CA CANCER J CLIN 2021;71:381–406

Brain and Other Central Nervous System Tumor Statistics, 2021

Kimberly D. Miller, MPH [1]; Quinn T. Ostrom, PhD, MPH [2,3]; Carol Kruchko, BA [2]; Nirav Patil, MBBS, MPH[2,4]; Tarik Tihan, MD, PhD[5]; Gino Cioffi, MPH[2,6]; Hannah E. Fuchs, BS[1]; Kristin A. Waite, PhD [2,6]; Ahmedin Jemal, DVM, PhD[1]; Rebecca L. Siegel, MPH [1]; Jill S. Barnholtz-Sloan, PhD[2,6,7]

[1]Surveillance and Health Equity Science, American Cancer Society, Atlanta, Georgia; [2]Central Brain Tumor Registry of the United States, Hinsdale, Illinois; [3]Department of Neurosurgery, Duke University School of Medicine, Durham, North Carolina; [4]Research and Education Institute, University Hospitals, Cleveland, Ohio; [5]Neuropathology Division, University of California, San Francisco, California; [6]Trans Divisional Research Program (TDRP), Division of Cancer Epidemiology and Genetics (DCEG), National Cancer Institute, Bethesda, Maryland; [7]Center for Biomedical Informatics & Information Technology (CBIIT), National Cancer Institute, Bethesda, Maryland.

The last 2 authors contributed equally to this article.

Corresponding Author: Kimberly D. Miller, MPH, American Cancer Society, Inc, 250 Williams Street NW, Atlanta, GA 30303 (kimberly.miller@cancer.org).

DISCLOSURES: Funding for the Central Brain Tumor Registry of the United States (CBTRUS) was provided by the Centers for Disease Control and Prevention (CDC) under contract no. 75D30119C06056 and by the American Brain Tumor Association, The Sontag Foundation, Novocure, the Musella Foundation, National Brain Tumor Society, the Pediatric Brain Tumor Foundation, the Uncle Kory Foundation, and the Zelda Dorin Tetenbaum Memorial Fund, as well as private and in-kind donations.

The contents of this article solely the responsibility of the authors and do not necessarily represent the official views of the CDC or the National Cancer Institute.

We acknowledge Lindsey Torre, MSPH, for her early contributions to the text and figures. The CBTRUS data were provided through an agreement with the CDC's National Program of Cancer Registries. In addition, CBTRUS used data from the research data files of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and the National Center for Health Statistics National Vital Statistics System. CBTRUS acknowledges and appreciates these contributions to this report and to cancer surveillance in general.

doi: 10.3322/caac.21693. Available online at cacancerjournal.com

Abstract: Brain and other central nervous system (CNS) tumors are among the most fatal cancers and account for substantial morbidity and mortality in the United States. Population-based data from the Central Brain Tumor Registry of the United States (a combined data set of the National Program of Cancer Registries [NPCR] and Surveillance, Epidemiology, and End Results [SEER] registries), NPCR, National Vital Statistics System and SEER program were analyzed to assess the contemporary burden of malignant and nonmalignant brain and other CNS tumors (hereafter brain) by histology, anatomic site, age, sex, and race/ethnicity. Malignant brain tumor incidence rates declined by 0.8% annually from 2008 to 2017 for all ages combined but increased 0.5% to 0.7% per year among children and adolescents. Malignant brain tumor incidence is highest in males and non-Hispanic White individuals, whereas the rates for nonmalignant tumors are highest in females and non-Hispanic Black individuals. Five-year relative survival for all malignant brain tumors combined increased between 1975 to 1977 and 2009 to 2015 from 23% to 36%, with larger gains among younger age groups. Less improvement among older age groups largely reflects a higher burden of glioblastoma, for which there have been few major advances in prevention, early detection, and treatment the past 4 decades. Specifically, 5-year glioblastoma survival only increased from 4% to 7% during the same time period. In addition, important survival disparities by race/ethnicity remain for childhood tumors, with the largest Black-White disparities for diffuse astrocytomas (75% vs 86% for patients diagnosed during 2009-2015) and embryonal tumors (59% vs 67%). Increased resources for the collection and reporting of timely consistent data are critical for advancing research to elucidate the causes of sex, age, and racial/ethnic differences in brain tumor occurrence, especially for rarer subtypes and among understudied populations. **CA Cancer J Clin 2021;71:381-406. © 2021 The Authors. CA: A Cancer Journal for Clinicians published by Wiley Periodicals LLC on behalf of American Cancer Society. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.**

Keywords: brain tumors, Central Brain Tumor Registry of the United States (CBTRUS), central nervous system tumors, epidemiology

Introduction

Malignant and nonmalignant brain and other central nervous system (CNS) tumors comprise a diverse constellation of over 100 histologically distinct subtypes with varying descriptive epidemiology, clinical characteristics, treatments, and outcomes. Although primary malignant brain and other CNS tumors are rare in the United States, they account for a disproportionate burden of cancer mortality because of their high fatality rate; only one-third of individuals survive at least 5 years after diagnosis.[1] The classification and reporting of these tumors have rapidly changed in recent years in parallel with expanding molecular understanding and advances in detection and diagnosis, although much of the etiology remains unknown. This article provides an overview of primary malignant and nonmalignant brain and other CNS tumor incidence,

mortality, and survival rates and trends in the United States, as well as differences in occurrence by major histologic subtype, anatomic site, geography, race/ethnicity, and sex.

Materials and Methods

Data Sources

De-identified incidence data from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) program and the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) were combined by the Central Brain Tumor Registry of the United States (CBTRUS), the only population-based registry focusing exclusively on primary brain and other central nervous system (CNS) tumors in the United States.[2] The SEER program and the NPCR collect population-based cancer incidence data that combined cover the entire US population. Federal law mandates the collection of population-based cancer data for the registries participating in the NPCR (SEER registries voluntarily comply) and was expanded in 2002 to include benign and borderline (nonmalignant) brain tumors beginning with the 2004 data year, in recognition of substantial morbidity imposed by these neoplasms.[3] The resulting combined SEER and NPCR dataset curated by CBTRUS includes all primary brain and other CNS tumors diagnosed in the United States and was the source herein for cross-sectional incidence rates (2013-2017) and long-term incidence trends (2000-2017 for malignant tumors; 2004-2017 for nonmalignant tumors).[4] Malignant tumor trends were based on data from 2000 to 2017 to allow for the inclusion of most states; 7 states (Arkansas, Mississippi, and South Dakota and nondual-funded SEER registries, including Utah, Connecticut, New Mexico, and Hawaii) did not report incidence data for ≥1 year during the study period and were excluded. The methods for the abstraction and compilation of this dataset are described elsewhere.[2] Incidence rates for Puerto Rico were excluded to provide comparability to previously published statistics but are available in Supplementary Materials to the annual 2020 CBTRUS report.[2]

Contemporary relative survival rates were based on data from the NPCR and included cases diagnosed in 45 states during 2009 through 2015 for malignant and nonmalignant tumors (all patients followed through 2016), covering approximately 94% of the US population.[5] Historical survival data for malignant tumors only, based on the SEER 9 registries (Connecticut, Iowa, Hawaii, New Mexico, and Utah and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound) and covering 9% of the US population, were used to analyze long-term survival trends for all malignant tumors combined and glioblastoma.[6] National mortality data, provided by the National Center for Health Statistics, were obtained via the SEER program's SEER*Stat software for malignant brain and other CNS tumor deaths occurring from 1970 through 2018.[7]

Classification

Cases were classified according to the *International Classification of Diseases for Oncology, third edition* (ICD-O-3) (topography codes C30.0, C70-C72, C75.1-C75.3).[8] Because this definition is inclusive of cases diagnosed in the pituitary (C75.1) and pineal (C75.3) glands and the craniopharyngeal duct (C75.2), as well as olfactory tumors of the nasal cavity (C30.0; morphology codes 9522-9523), rates for brain and other CNS tumors combined presented herein may differ from those elsewhere based on the SEER/World Health Organization (WHO) site recode alone. Cases were defined using behavior codes /3 for malignant tumors and /0 and /1 for nonmalignant (ie, /0, benign behaviors, and /1, borderline behaviors). Incident cases were further stratified by histologic subtype; major histology categories for cases in all ages were defined according the CBTRUS 2012 histology grouping (Table 1),[2] based on the *2007 WHO Classification of Tumors of the Central Nervous System* (2007 WHO classification). It is important to note that, although pilocytic astrocytomas are considered nonmalignant in clinical practice, they have historically been coded by central cancer registries as malignant (ICD-O-3 behavior code /3) and are included as such herein for consistency with the North American Association of Central Cancer Registries uniform data standards and the International Agency for Research on Cancer.

Histologic groups in children (ages birth to 14 years) and adolescents (ages 15-19 years) were also classified according to the *International Classification of Childhood Cancer, third edition* where data for these age groups are presented separately without comparison to groups aged ≥20 years.[9] Again, according to North American Association of Central Cancer Registries uniform data standards and the International Agency for Research on Cancer, pilocytic astrocytoma was coded as malignant for childhood and adolescent tumors.[10]

Revisions in the classification of malignant and nonmalignant brain tumor cases over time have increasingly incorporated molecular markers into the nomenclature to better reflect clinical characteristics and prognosis. Although the histologic subtypes presented herein are aligned with the 2007 WHO classification in concordance with the 2020 CBTRUS report (Table 1), current definitions for case reporting as of January 2018 have been based on the *2016 WHO Classification of Tumors of the Central Nervous System* (2016 WHO classification).[11] Whereas the 2021 CBTRUS report will reflect these changes, data in this report and the 2020 CBTRUS report were collected before widespread implementation of these latest changes and, in general, also reflect the prevailing classification at the time of data collection, including the 2000 *Classification of Tumors of the Central Nervous System* (2000 WHO classification) for data collected in the early 2000s. These differences in case reporting and coding, as well as advances in imaging and other detection modalities, are reflected

TABLE 1. Brain and Other Central Nervous System Tumor Histology Codes Based on the Central Brain Tumor Registry of the United States 2012 Classification

HISTOLOGY	ICD-O-3 HISTOLOGY CODES
Tumors of neuroepithelial tissue	
Pilocytic astrocytoma[a]	9421, 9425[b]
Diffuse/anaplastic astrocytoma	
Diffuse astrocytoma	9400, 9410, 9411, 9420
Anaplastic astrocytoma	9401
Unique astrocytoma variants	9381, 9384, 9424
Glioblastoma	9440, 9441, 9442/3
Oligodendroglioma/anaplastic oligodendroglioma	
Oligodendroglioma	9450
Anaplastic oligodendroglioma	9451, 9460
Oligoastrocytic tumors (mixed glioma)[c]	9382
Ependymal tumors	9383, 9391, 9392, 9393, 9394
Glioma malignant, NOS	9380, 9431[b], 9432[b]
Embryonal tumors	8963, 9364, 9470-9474, 9480, 9490, 9500-9502, 9508
Medulloblastoma	9470-9472, 9474
Atypical teratoid/rhabdoid tumor	9508
Primitive neuroectodermal tumor[c]	9473
Other neuroepithelial tumors	
Choroid plexus tumors	9390
Neuronal and mixed neuronal-glial tumors	8680, 8681, 8690, 8693, 9412, 9413, 9442/1, 9492 (excluding site C75.1), 9493, 9505, 9506, 9509, 9522, 9523
Tumors of the pineal region	9360, 9361, 9362, 9395[b]
All other neuroepithelial tumors	9363, 9423, 9430, 9444
Tumors of cranial and spinal nerves	
Nerve sheath tumors	9540, 9541, 9550, 9560, 9561, 9570, 9571
Other tumors of cranial and spinal nerves	9562
Tumors of meninges	
Meningioma	9530-9534, 9537-9539
Mesenchymal tumors	8324, 8800-8806, 8810, 8815, 8824, 8830, 8831, 8835, 8836, 8850-8854, 8857, 8861, 8870, 8880, 8890, 8897, 8900-8902, 8910, 8912, 8920, 8921, 8935, 8990, 9040, 9136, 9150, 9170, 9180, 9210, 9241, 9260, 9373
Other neoplasms related to the meninges	
Primary melanocytic lesions	8720, 8728, 8770, 8771
All other neoplasms related to the meninges	9161, 9220, 9231, 9240, 9243, 9370-9372, 9535
Lymphomas and hematopoietic neoplasms	9590, 9591, 9596, 9650-9655, 9659, 9661-9665, 9667, 9670, 9671, 9673, 9675, 9680, 9684, 9687, 9690, 9691, 9695, 9698, 9699, 9701, 9702, 9705, 9714, 9719, 9727-9729, 9731, 9733, 9734, 9740, 9741, 9750-9758, 9760, 9766, 9823, 9826, 9827, 9832, 9837, 9860, 9861, 9866, 9930, 9970
Germ cell tumors and cysts	8020, 8440, 9060, 9061, 9064, 9065, 9070-9072, 9080-9085, 9100, 9101
Tumors of sellar region	
Tumors of the pituitary	8040, 8140, 8146, 8246, 8260, 8270- 8272, 8280, 8281, 8290, 8300, 8310, 8323, 9492 (site C75.1 only), 9582
Pituitary adenoma	8272
Craniopharyngioma	9350, 9351, 9352
Unclassified tumors	
Hemangioma	9120-9123, 9125, 9130, 9131, 9133, 9140
Neoplasm, unspecified	8000-8005, 8010, 8021
All other	8320, 8452, 8710, 8711, 8713, 8811, 8840, 8896, 8980, 9173, 9503, 9580

Abbreviations: ICD-O-3, International Classification of Diseases for Oncology, third edition; NOS: not otherwise specified.
[a]Although the World Health Organization classifies pilocytic astrocytoma as a nonmalignant tumor, this histology has been historically classified as malignant for mandatory US cancer registry reporting.
[b]Histology was included only starting with diagnosis year 2015.
[c]These terms are no longer applicable in the 2016 World Health Organization classification but are included in this report for consistency with the 2020 Central Brain Tumor Registry of the United States report and for historical reference.

in incidence rates for specific subtypes; thus, subtype-specific incidence trends should be interpreted with caution.

Deaths from malignant brain and other CNS tumors were identified according to the *International Classification of Diseases, 10th revision*.[12] It should be noted that mortality statistics do not include information by histology and, as such, mortality rates herein are not directly comparable to incidence.

Analysis

All incidence and death rates were age-standardized to the 2000 US standard population and are expressed per 100,000 population, as calculated by SEER*Stat software (version 8.3.8). Incidence and mortality rate ratios were calculated with 95% confidence intervals (CIs). SEER*Stat software was also used to calculate observed median and relative survival, with the latter generated using National Center for Health Statistics life tables stratified by age, sex, and race/ethnicity. The annual percent change in rates was quantified using the Joinpoint Regression Program (version 4.8.0.1).[13] All statistical tests were 2-sided, and a *P* value <.05 was considered significant.

Selected Findings for All Brain and Other CNS Tumors Combined

Contemporary Incidence, Survival, and Mortality

Malignant brain and other CNS tumors account for a small proportion (approximately 1%) of all invasive cancer cases in the United States, but are the most commonly diagnosed solid tumor in children and adolescents and the leading cause of cancer death among males aged <40 years and females aged <20 years.[1] In 2021, an estimated 83,570 individuals will be diagnosed with brain and other CNS tumors in the United States (24,530 malignant tumors and 59,040 nonmalignant tumors), and 18,600 people will die from the disease.[1,2] Malignant tumors account for less than one-third of all brain and other CNS tumors diagnosed in the United States (Fig. 1) but the majority of deaths from the disease.

The risk of being diagnosed with a brain or other CNS tumor increases with age, reflecting the age-risk profile of the 2 predominate histologic subtypes for malignant and nonmalignant tumors, respectively: glioblastoma, which accounts for nearly one-half (49%) of all malignant tumors in all ages combined, and nonmalignant meningioma, which accounts for more than one-half (54%) of nonmalignant tumors (Fig. 1 and Tables 2-3). Malignant brain and other CNS tumors are more common in males than in females,

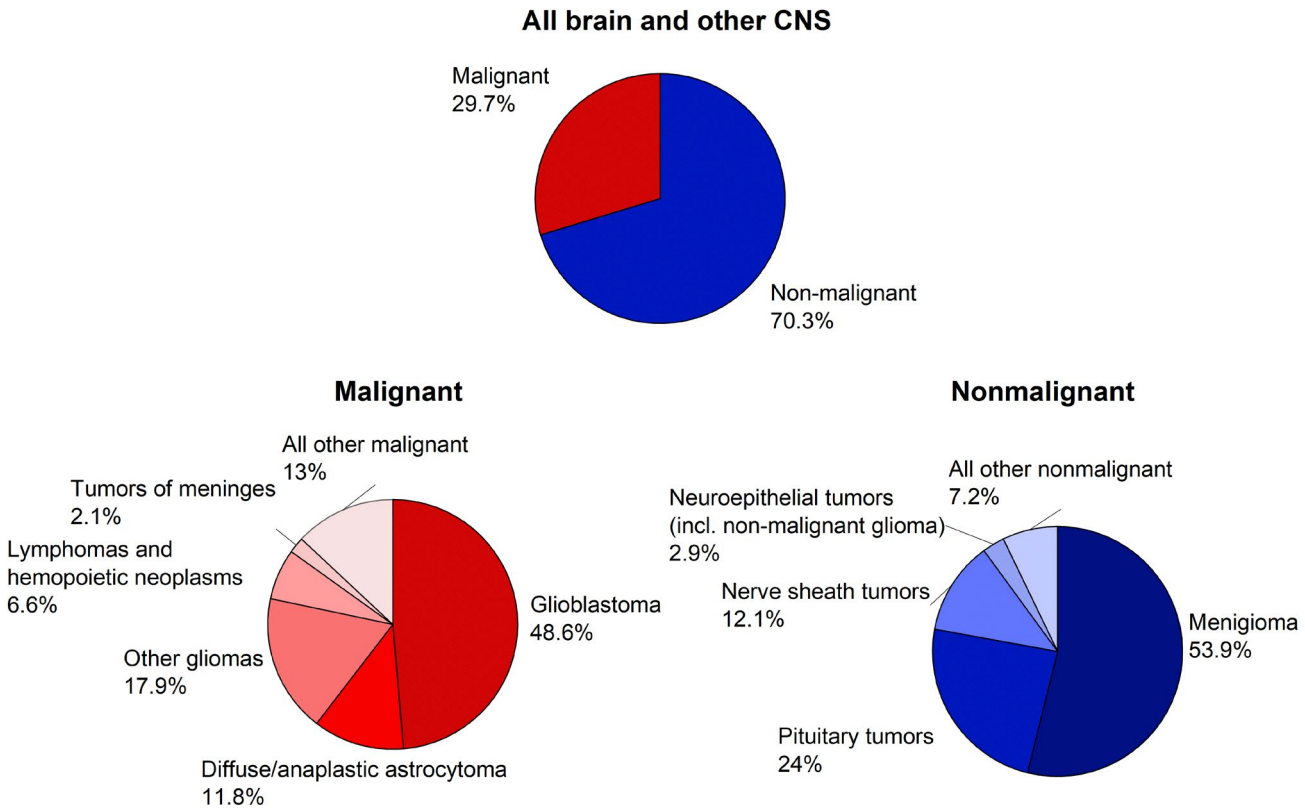

FIGURE 1. Distribution of Brain and Other Central Nervous System (CNS) Tumors by Behavior and Major Histology Type, 2013 to 2017. Pilocytic astrocytoma is clinically considered nonmalignant but is included in the malignant category according to historical convention for cancer reporting. Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

whereas the reverse is true for nonmalignant tumors (Fig. 2). For malignant tumors, sex differences are greatest for adults aged ≥45 years, among whom rates in females are 30% lower than those in males (female-to-male incidence rate ratio, 0.69; 95% CI, 0.68-0.70). Sex differences for nonmalignant tumors peak in ages 25 to 29 years, with the rate in females double that in males (female-to-male incidence rate ratio, 2.14; 95% CI, 2.05-2.25), reflecting the high burden of pituitary adenomas in females of this age group. However, pituitary tumor incidence decreases in females with advancing age, and sex differences in older adults are driven primarily by nonmalignant meningioma (Fig. 2 and Table 3). Sex differences in lifetime exposure to endogenous hormones have been proposed as a cause for this differential risk, since rates in children are generally similar, but results in published cohort studies have been inconsistent because of obstacles in long-term hormone measurement.[14]

Malignant brain tumor incidence rates are highest in individuals who are non-Hispanic White (8.0 cases diagnosed per 100,000 in both sexes combined during 2013-2017) and lowest in Asian or Pacific Islander individuals (3.4 cases per 100,000), with patterns for mortality following suit (Fig. 3). These racial differences for all ages combined are primarily driven by the higher rates of glioblastoma in non-Hispanic White adults (Table 4). Conversely, nonmalignant tumor incidence rates for all ages combined are highest in those who are non-Hispanic Black (19.9 cases diagnosed per 100,000 population during 2013-2017) (Fig. 3), reflecting the high burden of nonmalignant meningioma in non-Hispanic Black adults (Table 5). Some studies have reported that malignant brain tumor rates are higher in urban counties and among those with higher socioeconomic status, although the association is strongest for non-Hispanic Whites, and further studies are needed to elucidate the drivers of these patterns.[15,16] Wide geographic variation by state has also been noted for brain and other CNS tumor incidence, although this is thought to at least partly reflect differences in reporting across registries (for nonmalignant tumors) as well as differences in demographics.[2]

Figure 4 presents 5-year relative survival for malignant and nonmalignant brain tumors diagnosed during 2009 through 2015 by histology and age. Five-year survival for patients diagnosed with malignant tumors was 36% overall, reflecting the low survival for glioblastoma (7%). However, overall survival for patients with malignant tumors varied dramatically by age, ranging from approximately 80% in children and adolescents to ≤30% in adults aged ≥40 years (Fig. 4). There was comparatively less variation for nonmalignant tumors, for which 5-year survival ranged from 84% among individuals aged ≥65 years to ≥95% among those aged <65 years. By race/ethnicity, 5-year survival during 2009 through 2015 for malignant brain and other CNS tumors for all ages combined ranged from 31% in non-Hispanic White patients to 48% in those who were Hispanic.[5] It is important to note, however, that higher survival among Hispanic patients is due in part to loss to follow-up, whereas lower survival among non-Hispanic White patients reflects a higher burden of glioblastoma and other diffuse gliomas. Notably, in one study, higher survival for non-White patients who had glioma compared with those who were non-Hispanic White persisted after adjusting for socioeconomic status, age, and extent of surgical resection and when the analysis was confined to patients with glioblastoma who received both chemotherapy and radiation.[16] Survival patterns in children, which differ from those for all ages combined, are discussed in a section below.

Trends in Incidence, Survival, and Mortality

Overall malignant brain and other CNS tumor incidence rates for all ages combined declined by approximately 0.8% annually during 2008 through 2017, reflecting trends in adults aged ≥20 years (Fig. 5). Rates for malignant tumors by race/ethnicity also declined for all groups except for Asian and Pacific Islander and American Indian/Alaska Native American individuals, among whom rates were stable. Conversely, in contrast to rates for malignant tumors, overall incidence rates for nonmalignant tumors have been on the rise; however, this likely reflects improvements and advances in case finding and reporting.[17]

Relative survival has improved for all malignant tumors combined, from 23% for patients diagnosed during 1975 through 1977 in the oldest SEER registries[6] to 36% for patients diagnosed during 2009 through 2015 in the NPCR registries (Fig. 4), with increases in every age group (Fig. 6). The largest gains in survival occurred for individuals aged 20 to 39 years, for whom 5-year survival increased from 44% to 73%. Less improvement in survival among older age groups was largely driven by a lack of improvement for glioblastoma survival (Fig. 6), which increased slightly from 4% for patients diagnosed during 1975 through 1977[6] to 7% for those diagnosed during 2009 through 2015 (Fig. 4).

Mortality rates slightly increased from 2009 through 2018 by approximately 0.4% per year,[7] although the upward trend was limited to patients aged ≥65 years (0.7% annually); rates in those aged <65 years were stable. Reasons for the increase are unknown but may in part reflect reductions in misclassification on death certificates because of increased awareness.

Risk Factors for Brain and Other CNS Tumors

Research is ongoing regarding hereditary and environmental/behavioral risk factors for brain and other CNS tumors, although the rarity of many subtypes has caused glioma-based studies to predominate much of the literature.

TABLE 2. Malignant Brain and Other Central Nervous System Tumor Age-adjusted Incidence Rates by Sex and Age[a] (CBTRUS Data Provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013-2017 [Varying])

	ALL AGES COMBINED		BIRTH TO 14 YEARS		15-19 YEARS		20-39 YEARS		40-64 YEARS		≥65 YEARS	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Both sexes combined												
All brain and CNS combined	7.08		3.87		2.60		3.39		7.96		21.26	
Tumors of neuroepithelial tissue	6.03	84.8	3.57	92.8	2.21	84.9	3.05	90.0	6.98	87.5	16.73	78.8
Pilocytic astrocytoma[b]	0.35	4.2	1.07	27.7	0.59	22.6	0.19	5.9	0.09	1.0	0.05	0.3
Diffuse and anaplastic astrocytomas	0.87	11.8	0.32	8.4	0.35	13.3	0.92	27.1	1.05	12.3	1.60	7.6
Unique astrocytoma variants	0.05	0.6	0.05	1.4	0.08	2.9	0.05	1.5	0.03	0.4	0.07	0.3
Glioblastoma	3.23	48.6	0.16	4.1	0.23	8.7	0.62	17.6	4.33	57.1	13.33	62.7
Oligodendroglioma/anaplastic oligodendroglioma	0.35	4.5	0.03	0.9	0.10	3.8	0.44	12.7	0.57	6.3	0.29	1.4
Oligoastrocytic tumors (mixed glioma)	0.10	1.3	0.01	0.3	0.02	1.0	0.15	4.3	0.14	1.5	0.08	0.4
Ependymal tumors	0.25	3.2	0.28	7.2	0.14	5.6	0.21	6.1	0.29	3.3	0.25	1.2
Glioma malignant, NOS	0.51	6.6	0.87	22.5	0.41	15.8	0.29	8.6	0.33	3.9	0.91	4.2
Embryonal tumors	0.23	2.7	0.69	18.0	0.21	7.9	0.13	4.0	0.05	0.6	0.03	0.1
Other neuroepithelial tumors[c]	0.10	1.3	0.09	2.5	0.09	3.3	0.07	2.1	0.11	1.3	0.12	0.6
Tumors of cranial and spinal nerves	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.2	0.03	0.1
Nerve sheath tumors	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.2	0.03	0.1
Tumors of meninges	0.14	2.1	0.03	0.7	0.03	1.3	0.07	1.9	0.19	2.4	0.47	2.2
Meningioma	0.10	1.4	0.01	0.2	—	—	0.03	0.8	0.12	1.6	0.39	1.8
Mesenchymal tumors	0.03	0.4	0.02	0.4	—	—	0.02	0.7	0.04	0.5	0.05	0.2
Other neoplasms related to the meninges[d]	0.02	0.3	—	—	0.02	0.6	0.02	0.5	0.03	0.3	0.03	0.1
Lymphomas and hemopoietic neoplasms	0.45	6.6	0.03	0.7	0.04	1.5	0.12	3.5	0.50	6.5	1.99	9.3
Germ cell tumors and cysts	0.07	0.9	0.16	4.2	0.25	9.8	0.06	2.0	0.01	0.1	—	—
Tumors of sellar region	0.01	0.1	—	—	—	—	0.01	0.2	0.01	0.2	0.02	0.1
Tumors of the pituitary	0.01	0.1	—	—	—	—	0.01	0.2	0.01	0.2	0.02	0.1
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.37	5.4	0.06	1.5	0.06	2.2	0.07	2.1	0.25	3.2	2.02	9.5
Males												
All brain and CNS combined	8.30		4.11		2.92		3.83		9.42		25.78	
Tumors of neuroepithelial tissue	7.12	86.1	3.76	91.7	2.35	80.5	3.41	88.8	8.36	88.6	20.88	81.8
Pilocytic astrocytoma[b]	0.36	3.9	1.07	26.0	0.66	22.6	0.19	5.3	0.09	0.8	0.06	0.2
Diffuse and anaplastic astrocytomas	1.00	11.7	0.35	8.4	0.35	12.0	1.04	27.2	1.21	12.0	1.88	7.4

TABLE 2. (Continued)

	ALL AGES COMBINED		BIRTH TO 14 YEARS		15-19 YEARS		20-39 YEARS		40-64 YEARS		≥65 YEARS	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Unique astrocytoma variants	0.05	0.6	0.06	1.4	0.08	2.7	0.05	1.4	0.04	0.4	0.08	0.3
Glioblastoma	4.03	50.7	0.17	4.1	0.25	8.6	0.74	18.8	5.36	59.3	16.86	65.9
Oligodendroglioma/anaplastic oligodendroglioma	0.39	4.5	0.04	0.9	0.08	2.9	0.49	12.4	0.64	6.0	0.34	1.4
Oligoastrocytic tumors (mixed glioma)	0.11	1.3	0.02	0.4	—	—	0.18	4.7	0.15	1.4	0.11	0.5
Ependymal tumors	0.27	3.2	0.30	7.5	0.15	5.1	0.21	5.5	0.31	3.1	0.33	1.4
Glioma malignant, NOS	0.53	6.0	0.85	20.6	0.43	14.9	0.28	7.4	0.37	3.7	1.05	3.8
Embryonal tumors	0.27	2.9	0.83	20.2	0.23	7.9	0.16	4.3	0.06	0.5	0.04	0.1
Other neuroepithelial tumors[c]	0.11	1.3	0.09	2.3	0.10	3.3	0.07	1.9	0.13	1.3	0.14	0.6
Tumors of cranial and spinal nerves	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.2	0.03	0.1
Nerve sheath tumors	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.2	0.03	0.1
Tumors of meninges	0.15	1.7	0.03	0.7	—	—	0.07	1.7	0.19	2.0	0.48	1.8
Meningioma	0.09	1.1	—	—	—	—	0.02	0.5	0.11	1.2	0.39	1.5
Mesenchymal tumors	0.03	0.4	0.02	0.4	—	—	0.03	0.7	0.04	0.4	0.04	0.2
Other neoplasms related to the meninges[d]	0.02	0.3	—	—	—	—	0.02	0.4	0.03	0.3	0.04	0.2
Lymphomas and hemopoietic neoplasms	0.49	6.0	0.03	0.8	0.05	1.7	0.15	3.9	0.55	6.0	2.14	8.3
Germ cell tumors and cysts	0.11	1.2	0.21	5.0	0.43	14.8	0.11	3.3	0.01	0.1	—	—
Tumors of sellar region	0.01	0.1	—	—	—	—	—	—	0.02	0.2	0.03	0.1
Tumors of the pituitary	0.01	0.1	—	—	—	—	—	—	0.02	0.2	0.03	0.1
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.40	4.6	0.06	1.5	0.06	2.2	0.08	1.9	0.28	3.1	2.21	7.9
Females												
All brain and CNS combined	6.01		3.61		2.26		2.95		6.56		17.73	
Tumors of neuroepithelial tissue	5.06	83.1	3.38	94.1	2.06	90.9	2.69	91.5	5.67	86.1	13.48	75.5
Pilocytic astrocytoma[b]	0.34	4.5	1.07	29.7	0.51	22.6	0.19	6.6	0.09	1.2	0.05	0.3
Diffuse and anaplastic astrocytomas	0.76	11.8	0.30	8.3	0.34	15.0	0.79	27.0	0.89	12.6	1.38	7.8
Unique astrocytoma variants	0.04	0.6	0.05	1.4	0.07	3.2	0.04	1.6	0.02	0.4	0.06	0.3
Glioblastoma	2.54	46.0	0.15	4.0	0.20	8.9	0.49	16.1	3.34	54.0	10.56	59.0
Oligodendroglioma/anaplastic oligodendroglioma	0.31	4.5	0.03	0.8	0.12	5.1	0.39	13.2	0.50	6.6	0.24	1.4
Oligoastrocytic tumors (mixed glioma)	0.08	1.2	—	—	0.03	1.5	0.11	3.8	0.13	1.7	0.07	0.4
Ependymal tumors	0.22	3.3	0.25	6.9	0.14	6.2	0.21	7.0	0.26	3.6	0.19	1.1
Glioma malignant, NOS	0.49	7.3	0.89	24.7	0.39	17.1	0.29	10.2	0.30	4.3	0.80	4.7

TABLE 2. (Continued)

	ALL AGES COMBINED		BIRTH TO 14 YEARS		15-19 YEARS		20-39 YEARS		40-64 YEARS		≥65 YEARS	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Embryonal tumors	0.19	2.5	0.55	15.3	0.18	7.9	0.10	3.7	0.04	0.6	0.02	0.1
Other neuroepithelial tumors[c]	0.09	1.3	0.10	2.7	0.08	3.5	0.07	2.4	0.09	1.3	0.10	0.6
Tumors of cranial and spinal nerves	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.3	0.03	0.2
Nerve sheath tumors	0.01	0.2	—	—	—	—	0.01	0.3	0.02	0.3	0.03	0.2
Tumors of meninges	0.14	2.5	0.03	0.7	0.04	2.0	0.07	2.3	0.19	2.9	0.46	2.6
Meningioma	0.10	1.8	—	—	—	—	0.03	1.1	0.13	2.0	0.39	2.2
Mesenchymal tumors	0.03	0.4	0.01	0.3	—	—	0.02	0.7	0.03	0.5	0.05	0.3
Other neoplasms related to the meninges[d]	0.02	0.3	—	—	—	—	0.01	0.5	0.03	0.4	0.02	0.1
Lymphomas and hemopoietic neoplasms	0.41	7.3	0.02	0.5	0.03	1.4	0.09	2.9	0.45	7.2	1.89	10.4
Germ cell tumors and cysts	0.04	0.5	0.11	3.1	0.07	3.1	0.01	0.4	—	—	—	—
Tumors of sellar region	0.01	0.1	—	—	—	—	—	—	0.01	0.2	—	—
Tumors of the pituitary	0.01	0.1	—	—	—	—	—	—	0.01	0.2	—	—
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.34	6.4	0.05	1.4	0.05	2.3	0.07	2.4	0.21	3.3	1.87	11.2

Abbreviations: —, <16 cases were diagnosed during 2013-2017; CNS, central nervous system; NOS, not otherwise specified.
[a]Rates are per 100,000 and age-adjusted to the 2000 US standard population.
[b]Although the World Health Organization classifies pilocytic astrocytoma as a nonmalignant tumor, this histology has been historically classified as malignant for mandatory US cancer registry reporting.
[c]In addition to the 2012 Central Brain Tumor Registry of the United States (CBTRUS) histology group morphology codes for other neuroepithelial tumors, this category also includes a small number of choroid plexus tumors, neuronal and mixed neuronal glial tumors, and tumors of the pineal region.
[d]In addition to the 2012 CBTRUS histology group morphology codes for other tumors relative to the meninges, this category also includes a small number of primary melanocytic lesions.

TABLE 3. Nonmalignant Brain and Other Central Nervous System Tumor Age-Adjusted Incidence Rates by Sex and Age[a] (CBTRUS Data Provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013-2017 [Varying])

	ALL AGES COMBINED		BIRTH TO 14 YEARS		15-19 YEARS		20-39 YEARS		40-64 YEARS		≥65 YEARS	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Both sexes combined												
All brain and CNS combined	16.71		1.96		4.49		9.28		22.11		52.36	
Tumors of neuroepithelial tissue	0.54	2.9	0.59	30.4	0.73	16.3	0.54	6.1	0.50	2.1	0.36	0.7
Unique astrocytoma variants	0.02	0.1	0.07	3.5	0.03	0.7	0.01	0.2	0.01	<0.1	—	—
Ependymal tumors	0.17	1.0	0.04	1.9	0.08	1.7	0.18	2.0	0.27	1.1	0.21	0.4
Embryonal tumors	0.01	<0.1	—	—	—	—	0.01	0.1	0.01	<0.1	—	—
Other neuroepithelial tumors[b]	0.33	1.7	0.48	24.7	0.62	13.7	0.34	3.8	0.22	0.9	0.13	0.3
Tumors of cranial and spinal nerves	2.02	12.1	0.28	14.3	0.43	9.5	1.20	12.8	3.37	15.3	4.47	8.8
Nerve sheath tumors	2.02	12.1	0.28	14.3	0.42	9.5	1.20	12.8	3.37	15.3	4.46	8.8
Tumors of meninges	8.95	55.2	0.15	8.0	0.48	10.7	2.48	25.8	11.39	52.9	37.28	70.8
Meningioma	8.72	53.9	0.09	4.8	0.32	7.0	2.26	23.3	11.08	51.5	36.94	70.1
Mesenchymal tumors	0.06	0.3	0.04	2.3	0.04	0.8	0.04	0.5	0.07	0.3	0.09	0.2
Other neoplasms related to the meninges[c]	0.17	1.0	0.02	0.8	0.13	2.9	0.18	2.0	0.24	1.0	0.25	0.5
Germ cell tumors and cysts	0.03	0.2	0.05	2.8	0.03	0.7	0.03	0.3	0.02	0.1	0.02	<0.1
Tumors of sellar region	4.38	25.1	0.60	30.8	2.42	53.9	4.49	49.1	5.94	25.8	8.03	15.5
Tumors of the pituitary	4.19	24.0	0.36	18.6	2.25	50.2	4.36	47.7	5.72	24.8	7.8	15.0
Craniopharyngioma	0.19	1.1	0.24	12.2	0.17	3.7	0.13	1.4	0.22	1.0	0.23	0.5
Unclassified tumors	0.79	4.6	0.26	13.7	0.39	8.8	0.54	6.0	0.89	3.9	2.21	4.2
Males												
All brain and CNS combined	12.80		1.94		3.20		6.20		16.45		42.69	
Tumors of neuroepithelial tissue	0.58	4.3	0.64	33.1	0.79	24.6	0.58	9.7	0.56	3.2	0.41	1.1
Unique astrocytoma variants	0.03	0.2	0.07	3.9	0.04	1.1	0.02	0.3	—	—	—	—
Ependymal tumors	0.21	1.7	0.04	2.0	0.09	2.7	0.22	3.7	0.33	1.9	0.28	0.7
Embryonal tumors	0.01	<0.1	—	—	—	—	—	—	—	—	—	—
Other neuroepithelial tumors[b]	0.34	2.5	0.52	26.9	0.66	20.7	0.33	5.7	0.22	1.2	0.13	0.3
Tumors of cranial and spinal nerves	2.01	16.1	0.29	15.0	0.44	13.8	1.13	18.0	3.30	19.9	4.72	11.8
Nerve sheath tumors	2.01	16.1	0.29	15.0	0.44	13.6	1.13	18.0	3.30	19.9	4.71	11.8
Tumors of meninges	5.41	42.2	0.15	7.7	0.43	13.4	1.43	22.7	5.90	36.9	24.93	56.9
Meningioma	5.17	40.3	0.09	4.4	0.28	8.7	1.20	18.9	5.55	34.9	24.55	56.0
Mesenchymal tumors	0.06	0.4	0.05	2.5	0.03	1.0	0.04	0.7	0.08	0.4	0.08	0.2
Other neoplasms related to the meninges[c]	0.19	1.4	0.01	0.8	0.12	3.8	0.19	3.1	0.27	1.6	0.30	0.7

TABLE 3. (Continued)

	ALL AGES COMBINED		BIRTH TO 14 YEARS		15-19 YEARS		20-39 YEARS		40-64 YEARS		≥65 YEARS	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Germ cell tumors and cysts	0.03	0.2	0.06	3.3	0.03	0.9	0.03	0.4	0.02	0.1	0.02	0.1
Tumors of sellar region	4.01	31.5	0.52	26.7	1.14	35.6	2.57	41.4	5.86	35.1	10.39	25.1
Tumors of the pituitary	3.81	30.0	0.26	13.5	0.99	31.0	2.45	39.4	5.63	33.7	10.15	24.5
Craniopharyngioma	0.20	1.5	0.25	13.2	0.15	4.6	0.12	2.0	0.23	1.3	0.24	0.6
Unclassified tumors	0.74	5.6	0.27	14.1	0.37	11.6	0.47	7.7	0.80	4.8	2.23	5.1
Females												
All brain and CNS combined	20.31		1.98		5.83		12.41		27.55		59.93	
Tumors of neuroepithelial tissue	0.49	2.0	0.53	27.6	0.68	11.6	0.51	4.3	0.44	1.5	0.32	0.5
Unique astrocytoma variants	0.02	0.1	0.06	3.1	—	—	0.01	0.1	0.01	<0.1	—	—
Ependymal tumors	0.14	0.6	0.03	1.8	0.07	1.1	0.15	1.2	0.20	0.7	0.16	0.3
Embryonal tumors	0.01	<0.1	—	—	—	—	0.01	0.1	0.01	<0.1	—	—
Other neuroepithelial tumors[b]	0.32	1.3	0.43	22.5	0.57	9.8	0.34	2.9	0.23	0.7	0.14	0.2
Tumors of cranial and spinal nerves	2.03	9.9	0.26	13.6	0.41	7.1	1.27	10.2	3.44	12.6	4.28	7.1
Nerve sheath tumors	2.03	9.9	0.26	13.6	0.41	7.1	1.27	10.2	3.44	12.6	4.27	7.1
Tumors of meninges	12.07	62.5	0.16	8.2	0.54	9.2	3.54	27.4	16.65	62.1	46.95	78.4
Meningioma	11.86	61.5	0.10	5.2	0.36	6.1	3.32	25.5	16.38	61.1	46.65	77.9
Mesenchymal tumors	0.06	0.3	0.04	2.1	0.04	0.7	0.05	0.4	0.07	0.2	0.10	0.2
Other neoplasms related to the meninges[c]	0.15	0.7	0.02	0.9	0.14	2.4	0.18	1.5	0.20	0.7	0.21	0.3
Germ cell tumors and cysts	0.03	0.1	0.04	2.2	0.03	0.5	0.02	0.2	0.02	0.1	0.02	<0.1
Tumors of sellar region	4.84	21.5	0.68	35.1	3.76	64.4	6.44	52.9	6.03	20.4	6.17	10.2
Tumors of the pituitary	4.65	20.6	0.46	23.9	3.57	61.2	6.31	51.9	5.81	19.6	5.95	9.8
Craniopharyngioma	0.19	0.8	0.22	11.2	0.19	3.2	0.13	1.1	0.21	0.8	0.22	0.4
Unclassified tumors	0.84	4.0	0.26	13.3	0.42	7.2	0.62	5.1	0.97	3.4	2.20	3.8

Abbreviations: —, <16 cases were diagnosed during 2013-2017; CNS, central nervous system; NOS, not otherwise specified.
[a]Rates are per 100,000 and are age-adjusted to the 2000 US standard population.
[b]In addition to the 2012 Central Brain Tumor Registry of the United States (CBTRUS) histology group morphology codes for other neuroepithelial tumors, this category also includes choroid plexus tumors, neuronal and mixed neuronal glial tumors, and tumors of the pineal region.
[c]In addition to the 2012 CBTRUS histology group morphology codes for other tumors relative to the meninges, this category also includes primary melanocytic lesions.

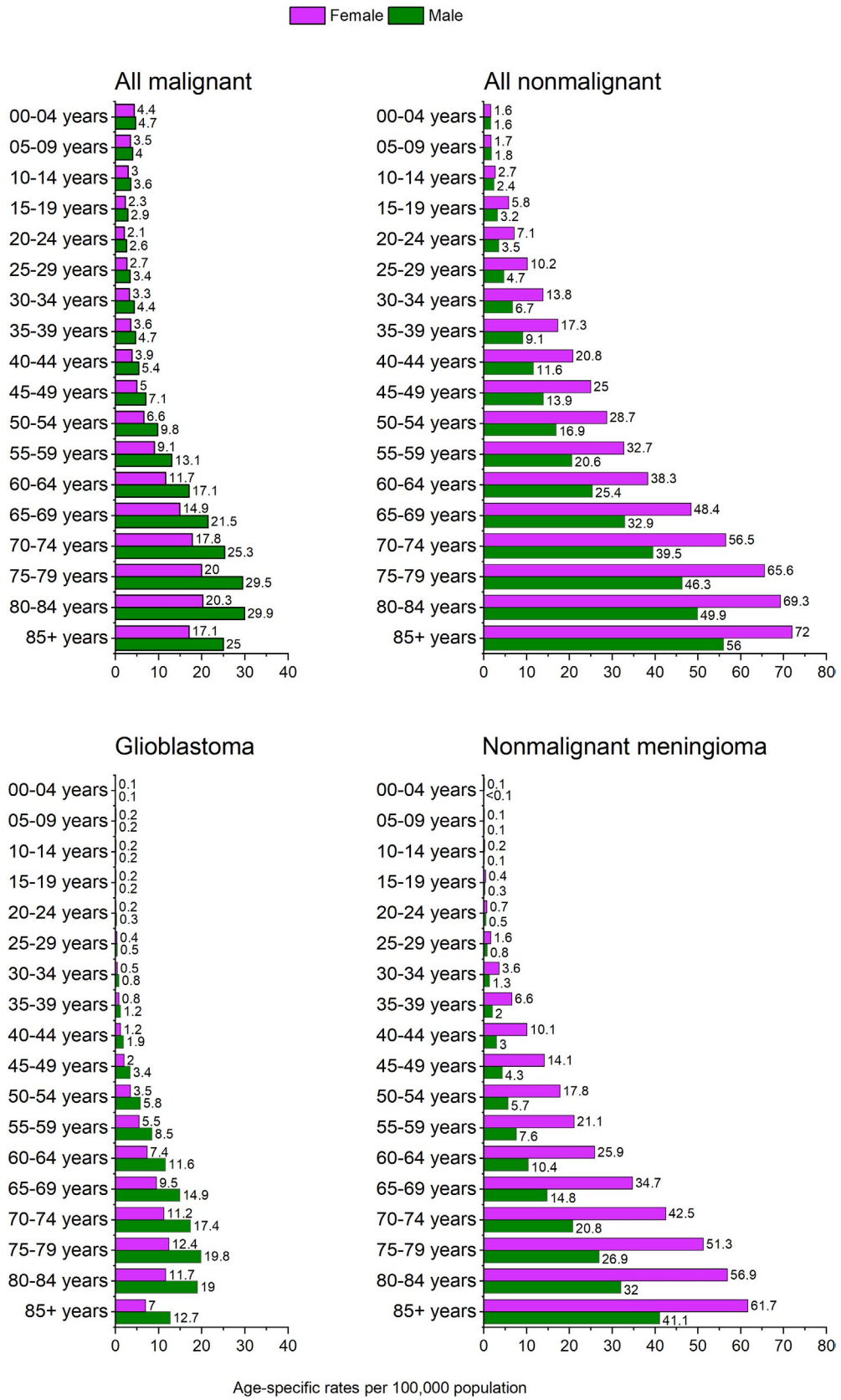

FIGURE 2. Age-Specific Malignant and Nonmalignant Brain and Other Central Nervous System (CNS) Tumor Incidence Rates by Sex, 2013 to 2017. Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

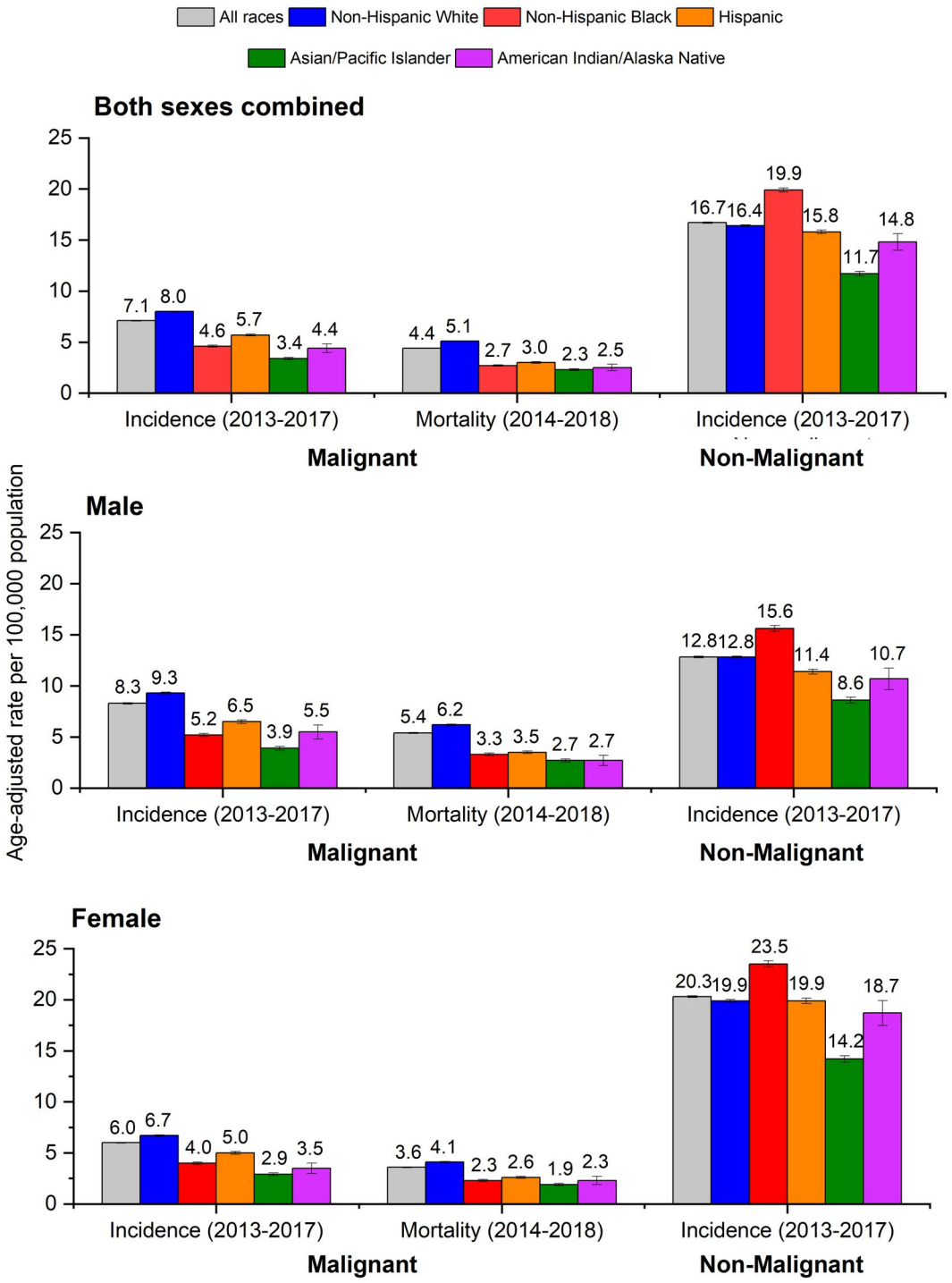

FIGURE 3. Malignant and Nonmalignant Brain and Other Central Nervous System (CNS) Tumor Incidence and Mortality by Sex and Race/Ethnicity, 2013 to 2018. American Indian/Alaska Native rates reflect rates in Preferred/Referred Health Care Delivery Area counties. Rates are age adjusted to the 2000 US standard population. Error bars represent 95% confidence intervals. Data sources: Incidence, Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying); mortality, National Center for Health Statistics, Centers for Disease Control and Prevention, 2020.

The only established environmental risk factor for all brain tumors is exposure to ionizing radiation; the association appears to be stronger for meningioma and in younger patients with glioma.[14,18] Individuals who received cranial radiation as treatment for acute lymphocytic leukemia in their youth are at particular risk of subsequent primary brain tumors.[19]

Although a hereditary component has been noted for some brain tumors, this accounts for a very small proportion of cases.[20] Certain Mendelian syndromes are linked to an increased risk for specific types, such as familial adenomatous polyposis and Turcot syndrome type 1 and type 2 for medulloblastoma and gliomas.[14] Several germline mutations have been

TABLE 4. Malignant Brain and Other Central Nervous System Tumor Age-Adjusted Incidence Rates in Adults Aged ≥20 Years by Sex and Race/Ethnicity[a] (CBTRUS Data Provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013-2017 [Varying])

	ALL RACES		NON-HISPANIC WHITE		NON-HISPANIC BLACK		HISPANIC		ASIAN/PACIFIC ISLANDER		AMERICAN INDIAN/ ALASKA NATIVE	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Both sexes combined												
All brain and CNS combined	8.50		9.54		5.22		6.89		3.89		5.33	
Tumors of neuroepithelial tissue	7.15	83.9	8.20	85.1	4.06	78.9	5.48	81.2	2.78	72.7	4.19	80.2
Pilocytic astrocytoma[b]	0.12	1.3	0.15	1.2	0.10	2.1	0.08	1.6	0.04	1.2	—	—
Diffuse and anaplastic astrocytomas	1.09	12.1	1.30	12.0	0.60	11.8	0.76	12.5	0.46	12.4	0.69	14.6
Unique astrocytoma variants	0.04	0.5	0.05	0.4	0.03	0.7	0.04	0.7	0.04	1.0	—	—
Glioblastoma	4.45	54.4	5.05	56.7	2.45	47.3	3.39	45.8	1.60	40.6	2.60	46.3
Oligodendroglioma/anaplastic oligodendroglioma	0.47	4.9	0.56	4.7	0.22	4.2	0.36	6.4	0.20	5.5	0.32	7.2
Oligoastrocytic tumors (mixed glioma)	0.13	1.4	0.17	1.4	0.05	1.0	0.09	1.6	0.06	1.6	—	—
Ependymal tumors	0.25	2.7	0.28	2.5	0.17	3.3	0.23	4.0	0.12	3.4	—	—
Glioma malignant, NOS	0.42	4.7	0.46	4.5	0.32	6.1	0.35	5.3	0.18	4.7	0.25	4.7
Embryonal tumors	0.08	0.8	0.08	0.7	0.05	1.2	0.09	1.9	0.02	0.7	—	—
Other neuroepithelial tumors[c]	0.10	1.1	0.10	1.0	0.06	1.2	0.08	1.5	0.06	1.6	—	—
Tumors of cranial and spinal nerves	0.02	0.2	0.01	0.1	0.02	0.3	0.03	0.4	—	—	—	—
Nerve sheath tumors	0.02	0.2	0.01	0.1	0.02	0.3	0.03	0.4	—	—	—	—
Tumors of meninges	0.19	2.2	0.18	1.9	0.23	4.3	0.19	2.7	0.18	4.5	—	—
Meningioma	0.13	1.6	0.12	1.3	0.19	3.4	0.13	1.8	0.13	3.1	—	—
Mesenchymal tumors	0.03	0.4	0.04	0.3	0.02	0.5	0.03	0.5	0.04	1.1	—	—
Other neoplasms related to the meninges[d]	0.02	0.3	0.02	0.2	0.02	0.4	0.03	0.5	—	—	—	—
Lymphomas and hemopoietic neoplasms	0.62	7.4	0.60	6.7	0.45	8.5	0.69	9.3	0.61	15.3	0.52	9.4
Germ cell tumors and cysts	0.03	0.3	0.03	0.2	0.02	0.4	0.02	0.6	0.03	0.8	—	—
Tumors of sellar region	0.01	0.1	0.01	0.1	0.02	0.4	0.01	0.2	—	—	—	—
Tumors of the pituitary	0.01	0.1	0.01	0.1	0.02	0.4	0.01	0.2	—	—	—	—
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.49	5.9	0.50	5.8	0.42	7.2	0.47	5.5	0.27	6.0	0.42	6.9
Males												
All brain and CNS combined	10.10		11.28		6.14		7.97		4.50		6.40	
Tumors of neuroepithelial tissue	8.61	85.7	9.81	86.8	4.93	81.7	6.35	81.5	3.33	75.2	5.10	81.3
Pilocytic astrocytoma[b]	0.13	1.2	0.15	1.1	0.10	1.8	0.08	1.5	0.05	1.2	—	—

TABLE 4. (Continued)

	ALL RACES		NON-HISPANIC WHITE		NON-HISPANIC BLACK		HISPANIC		ASIAN/PACIFIC ISLANDER		AMERICAN INDIAN/ ALASKA NATIVE	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Diffuse and anaplastic astrocytomas	1.26	12.1	1.49	12.0	0.69	11.9	0.84	12.5	0.56	13.4	0.83	14.8
Unique astrocytoma variants	0.05	0.5	0.06	0.4	0.03	0.6	0.04	0.7	—	—	—	—
Glioblastoma	5.57	56.7	6.28	59.0	3.11	50.5	4.06	46.7	2.00	43.3	3.19	46.3
Oligodendroglioma/anaplastic oligodendroglioma	0.53	4.9	0.63	4.7	0.26	4.4	0.36	6.1	0.23	5.6	—	—
Oligoastrocytic tumors (mixed glioma)	0.15	1.4	0.19	1.4	0.06	1.0	0.11	1.7	0.06	1.6	—	—
Ependymal tumors	0.28	2.7	0.31	2.5	0.18	3.0	0.25	3.8	0.10	2.6	—	—
Glioma malignant, NOS	0.45	4.3	0.49	4.0	0.37	5.9	0.41	5.2	0.18	4.0	—	—
Embryonal tumors	0.09	0.9	0.10	0.7	0.06	1.3	0.10	2.0	—	—	—	—
Other neuroepithelial tumors[c]	0.11	1.1	0.12	1.0	0.07	1.2	0.09	1.5	0.08	1.7	—	—
Tumors of cranial and spinal nerves	0.02	0.2	0.02	0.1	—	—	0.02	0.3	—	—	—	—
Nerve sheath tumors	0.02	0.2	0.02	0.1	—	—	0.02	0.3	—	—	—	—
Tumors of meninges	0.19	1.9	0.19	1.6	0.20	3.2	0.19	2.4	0.17	3.8	—	—
Meningioma	0.13	1.2	0.12	1.1	0.17	2.5	0.12	1.4	0.12	2.4	—	—
Mesenchymal tumors	0.04	0.4	0.04	0.3	—	—	0.03	0.5	—	—	—	—
Other neoplasms related to the meninges[d]	0.03	0.3	0.03	0.2	—	—	0.03	0.5	—	—	—	—
Lymphomas and hemopoietic neoplasms	0.67	6.7	0.65	6.1	0.44	7.3	0.80	9.4	0.67	14.6	0.50	8.4
Germ cell tumors and cysts	0.05	0.5	0.05	0.4	0.04	0.8	0.04	0.9	0.04	1.3	—	—
Tumors of sellar region	0.02	0.1	0.01	0.1	0.03	0.5	0.02	0.3	—	—	—	—
Tumors of the pituitary	0.01	0.1	0.01	0.1	0.03	0.5	0.02	0.3	—	—	—	—
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.54	5.0	0.55	4.9	0.47	6.2	0.54	5.1	0.26	4.7	—	—
Females												
All brain and CNS combined	7.10		7.98		4.48		5.95		3.39		4.44	
Tumors of neuroepithelial tissue	5.87	81.8	6.75	82.9	3.37	75.8	4.72	80.9	2.33	69.9	3.43	78.8
Pilocytic astrocytoma[b]	0.12	1.4	0.15	1.3	0.11	2.5	0.08	1.7	—	—	—	—
Diffuse and anaplastic astrocytomas	0.94	12.1	1.13	12.1	0.52	11.6	0.68	12.6	0.37	11.3	0.57	14.4
Unique astrocytoma variants	0.04	0.5	0.04	0.4	0.03	0.8	0.04	0.6	0.04	1.3	—	—
Glioblastoma	3.49	51.6	3.97	53.8	1.93	43.7	2.82	44.7	1.27	37.6	2.12	46.3
Oligodendroglioma/anaplastic oligodendroglioma	0.41	4.9	0.50	4.8	0.18	3.9	0.35	6.8	0.17	5.3	—	—
Oligoastrocytic tumors (mixed glioma)	0.11	1.3	0.14	1.3	0.05	1.1	0.08	1.5	0.05	1.5	—	—

TABLE 4. (Continued)

	ALL RACES		NON-HISPANIC WHITE		NON-HISPANIC BLACK		HISPANIC		ASIAN/PACIFIC ISLANDER		AMERICAN INDIAN/ ALASKA NATIVE	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Ependymal tumors	0.23	2.8	0.25	2.5	0.16	3.7	0.22	4.4	0.14	4.3	—	—
Glioma malignant, NOS	0.39	5.2	0.43	5.1	0.28	6.3	0.30	5.4	0.18	5.4	—	—
Embryonal tumors	0.06	0.8	0.07	0.6	0.05	1.1	0.08	1.8	—	—	—	—
Other neuroepithelial tumors[c]	0.08	1.1	0.09	1.0	0.06	1.2	0.07	1.4	0.05	1.5	—	—
Tumors of cranial and spinal nerves	0.02	0.2	0.01	0.2	—	—	0.03	0.5	—	—	—	—
Nerve sheath tumors	0.02	0.2	0.01	0.2	—	—	0.03	0.5	—	—	—	—
Tumors of meninges	0.19	2.7	0.18	2.3	0.25	5.5	0.18	3.1	0.19	5.4	—	—
Meningioma	0.14	2.0	0.13	1.7	0.20	4.3	0.14	2.2	0.14	3.9	—	—
Mesenchymal tumors	0.03	0.4	0.04	0.4	0.02	0.6	0.02	0.4	—	—	—	—
Other neoplasms related to the meninges[d]	0.02	0.3	0.02	0.2	0.03	0.6	0.03	0.5	—	—	—	—
Lymphomas and hemopoietic neoplasms	0.56	8.2	0.55	7.6	0.45	9.8	0.59	9.2	0.55	16.1	0.52	10.6
Germ cell tumors and cysts	0.01	0.1	0.01	0.0	—	—	—	—	—	—	—	—
Tumors of sellar region	0.01	0.1	0.01	0.1	—	—	—	—	—	—	—	—
Tumors of the pituitary	0.01	0.1	0.01	0.1	—	—	—	—	—	—	—	—
Craniopharyngioma	—	—	—	—	—	—	—	—	—	—	—	—
Unclassified tumors	0.45	7.0	0.46	6.9	0.39	8.2	0.42	6.1	0.28	7.5	—	—

Abbreviations: —, <16 cases were diagnosed during 2013-2017; CNS, central nervous system; NOS, not otherwise specified.
[a]Rates are per 100,000 and are age-adjusted to the 2000 US standard population. Rates for American Indians and Alaska Natives are based on Preferred/Referred Care Delivery Area counties.
[b]Although the World Health Organization classifies pilocytic astrocytoma as a nonmalignant tumor, this histology has been historically classified as malignant for mandatory US cancer registry reporting.
[c]In addition to the 2012 Central Brain Tumor Registry of the United States (CBTRUS) histology group morphology codes for other neuroepithelial tumors, this category also includes a small number of choroid plexus tumors, neuronal and mixed neuronal glial tumors, and tumors of the pineal region.
[d]In addition to the 2012 CBTRUS histology group morphology codes for other tumors relative to the meninges, this category also includes a small number of primary melanocytic lesions.

TABLE 5. Nonmalignant Brain and Other Central Nervous System Tumor Age-Adjusted Incidence Rates in Adults Aged ≥20 Years by Sex and Race/Ethnicity[a] (CBTRUS Data Provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013-2017 [Varying])

	ALL RACES		NON-HISPANIC WHITE		NON-HISPANIC BLACK		HISPANIC		ASIAN/PACIFIC ISLANDER		AMERICAN INDIAN/ ALASKA NATIVE	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Both sexes combined												
All brain and CNS combined	22.37		21.96		27.05		21.17		15.79		20.04	
Tumors of neuroepithelial tissue	0.49	2.0	0.58	2.2	0.31	1.3	0.37	2.2	0.17	1.2	0.38	2.4
Unique astrocytoma variants	0.01	<0.1	0.01	<0.1	0.01	<0.1	0.01	0.1	—	—	—	—
Ependymal tumors	0.22	1.0	0.27	1.1	0.12	0.5	0.17	1.0	0.06	0.4	—	—
Embryonal tumors	0.01	<0.1	0.01	<0.1	—	—	—	—	—	—	—	—
Other neuroepithelial tumors[b]	0.25	1.0	0.30	1.1	0.18	0.7	0.18	1.1	0.11	0.8	0.19	1.3
Tumors of cranial and spinal nerves	2.70	12.1	3.04	13.5	1.38	5.3	1.86	9.4	2.24	15.1	2.08	11.6
Nerve sheath tumors	2.70	12.1	3.04	13.5	1.38	5.3	1.85	9.4	2.24	15.1	2.08	11.6
Tumors of meninges	12.44	56.9	12.34	59.3	14.65	53.0	11.57	49.5	8.87	53.9	10.59	48.8
Meningioma	12.16	55.7	12.04	58.1	14.41	52.0	11.33	48.2	8.72	52.9	10.39	47.6
Mesenchymal tumors	0.06	0.3	0.07	0.3	0.05	0.2	0.06	0.3	0.03	0.2	—	—
Other neoplasms related to the meninges[c]	0.22	0.9	0.23	1.0	0.19	0.7	0.18	1.0	0.12	0.8	—	—
Germ cell tumors and cysts	0.02	0.1	0.02	0.1	0.02	0.1	0.03	0.1	—	—	—	—
Tumors of sellar region	5.73	24.5	4.97	20.5	9.66	36.6	6.34	33.9	3.91	26.1	5.74	31.2
Tumors of the pituitary	5.54	23.7	4.80	19.8	9.33	35.3	6.17	33.0	3.78	25.2	5.53	30.1
Craniopharyngioma	0.18	0.8	0.16	0.7	0.33	1.3	0.17	0.9	0.13	0.8	—	—
Unclassified tumors	0.98	4.3	0.99	4.4	1.03	3.8	1.01	4.9	0.58	3.6	1.26	5.9
Males												
All brain and CNS combined	17.03		16.93		21.13		15.11		11.48		14.34	
Tumors of neuroepithelial tissue	0.54	3.1	0.64	3.3	0.34	1.9	0.40	3.5	0.18	1.8	0.49	4.6
Unique astrocytoma variants	0.01	<0.1	0.01	<0.1	—	—	—	—	—	—	—	—
Ependymal tumors	0.28	1.6	0.34	1.8	0.15	0.8	0.20	1.7	0.08	0.7	—	—
Embryonal tumors	0.01	<0.1	0.00	<0.1	—	—	—	—	—	—	—	—
Other neuroepithelial tumors[b]	0.25	1.4	0.29	1.4	0.17	1.0	0.18	1.7	0.09	1.0	—	—
Tumors of cranial and spinal nerves	2.69	16.2	3.04	18.0	1.28	6.5	1.69	12.5	2.25	21.4	1.96	16.0
Nerve sheath tumors	2.68	16.2	3.03	17.9	1.28	6.5	1.69	12.5	2.25	21.4	1.96	16.0
Tumors of meninges	7.50	43.7	7.49	45.5	9.16	41.1	6.47	37.2	5.01	40.6	5.93	35.6
Meningioma	7.19	41.9	7.16	43.7	8.88	39.7	6.22	35.2	4.84	39.1	5.76	34.2

TABLE 5. (Continued)

	ALL RACES		NON-HISPANIC WHITE		NON-HISPANIC BLACK		HISPANIC		ASIAN/PACIFIC ISLANDER		AMERICAN INDIAN/ ALASKA NATIVE	
	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %	RATE	CASES, %
Mesenchymal tumors	0.06	0.4	0.07	0.4	0.05	0.3	0.06	0.4	—	—	—	—
Other neoplasms related to the meninges[c]	0.24	1.4	0.26	1.4	0.22	1.2	0.20	1.6	0.12	1.2	—	—
Germ cell tumors and cysts	0.02	0.1	0.03	0.1	—	—	0.02	0.2	—	—	—	—
Tumors of sellar region	5.36	31.6	4.81	27.8	9.36	45.8	5.56	40.1	3.51	31.7	4.90	36.3
Tumors of the pituitary	5.17	30.5	4.64	26.8	9.02	44.1	5.40	38.8	3.35	30.3	4.70	34.7
Craniopharyngioma	0.19	1.1	0.17	1.0	0.33	1.7	0.16	1.3	0.15	1.4	—	—
Unclassified tumors	0.92	5.3	0.93	5.3	0.97	4.5	0.97	6.4	0.53	4.4	1.05	7.5
Females												
All brain and CNS combined	27.27		26.65		31.97		26.74		19.36		25.31	
Tumors of neuroepithelial tissue	0.45	1.5	0.53	1.6	0.29	0.9	0.34	1.5	0.17	0.9	—	—
Unique astrocytoma variants	0.01	<0.1	0.01	<0.1	—	—	—	—	—	—	—	—
Ependymal tumors	0.17	0.6	0.21	0.6	0.10	0.3	0.15	0.6	0.05	0.3	—	—
Embryonal tumors	0.01	<0.1	0.01	<0.1	—	—	—	—	—	—	—	—
Other neuroepithelial tumors[b]	0.26	0.8	0.31	0.9	0.18	0.6	0.18	0.8	0.12	0.6	—	—
Tumors of cranial and spinal nerves	2.73	9.9	3.06	11.0	1.48	4.7	2.02	7.8	2.23	12.1	2.20	9.4
Nerve sheath tumors	2.73	9.9	3.06	11.0	1.48	4.7	2.01	7.8	2.23	12.1	2.20	9.4
Tumors of meninges	16.81	64.2	16.76	67.2	18.90	59.1	15.99	55.6	11.99	60.3	14.72	55.3
Meningioma	16.56	63.4	16.48	66.3	18.69	58.4	15.76	54.7	11.84	59.5	14.50	54.2
Mesenchymal tumors	0.07	0.2	0.07	0.2	0.05	0.2	0.07	0.3	—	—	—	—
Other neoplasms related to the meninges[c]	0.19	0.7	0.21	0.7	0.16	0.5	0.16	0.7	0.12	0.7	—	—
Germ cell tumors and cysts	0.02	0.1	0.02	0.1	—	—	—	—	—	—	—	—
Tumors of sellar region	6.21	20.6	5.22	16.3	10.19	31.8	7.29	30.8	4.32	23.3	6.70	28.7
Tumors of the pituitary	6.03	19.9	5.06	15.7	9.87	30.7	7.11	30.1	4.22	22.8	6.48	27.8
Craniopharyngioma	0.18	0.6	0.16	0.5	0.33	1.0	0.18	0.7	0.10	0.6	—	—
Unclassified tumors	1.05	3.8	1.06	3.9	1.08	3.4	1.07	4.1	0.63	3.2	1.40	5.2

Abbreviations: —, <16 cases were diagnosed during 2013-2017; CNS, central nervous system; NOS, not otherwise specified.
[a]Rates are per 100,000 and are age-adjusted to the 2000 US standard population. Rates for American Indians and Alaska Natives are based on Preferred/Referred Care Delivery Area counties.
[b]In addition to the 2012 Central Brain Tumor Registry of the United States (CBTRUS) histology group morphology codes for other neuroepithelial tumors, this category also includes choroid plexus tumors, neuronal and mixed neuronal glial tumors, and tumors of the pineal region.
[c]In addition to the 2012 CBTRUS histology group morphology codes for other tumors relative to the meninges, this category also includes primary melanocytic lesions.

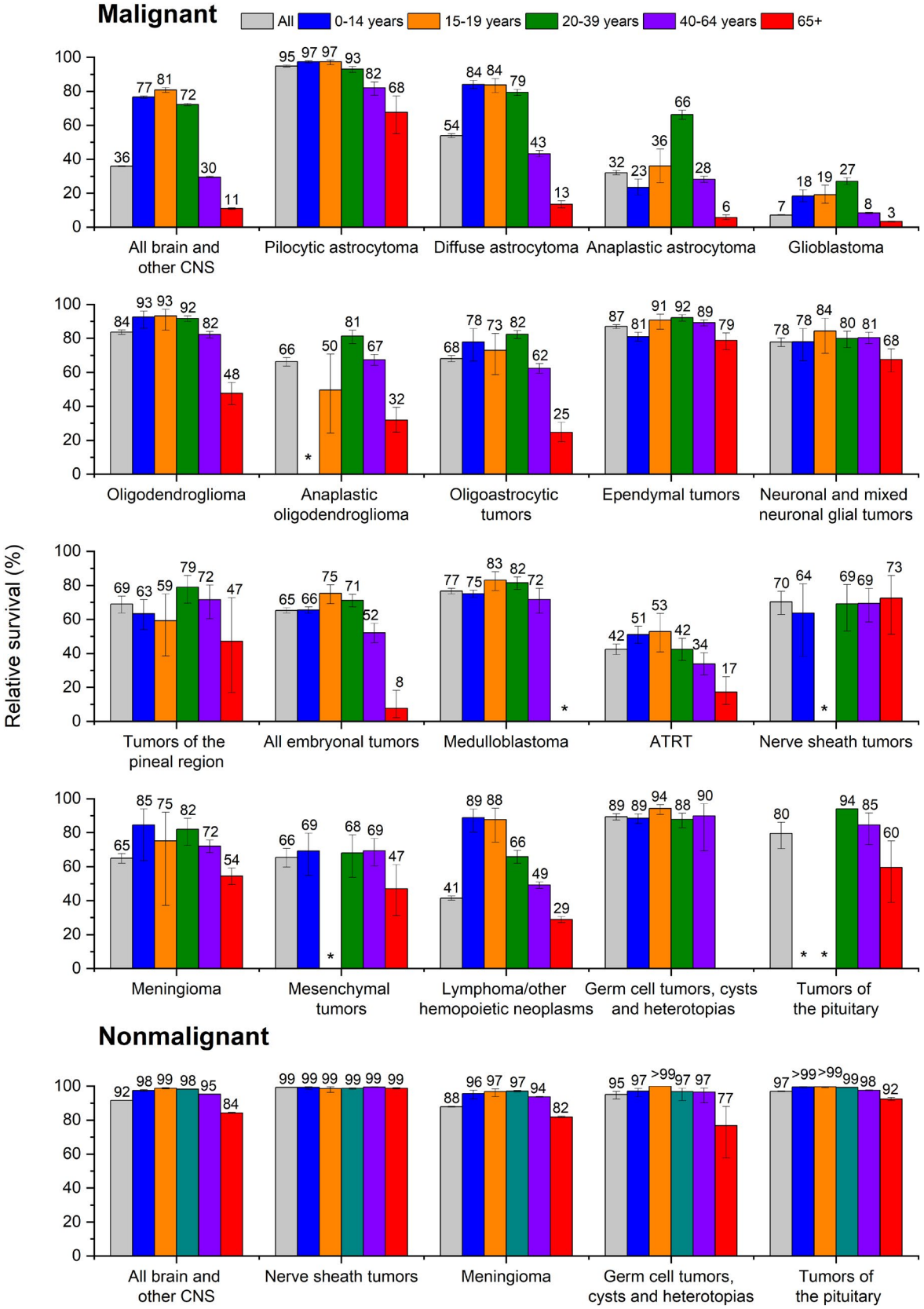

FIGURE 4. Five-Year Relative Survival for Selected Brain and Other Central Nervous System (CNS) Tumors by Histology by Age, 2009 to 2015. *The survival estimate is suppressed because <16 cases were diagnosed. All patients were diagnosed during 2009 to 2015 and followed through 2016. Error bars indicate 95% confidence intervals. Pilocytic astrocytoma is considered nonmalignant in clinical practice but is included in the malignant category according to historical convention for US cancer reporting. ATRT indicates atypical teratoid rhabdoid tumor. Data source: National Program of Cancer Registries survival database.

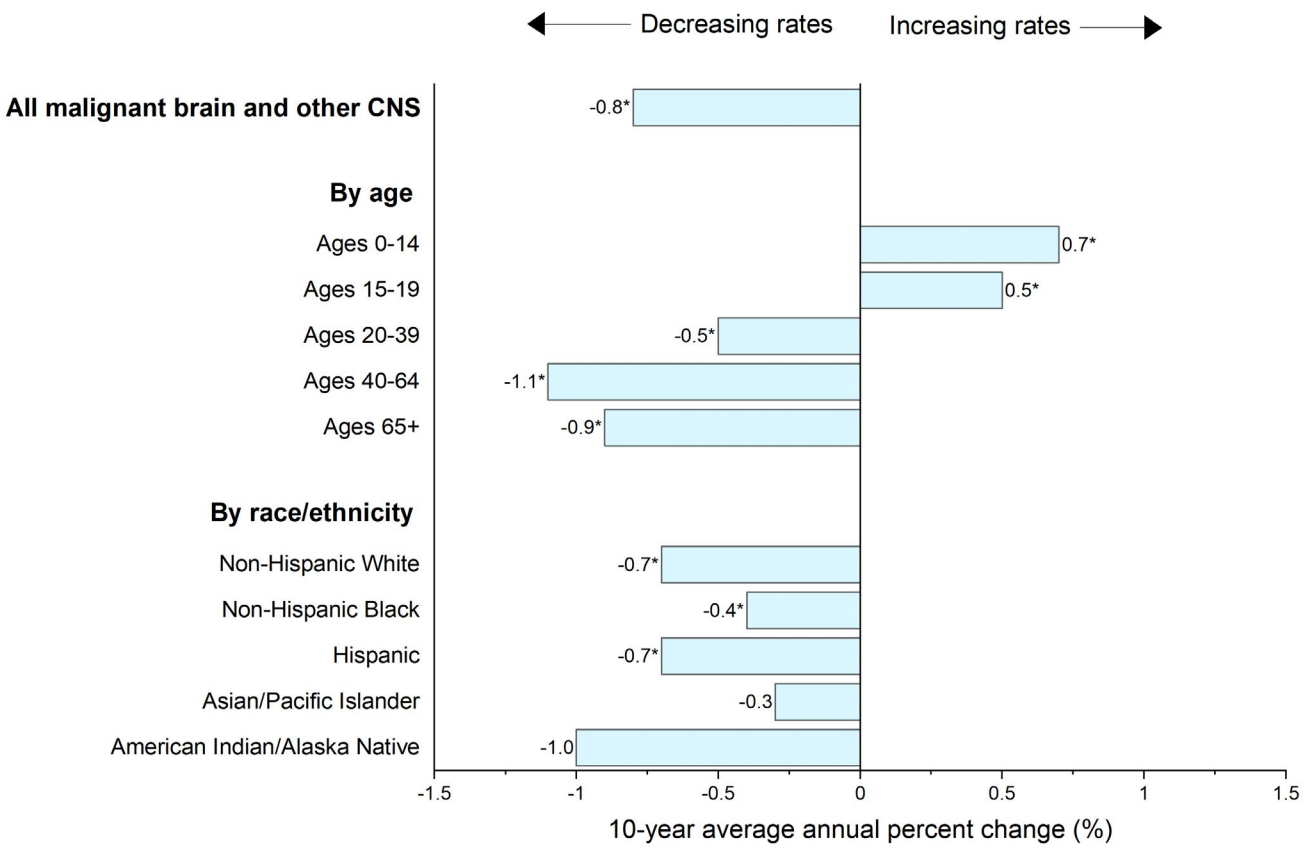

FIGURE 5. Ten-Year Average Annual Percent Change in Malignant Brain and Other Central Nervous System (CNS) Tumor Incidence Rates by Age and Race/Ethnicity, United States, 2008 to 2017. American Indian/Alaska Native rates reflect rates in Preferred/Referred Health Care Delivery Area counties. Joinpoints are based on data from 2000 to 2017 for incidence, allowing for up to 3 joinpoints. *The average annual percent change is statistically significantly different from zero ($P < .05$). Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

associated with an increased risk of brain tumors for specific histologic types, although most of these studies were conducted among older populations of European ancestry, and data are limited for children and other racial/ethnic groups.[14,21]

Major Brain and Other CNS Tumor Types in Adults

Brain and other CNS tumors are extremely heterogeneous. The section below provides information on major malignant and nonmalignant subtypes in adults aged ≥20 years. The descriptive epidemiology, treatment, and prognosis of brain and other CNS tumors in children (ages birth to 14 years) and adolescents (ages 15-19 years) differ substantially from adults and are presented in a subsequent section.

Malignant Gliomas

Overview

Gliomas are a subset of neuroepithelial tumors that have histologic features similar to normal glial cells (astrocytes, oligodendrocytes, and ependymal cells). It is important to note that, although pilocytic astrocytoma is reported as malignant in population-based cancer registry data according to historical convention, it is categorized as nonmalignant by the WHO and considered as such in clinical practice.[10] Therefore, in clinical practice, malignant gliomas refer to glioblastoma and other aggressive diffuse gliomas (eg, grade 3 anaplastic astrocytoma and oligodendroglioma).

Although gliomas may occur throughout the brain and other CNS, diffuse gliomas are most commonly diagnosed in the supratentorial region of the brain (the lobes of the cerebrum) (Fig. 7). Diffuse gliomas predominate among adults, with some variation in subtype by age. Specific risk factors for glioma beyond those described previously for all brain and other CNS tumors combined (see Risk Factors for Brain and Other CNS Tumors, above) are largely unknown, although recent studies have demonstrated that an atopic history in adults may be protective.[22]

The classification of gliomas has changed rapidly in recent years, and the distinction for several subtypes is currently determined molecularly by the presence of mutations in the *IDH-1/IDH-2* genes and 1p/19q codeletion according to the 2016 WHO classification.[12] This has important implications for the descriptive epidemiology of gliomas. For example, recent molecular studies have demonstrated that oligoastrocytoma is more appropriately classified as either

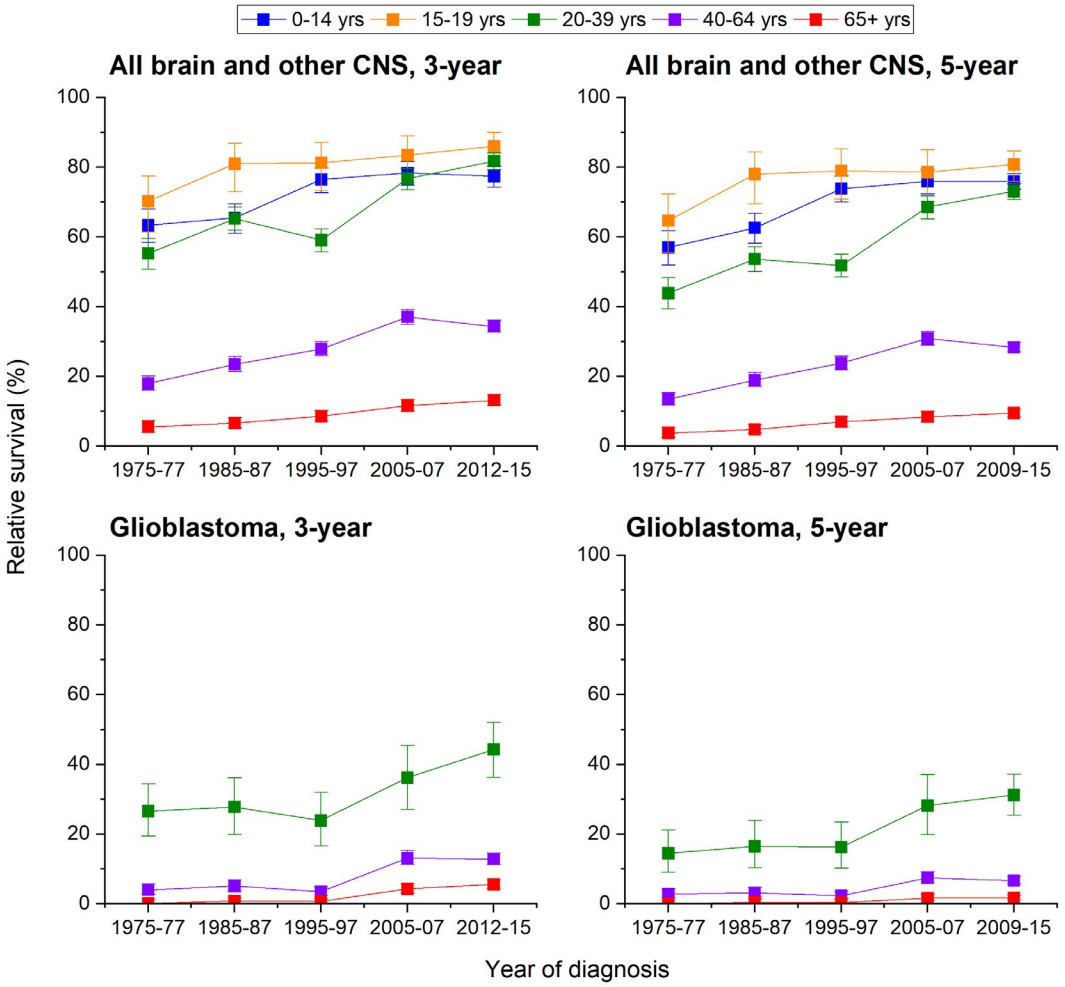

FIGURE 6. Trends in 5-Year and 3-Year Relative Survival for All Malignant Brain and Other Central Nervous System (CNS) Tumors Combined and Glioblastoma, 1975 to 2015. Error bars indicate 95% confidence intervals. Data source: Surveillance, Epidemiology, and End Results (SEER) 9 registries, 2020.

astrocytoma or oligodendroglioma, rather than as a distinct histologic type. Thus, in the 2016 WHO classification the term *oligoastrocytoma* is discouraged and assigned a *not otherwise specified* designation. Herein, the data presented for oligoastrocytic tumors are reported for historical reference. These tumors will not be included in the upcoming WHO 2021 classification scheme as a separate entity.

Glioblastoma

Glioblastoma is a grade 4 tumor usually of astrocytic cell lineage and is the most commonly diagnosed malignant brain and other CNS tumor in the United States, accounting for 54% of malignant cases in adults (Table 4). Glioblastoma incidence increases with age, with the highest rates occurring among those aged 75 to 84 years (Fig. 2). As with other gliomas, it is more common in males than in females (5.6 vs 3.5 cases per 100,000 population, respectively, during 2013-2017) (Table 4).[5] Rates in non-Hispanic White adults (5.1 cases per 100,000) are more than double those in non-Hispanic Black adults (2.5 cases per 100,000) and American Indian/Alaska Native adults (2.6 cases per 100,000) and are >3-fold the rates in those who are Asian or Pacific Islander (1.6 cases per 100,000) for reasons that are largely unknown (Table 4). Racial/ethnic differences are unlikely to be due to detection bias because of the symptomatic and aggressive nature of glioblastomas.[23] As with other gliomas, the risk of glioblastoma increases with higher socioeconomic status, although this association is significant among White individuals only.[16] The reason for this association of glioblastoma risk with socioeconomic status is unknown.

From 2008 to 2017, incidence rates for glioblastoma were stable (Fig. 8). Although there have been advances in glioblastoma treatment, such as maximal surgical resection with concurrent radiation and alkylating chemotherapy, followed by adjuvant alkylating chemotherapy, the 5-year relative survival for patients who had glioblastoma diagnosed during 2009 through 2015 remained low, ranging from 3% in adults aged ≥65 years to 27% among those aged 20 to 39 years (Fig. 4). Survival is higher for females and non-White patients after adjusting for treatment differences.[23,24] However, in one study, Black patients had lower survival

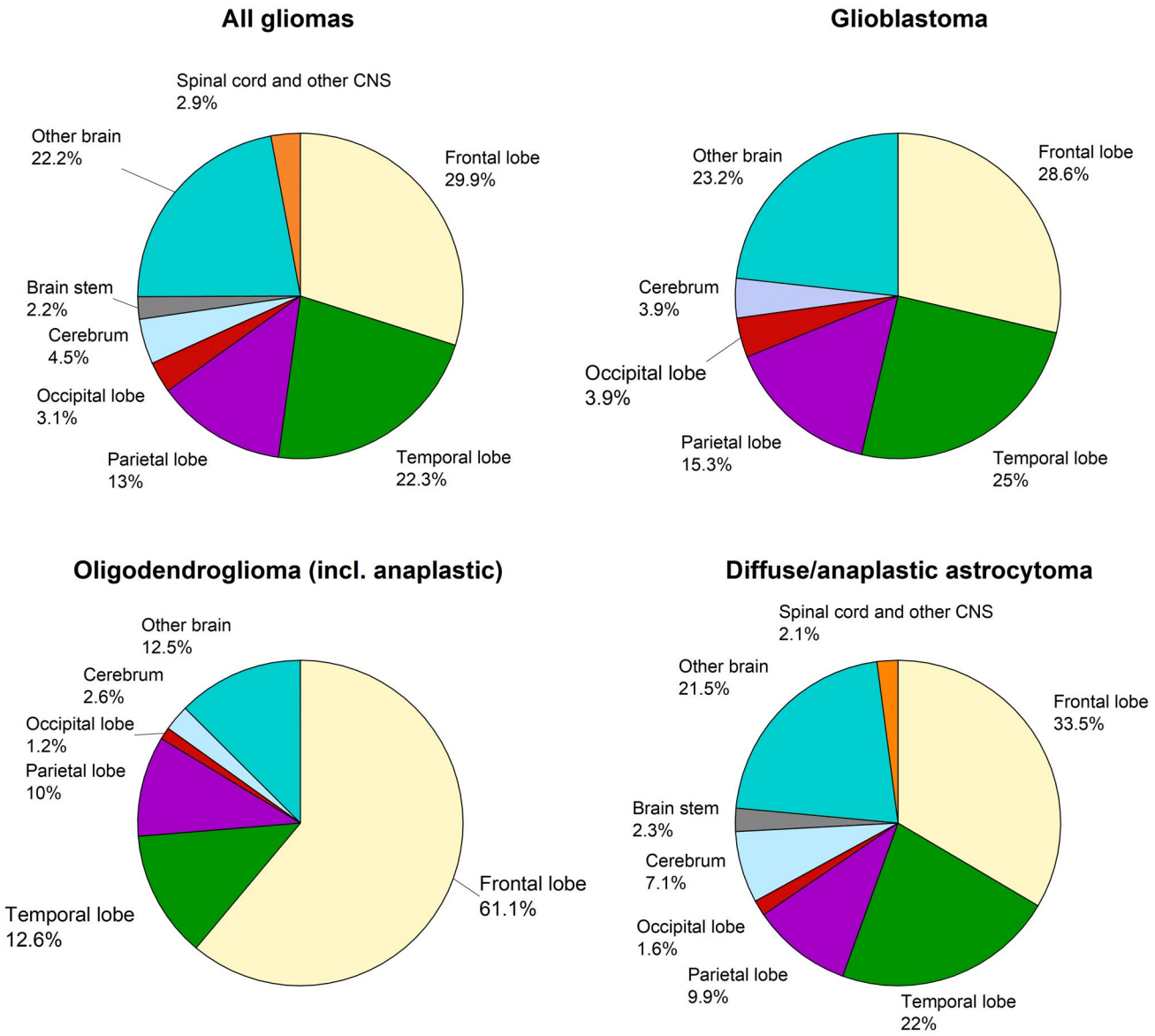

FIGURE 7. Distribution of Malignant Gliomas by Histology and Anatomic Subsite Among Adults Aged ≥20 Years, 2013 to 2017. Other brain includes a small proportion of cases in the ventricle and cerebellum; for glioblastoma and oligodendroglioma, this category also includes a small proportion of brainstem cases. Spinal cord and other central nervous system (CNS) includes a small number of tumors occurring in the meninges, cranial nerves, pituitary and craniopharyngeal ducts, and the pineal region. Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

than non-Hispanic White patients before adjustment for radiation and chemotherapy receipt, suggesting that substantial disparities in access to care persist for Black patients with glioblastoma.[16]

Other diffuse gliomas

Diffuse gliomas other than glioblastoma are largely diagnosed as WHO grade 3 and 4 tumors. Diffuse or anaplastic astrocytomas have an anatomic subsite distribution similar to that of glioblastoma, whereas oligodendrogliomas are slightly more commonly diagnosed in the supratentorial region (Fig. 7). Like glioblastoma, incidence rates for other diffuse gliomas generally increase with age, with the exceptions of oligodendroglioma and anaplastic oligodendroglioma, for which rates peak in patients aged 40 to 64 years (Fig. 9). Because of the rarity of glioblastoma in younger age groups, other diffuse gliomas account for a larger proportion of glioma cases in patients aged 20 to 39 years compared with those aged ≥65 years, although overall rates are lower. Incidence and survival trends for gliomas should be interpreted with caution because of changes in classification (Fig. 8). In particular, contemporary rates are likely already impacted by registries that were early adopters of the WHO coding changes for oligoastrocytoma, which is no longer considered a distinct entity but is classified as either astrocytoma or oligodendroglioma based on molecular markers.

Five-year relative survival for other diffuse gliomas is higher in younger adults, ranging from 66% to 92% in those

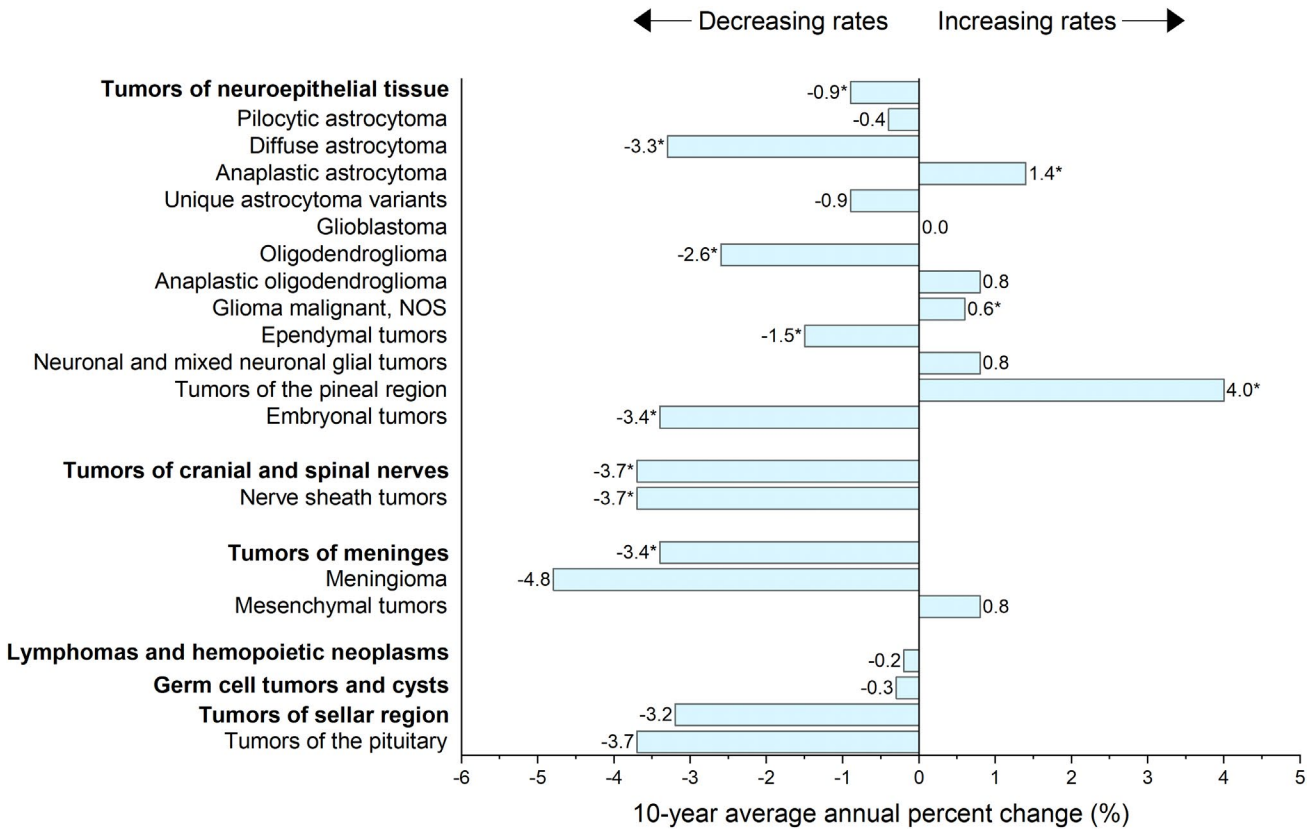

FIGURE 8. Ten-Year Average Annual Percent Change in Malignant Brain and Other Central Nervous System Tumor Incidence Rates Among Adults Aged ≥20 Years by Histology, United States, 2008 to 2017. Pilocytic astrocytoma is considered nonmalignant in clinical practice but is included in the malignant category according to historical convention for US cancer reporting. *The average annual percent change is statistically significantly different from zero ($P < .05$). NOS indicates not otherwise specified. Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

aged 20 to 39 years for the most common histologic types compared with 6% to 48% among those aged ≥65 years. Regardless of age, however, 5-year survival is lower for astrocytomas than for oligodendrogliomas.

Nonmalignant meningioma

Nonmalignant meningioma is the most frequently diagnosed nonmalignant brain and other CNS tumor in adults, accounting for 56% of nonmalignant cases in ages ≥20 years (Table 5). It most commonly occurs in the cerebral meninges (as opposed to the spinal meninges). Nonmalignant meningioma incidence is highest in adults aged ≥65 years and in females, among whom rates are >2-fold of those in males (Fig. 2).[5] Rates are also significantly higher in non-Hispanic Black adults than in other racial/ethnic groups for reasons that are unknown (Table 5).

During 2008 through 2017, nonmalignant meningioma incidence rates increased by 0.9% per year, which is likely due in part to advances in detection and improvements in reporting after the expansion of federally mandated reporting for NPCR registries in 2004 to include benign and borderline brain tumors.[17] Five-year relative survival for patients diagnosed during 2009 through 2015 was ≥94% among individuals aged <65 years compared to 82% in those aged ≥65 years (Fig. 4), with rates slightly lower for adult patients diagnosed with meningioma in the cerebral meninges (88%) as opposed to the spinal meninges (97%).[5] Patients who are older, male, and/or Black have poorer survival,[25] perhaps partly because of treatment differences. For example, in one study of cerebral meningiomas, patients who were younger, White, or female were more likely to undergo surgical resection, which was associated with higher 3-year observed survival (93% vs 88% in those not receiving resection).[26]

Nonmalignant tumors of the pituitary

Nonmalignant tumors of the sellar region, particularly pituitary adenomas (also known as pituitary neuroendocrine tumors [PITNET], per current WHO terminology), are the second most common intracranial tumor in adults in the United States after meningioma, accounting for approximately one-quarter of all nonmalignant brain and other CNS cases in adults (Table 5). Pituitary adenomas may be functional, wherein the tumor causes the pituitary gland to overproduce hormones, or nonfunctional; nonfunctional tumors may lead to underproduction of hormones if the tumor is large enough to compress the pituitary stalk and cause the

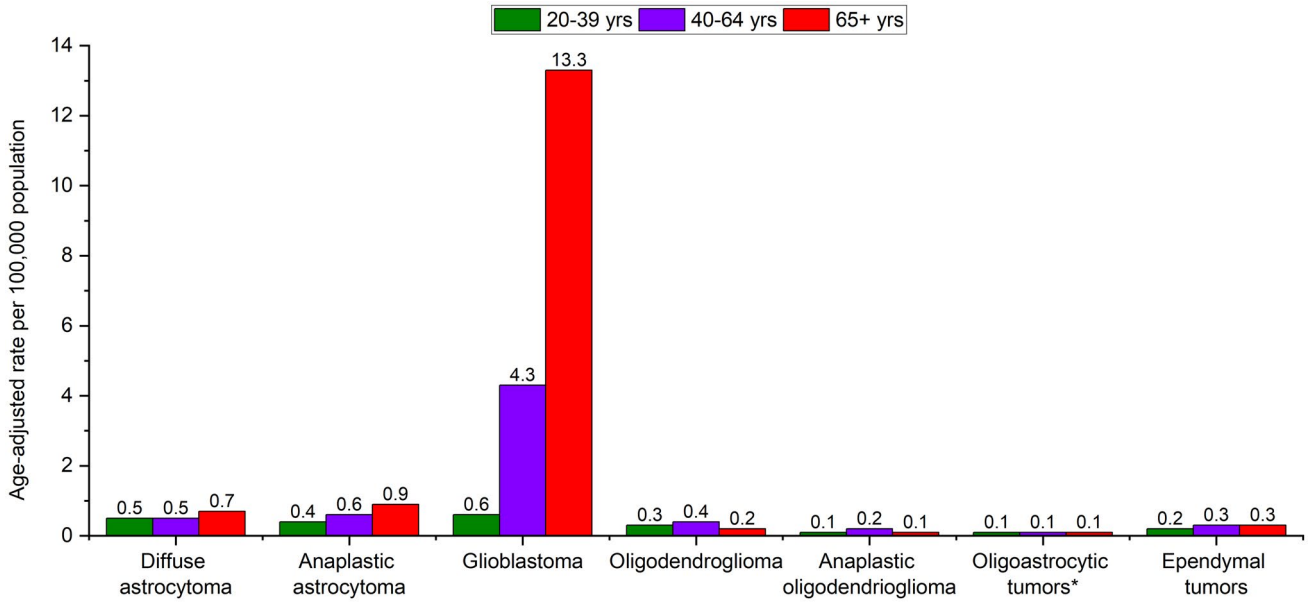

FIGURE 9. Incidence Rates for Specified Malignant Gliomas by Age in Adults Aged ≥20 Years, 2013 to 2017. Rates are limited to Central Brain Tumor Registry of the United States (CBTRUS) definitions for glioma morphology. *These tumors are no longer considered separate from astrocytomas or oligodendrogliomas according to the 2016 World Health Organization central nervous system classification. Data source: CBTRUS data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

gland to stop regulating hormones correctly. During 2013 through 2017, rates in adults were slightly higher in females than in males overall (6.0 vs 5.2 cases per 100,000, respectively) (Table 5), although the sex disparity varies greatly by age. For example, among individuals aged 20 to 24 years, rates in females were 4-fold higher than those in males (2.8 vs 0.7 cases per 100,000, respectively); whereas, among those aged 80 to 84 years, rates in males were nearly double those in females (6.4 vs 3.3 cases per 100,000, respectively).[5] Incidence rates were highest in non-Hispanic Black adults (9.3 cases per 100,000) and lowest in Asian and Pacific Islander adults (3.8 cases per 100,000) (Table 5). Although incidence rates increased by 1.5% annually in adults during 2007 through 2018, this uptick is likely because of increased case capture and reporting of nonmalignant tumors rather than a true disease increase.

Pituitary tumors are often diagnosed because they frequently lead to symptoms of endocrine dysfunction via the overproduction or underproduction of hormones.[27] Symptoms of endocrine dysfunction may include galactorrhea, infertility, and/or signs of classical endocrine-related syndromes, such as hyperprolactinemia, acromegaly, and Cushing disease. Some tumors may also cause clinically significant nonendocrine signs and symptoms, depending on their location and size, such as visual impairment; however, tumors are also sometimes found incidentally on radiographs in asymptomatic patients. Five-year relative survival for patients diagnosed during 2009 through 2015 was among the highest for brain and other CNS tumors, ranging from 92% in those aged ≥65 years to 99% in those aged 20 to 39 years. Although some tumors do not require immediate intervention, they have important implications for quality of life given their potential to cause long-term endocrine dysfunction.[28] Therapy for pituitary tumors depends on the specific type of tumor and may include transsphenoidal surgery, pituitary-directed medications (eg, somatostatin receptor ligands, dopamine agonists), and/or radiation.[27] Transsphenoidal surgery is frequently the first-line therapy for functioning pituitary adenomas, with the exception of prolactinomas, for which patients typically receive a dopamine agonist as first-line therapy. Treatment should be managed with a team including both experts in endocrinology and neurosurgery when indicated.

Brain and Other CNS System Tumor Subtypes in Children and Adolescents

The distribution of brain and other CNS tumors common in children (aged birth to 14 years) and adolescents (aged 15-19 years) differs substantially from that in adults. Notably, in contrast to adults, rates are generally similar by sex overall, and, although incidence rates are highest in non-Hispanic White children as in adults, mortality rates in non-Hispanic White and non-Hispanic Black children are equivalent (0.7 deaths per 100,000; mortality rate ratio, 1.03; 95% CI, 0.91-1.16).[7] It is also notable that, in contrast to declining trends in adults, incidence rates among children and adolescents

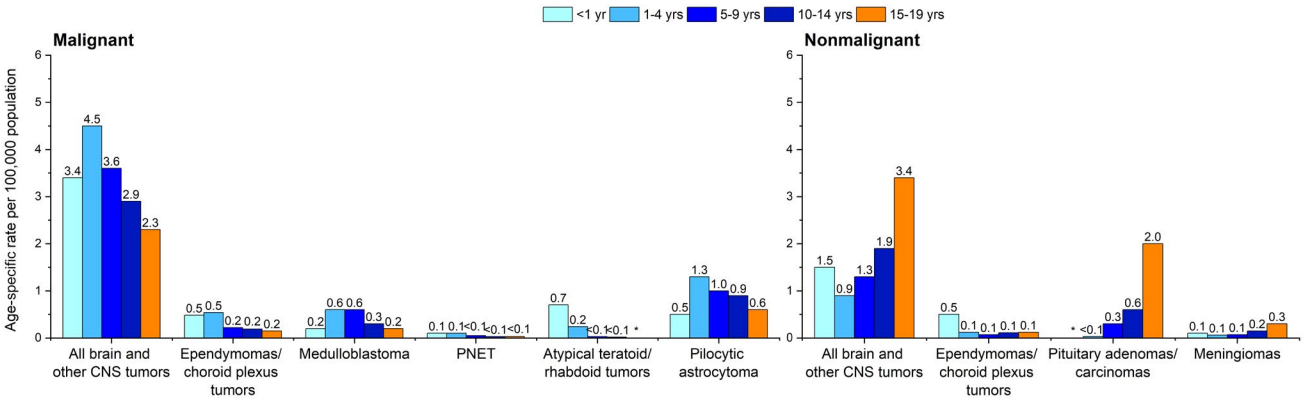

FIGURE 10. Incidence Rates for Selected Malignant and Nonmalignant Brain and Other Central Nervous System (CNS) Tumors in Children and Adolescents, 2013 to 2017. Pilocytic astrocytoma is considered nonmalignant in clinical practice but is included in the malignant category according to historical convention for US cancer reporting. *Rates are not shown because of sparse data (<16 cases during 2013-2017). PNET indicates primitive neuroectodermal tumor. Data source: Central Brain Tumor Registry of the United States data provided by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, 2013 to 2017 (varying).

increased slightly by 0.7% and 0.5% annually during 2008 through 2017, respectively.

Childhood and adolescent brain and other CNS tumors are broadly classified into 2 categories, glial and neuronal tumors.[29] The most common gliomas in children are astrocytomas, oligodendrogliomas, ependymomas, brainstem gliomas (including the rare but highly fatal diffuse midline glioma, previously referred to as diffuse intrinsic pontine glioma, for which population-based data are not available because of the lack of a specific ICD-O-3 site code for the pons), and optic nerve gliomas. Most notably, pilocytic astrocytomas are substantially more common in children and adolescents compared with adults, accounting for one-quarter of all cases reported as malignant (see the discussion of pilocytic astrocytoma coding in historical surveillance data, above) (Table 1).[4] Most neuronal tumors are embryonal in nature, with the most common subtypes including medulloblastoma, atypical teratoid/rhabdoid tumors, and CNS primitive neuroectodermal tumors.[29] Germ cell tumors and cystic tumors are also more common among children and adolescents than among adults.

Whereas malignant tumor rates peak in children aged 1 to 4 years and decline thereafter, nonmalignant tumor incidence rates decrease immediately after infancy but subsequently continue to rise into adolescence (Fig. 10), mirroring the patterns of the most common subtypes—malignant astrocytomas and nonmalignant pituitary tumors and meningiomas, respectively. Notably, rates for atypical teratoid/rhabdoid tumors are highest in infants and subsequently decline,[30] whereas medulloblastoma occurs most commonly between ages 1 and 10 years.

Five-year relative survival for children and adolescents diagnosed with malignant tumors during 2009 through 2015 varied substantially by subtype (Fig. 4). By race/ethnicity, 5-year survival was lowest in patients who were non-Hispanic Black (70%) and highest in those who were non-Hispanic White (79%), in contrast to patterns in adults. In other population-based studies, the disparity among children persisted after adjustment for stage, anatomic location, and histology.[31,32] The racial disparity among children likely reflects less access to appropriate treatment and clinical trial enrollment among non-White patients.[32] Differences in survival between non-Hispanic Black and non-Hispanic White children were largest for diffuse astrocytomas (75% vs 86%, respectively) and embryonal tumors (59% vs 67%, respectively), whereas survival for several other histologic types was similar.[5]

Long-Term and Late Effects Among Patients With Brain and Other CNS Tumors

Patients with a history of a malignant or nonmalignant brain or other CNS tumor frequently have long-term and late physical and psychosocial effects related to the tumor and/or its treatment, with variation by type of tumor, tumor location, patient characteristics, environmental factors, and treatment received.[33] It is also important to note that, despite high survival rates, nonmalignant tumors may confer substantial long-term morbidity.[28,33]

Childhood and adolescent cancer survivors are at particular risk of long-term and late effects because of the insult to the developing brain during cranial irradiation, surgical treatment, and the toxicity of chemotherapeutic agents.[34,35] Compared with their cancer-free siblings, survivors of childhood brain and other CNS tumors in the Childhood Cancer Survivor Study were at elevated risk for endocrine disorders, including hypothyroidism, as well as cardiovascular problems such as blood clots.[36] One study also showed that childhood cancer survivors of nonpituitary and noncraniopharyngioma brain and other CNS tumors similarly had a

higher prevalence of weight gain, overweight, and/or obesity (33% vs 13% in the age-matched general population).[37]

There is growing recognition in survivorship research for a more expansive focus regarding long-term cognitive outcomes other than intelligence (eg, memory and attention problems), given the potential impact of these tumors and their treatment on social functioning and quality of life for patients.[33] Although advances in treatment have led to improvements in long-term cognitive and psychosocial functioning among brain and other CNS tumor survivors, poor outcomes continue to cause substantial morbidity and decreased quality of life for patients, particularly those who were diagnosed as children or adolescents.[33,38-40] Compared with cancer-free siblings, adult survivors of childhood malignant brain tumors in the Childhood Cancer Survivor Study reported less educational attainment, higher levels of unemployment, lower income levels, and were less likely to be married.[38] In addition, the prevalence of depression was significantly higher in survivors compared with siblings, and non-White survivors experienced higher levels of distress than those who were White. Similar findings have been reported for survivors of nonmalignant tumors.[39]

Limitations

There are important limitations to consider regarding the data presented herein. First, incidence trends should be interpreted with caution because rates were not adjusted for delays in case reporting, and data are only available through 2017, before widespread implementation of the 2016 WHO classification in the United States. As previously noted, pilocytic astrocytomas are included with malignant brain and other CNS tumors herein, consistent with historical reporting convention in the United States; however, these tumors are broadly considered nonmalignant by the WHO and in clinical practice. In addition, incidence information is not available for some rare tumors, such as diffuse midline glioma, because of lack of specificity regarding specific anatomic site in ICD-O-3 coding. Similarly, mortality data are not available for specific histologic types because this information is not available in ICD-10. Nonmalignant brain tumor mortality data are not presented because of concerns in the accuracy of reporting and the low rate of deaths for these tumors. Importantly, mortality trends should not be compared directly with incidence trends in this report, particularly because of widespread variation in incidence reporting across registries, as well as small underlying differences in anatomic site definitions. Finally, no mechanism currently exists for central pathology review of cases within the US cancer registry system. Thus, histology code assignment is based on the information contained in the patient's medical record at the time of case registration; the WHO classification was revised in 1993, 2000, 2007, and 2016.

Conclusion

Malignant and nonmalignant brain and other CNS tumors exhibit wide heterogeneity in occurrence by age, sex, and race/ethnicity, and they cause substantial morbidity and mortality in the United States. Because of the aggressive nature of many malignant subtypes and limited knowledge regarding etiology, ongoing updates of the descriptive epidemiology of these tumors is essential. To that end, expansion of resources for central cancer registries to collect and report data in a way that is timely, specific, and broadly consistent across the United States is necessary to advance biologic understanding of brain and other CNS tumors. In addition, ongoing research is needed to elucidate the causes of sex, age, and racial/ethnic differences in occurrence, especially for rarer subtypes and understudied populations. Racial/ethnic disparities in treatment access and receipt should also be further explored. ■

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *CA Cancer J Clin.* 2021;71:7-33.
2. 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(12 suppl 2):iv1-iv96.
3. 107th Congress. Benign Brain Tumor Cancer Registries Amendment Act. 107 *Cong Rec.* §260 (2002). Accessed January 17, 2021. govinfo.gov/app/details/CREC-2002-08-01/CREC-2002-08-01-pt2-PgS8022-3
4. Central Brain Tumor Registry of the United States (CBTRUS). SEER*Stat Database. Centers for Disease Control and Prevention National Program of Cancer Registries and National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Incidence Data (1995-2017). CBTRUS; 2019.
5. National Program of Cancer Registries (NPCR). SEER*Stat Database: NPCR Survival Analytic File—2001-2016. US Department of Health and Human Services, Centers for Disease Control and Prevention; 2020.
6. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Incidence-SEER Research Data, 9 Registries, November 2019 Submission (1975-2017)-Linked To County Attributes-Time Dependent (1990-2017) Income/Rurality, 1969-2018 Counties. National Cancer Institute, Division of Cancer Control & Population Sciences, Surveillance Research Program; 2020.
7. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Database: Mortality-All COD, Aggregated With State, Total U.S. (1990-2018) [underlying mortality data provided by the National Center for Health Statistics]. National Cancer Institute, Division of Cancer Control & Population Sciences, Surveillance Research Program; 2020.
8. Fritz A, Percy C, Jack A, et al, eds. International Classification of Diseases for Oncology. 3rd ed. World Health Organization/International Agency for Research on Cancer; 2000. Accessed March 1, 2020. codes.iarc.fr/

9. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. *Cancer*. 2005;103:1457-1467.
10. Ostrom QT, Kruchko C, Barnholtz-Sloan JS. Pilocytic astrocytomas: where do they belong in cancer reporting? *Neuro Oncol*. 2020;22:298-300.
11. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131:803-820.
12. World Health Organization. International Statistical Classification of Diseases and Related Health Problems (ICD). 10th Revision. World Health Organization; 2013. Accessed March 1, 2020. who.int/classifications/icd/en/
13. National Cancer Institute. Joinpoint Regression Program, Version 4.7.0.0. Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute; 2019.
14. Ostrom QT, Adel Fahmideh M, Cote DJ, et al. Risk factors for childhood and adult primary brain tumors. *Neuro Oncol*. 2019;21:1357-1375.
15. Porter AB, Lachance DH, Johnson DR. Socioeconomic status and glioblastoma risk: a population-based analysis. *Cancer Causes Control*. 2015;26:179-185.
16. Cote DJ, Ostrom QT, Gittleman H, et al. Glioma incidence and survival variations by county-level socioeconomic measures. *Cancer*. 2019;125:3390-3400.
17. Li XR, Kruchko C, Wu XC, et al. Are benign and borderline brain tumors underreported? *J Registry Manag*. 2016;43:187-194.
18. Braganza MZ, Kitahara CM, Berrington de Gonzalez A, Inskip PD, Johnson KJ, Rajaraman P. Ionizing radiation and the risk of brain and central nervous system tumors: a systematic review. *Neuro Oncol*. 2012;14:1316-1324.
19. Davis F, Il'yasova D, Rankin K, McCarthy B, Bigner DD. Medical diagnostic radiation exposures and risk of gliomas. *Radiat Res*. 2011;175:790-796.
20. Wrensch M, Lee M, Miike R, et al. Familial and personal medical history of cancer and nervous system conditions among adults with glioma and controls. *Am J Epidemiol*. 1997;145:581-593.
21. Rice T, Lachance DH, Molinaro AM, et al. Understanding inherited genetic risk of adult glioma—a review. *Neurooncol Pract*. 2016;3:10-16.
22. Wigertz A, Lonn S, Schwartzbaum J, et al. Allergic conditions and brain tumor risk. *Am J Epidemiol*. 2007;166:941-950.
23. 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;4:1254-1262.
24. Ostrom QT, Rubin JB, Lathia JD, Berens ME, Barnholtz-Sloan JS. Females have the survival advantage in glioblastoma. *Neuro Oncol*. 2018;20:576-577.
25. Achey RL, Gittleman H, Schroer J, Khanna V, Kruchko C, Barnholtz-Sloan JS. Nonmalignant and malignant meningioma incidence and survival in the elderly, 2005-2015, using the Central Brain Tumor Registry of the United States. *Neuro Oncol*. 2019;21:380-391.
26. Cahill KS, Claus EB. Treatment and survival of patients with nonmalignant intracranial meningioma: results from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. Clinical article. *J Neurosurg*. 2011;115:259-267.
27. Varlamov EV, McCartney S, Fleseriu M. Functioning pituitary adenomas—current treatment options and emerging medical therapies. *Eur Endocrinol*. 2019;15:30-40.
28. Worrell SL, Kirschner ML, Shatz RS, Sengupta S, Erickson MG. Interdisciplinary approaches to survivorship with a focus on the low-grade and benign brain tumor populations. *Curr Oncol Rep*. 2021;23:19.
29. Adel Fahmideh M, Scheurer ME. Pediatric brain tumors: descriptive epidemiology, risk factors, and future directions. *Cancer Epidemiol Biomarkers Prev*. 2021;30:813-821.
30. Ostrom QT, Chen Y, de Blank PM, et al. The descriptive epidemiology of atypical teratoid/rhabdoid tumors in the United States, 2001-2010. *Neuro Oncol*. 2014;16:1392-1399.
31. Siegel DA, Li J, Ding H, Singh SD, King JB, Pollack LA. Racial and ethnic differences in survival of pediatric patients with brain and central nervous system cancer in the United States. *Pediatr Blood Cancer*. 2019;66:e27501.
32. Mitchell HK, Morris M, Ellis L, Abrahao R, Bonaventure A. Racial/ethnic and socioeconomic survival disparities for children and adolescents with central nervous system tumours in the United States, 2000-2015. *Cancer Epidemiol*. 2020;64:101644.
33. Oyefiade A, Paltin I, De Luca CR, et al. Cognitive risk in survivors of pediatric brain tumors. *J Clin Oncol*. 2021;39:1718-1726.
34. Padovani L, Andre N, Constine LS, Muracciole X. Neurocognitive function after radiotherapy for paediatric brain tumours. *Nat Rev Neurol*. 2012;8:578-588.
35. Turner CD, Rey-Casserly C, Liptak CC, Chordas C. Late effects of therapy for pediatric brain tumor survivors. *J Child Neurol*. 2009;24:1455-1463.
36. Gurney JG, Kadan-Lottick NS, Packer RJ, et al. Endocrine and cardiovascular late effects among adult survivors of childhood brain tumors: Childhood Cancer Survivor Study. *Cancer*. 2003;97:663-673.
37. van Schaik J, van Roessel IMAA, Schouten-van Meeteren NAYN, et al. High prevalence of weight gain in childhood brain tumor survivors and its association with hypothalamic-pituitary dysfunction. *J Clin Oncol*. 2021;39:1264-1273.
38. Zebrack BJ, Gurney JG, Oeffinger K, et al. Psychological outcomes in long-term survivors of childhood brain cancer: a report from the Childhood Cancer Survivor Study. *J Clin Oncol*. 2004;22:999-1006.
39. Ris MD, Leisenring WM, Goodman P, et al. Neuropsychological and socioeconomic outcomes in adult survivors of pediatric low-grade glioma. *Cancer*. 2019;125:3050-3058.
40. Gurney JG, Krull KR, Kadan-Lottick N, et al. Social outcomes in the Childhood Cancer Survivor Study cohort. *J Clin Oncol*. 2009;27:2390-2395.