JAMA Oncology | Original Investigation

Adult Glioma Incidence and Survival by Race or Ethnicity in the United States From 2000 to 2014

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IMPORTANCE Glioma is the most commonly occurring malignant brain tumor in the United States, and its incidence varies by age, sex, and race or ethnicity. Survival after brain tumor diagnosis has been shown to vary by these factors.

OBJECTIVE To quantify the differences in incidence and survival rates of glioma in adults by race or ethnicity.

DESIGN, SETTING, AND PARTICIPANTS This population-based study obtained incidence data from the Central Brain Tumor Registry of the United States and survival data from Surveillance, Epidemiology, and End Results registries, covering the period January 1, 2000, to December 31, 2014. Average annual age-adjusted incidence rates with 95% CIs were generated by glioma histologic groups, race, Hispanic ethnicity, sex, and age groups. One-year and 5-year relative survival rates were generated by glioma histologic groups, race, Hispanic ethnicity, and insurance status. The analysis included 244 808 patients with glioma diagnosed in adults aged 18 years or older. Data were collected from January 1, 2000, to December 31, 2014. Data analysis took place from December 11, 2017, to January 31, 2018.

RESULTS Overall, 244 808 patients with glioma were analyzed. Of these, 150 631 (61.5%) were glioblastomas, 46 002 (18.8%) were non-glioblastoma astrocytomas, 26 068 (10.7%) were oligodendroglial tumors, 8816 (3.6%) were ependymomas, and 13 291 (5.4%) were other glioma diagnoses in adults. The data set included 137 733 males (56.3%) and 107 075 (43.7%) females. There were 204 580 non-Hispanic whites (83.6%), 17 321 Hispanic whites (7.08%), 14 566 blacks (6.0%), 1070 American Indians or Alaska Natives (0.4%), and 5947 Asians or Pacific Islanders (2.4%). Incidences of glioblastoma, non-glioblastoma astrocytoma, and oligodendroglial tumors were higher among non-Hispanic whites than among Hispanic whites (30% lower overall), blacks (52% lower overall), American Indians or Alaska Natives (58% lower overall), or Asians or Pacific Islanders (52% lower overall). Most tumors were more common in males than in females across all race or ethnicity groups, with the great difference in glioblastoma where the incidence was 60% higher overall in males. Most tumors (193 329 [79.9%]) occurred in those aged 45 years or older, with differences in incidence by race or ethnicity appearing in all age groups. Survival after diagnosis of glioma of different subtypes was generally comparable among Hispanic whites, blacks, and Asians or Pacific Islanders but was lower among non-Hispanic whites for many tumor types, including glioblastoma, irrespective of treatment type.

CONCLUSIONS AND RELEVANCE Incidence of glioma and 1-year and 5-year survival rates after diagnosis vary significantly by race or ethnicity, with non-Hispanic whites having higher incidence and lower survival rates compared with individuals of other racial or ethnic groups. These findings can inform future discovery of risk factors and reveal unaddressed health disparities.

Supplemental content

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JAMA Oncol. 2018;4(9):1254-1262. doi:10.1001/jamaoncol.2018.1789
Published online June 21, 2018.

Glioma is the most commonly occurring type of malignant brain tumor in the United States, with an average annual age-adjusted incidence rate (AAAIR) of 6.0 per 100 000 population from 2010 to 2014,[1] and causes significant morbidity and mortality. Glioblastoma, the most commonly occurring type of glioma, has a 5-year survival rate of approximately 5%.[1] Age and extent of resection (EOR) are 2 of the strongest prognostic factors in glioblastoma.[2] Incidence of glioma varies substantially by age, sex, and race or ethnicity; in the United States, incidence is highest among non-Hispanic whites.[1] Glioma incidence also varies globally, with the highest rates in the United States, Canada, Australia, and Northern Europe.[3] Lifetime risk of developing a malignant brain tumor is more than twice as high among non-Hispanic whites (715/100,000) compared with blacks (347/100,000) and is 25% higher compared with Hispanic whites (559/100,000).[4] Survival rates after a diagnosis of malignant brain tumor also vary by race or ethnicity.[5,6]

The few validated risk factors for glioma include history of allergies or atopic disease (which decreases risk) and exposure to ionizing radiation (which increases risk).[7] These risk factors explain a small proportion of glioma incidence and do not fully explain racial or ethnic differences in incidence. The purpose of this study was to use population-based data to quantify differences in glioma incidence and survival by race or ethnicity.

Key Points

Question Are there differences in glioma incidence and survival by race or ethnicity in the United States?

Findings In this population-based analysis of 244 808 patients with glioma, non-Hispanic whites had the highest incidence and the lowest relative survival rates in most histologies.

Meaning Differences in incidence and survival by race or ethnicity can inform future discovery of risk factors and reveal unaddressed health disparities.

Methods

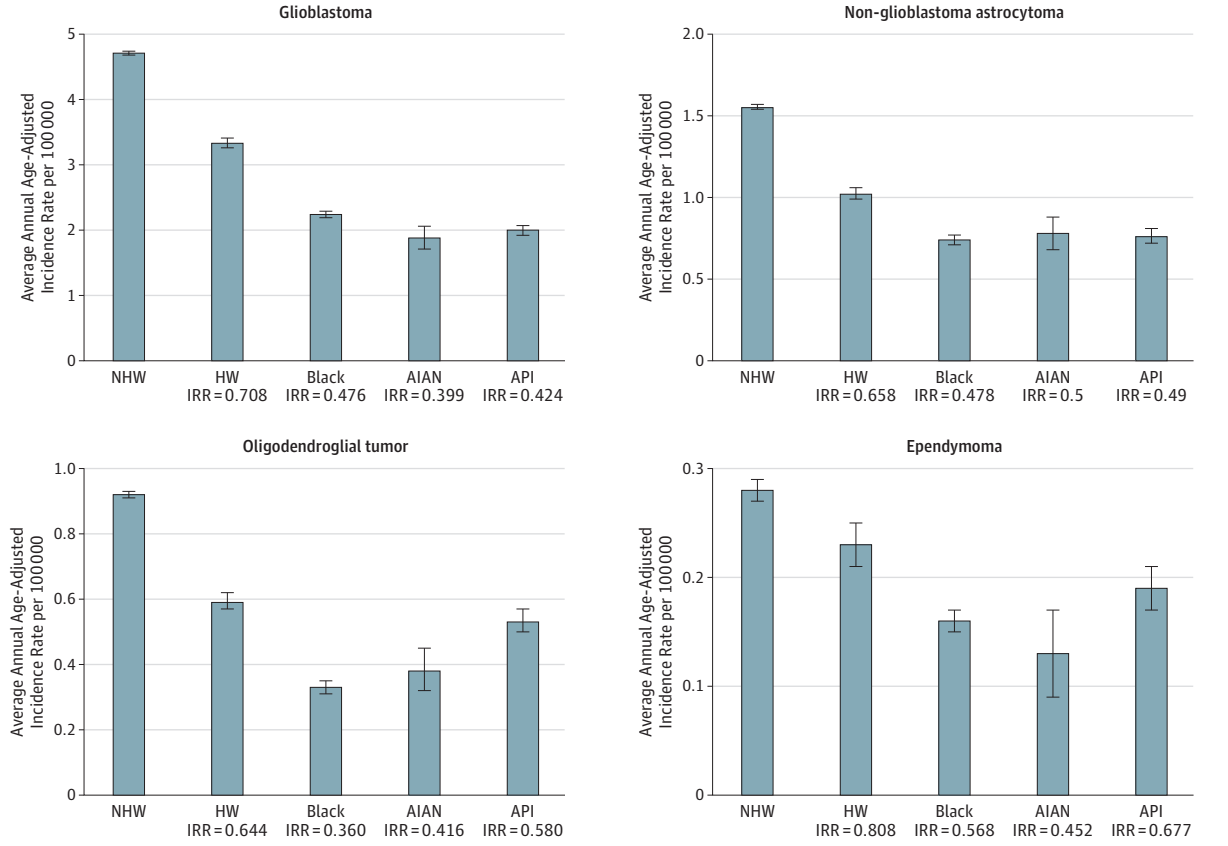
Data were obtained from the Central Brain Tumor Registry of the United States, through a data-release agreement with the Centers for Disease Control and Prevention National Program of Cancer Registries, which includes incidence data from approximately 99.9% of the US population.[1,7] These data are derived from 51 central cancer registries (in 50 states and Washington, DC). The AAAIRs with 95% CIs were generated for adults (aged 18 years or older) using the SEER*Stat software, version 8.3.4 (Surveillance, Epidemiology, and End Results [SEER] Program). These data from January 1, 2000, to December 31, 2014, included glioma histologic groups, race or Hispanic ethnicity[8] (non-Hispanic white, Hispanic white, black, Asian or Pacific Islander, and American Indian or Alaska Native), sex, and age groups (18-34, 35-44, 45-54, 55-64, 65-74, and 75 years or older). Race information is abstracted by cancer registrars from medical records, which have been shown to have high sensitivity for blacks and moderate sensitivity for Hispanic whites.[9,10] Hispanic ethnicity is further classified using the North American Association of Central Cancer Registries Hispanic Identification algorithm, which uses a combination of data fields (medical record, birthplace, race, and surname) to directly and indirectly classify cases.[8] The data set used in this study was deidentified, and as a result the study protocol was ruled exempt from review by the University Hospitals Cleveland Medical Center Institutional Review Board. No patient informed consent was directly obtained. Data were collected from January 1, 2000, to December 31, 2014. Data analysis took place from December 11, 2017, to January 31, 2018.

All rates were standardized to the 2000 US population and reported per 100 000 population to adjust for differences in age distribution among racial or ethnic populations. Incidence rate ratios were generated from these standardized rates. Histologic groups were classified using the *International Classification of Diseases for Oncology, Third Edition,* codes and were defined according to the histologic grouping scheme of the Central Brain Tumor Registry of the United States (eTable 1 in the Supplement).[11,12] Only malignant cases (*International Classification of Diseases for Oncology, Third Edition,* behavior code of /3) were included. Joinpoint Regression Program, version 4.2.02[13] (SEER Program), was used to estimate incidence time trends as well as annual percentage change and 95% CIs. Figures were created in R, version 3.2.3[14] (R Foundation for Statistical Computing), using ggplot2[15] and SEER2R statistical packages.[16]

Most central cancer registries in the United States do not conduct active follow-up for outcomes. These data are publicly available from the National Cancer Institute SEER Program, which represents a subset (approximately 28%) of the cases included in the Central Brain Tumor Registry of the United States data set.[13,14,17] Survival data from 2000 to 2014 for adults at the time of diagnosis with histologic confirmation were included in survival analyses (followed until December 31, 2014, regardless of year of diagnosis). A custom data set was obtained containing additional treatment data fields, including chemotherapy and radiation treatments.[17] Although the treatment information in the SEER registries has been shown to have high positive predictive value (95% for radiation and 90% for chemotherapy),[18] its sensitivity is only moderate. The SEER Program strongly recommends that "no" values are treated as missing data and comparisons are not made between individuals identified as having treatment and those identified as having no treatment. As a result, treatment groups were defined using "yes" values for beam radiation and/or chemotherapy (see eTable 2 in the Supplement for information on treatment data completeness).

One-year and 5-year relative survival (RS) rates were generated using SEER*Stat, version 8.3.4, by glioma histologic groups, race or ethnicity, and insurance status (available only for diagnosis years 2007 to 2014). Insurance status completeness is known to be poor for persons older than 65 years, who may be classified as being uninsured or having private insurance when they are Medicare-eligible. As a result, these data were used to evaluate survival in individuals aged 18 to 64 years only. Additional survival analyses were performed using Cox

Figure 1. Average Annual Age-Adjusted Incidence Rates and 95% Confidence Intervals for Selected Glioma Histologies by Race or Ethnicity and Incidence Rate Ratios (IRRs) Compared With Non-Hispanic Whites (NHW), 2000-2014



AIAN indicates American Indian or Alaska Native; API, Asian or Pacific Islander; HW, Hispanic white.

proportional hazard models adjusted for age and EOR in R, version 3.2.3 (R Foundation for Statistical Computing). We calculated 95% CIs using the method described in Tiwari et al[19] and *P* values for incidence rate ratios were calculated using the method documented in Fay et al.[20] All *P* values were 1-sided, and associations were considered significant at $P < .05$.

Results

Overall, from 2000 to 2014, there were 244 808 patients with glioma. Of these, 150 631 (61.5%) were glioblastomas, 46 002 (18.8%) were non-glioblastoma astrocytomas, 26 068 (10.7%) were oligodendroglial tumors, 8816 (3.6%) were ependymomas, and 13 291 (5.4%) were other glioma diagnoses in adults (eTable 3 in the Supplement). The data set included 137 733 males (56.3%) and 107 075 (43.7%) females. There were 204 580 non-Hispanic whites (83.6%), 17 321 Hispanic whites (7.08%), 14 566 blacks (6.0%), 1070 American Indians or Alaska Natives (0.4%), and 5947 Asians or Pacific Islanders (2.4%).

Glioblastoma incidence was highest in non-Hispanic whites (AAAIR, 4.71; 95% CI, 4.69-4.74) and lowest in American Indians or Alaska Natives (AAAIR, 1.88; 95% CI, 1.71-2.06), where incidence was approximately 40% that of non-Hispanic whites (**Figure 1**; eTable 3 in the Supplement). Incidence was highest in males (incidence rate ratio [IRR], 1.59; $P < .005$). The male to female IRR was highest in Asians or Pacific Islanders (IRR, 1.65) and lowest in Hispanic whites (IRR, 1.49). The median age varied by race or ethnicity, with non-Hispanic whites having the highest median age (64 years) and blacks and American Indians or Alaska Natives having the lowest (59 years). Incidence rates were highest in the age 65 years or older group (eFigure and eTable 4 in the Supplement).

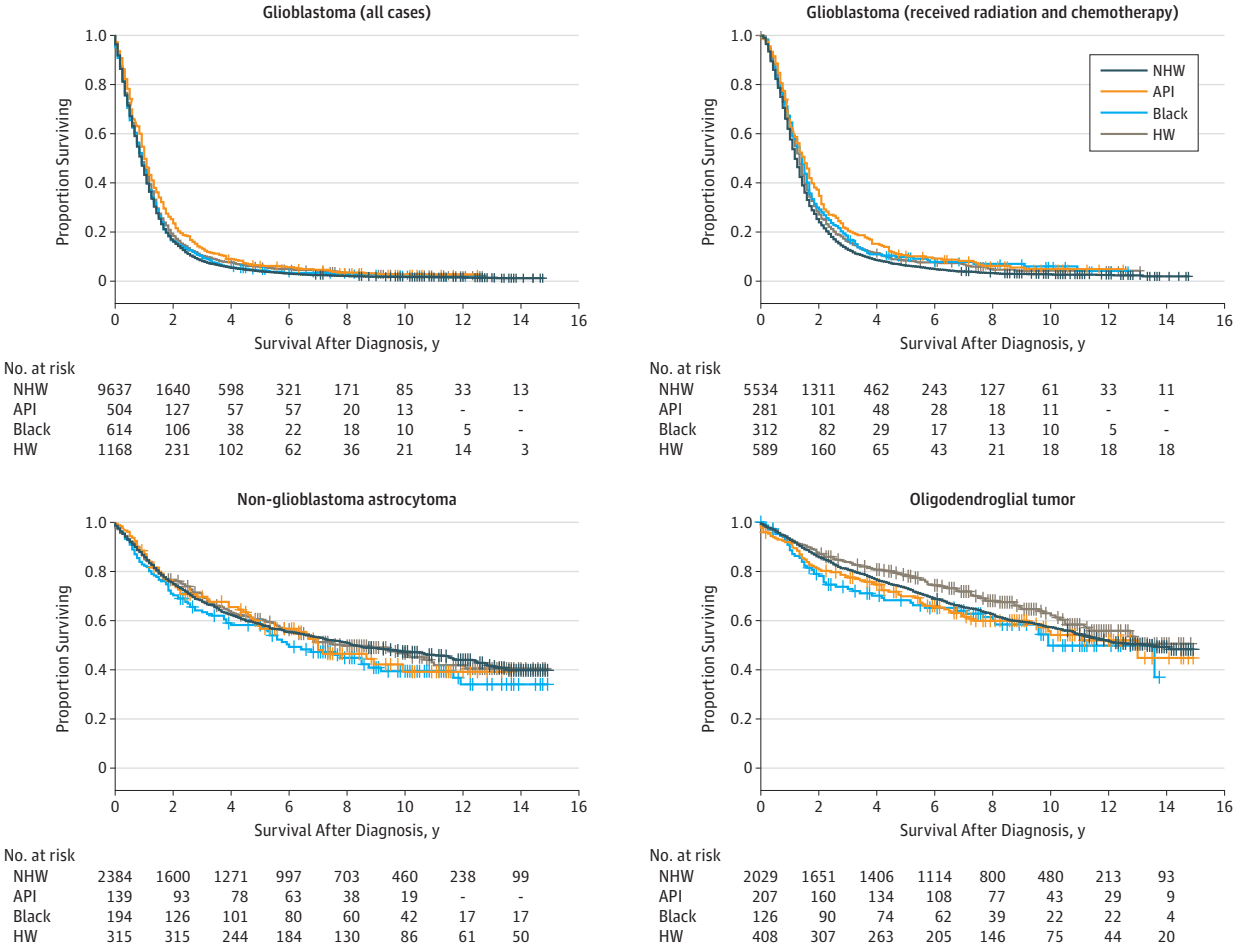
Overall, the 1-year RS after diagnosis was 41.4% (95% CI, 40.8-42.0) and the 5-year RS was 5.4% (95% CI, 5.1-5.7) (**Table**). The highest 5-year RS was observed in Asians or Pacific Islanders (8.8%; 95% CI, 7.0-10.9) and the lowest in non-Hispanic whites (4.8%; 95% CI, 4.5-5.2). To evaluate the potential period effects between the pre- and post-Stupp treatment (concurrent radiation and temozolomide[21]) protocol eras (2000-2004 and 2005-2014), RS was evaluated separately within each period. The RS was generally higher in the post-Stupp era (Table). There was no change in the 5-year RS for Asians or Pacific Islanders between the 2 periods, whereas the 1-year RS increased from 39.3% (95% CI, 33.9-44.6) to 54.2% (95% CI, 50.8-57.4). Among those who received radiation, the 1-year RS was highest in Asians or Pacific Islanders (63.1%), whereas the 5-year RS was highest in Hispanic whites (9.6%). For those who

Table. One-Year and 5-Year Relative Survival Rates and 95% CIs for Selected Glioma Histologies in Adults by Race or Ethnicity and Diagnosis Periods, 2000-2014

Histologic Group	Race or Ethnicity	Diagnosis Years 2000-2014			Diagnosis Years 2000-2004			Diagnosis Years 2005-2014		
		No.	% (95% CI)		No.	% (95% CI)		No.	% (95% CI)	
			1-Year RS	5-Year RS		1-Year RS	5-Year RS		1-Year RS	5-Year RS
Glioblastoma	All groups	30 880	41.4 (40.8-42.0)	5.4 (5.1-5.7)	9223	34.4 (33.5-35.4)	4.3 (3.9-4.7)	21 657	44.6 (43.9-45.3)	5.8 (5.4-6.2)
	Non-Hispanic white	24 635	40.7 (40.1-41.3)	4.8 (4.5-5.2)	7581	34.1 (33.0-35.2)	3.9 (3.4-4.3)	17 054	43.8 (43.1-44.6)	5.2 (4.7-5.6)
	Hispanic white	2972	42.9 (41.0-44.8)	7.8 (6.7-9.0)	783	37.4 (33.9-40.8)	6.3 (4.7-8.2)	2189	45.1 (42.8-47.3)	8.4 (7.0-10.0)
	Black	1758	42.0 (39.6-44.3)	6.8 (5.5-8.4)	487	32.7 (28.5-37.0)	4.6 (2.9-6.8)	1271	45.7 (42.8-48.5)	7.8 (6.0-9.9)
	API	1331	50.2 (47.4-53.0)	8.8 (7.0-10.9)	334	39.3 (33.9-44.6)	8.8 (5.9-12.3)	997	54.2 (50.8-57.4)	8.1 (5.9-10.7)
Non-glioblastoma astrocytomas	All groups	10 259	72.4 (71.5-73.3)	44.4 (43.3-45.5)	3443	68.8 (67.2-70.3)	42.0 (40.3-43.7)	6816	74.3 (73.2-75.4)	45.6 (44.2-47.0)
	Non-Hispanic white	7648	71.3 (70.2-72.3)	43.2 (41.9-44.4)	2630	67.5 (65.7-69.3)	40.7 (38.8-42.7)	5018	73.3 (72.0-74.6)	44.4 (42.7-46.0)
	Hispanic white	1270	76.0 (73.5-78.4)	50.8 (47.5-53.9)	411	72.7 (68.0-76.8)	48.6 (43.4-53.5)	859	77.8 (74.6-80.6)	52.1 (47.9-56.1)
	Black	675	72.2 (68.5-75.5)	45.4 (41.1-49.5)	236	71.3 (64.9-76.7)	45.8 (39.2-52.2)	439	72.8 (68.2-76.9)	44.5 (38.9-50.0)
	API	540	78.2 (74.3-81.6)	44.1 (39.1-49.0)	144	75.8 (67.8-82.1)	38.9 (30.8-47.0)	396	79.2 (74.5-83.0)	46.6 (40.3-52.7)
Oligodendroglial tumors	All	6396	90.4 (89.6-91.1)	70.1 (68.8-71.3)	2238	89.4 (88.0-90.6)	67.6 (65.5-69.5)	4158	91.0 (90.0-91.8)	71.8 (70.1-73.4)
	Non-Hispanic white	4647	90.2 (89.3-91.1)	70.0 (68.5-71.4)	1694	89.1 (87.5-90.5)	67.9 (65.5-70.1)	2953	90.9 (89.7-91.9)	71.4 (69.3-73.3)
	Hispanic white	906	90.7 (88.5-92.5)	73.9 (70.3-77.1)	267	89.7 (85.2-92.8)	72.3 (66.1-77.5)	639	91.2 (88.6-93.3)	74.9 (70.4-78.8)
	Black	292	89.5 (85.1-92.7)	63.8 (57.1-69.7)	94	85.7 (76.5-91.5)	56.8 (45.7-66.5)	198	91.4 (86.1-94.7)	68.0 (59.5-75.1)
	API	454	91.5 (88.4-93.8)	67.5 (62.2-72.2)	149	92.1 (86.4-95.5)	61.4 (52.9-68.8)	305	91.2 (87.2-94.0)	72.4 (65.4-78.1)
Ependymoma	All	2032	94.3 (93.1-95.3)	88.0 (86.2-89.6)	646	93.9 (91.7-95.6)	86.3 (83.0-89.0)	1386	94.5 (93.0-95.7)	89.0 (86.7-90.9)
	Non-Hispanic white	1395	94.2 (92.8-95.4)	88.2 (86.0-90.1)	462	93.9 (91.2-95.9)	86.4 (82.4-89.6)	933	94.4 (92.5-95.8)	89.1 (86.3-91.3)
	Hispanic white	328	94.9 (91.6-96.9)	88.9 (83.7-92.4)	102	98.3 (91.7-99.7)	89.0 (79.6-94.2)	226	93.2 (88.6-96.0)	89.1 (82.6-93.3)
	Black	165	93.0 (87.4-96.1)	84.8 (77.0-90.2)	Not presented	Not presented	Not presented	118	95.0 (88.6-97.9)	85.0 (74.8-91.3)
	API	114	93.7 (86.9-97.0)	84.2 (74.7-90.4)	Not presented	Not presented	Not presented	81	96.2 (87.9-98.8)	86.4 (73.7-93.3)
Other gliomas	All	1247	65.8 (63.0-68.4)	41.0 (38.0-44.1)	437	62.1 (57.3-66.5)	36.8 (32.2-41.5)	810	68.0 (64.4-71.2)	44.0 (39.9-48.0)
	Non-Hispanic white	897	65.0 (61.7-68.1)	40.7 (37.1-44.2)	328	63.8 (58.3-68.8)	37.8 (32.4-43.2)	569	65.8 (61.5-69.7)	42.9 (38.1-47.6)
	Hispanic white	159	69.2 (60.8-76.1)	44.0 (35.0-52.6)	Not presented	Not presented	Not presented	113	73.5 (63.7-81.0)	48.1 (36.7-58.6)
	Black	101	65.6 (55.0-74.2)	44.8 (33.7-55.2)	Not presented	Not presented	Not presented	62	73.0 (59.2-82.8)	48.0 (32.5-61.9)
	API	71	70.0 (57.2-79.7)	35.6 (22.5-48.9)	Not presented	Not presented	Not presented	Not presented	Not presented	Not presented

Abbreviations: API, Asian or Pacific Islander; RS, relative survival.

Figure 2. Survival Curves by Histologic Subtype for Individuals Who Received Resection by Race or Ethnicity, Adjusted by Age and Extent of Resection (Subtotal vs Gross Total), 2000-2014



Glioblastoma survival is significantly improved for people who are not non-Hispanic whites (HNW). No significant differences were observed in survival for non-glioblastoma astrocytoma or oligodendroglial tumors.

API indicates Asian or Pacific Islander; HW, Hispanic white.

received both radiation and chemotherapy, the 1-year and 5-year RS rates were highest in Asians or Pacific Islanders (67.1% and 10.1%) and lowest in non-Hispanic whites (57.2% and 6.6%). For persons aged 18 to 34 years, non-Hispanic whites had the highest 1-year and 5-year survival (78.6% and 27.0%) (eTable 5 in the Supplement). In the 35 to 44 years age cohort, survival was highest among Hispanic whites, with a 1-year RS of 69.6% and a 5-year RS of 19.3%. For all cohorts aged 45 years or older, Asians or Pacific Islanders had the highest survival rate. When survival models were adjusted for EOR and age, being Asian or Pacific Islander was a significant predictor of increased survival ($P = 2.4\text{x}10^{-5}$; **Figure 2**; eTable 6 in the Supplement). Among only those who received surgery, radiation, and chemotherapy, all racial or ethnic groups had significantly improved survival compared with non-Hispanic whites (see eTable 2 in the Supplement for the completeness of treatment information).

Non-glioblastoma astrocytoma incidence was highest in non-Hispanic whites (AAAIR, 1.55; 95% CI, 1.54-1.57) and lowest in blacks (AAAIR, 0.74; 95% CI, 0.72-0.77), where incidence was approximately 48% that of non-Hispanic whites (Figure 1; eTable 3 in the Supplement). Overall incidence was highest in males (IRR, 1.35; $P < .005$). The male to female IRR was highest in non-Hispanic whites (IRR, 1.55) and Asians or Pacific Islanders (IRR, 1.55) but lowest in American Indians or Alaska Natives, where no significant sex difference was observed (IRR, 1.08; $P = .58$). The median age varied by race or ethnicity, with non-Hispanic whites having the highest (50 years) and Hispanic whites, Asians or Pacific Islanders, and American Indians or Alaska Natives having the lowest (41 years). Incidence rates were highest in the 65-74 years age cohort in all race or ethnicity groups except Asians or Pacific Islanders, where the highest incidence was in persons 75 years or older (eFigure and eTable 4 in the Supplement).

Overall, the 1-year RS after diagnosis of non-glioblastoma astrocytomas was 72.4% (95% CI, 71.5-73.3) and the 5-year RS was 44.4% (95% CI, 43.3-45.5) (Table). The highest 5-year RS was observed in Hispanic whites (50.8%; 95% CI, 47.5-53.9)

and the lowest in non-Hispanic whites (43.2%; 95% CI, 41.9-44.4). For persons aged 18 to 44 years, non-Hispanic whites had the highest 1-year and 5-year RS, whereas in older age groups the highest 5-year RS was in Hispanic whites (eTable 5 in the Supplement). When survival models were adjusted for EOR and age, there was no significant association between survival and any race or ethnicity group (Figure 2; eTable 6 in the Supplement).

Oligodendroglial tumors incidence was highest in non-Hispanic whites (AAAIR, 0.92; 95% CI, 0.91-0.93) and lowest in blacks (AAAIR, 0.33; 95% CI, 0.31-0.35), where incidence was approximately 36% that of non-Hispanic whites (Figure 1; eTable 3 in the Supplement). Overall incidence was highest in males (IRR, 1.33; $P < .005$). The male to female IRR was highest in non-Hispanic whites (IRR, 1.33) and lowest in Hispanic whites, where there was no significant sex difference (IRR, 1.17). The median age varied by race or ethnicity, with the highest in non-Hispanic whites (44 years) and the lowest in American Indians or Alaska Natives (36 years). Incidence rates were highest in the 35 to 44 years age cohort in non-Hispanic whites, blacks, and Asians or Pacific Islanders; incidence rate in American Indians or Alaska Natives was highest in the 18 to 34 years cohort; and incidence rate in Hispanic whites was highest in the 45 to 54 years age group (eFigure and eTable 4 in the Supplement).

Overall, the 1-year RS after diagnosis of oligodendroglial tumors was 90.4% (95% CI, 89.6-91.1) and the 5-year RS was 70.0% (95% CI, 68.5-71.4) (Table). The highest 5-year RS was observed in Hispanic whites (73.9%; 95% CI, 70.3-77.1) and lowest in blacks (63.8%; 95% CI, 57.1-69.7). The 1-year and 5-year RS increased from 2005 to 2014, but these increases were minimal. For individuals aged 18 to 44 years, non-Hispanic whites had the highest 1-year and 5-year RS, whereas in older age groups, the highest 5-year RS was in Hispanic whites (eTable 5 in the Supplement). When survival models were adjusted for EOR and age, no significant association was found between survival rate and any race or ethnicity group (Figure 2; eTable 6 in the Supplement).

Ependymoma incidence was highest in non-Hispanic whites (AAAIR, 0.29; 95% CI, 0.28-0.29) and lowest in American Indians or Alaska Natives (AAAIR, 0.13; 95% CI, 0.09-0.17), where incidence was approximately 45% that of non-Hispanic whites (Figure 1; eTable 3 in the Supplement). Incidence of ependymoma was slightly higher in males (IRR, 1.33; $P < .005$). The male to female IRR was highest in non-Hispanic whites (IRR, 1.11), and there was no significant sex difference in incidence in any other group. The median age varied by race or ethnicity, with non-Hispanic whites having the highest (59 years) and Hispanic whites having the lowest (47 years). Incidence of ependymoma was highest in the 45 to 74 years age group in all race or ethnicity groups (eFigure and eTable 4 in the Supplement). Overall, the 1-year RS after diagnosis of ependymoma was 94.3% (95% CI, 93.1-95.3) and the 5-year RS was 88.0% (95% CI, 86.2-89.6) (Table). The highest 5-year RS was observed in Hispanic whites (88.9%; 95% CI, 83.7-92.4) and lowest in Asians or Pacific Islanders (84.2%; 95% CI, 74.7-90.4). No notable changes were observed in the 1-year and 5-year RS rates between 2000 to 2004 and 2005 to 2014.

Discussion

The present study of glioma incidence and survival across a 14-year period demonstrates substantial variation by race or ethnicity, using data from 99.9% of the US population to derive incidence rates and data from approximately 28% of the population to obtain survival rates.[22,23] Non-Hispanic whites had the highest incidence of all glioma subtypes, consistent with what has been previously reported.[1,18,21] The median age of diagnosis for all histologies was highest also among non-Hispanic whites. There was a male preponderance in incidence of most glioma histologies among all examined racial or ethnic groups, and the scale of the male to female IRR was similar among all race or ethnicity groups. Analyses have consistently found higher glioma incidence in non-Hispanic whites as well as in countries with high proportions of individuals with mostly European ancestry.[1,3] The reason for this finding may be, to some extent, the variation in genetic risk susceptibility for glioma, but to date no studies have examined the inherited risk variants associated with glioma risk in blacks or Hispanic whites.

A portion of this incidence difference may be the result of several biases. Incidence estimates are sensitive to ascertainment bias, because of differential access to health care or the variation in diagnostic procedure. Non-Hispanic whites often have improved access to health care, which may lead to earlier or more accurate diagnosis.[22,23] Glioma is usually symptomatic (incidental diagnoses represent approximately 2% to 6% of diagnoses in case series studies[24-26]) and often presents with substantial symptoms, including seizures and cognitive impairments. As a result, the chance of ascertainment bias resulting in considerable underdiagnosis is small. Heterogeneous reporting guidelines or the application of histologic classification schemes could result in spuriously different rates among racial or ethnic groups. There is no central pathology review of tumor samples in the data used for this analysis, but it is possible that "true" histologic classification could be confounded with race or ethnicity. Although these factors may affect incidence rates, they fail to explain the incidence difference between non-Hispanic whites and other groups.

Previous analyses have found substantial associations between increased socioeconomic status and glioma, which may contribute to differences in incidence by race or ethnicity.[27-29] A previous SEER analysis found increased incidence of glioma in areas of higher socioeconomic status after adjusting for sex, race, and age.[28] In Sweden, the highest glioma incidence was among those with family incomes in the highest quartile (odds ratio [OR], 1.5; 95% CI, 1.1-2.1), after adjusting for sex, age, and geographic region.[29] The underlying risk factors responsible for differential incidence by socioeconomic status are unknown but could be partially the result of confounding with known or currently unknown risk factors.[30,31] The population distribution of the SEER registries approximates that these registries contain a greater proportion of persons who are not non-Hispanic white in the SEER data, which may affect race-specific survival estimates.[32-34] These registries contain greater proportions of foreign-born individuals, who have less than a

high school diploma compared with the general US population, which may also affect survival estimates.[35]

This analysis found that non-Hispanic whites had poorer outcomes after diagnosis of glioblastoma when compared with all other groups. This pattern was present in both the pre- and post-Stupp protocol era period analyses (Table) among those who received treatment beyond resection (eTable 7 in the Supplement) as well as after adjustment for age and EOR (Figure 2). A large US meta-analysis previously reported that blacks have lower 5-year survival rate compared with whites after diagnosis of central nervous system cancers.[36] These disparities were reduced after adjustment for disease severity, treatment type, and the underlying mortality rate. Curry et al[5] remark that blacks presented with greater disease severity and that there is lower annual cancer-associated craniotomy case volume in the National Inpatient Sample data for patients with Medicaid insurance. Variations in health care access and severity at the time of presentation are likely substantial contributors to the variation in survival patterns.

Furthermore, this analysis found that non-Hispanic whites have a lower survival rate compared with other racial or ethnic groups. People who are not non-Hispanic whites have comparatively low numbers of cases, and some of the observed differences may be the result of these low numbers. These findings are in line with those of some previously reported analyses, such as a SEER study that found increased survival in blacks compared with whites after diagnosis of a central nervous system tumor.[37] These differences were consistently observed within sex and across age strata. Both 1-year and 5-year survival rates were lower among non-Hispanic whites, particularly compared with Hispanic whites, regardless of treatment type. This previous analysis also found that differences persisted in glioblastoma among those who received radiation and chemotherapy, suggesting that health care access is not sufficient to explain survival differences.

In older cohorts who have universal access to Medicare, access to health care and treatment type may not adequately explain differential survival rates. For all ages, other factors should be explored in future studies. Survival after diagnosis of cancer of other sites has been shown to correlate with many factors that also vary by race or ethnicity, including body mass index, smoking status, and religious service attendance.[38-40] Although prediagnostic body mass index has been associated with shorter survival after diagnosis of glioma, these additional factors have not all been sufficiently explored.[41] Non-Hispanic whites had the highest RS in younger cohorts in age-stratified analyses (eTable 4 in the Supplement). Compared with persons aged 65 years or older who are eligible for Medicare, young persons diagnosed with cancer may not have access to health insurance. Access to health insurance among young adult oncology patients varies significantly by socioeconomic status, race, and ethnicity.[42,43] When survival analyses were performed for glioblastoma stratified by insurance status within the 18 to 64 years age cohorts, non-Hispanic whites had the poorest survival within each cohort (eTable 8 in the Supplement). This finding suggests that the observed survival benefit among non-Hispanic whites in younger cohorts may be, to some extent, due to differences in health care access.

Limitations

This study has limitations. The data used for this analysis are limited in the variables available for each individual. Many of these factors may be associated with differences in survival, including comorbidities, tumor volume and location, EOR, Karnofsky performance status, and treatment pattern.[2,21] Cancer registry data represent the most complete data set for characterizing patterns of cancer incidence and survival, but several limitations are inherent in this type of data, including known problems with completeness of treatment information.[18] The 2016 World Health Organization Classification of Tumors of the Central Nervous System summary contains considerable revisions to glioma histologic classification.[44] The largest of these revisions is the incorporation of isocitrate dehydrogenase 1/2 mutation status and 1p/19q codeletion status into the diagnostic criteria for astrocytoma and oligodendroglioma. This revision also resulted in the elimination of oligoastrocytoma as a valid glioma histologic subtype.[45] To date, data on isocitrate dehydrogenase 1/2 mutation status have not been collected in both the National Program of Cancer Registries or SEER systems, although collection will begin in 2018. Since 2011, 1p/19q codeletion status has been required by SEER registries, but completeness varies significantly by histologic subtype.[46] As a result, these molecular classifications were not incorporated into this analysis, and it is not possible to assess whether these may be driving the observed survival differences. An analysis of time trends by race or ethnicity and glioma histologic subtype (eTable 9 in the Supplement) shows substantial decreases in incidence of oligodendroglial tumors in all groups over the period examined in this study, which may be the result of changing classification schemes.

Conclusions

To our knowledge, this study represents the most complete and up-to-date reporting of patterns of glioma incidence and survival by race or ethnicity in the United States. These estimates of incidence are population-based and include approximately 99.9% of the US population, while SEER data cover approximately 28% of the population.[22] Incidence and survival patterns of most glioma histologies varied significantly by race or ethnicity, with non-Hispanic whites having higher incidence and lower survival compared with individuals of other race or ethnicity. Further examination is necessary to determine the factors that contribute to these differences. Expanding investigations of germline genetic associations in blacks and Hispanic whites may identify genetic contributions to incidence differences. Somatic characterization of tumors in multiethnic cohorts is also necessary to determine that the observed survival differences may not be due to differences in proportions of molecular subtypes within histologic subtypes among racial or ethnic groups. Examination of treatment patterns in databases with more extensive clinical information is necessary to determine the extent to which health care access may affect differences in outcomes.

ARTICLE INFORMATION

Accepted for Publication: April 3, 2018.

Published Online: June 21, 2018. doi:10.1001/jamaoncol.2018.1789

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Obtained funding: Kruchko.
Administrative, technical, or material support: Cote, Kruchko.
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Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported by research training grant RP160097T from the Cancer Prevention and Research Institute of Texas (Dr Ostrom) and training grant T32 CA 009001 from the National Institutes of Health (Mr Cote). The Central Brain Tumor Registry of the United States was funded by contract no. 2016-M-9030 from the Centers for Disease Control and Prevention and by the Sontag Foundation, Novocure, AbbVie along with the Musella Foundation, the Children's Brain Tumor Foundation, National Brain Tumor Society, the Pediatric Brain Tumor Foundation, the Zelda Dorin Tetenbaum Memorial Fund, and private and in-kind donations.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The views expressed herein are solely the responsibility of the authors and do not necessarily reflect the official views of the Centers for Disease Control and Prevention.

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