers, positive AUDIT-C screens may also represent the use of alcohol as a coping mechanism for a recent tumor diagnosis.[24]

Smoking history was found only to be associated with intracranial metastases, most likely accounted for by the strong association between smoking and non-intracranial cancers.[82] Consistent with previous investigations, no association between meningiomas and smoking was observed in our cohort.[14,46,59,63]

Pituitary adenomas were the only tumor type to exhibit a positive correlation with psychiatric history.[70,85,92] The psychiatric disorders experienced by those with pituitary adenomas may be due to the pituitary tumor itself, treatment, or hormonal changes in the hypothalamic-pituitary axis – regardless, primary treating clinicians should have heightened awareness that such a patient population may require ancillary psychiatric care.[85] Unlike pituitary adenomas, vestibular schwannomas exhibited decreased odds of depression and other psychiatric disorders.

Family history

Family history of cancer is an established risk factor for brain tumors, consistent with our overall cohort, as well as when stratified among gliomas and vestibular schwannomas.[15,16,32,95] For benign meningiomas specifically, as in our cohort, two prior investigations suggest that having a first degree relative with a meningioma significantly increases the odds of diagnosis, as does a personal history of cancer.[23,53]

Tumor size at diagnosis associated with race

Several racial disparities were highlighted when examining tumor size at the time of diagnosis [Table 3]. For benign meningiomas, Asians, NHPI, and Hispanics exhibited tumors nearly two-fold larger than Whites with the difference between NHPI and Whites are statically significant. While the finding among NHPI is unique, prior surveillance data from the United States corroborate our data, demonstrating that Black, Hispanic, and Asian populations often present with larger tumors than Whites.[8] Among gliomas, NHPI presented with significantly larger tumors than both Whites and Asians, while Asians had smaller gliomas than Whites; such differences may account the lower mortality rates among Asian glioma patients, provided the correlation between larger tumor size and worse survival.[12,20,43,68] For vestibular schwannomas, both Asians and NHPI had smaller tumors relative to Whites. Overall, these large tumor sizes among NHPI demonstrate a delay to diagnosis and, thus, carry important implications toward survival and outcome.[20,40] The results are likely due to the documented disparities in healthcare access that NHPI faces.[27]

Limitations

Although this exploratory study identified several novel correlations, the findings should be considered in the context of several limitations. First, the study is retrospective and relies on accurate documentation by healthcare workers.

The reliance on ICD codes for case ascertainment leads to susceptibility to administrative errors in data entry, meaning that cases could be inadvertently undetected. Furthermore, certain social history and psychiatric risk factors may be susceptible to recall bias or patient's reluctance to disclose due to stigmatization of mental health. Finally, a limited sample size may have decreased statistical power.

CONCLUSION

This study identified several sociodemographic differences in intracranial tumors, which, in turn, may have implications for diagnosis, treatment, and healthcare policy. For benign meningiomas, gliomas, and vestibular schwannomas, NHPI presented with significantly larger tumor volumes at diagnosis than Whites and/or Asians. There were greater odds of diagnosis of benign meningiomas among NAAN, increased odds of diagnosis of gliomas among Whites (reduced among Asians), and increased odds of pituitary adenomas among NHPI (reduced among Whites). Affluence was associated with a diagnosis of malignant meningioma, vestibular schwannoma, and intracranial metastases. Hence, among brain tumors, there are key healthcare disparities that may implicate survival outcomes being linked to a patient's sociodemographic background.

Authors' contributions

All authors contributed equally to the development of this project and manuscript.

Availability of data and material

Data supporting this study can be made available upon reasonable request. Further data can be found in Supplementary Table 1 (number of patients stratified by tumor dimensions, sociodemographics, and medical comorbidities) and Supplementary Tables 2a-c (multivariable logistic regression).

Code availability

Code supporting this study can be made available on reasonable request.

Ethics approval

The Institutional Review Board approval was obtained before the study from the University of Hawaii, Office of Research Compliance (protocol number: 2020-01010).

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Ahn S, Han K, Lee JE, Jeun SS, Park YM, Yang SH. Associations of general and abdominal obesity with the risk of glioma development. Cancers (Basel) 2021;13:2859.
2. Aldape K, Brindle KM, Chesler L, Chopra R, Gajjar A, Gilbert MR, *et al*. Challenges to curing primary brain tumours. Nat Rev Clin Oncol 2019;16:509-20.
3. Alentorn A, Hoang-Xuan K, Mikkelsen T. Presenting signs and symptoms in brain tumors. Handb Clin Neurol 2016;134:19-26.
4. Almeida J, Costa J, Coelho P, Cea V, Galesio M, Noronha JP, *et al*. Adipocyte proteome and secretome influence inflammatory and hormone pathways in glioma. Metab Brain Dis 2019;34:141-52.
5. Alther B, Mylius V, Weller M, Gantenbein AR. From first symptoms to diagnosis: Initial clinical presentation of primary brain tumors. Clin Transl Neurosci 2020;4:17.
6. Altuntaş SÇ, Evran M, Sert M, Tetiker T. Markers of metabolic syndrome in patients with pituitary adenoma: A case series of 303 patients. Horm Metab Res 2019;51:709-13.
7. Aluli NE. Prevalence of obesity in a Native Hawaiian population. Am J Clin Nutr 1991;53:1556S-60.
8. Anzalone CL, Glasgow AE, Van Gompel JJ, Carlson ML. Racial differences in disease presentation and management of intracranial meningioma. J Neurol Surg B Skull Base 2019;80:555-61.
9. Assi HI, Hilal L, Abu-Gheida I, Berro J, Sukhon F, Skaf G, *et al*. Demographics and outcomes of meningioma patients treated at a tertiary care center in the Middle East. Clin Neurol Neurosurg 2020;195:105846.
10. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG, World Health Organization. AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care. Geneva: World Health Organization; 2001.
11. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, *et al*. Alcohol consumption and site-specific cancer risk: A comprehensive dose-response meta-analysis. Br J Cancer 2015;112:580-93.
12. Barnholtz-Sloan JS, Maldonado JL, Williams VL, Curry WT, Rodkey EA, Barker FG 2nd, *et al*. Racial/ethnic differences in survival among elderly patients with a primary glioblastoma. J Neurooncol 2007;85:171-80.

13. Baumgartner ET, Grossmann B, Fuddy L. Hawaii's near-universal health insurance--lessons learned. J Health Care Poor Underserved 1993;4:194-202.
14. Benson VS, Pirie K, Green J, Casabonne D, Beral V, Million Women Study Collaborators. Lifestyle factors and primary glioma and meningioma tumours in the Million Women Study cohort. Br J Cancer 2008;99:185-90.
15. Blumenthal DT, Cannon-Albright LA. Familiality in brain tumors. Neurology 2008;71:1015-20.
16. Bondy ML, Scheurer ME, Malmer B, Barnholtz-Sloan JS, Davis FG, Il'yasova D, *et al*. Brain tumor epidemiology: Consensus from the brain tumor epidemiology consortium. Cancer 2008;113:1953-68.
17. Brokinkel B, Hess K, Mawrin C. Brain invasion in meningiomas-clinical considerations and impact of neuropathological evaluation: A systematic review. Neuro Oncol 2017;19:1298-307.
18. Buckingham RS, Cornforth LL, Whitwell KJ, Lee RB. Visual acuity, optical, and eye health readiness in the military. Mil Med 2003;168:194-8.
19. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): An effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol use disorders identification test. Arch Intern Med 1998;158:1789-95.
20. Chaichana KL, Chaichana KK, Olivi A, Weingart JD, Bennett R, Brem H, *et al*. Surgical outcomes for older patients with glioblastoma multiforme: Preoperative factors associated with decreased survival. Clinical article. J Neurosurg 2011;114:587-94.
21. Chatterjee J, Sanapala S, Cobb O, Bewley A, Goldstein AK, Cordell E, *et al*. Asthma reduces glioma formation by T cell decorin-mediated inhibition of microglia. Nat Commun 2021;12:7122.
22. Chen P, Aldape K, Wiencke JK, Kelsey KT, Miike R, Davis RL, *et al*. Ethnicity delineates different genetic pathways in malignant glioma. Cancer Res 2001;61:3949-54.
23. Claus EB, Calvocoressi L, Bondy ML, Schildkraut JM, Wiemels JL, Wrensch M. Family and personal medical history and risk of meningioma. J Neurosurg 2011;115:1072-7.
24. Cooper ML, Russell M, George WH. Coping, expectancies, and alcohol abuse: A test of social learning formulations. J Abnorm Psychol 1988;97:218-30.
25. Corona AP, Oliveira JC, Souza FP, Santana LV, Rêgo MA. Risk factors associated with vestibulocochlear nerve schwannoma: Systematic review. Braz J Otorhinolaryngol 2009;75:593-615.
26. Curry WT Jr., Barker FG 2nd. Racial, ethnic and socioeconomic disparities in the treatment of brain tumors. J Neurooncol 2009;93:25-39.
27. Dachs GU, Currie MJ, McKenzie F, Jeffreys M, Cox B, Foliaki S, *et al*. Cancer disparities in indigenous Polynesian populations: Māori, Native Hawaiians, and Pacific people. Lancet Oncol 2008;9:473-84.
28. Das A, Tan WL, Teo J, Smith DR. Glioblastoma multiforme in an Asian population: Evidence for a distinct genetic pathway. J Neurooncol 2002;60:117-25.
29. Dubrow R, Darefsky AS. Demographic variation in incidence of adult glioma by subtype, United States, 1992-2007. BMC Cancer 2011;11:325.
30. Escarce JJ, Kapur K. Access to and quality of health care. Washington, DC: National Academies Press; 2006.
31. Ferrer VP, Moura Neto V, Mentlein R. Glioma infiltration and extracellular matrix: Key players and modulators. Glia 2018;66:1542-65.
32. Fisher JL, Schwartzbaum JA, Wrensch M, Wiemels JL. Epidemiology of brain tumors. Neurol Clin 2007;25:867-90, vii.
33. Foley RW, Shirazi S, Maweni RM, Walsh K, McConn Walsh R, Javadpour M, *et al*. Signs and symptoms of acoustic neuroma at initial presentation: An exploratory analysis. Cureus 2017;9:e1846.
34. Galeone C, Malerba S, Rota M, Bagnardi V, Negri E, Scotti L, *et al*. A meta-analysis of alcohol consumption and the risk of brain tumours. Ann Oncol 2013;24:514-23.
35. Ghaffari-Rafi A, Mehdizadeh R, Ghaffari-Rafi S, Castillo JA Jr., Rodriguez-Beato FY, Leon-Rojas J. Demographic and socioeconomic disparities of pituitary adenomas and carcinomas in the United States. J Clin Neurosci 2022;98:96-103.
36. Ghaffari-Rafi A, Mehdizadeh R, Ghaffari-Rafi S, Leon-Rojas J. Demographic and socioeconomic disparities of benign and malignant spinal meningiomas in the United States. Neurochirurgie 2021;67:112-8.
37. Ghaffari-Rafi A, Mehdizadeh R, Ko AW, Ghaffari-Rafi S, Leon-Rojas J. Demographic and socioeconomic disparities of benign cerebral meningiomas in the United States. J Clin Neurosci 2021;86:122-8.
38. Ghaffari-Rafi A, Samandouras G. Effect of treatment modalities on progression-free survival and overall survival in molecularly subtyped World Health Organization grade II diffuse gliomas: A systematic review. World Neurosurg 2020;133:366-80.e2.
39. Grimes DA, Schulz KF. Compared to what? Finding controls for case-control studies. Lancet 2005;365:1429-33.
40. Hale AT, Wang L, Strother MK, Chambless LB. Differentiating meningioma grade by imaging features on magnetic resonance imaging. J Clin Neurosci 2018;48:71-5.
41. Harding NJ, Birch JM, Hepworth SJ, McKinney PA. Atopic dysfunction and risk of central nervous system tumours in children. Eur J Cancer 2008;44:92-9.
42. Hess K, Spille DC, Adeli A, Sporns PB, Brokinkel C, Grauer O, *et al*. Brain invasion and the risk of seizures in patients with meningioma. J Neurosurg 2018;130:789-96.
43. Hodges TR, Labak CM, Mahajan UV, Wright CH, Wright J, Cioffi G, *et al*. Impact of race on care, readmissions, and survival for patients with glioblastoma: An analysis of the National Cancer Database. Neurooncol Adv 2021;3:vdab040.
44. Infante-Rivard C, Roncarolo F, Doucette K. Reliability of cancer family history reported by parents in a case-control study of childhood leukemia. Cancer Causes Control 2012;23:1665-72.
45. Inskip PD, Tarone RE, Hatch EE, Wilcosky TC, Fine HA, Black PM, *et al*. Sociodemographic indicators and risk of brain tumours. Int J Epidemiol 2003;32:225-33.
46. Johnson DR, Olson JE, Vierkant RA, Hammack JE, Wang AH, Folsom AR, *et al*. Risk factors for meningioma in postmenopausal women: Results from the Iowa Women's Health Study. Neuro Oncol 2011;13:1011-9.
47. Kendel F, Wirtz M, Dunkel A, Lehmkuhl E, Hetzer R, Regitz-Zagrosek V. Screening for depression: Rasch analysis of the

dimensional structure of the PHQ-9 and the HADS-D. J Affect Disord 2010;122:241-6.
48. Kotagal V, Langa KM, Plassman BL, Fisher GG, Giordani BJ, Wallace RB, *et al*. Factors associated with cognitive evaluations in the United States. Neurology 2015;84:64-71.
49. Kriston L, Hölzel L, Weiser AK, Berner MM, Härter M. Meta-analysis: Are 3 questions enough to detect unhealthy alcohol use? Ann Intern Med 2008;149:879-88.
50. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med 2001;16:606-13.
51. Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: A systematic review. Gen Hosp Psychiatry 2010;32:345-59.
52. Lazar M, Davenport L. Barriers to health care access for low income families: A review of literature. J Community Health Nurs 2018;35:28-37.
53. Malmer B, Henriksson R, Grönberg H. Familial brain tumours-genetics or environment? A nationwide cohort study of cancer risk in spouses and first-degree relatives of brain tumour patients. Int J Cancer 2003;106:260-3.
54. Mathew GD, Facer GW, Suh KW, Houser OW, O'Brien PC. Symptoms, findings, and methods of diagnosis in patients with acoustic neuroma. Laryngoscope 1978;88:1893-903, 1921.
55. McDowell BD, Wallace RB, Carnahan RM, Chrischilles EA, Lynch CF, Schlechte JA. Demographic differences in incidence for pituitary adenoma. Pituitary 2011;14:23-30.
56. McHugh ML. The chi-square test of independence. Biochem Med (Zagreb) 2013;23:143-9.
57. Melkonian SC, Weir HK, Jim MA, Preikschat B, Haverkamp D, White MC. Incidence of and trends in the leading cancers with elevated incidence among American Indian and Alaska Native Populations, 2012-2016. Am J Epidemiol 2021;190:528-38.
58. Mochizuki S, Iwadate Y, Namba H, Yoshida Y, Yamaura A, Sakiyama S, *et al*. Homozygous deletion of the p16/MTS-1/CDKN2 gene in malignant gliomas is infrequent among Japanese patients. Int J Oncol 1999;15:983-9.
59. Muskens IS, Wu AH, Porcel J, Cheng I, Le Marchand L, Wiemels JL, *et al*. Body mass index, comorbidities, and hormonal factors in relation to meningioma in an ethnically diverse population: The Multiethnic Cohort. Neuro Oncol 2019;21:498-507.
60. Navas-Acién A, Pollán M, Gustavsson P, Plato N. Occupation, exposure to chemicals and risk of gliomas and meningiomas in Sweden. Am J Ind Med 2002;42:214-27.
61. Nayak L, Iwamoto FM. Primary brain tumors in the elderly. Curr Neurol Neurosci Rep 2010;10:252-8.
62. Osawa T, Tosaka M, Nagaishi M, Yoshimoto Y. Factors affecting peritumoral brain edema in meningioma: Special histological subtypes with prominently extensive edema. J Neurooncol 2013;111:49-57.
63. Ostrom QT, Adel Fahmideh M, Cote DJ, Muskens IS, Schraw JM, Scheurer ME, *et al*. Risk factors for childhood and adult primary brain tumors. Neuro Oncol 2019;21:1357-75.
64. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, *et al*. CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States in 2012-2016. Neuro Oncol 2019;21:v1-100.
65. Ostrom QT, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2014-2018. Neuro Oncol 2021;23:iii1-105.
66. Ostrom QT, Cote DJ, Ascha M, Kruchko C, Barnholtz-Sloan JS. Adult glioma incidence and survival by race or ethnicity in the United States from 2000 to 2014. JAMA Oncol 2018;4:1254-62.
67. Ostrom QT, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States in 2013-2017. Neuro Oncol 2020;22:iv1-96.
68. Pan IW, Ferguson SD, Lam S. Patient and treatment factors associated with survival among adult glioblastoma patients: A USA population-based study from 2000-2010. J Clin Neurosci 2015;22:1575-81.
69. Park JS, Sade B, Oya S, Kim CG, Lee JH. The influence of age on the histological grading of meningiomas. Neurosurg Rev 2014;37:425-9; discussion 429.
70. Pengili T, Hashorva A, Prifti I, Lici M, Balani E. Cases where pituitary tumor is presented first with psychiatric signs are very rare. Eur Psychiatry 2017;41:S483.
71. Radley D, Baumgartner J, Collins S, Zephyrin L, Schneider E. Achieving racial and ethnic equity in US health care: A scorecard of state performance. New York: The Commonwealth Fund; 2021.
72. Reinert DF, Allen JP. The alcohol use disorders identification test: An update of research findings. Alcohol Clin Exp Res 2007;31:185-99.
73. Reznitsky M, Petersen MM, West N, Stangerup SE, Cayé-Thomasen P. Epidemiology of vestibular schwannomas - prospective 40-year data from an unselected national cohort. Clin Epidemiol 2019;11:981-6.
74. Robertson JT, Gunter BC, Somes GW. Racial differences in the incidence of gliomas: A retrospective study from Memphis, Tennessee. Br J Neurosurg 2002;16:562-6.
75. Schmid C, Goede DL, Hauser RS, Brändle M. Increased prevalence of high Body Mass Index in patients presenting with pituitary tumours: Severe obesity in patients with macroprolactinoma. Swiss Med Wkly 2006;136:254-8.
76. Schoemaker MJ, Swerdlow AJ, Auvinen A, Christensen HC, Feychting M, Johansen C, *et al*. Medical history, cigarette smoking and risk of acoustic neuroma: An international case-control study. Int J Cancer 2007;120:103-10.
77. Schüz J, Steding-Jessen M, Hansen S, Stangerup SE, Cayé-Thomasen P, Johansen C. Sociodemographic factors and vestibular schwannoma: A Danish nationwide cohort study. Neuro Oncol 2010;12:1291-9.
78. Shete S, Hosking FJ, Robertson LB, Dobbins SE, Sanson M, Malmer B, *et al*. Genome-wide association study identifies five susceptibility loci for glioma. Nat Genet 2009;41:899-904.
79. Sun T, Plutynski A, Ward S, Rubin JB. An integrative view on sex differences in brain tumors. Cell Mol Life Sci 2015;72:3323-42.
80. Tamiya T, Ono Y, Matsumoto K, Ohmoto T. Peritumoral brain edema in intracranial meningiomas: Effects of radiological and histological factors. Neurosurgery 2001;49:1046-51.
81. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: Foundation for Statistical Computing; 2013. p. 201. Available From: https://www

R-project org [Last accessed on 2024 Mar 08].
82. Tindle HA, Stevenson Duncan M, Greevy RA, Vasan RS, Kundu S, Massion PP, *et al*. Lifetime smoking history and risk of lung cancer: Results from the Framingham heart study. J Natl Cancer Inst 2018;110:1201-7.
83. Turner MC, Krewski D, Armstrong BK, Chetrit A, Giles GG, Hours M, *et al*. Allergy and brain tumors in the INTERPHONE study: Pooled results from Australia, Canada, France, Israel, and New Zealand. Cancer Causes Control 2013;24:949-60.
84. Weaver JL, McAlister WH. Vision readiness of the reserve forces of the U.S. Army. Mil Med 2001;166:64-6.
85. Weitzner MA, Kanfer S, Booth-Jones M. Apathy and pituitary disease: It has nothing to do with depression. J Neuropsychiatry Clin Neurosci 2005;17:159-66.
86. White MC, Espey DK, Swan J, Wiggins CL, Eheman C, Kaur JS. Disparities in cancer mortality and incidence among American Indians and Alaska Natives in the United States. Am J Public Health 2014;104 Suppl 3:S377-87.
87. Whittle IR. The dilemma of low grade glioma. J Neurol Neurosurg Psychiatry 2004;75:ii31-6.
88. Wiedmann MK, Brunborg C, Di Ieva A, Lindemann K, Johannesen TB, Vatten L, *et al*. Overweight, obesity and height as risk factors for meningioma, glioma, pituitary adenoma and nerve sheath tumor: A large population-based prospective cohort study. Acta Oncol 2017;56:1302-9.
89. Wiegand DA, Fickel V. Acoustic neuroma--the patient's perspective: Subjective assessment of symptoms, diagnosis, therapy, and outcome in 541 patients. Laryngoscope 1989;99:179-87.
90. Wigertz A, Lönn S, Hall P, Feychting M. Non-participant characteristics and the association between socioeconomic factors and brain tumour risk. J Epidemiol Community Health 2010;64:736-43.
91. Wigertz A, Lönn S, Schwartzbaum J, Hall P, Auvinen A, Christensen HC, *et al*. Allergic conditions and brain tumor risk. Am J Epidemiol 2007;166:941-50.
92. Wilcox JA, Naranjo J. Psychiatric manifestations of pituitary tumors. Psychosomatics 1997;38:396-7.
93. Wilcoxon F. Individual comparisons by ranking methods. Biom Bull, 1945;1:80-3.
94. Wrensch M, Jenkins RB, Chang JS, Yeh RF, Xiao Y, Decker PA, *et al*. Variants in the CDKN2B and RTEL1 regions are associated with high-grade glioma susceptibility. Nat Genet 2009;41:905-8.
95. Wrensch M, Lee M, Miike R, Newman B, Barger G, Davis R, *et al*. Familial and personal medical history of cancer and nervous system conditions among adults with glioma and controls. Am J Epidemiol 1997;145:581-93.

How to cite this article: Kim K, Lew RJ, Higashihara TJ, Yamashita S, Pang M, Stafford M, *et al*. Differences in tumor size, clinical, demographic, and socioeconomic profiles of central nervous system tumors among a racially diverse cohort: A retrospective case–control study. Surg Neurol Int. 2024;15:459. doi: 10.25259/SNI_190_2024