




Utility of Administrative Databases and Big Data on Understanding Glioma Treatment—A Systematic Review

Monica-Rae Owens¹ Sarah Nguyen¹ Michael Karsy² 

¹Department of Neurosurgery, University of Utah, Utah, United States

²University of Utah Health Care, University of Utah Health Hospitals and Clinics, Utah, United States

Address for correspondence Michael Karsy, MD, PhD, MSc, University of Utah Health Care, University of Utah Health Hospitals and Clinics, UT, United States (e-mail: michael.karsy@hsc.utah.edu).

Indian J Neurosurg 2022;11:104–117.

Abstract

Background Gliomas are a heterogeneous group of tumors where large multicenter clinical and genetic studies have become increasingly popular in their understanding. We reviewed and analyzed the findings from large databases in gliomas, seeking to understand clinically relevant information.

Methods A systematic review was performed for gliomas studied using large administrative databases up to January 2020 (e.g., National Inpatient Sample [NIS], National Surgical Quality Improvement Program [NSQIP], and Surveillance, Epidemiology, and End Results Program [SEER], National Cancer Database [NCDB], and others).

Results Out of 390 screened studies, 122 were analyzed. Studies included a wide range of gliomas including low- and high-grade gliomas. The SEER database ($n = 83$) was the most used database followed by NCDB ($n = 28$). The most common pathologies included glioblastoma multiforme (GBM) ($n = 67$), with the next category including mixes of grades II to IV glioma ($n = 31$). Common study themes involved evaluation of descriptive epidemiological trends, prognostic factors, comparison of different pathologies, and evaluation of outcome trends over time. Persistent health care disparities in patient outcomes were frequently seen depending on race, marital status, insurance status, hospital volume, and location, which did not change over time. Most studies showed improvement in survival because of advances in surgical and adjuvant treatments.

Conclusions This study helps summarize the use of clinical administrative databases in gliomas research, informing on socioeconomic issues, surgical outcomes, and adjuvant treatments over time on a national level. Large databases allow for some study questions that would not be possible with single institution data; however, limitations remain in data curation, analysis, and reporting methods.

Keywords

- ▶ administrative database
- ▶ glioma
- ▶ glioblastoma

DOI <https://doi.org/10.1055/s-0042-1742333>.
ISSN 2277-954X.

© 2022. Neurological Surgeons' Society of India. All rights reserved. This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)
Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Gliomas encompass the second most common type of brain tumor in the United States, while glioblastoma multiforme (GBM) accounts for the most common malignant primary brain tumor.¹ Multiple advances in treatment, including earlier imaging and detection, safer surgical resection, and adjuvant radiochemotherapy (RCT) have improved disease treatment.² Clinical variables, such as age and surgical resection, in addition to genetic factors have been helpful in stratifying patient risk. However, there remains heterogeneity in the outcomes of patients and treatment response.

The rise in the use of administrative databases and big data has been notable in neurosurgery, but their impact on glioma understanding remains limited.³ These studies often show multiple associative findings due to their significant sample sizes without distinction between statistical and clinical significance. Moreover, the clinical impact of these studies remains unclear. The purpose of this review was to accumulate and compare the lessons learned from big data regarding gliomas and identify future challenges for exploration.

Methods

We aimed to evaluate the impact of multicenter, publicly available administrative databases on clinically relevant information in the treatment of gliomas. A literature search of PubMed was performed using the following search terms: (National Surgical Quality Improvement Program OR NSQIP OR National Inpatient Sample OR NIS OR HCUP-NIS OR Kid's Inpatient Database OR HCUP-KID OR Surveillance, Epidemiology, and End Results Program OR SEER OR Pediatric Health Information Systems OR PHIS OR MarketScan OR Administrative database OR SEER OR SEER-Medicare OR CBTRUS OR NCDB OR NRD OR SID OR SASD OR CMS OR Vizient OR Premier OR PearlDiver OR Optum) AND (glioma OR glioblastoma OR astrocytoma OR oligodendroglioma OR anaplastic astrocytoma OR anaplastic oligodendroglioma [AO]). References from manuscripts were also reviewed to identify relevant studies.

Studies up to January 2020 and English-only manuscripts were included. Studies were reviewed independently by two reviewers (M.O., M.K.) to exclude case reports, reviews, and laboratory studies. The main study findings including prognostic factors, sample number, database type, World Health Organization (WHO) tumor status, tumor types, surgical complications, and surgical outcomes were noted. Papers were narrowed to those discussing low-grade glioma (LGG), including grade II gliomas, astrocytoma and oligodendroglioma, as well as high-grade gliomas (HGG), including anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), and GBM. Studies used a combination of histological and molecular classification, depending on the year of study. Several studies incorporated other glioma types that were excluded (**Supplemental discussion, ▶Fig. S1, ▶Table S1**). The Preferred Reporting

Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to draft this manuscript. Descriptive statistics are demonstrated where relevant.

Results

A total of 390 studies were screened and narrowed down to 122 studies (▶**Fig. 1**). Studies included AA only ($n=2$), AA with other pathologies ($n=3$), AO only ($n=2$), GBM ($n=67$), grades II to IV glioma ($n=31$), grade II glioma ($n=3$), HGG ($n=7$), mix of high-grade tumors ($n=1$), and oligodendroglioma ($n=6$) (▶**Table 1**). The most common databases included the NCDB ($n=28$) and SEER databases ($n=83$). A further breakdown of all studies into LGG and HGG was performed (▶**Figs. S1–S3**).

Low Grade Glioma

LGGs were evaluated as an aggregate group in three studies. One study on grade II gliomas showed that RCT did not improve survival compared with chemotherapy alone,⁴ and two others showed that greater extent of resection (EOR) improved prognosis.^{5,6} Unfortunately, these studies were limited by aggregating all LGGs, which often behave distinctly.

Six studies specifically evaluated oligodendroglioma,^{7–12} with two of these studies showing improved survival over the preceding 10 years (e.g., 2004–2013) mainly as a function of improved surgery and RCT.^{9,12} Achey et al evaluated the age-adjusted incidence rate from the Central Brain Tumor Registry of the United States from 2000 to 2013.⁷ A decreased incidence of oligodendroglioma and AO was seen, although this was possibly because of recent changes in molecular classification. Prognostic factors impacting survival for oligodendrogliomas in other studies included age, sex, race, and EOR.^{8,10–12} Alattar et al evaluated 3,406 patients with oligodendroglioma from 1999 to 2010 using the SEER database and demonstrated an improvement in OS after gross-total resection compared with AA or GBM.⁸ This finding was confirmed by Kinslow et al in their evaluation of 3135 cases from the SEER database data from 2004 to 2013; they also showed that EOR impacted survival in both oligodendroglioma and AO.¹⁰

Multiple studies have evaluated glioma by including either LGG as a broad category or comparing LGG with HGG.^{1,13–37} Several studies evaluated the epidemiology of gliomas and demonstrated increased likelihood in Caucasians, older, or male patients, patients with prior smoking history, women with prior breast cancer treatment, and insured patients.^{13–16,19} Plascak et al evaluated 24,230 glioma patients using the SEER database between 2000 and 2006; they showed a greater incidence of gliomas in countries with higher socioeconomic status, which suggested unequal distribution of diagnostic resources.¹⁹ Another study using the SEER database noted a decreasing incidence of gliomas and suggested there was a shift to increased diagnosis of GBM by pathological criteria over time.¹⁸ The vast majority of studies involving glioma have looked at prognostic factors. These studies have suggested that White race, younger age, more

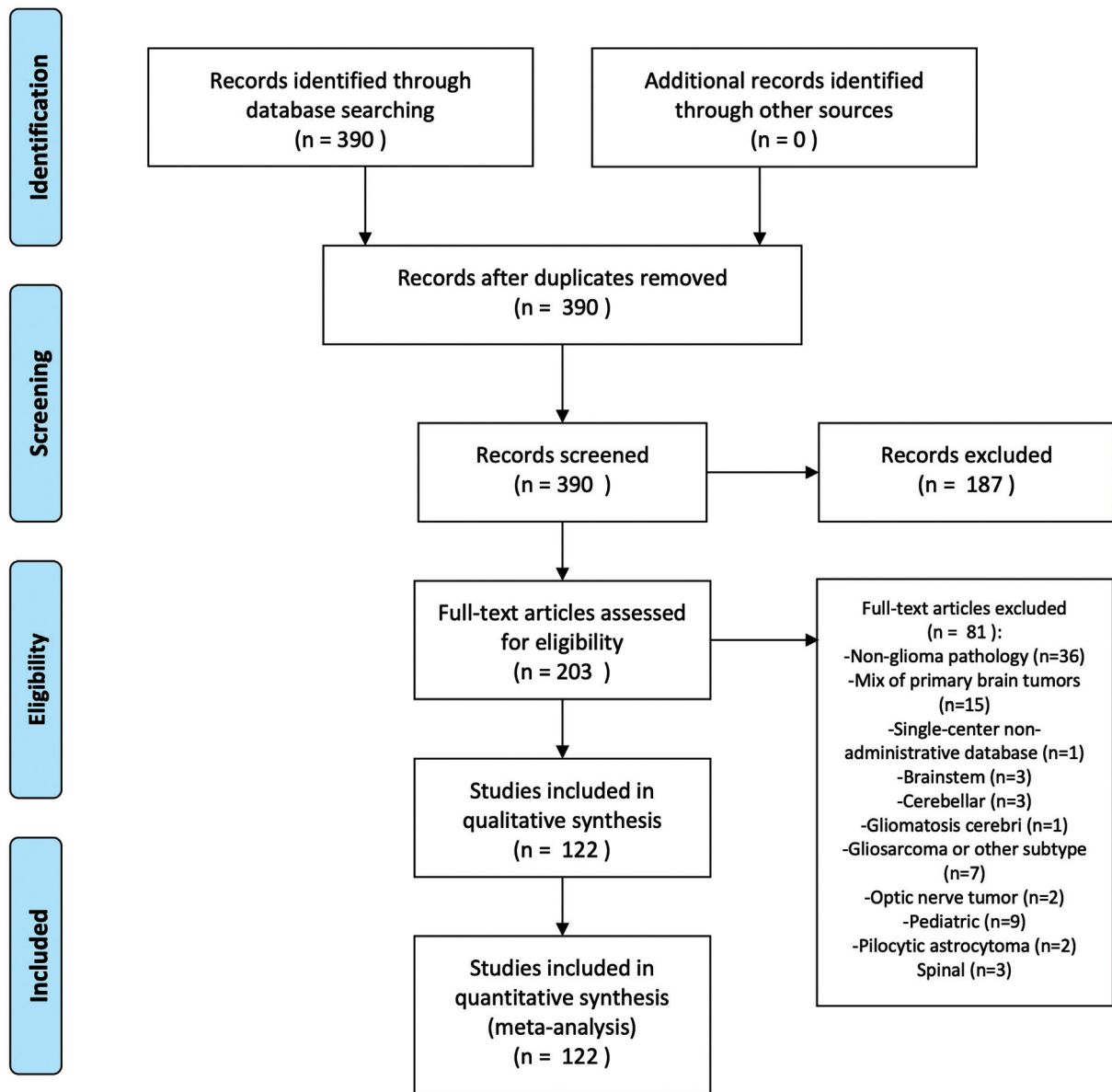


Fig. 1 The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of selected studies.

recent diagnosis, lower WHO grade or histology, marital status, better socioeconomic status, EOR, radiotherapy, radiochemotherapy, treatment at high-volume facilities, and tumor size positively impact patient prognosis.^{1,4,16,17,20–36} Missios et al evaluated 21,384 cases of glioma between 2005 and 2011 using the National Inpatient Sample (NIS) database and showed that perioperative complications were increased by greater age, coagulopathy, coronary artery disease, congestive heart failure, and smoking history.³⁷

Although these studies have had an impact by identifying consistent risk and prognostic factors, they are limited by aggregating glioma types, mostly as a limitation of lacking molecular data in nearly all multicenter databases. Moreover, both epidemiology and prognostic factor studies suggest geographic differences in outcomes because of medical resources and facilities but do little to address these inequalities or report in sufficient detail to confer

actionable insight. Despite improve standardization of glioma treatment with clinical guidelines, treatment variation likely still occurs, which is impacted by patient socioeconomics and remains poorly understood.

High-Grade Glioma

Several studies have evaluated and compared outcomes for AA and AO. Prognostic factors for AA included age, RCT, private insurance, higher income, tumor site, marital status, EOR, histology, and treatment with RT.^{38–44} Smoll et al specifically looked at 3,202 patients with AA between 1973 and 2006 in the SEER database, showing worsened mortality compared with matched controls.⁴³ A 5- and 10-year overall survival (OS) of 23.6% and 15.1% was identified, respectively. Age significantly impacted prognosis, however, improvement in survival was not seen over the study time period. In contrast, Shin et al evaluated 1,692 patients with

Table 1 Studies evaluating administrative studies/big data in LGG and HGG

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
NCDB	AA	4,807	2004–2013	Prognostic factors: RCT, age, private insurance, higher income	Shin ⁴⁰
SEER	AA	3,202	1973–2006	5-year OS 23.6%; prognostic factor: age (only 3 years postdiagnosis); 5 year survival unchanged over time	Smoll ⁴³
SEER	AA, AO	1,939	1973–2013	Prognostic factors: age, tumor site, marital status, EOR, histology, RT, surgery	Zhao ⁴⁴
SEER	AA, AO	390	1990–2008	Evaluated patients > 70 years of age; median OS 11 month; prognostic factors: EOR, RT, gender, marital status	Mukherjee ³⁸
SEER	AA, GBM	24717	1999–2010	Median OS (AA versus GBM with GTR) 64 versus 13 months; prognostic factors: EOR	Padwal ³⁹
NCDB	AO	1,643	2004–2013	Prognostic factors: race, age, RCT	Shin ⁴²
NCDB	AO	1,692	2004–2013	5-year OS 59.8%; prognostic factors: RCT, single-agent chemotherapy	Shin ⁴¹
NCDB	GBM	100,672	1998–2011	Median OS 7.5 months; prognostic factor: age, tumor histology, race, gender, education, insurance status, EOR, RCT, tumor location	Dressler ⁵⁶
NCDB	GBM	60,672	2004–2013	Median OS 8.1 months; prognostic factors: TMZ, high volume facility treatment; 2-month survival benefit in high-volume centers	Aulakh ⁵⁵
NCDB	GBM	738	2010–2012	Median OS (RCT) 15.6 months, 2-year OS 25.9%; limited benefit of RT in patients with MGMT methylation	Lee ⁶⁰
NCDB	GBM	448	2010–2013	Median OS (RCT) 8.7 months; prognostic factors: age, EOR, RCT;	Malakhov ⁵⁹
NCDB	GBM	4,598	1998–2011	Prognostic factor: long-course radiotherapy compared with short-course radiotherapy	Mak ⁵⁸
NCDB	GBM	114,979	1998–2012	Prognostic factor: RCT compared with radiation alone	Glaser ⁵⁷
NCDB	GBM	114,979	1998–2012	Prognostic factors: disparities in standard of care secondary to race, insurance status and institution of treatment	Rhome ⁶⁵
NCDB	GBM	5,252	2004–2012	Prognostic factor: single-agent chemotherapy with radiotherapy in elderly patients	Huang ¹¹¹
NCDB	GBM	89,839	2004–2013	Prognostic factor: patients treated in academic/research programs, high-volume centers	Hauser ⁶⁴
NCDB	GBM	27,865	2004–2013	Prognostic factor: GTR; no survival benefit of STR over biopsy	Trifiletti ⁶⁷
NCDB	GBM	1,223	2004–2014	Dose escalation not associated with survival; prognostic factors: age, comorbidity score, hospital volume (noncommunity centers), education level, income, insurance status, race, gender	Wegner ⁶⁸
NCDB	GBM	45,942	2004–2015	Prognostic factor: younger age, female gender, black ethnicity, higher KPS, and GTR over STR; delay > 8 weeks for radiochemotherapy detrimental after GTR; delay < 4 weeks for radiochemotherapy detrimental after STR	Buszek ⁶²
NCDB	GBM	45,268	2004–2016	Median OS was 12.8 months vs 8.3 months for patients with unifocal GBM or multifocal	Haque ⁶³

(Continued)

Table 1 (Continued)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				GBM; prognostic factor: radiochemotherapy; radiochemotherapy beneficial even if multifocal	
NCDB	GBM	13,489	2005–2012	Prognostic factors: delay in radiochemotherapy treatment	Yusuf ⁷⁶
NCDB	GBM	1,479	2006–2011	Prognostic factor: radiochemotherapy compared with radiation alone	Kole ⁶⁶
NCDB	GBM	12,725	2010–2012	Median OS (MGMTme versus MGMT-) 20 versus 15 months; prognostic factors: RCT in MGMTme tumors	Lee ⁶¹
NCDB; RTOG	GBM	40,396	1974–2002	Survival for patients in the RTOG database exceeded survival in patients in the NCDB group likely because patients in the RTOG database come from clinical trials which have specific enrollment criteria; prognostic factor: age	Siker ⁷³
SEER	GBM	9,103	1973–2006	Prognostic factor: age, marital status, resection	Walker ⁷⁵
SEER	GBM	21,783	1973–2007	Prognostic factors: EOR, RT	Zinn ⁷⁷
SEER	GBM	34,664	1973–2008	Prognostic factor: race (Asian/Pacific Islander), surgical resection, age, RT; improved survival over time	Thumma ⁷⁴
SEER	GBM	51,518	1973–2014	Prognostic factor: no prior history of cancer	Al-Husseini ⁷⁰
SEER	GBM	60,456	1973–2015	Prognostic factors: age, tumor size, tumor location, GTR, radiation, chemotherapy, brachytherapy	Bartek ⁷²
SEER	GBM	25,117	1985–2014	Prognostic factors: Hispanic Latino (GBM and GBM-GC), age, gender	Bin Abdulrahman ¹²⁰
SEER	GBM	10,987	1988–2001	Prognostic factors: marital status	Chang ⁷⁸
SEER	GBM	1,530	1991–1999	Prognostic factor: race	Barnholtz-Sloan ⁷¹
SEER	GBM	1,375	1991–2002	Median time post-resection to initiation of RT was 15 days; no impact of wait time on OS	Lai ¹²¹
SEER	GBM	1,273	1991–2007	No difference in patient outcomes between low- and high-readmission rate hospitals	Nuno ¹¹⁷
SEER	GBM	19,674	1993–2007	Improved survival over time	Darefsky ⁸⁰
SEER	GBM	4,137	1994–2002	Prognostic factors: age, marital status, and comorbidities	Iwamoto ⁸¹
SEER	GBM	1,652	1995–2009	Median OS of 7.4, 5.9 and 5.6 months for TMZ/RT, RT alone (2005–2009) and RT alone (1995–1999), respectively; benefit of TMZ addition to RT in later years	Arvold ⁹⁸
SEER	GBM	3,963	1997–2010	GTR supported as initial treatment and for recurrence	Chen ¹²²
SEER	GBM	3,784	1997–2010	Patients with postop infections showed no significant difference in survival	Chen ¹²³
SEER	GBM	22,777	1998–2007	Factors associated with omission of RT included older age, lower annual income, African–American race, Hispanic race, Asian–American race, unmarried status, and STR/Bx; use of radiation associated with improved OS	Aizer ⁶⁹
SEER	GBM	10,022	1998–2008	Patients surviving past 2 years have favorable conditional probability of survival	Johnson ⁸³
SEER	GBM	20,705	1998–2009		Noorbakhsh ⁸⁶

Table 1 (Continued)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				Benefit of 2–3 months survival after GTR in all age groups; lower rate of GTR in older patients	
SEER	GBM	342	1998–2009	Median OS 12 months; prognostic factors: EOR	Adams ⁸²
SEER	GBM	6,039	1999–2010	Prognostic factors: gender (female), married patients, ethnicity	Shah ⁸⁹
SEER	GBM	13,932	2000–2008	Benefit of TMZ to survival over time	Johnson ⁸⁴
SEER	GBM	6,586	2000–2008	Prognostic factor: gender (female)	Tian ⁹⁰
SEER	GBM	20,879	2000–2009	Benefit of TMZ and BZM to survival over time	Wachtel ⁹¹
SEER	GBM	302	2000–2010	Prognostic factors: supratentorial location, GTR, and later year of diagnosis	Lam ⁸⁵
SEER	GBM	14,675	2000–2010	Median OS 11 months; prognostic factors: age, gender, marriage status, race (non-Hispanics), region (northeast), nonlateralizing, small (< 3 cm), adjuvant radiation	Pan ⁸⁷
SEER	GBM	26,481	2000–2010	Prognostic factors: age, gender, race (non-White), socioeconomic status	Porter ⁸⁸
SEER	GBM	28,933	2000–2013	Improved survival with TMZ with radiation and adjuvant TMZ and then BEV after FDA approval	Zhu ⁹²
SEER	GBM	20,550	2000–2013	Prognostic factors: tumor size (< 5 cm), EOR, RCT	Shu ⁹⁶
SEER	GBM	6,919	2001–2006	Benefit of TMZ to survival over time	Koshy ⁹⁴
SEER	GBM	11,189	2001–2006	Cure fraction of 12% for young adults at 10 years	Smoll ⁹⁷
SEER	GBM	21,184	2001–2011	Prognostic factors: race (Latinos); possibly greater incidence of GBM-GC in Latinos	Shabihkhani ⁹⁵
SEER	GBM	5,991	2004–2008	Prognostic factors: age, marital status, median income; factors led to increased GTR and RT	Aneja ⁹³
SEER	GBM	24,262	2004–2013	Regional differences in survival and incidence in the US; prognostic factors: age, marital status, race, tumor laterality, WHO grade, disease extent, tumor size, tumor extension, RCT	Xu ¹¹⁹
SEER	GBM	24,348	2004–2013	Median survival 15, 15 and 5 months for pediatric, adult, and elderly, respectively	Li ¹¹⁶
SEER	GBM	30,767	2004–2015	Prognostic factors: marriage, age, race, middle-income counties	Xie ⁵²
SEER	GBM	5,607	2006–2010	Median OS of 8, 7, and 9 months in 2006, 2008, and 2010, respectively; improved survival with BZM	Johnson ¹⁰⁵
SEER	GBM	2,603	2006–2011	Benefit of BZM to survival	Davies ¹⁰²
SEER	GBM	13,665	2007–2012	Prognostic factors: insurance status, RT, marital status; improved OS over time	Rong ¹¹⁰
SEER	GBM	3,473	2010–2014	Prognostic factors: race (Asian–Pacific Islander)	Bohn ¹⁰¹
SEER; Broad Institute Genotype Tissue Expression project; UCSF 10K Immunomes-database	GBM		1973–2016	Increased expression of immunoregulatory molecules in the elderly	Ladomersky ¹⁰⁶
	GBM	5,029	1999–2007	Median survival was 4.9 months	Arvold ⁹⁹

(Continued)

Table 1 (Continued)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
SEER; Medicare database					
ACS-NSQIP	GBM	1,016	2012–2016	Patients' aged 65–89 years included; 3.4% 30-day death rate; 5.7% severe complication rate; 33% change in living disposition rate	Rahmani ¹⁰⁹
California Office of Statewide Health Planning & Development inpatient-discharge administrative database	GBM	18,506	1995–2010	13.2% 30-day readmission rate; each readmission represented an additional \$20,296 in median hospital charges on top of the \$72,029 in charges for the index neurosurgical admission	Marcus ¹⁰⁷
MarketScan	GBM	14,037	2007–2016	Functional mapping associated with decreased complications, reoperations, emergency department visits, and shorter lengths of stay; no difference in charges with functional versus no mapping	Pendharkar ¹⁰⁸
SEER	GBM	48,748	2000–2013	Multiple primary tumors associated with female gender, White race, smaller tumors	Nguyen ¹¹²
SEER	GBM	12,437	2002–2011	Hospice enrollment associated with older age, female gender, higher education, White race, lower median income	Forst ¹⁰⁴
Los Angeles County Cancer Surveillance Program, CCR, and SEER	GBM	38,567	1996–2006	Increased incidence of frontal, temporal and cerebellar GBM over time compared with other locations	Zada ¹¹³
SEER	GBM	21,493	1973–1997	Prognostic factor: race (white)	Barnholtz-Sloan ¹⁰⁰
SEER	GBM	1,181	1973–2015	Prognostic factors (for secondary malignancy): age, race, differentiated grade of cancer tissue, marital status, WHO grade, latency	Wang ¹¹⁸
SEER	GBM	37,581	2001–2011	Median OS 14 versus 11 months of metropolitan versus non-metropolitan; prognostic factors: urban area	Delavar ¹⁰³
FCDS	Glioma	14,092	1981–2013	Diagnostic factor: race (Caucasian more likely), age (older), gender (male), smoking status, insurance status	Persaud-Sharma ¹⁵
NCDB	Glioma	49,405	2004–2013	Proton beam therapy better median and 5-year OS compared with other radiation therapy	Jhaveri ¹⁷
NCDB	Glioma	5,036	2010–2014	Prognostic factors: female gender (GBMs)	Gittleman ²⁰
NIS	Glioma	21,384	2005–2011	Identified perioperative complication risk: age, coagulopathy, CAD, CHF, smoking	Missios ³⁷
SEER	Glioma	5,956	1973–2010	Prognostic factor: race (White)	Samaan ²¹
SEER	Glioma	49,124	1973–2014	Increased incidence of GBM versus non-GBM over time	Li ¹⁸
SEER	Glioma	389,415	1973–2014	Increased risk of gliomas in younger women after breast cancer treatment	Mezencev ¹⁴
SEER	Glioma	58,700	1975–2016	Prognostic factor: age	Zhou ¹²⁴
SEER	Glioma	22,427	1977–2000	Prognostic factors: age, gender, year of diagnosis; diagnostic factors: age, gender, later year of diagnosis	Hess ¹⁶
SEER	Glioma	24,340	1992–2007	Diagnostic factors: age, race (non-Hispanic White)	Dubrow ¹³
SEER	Glioma	1,067	1994–2002	Median OS 9, 4, 57 and 9 months for low-grade glioma, AA, OG, and AO, respectively; prognostic factors: age, WHO grade	Iwamoto ²⁵
SEER	Glioma	9,385	1999–2010		Dong ²⁴

Table 1 (Continued)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
				Improved survival for grade II and III gliomas over time	
SEER	Glioma	24,230	2000–2006	Greater incidence gliomas in counties with higher socioeconomic status	Plascak ¹⁹
SEER	Glioma	617	2000–2014	Prognostic factor: marital status	Long ²⁶
SEER	Glioma	244,808	2000–2014	Prognostic factor: race; non-Hispanic whites showed lower survival	Ostrom ¹
SEER	Glioma	43,324	2000–2016	Prognostic factor: marital status	Xie ²⁸
SEER	Glioma	50,170	2003–2012	Prognostic factor: socioeconomic status	Deb ²³
SEER	Glioma	10,591	2005–2013	Prognostic factor: age, race (White), non-cerebral tumor sites	Sun ⁵¹
SEER; Medicare database	Glioma	1,958	1991–1999	Prognostic factors: age, EOR, RT	Barnholtz-Sloan ⁵⁰
NCDB	Glioma	1,029	2004–2012	No difference between single- and multi-agent chemotherapy	Haque ¹²⁵
NCDB	Glioma	2,253	2004–2013	Prognostic factor: RCT	Wu ²⁷
NCDB	Glioma	5,539	2004–2014	Prognostic factor: high-volume facility	Zhu ²⁹
NCDB	Glioma	1,952	2010–2012	Prognostic factor: histology, RT	Youseff ³⁶
NCDB	Glioma	1,032	2010–2013	Prognostic factor: WHO grade, tumor size	Jairam ³²
SEER	Glioma	2,009	1973–2001	Prognostic factor: gender (female), age, race (White), WHO grade, later year of diagnosis; improved survival over time	Claus ³⁰
SEER	Glioma	2,825	1973–2011	Indicated lack of OS improvement for LGG; suggested importance of molecular markers	Claus ³¹
SEER	Glioma	42,622	2000–2013	Evaluated primary and secondary GBM	Nguyen ³⁴
SEER	Glioma	5,037	2001–2006	Patients diagnosed with LGG 17X more likely to die than general population; older patients with LGG 31X more likely to die than young adults in first year	Smoll ³⁵
SEER	Glioma	3,732	2004–2013	Prognostic factors: age, marital status, tumor site, histological type, tumor size, surgery, and sex	Zhao ²²
SEER	Glioma	561	2006–2012	Prognostic factor: EOR	Diaz-Aguilar ¹²⁶
SEER, TCGA	Glioma	1,278	1999–2016	Overlap of risk genes in Alzheimer disease and gliomas (TREM2, SPI1, CD33, and INPP5D)	Lehrer ³³
NCDB	Grade II glioma	1,054	2004–2013	RCT not associated with higher survival in comparison to chemotherapy alone	Jhaveri ¹⁷
SEER	Grade II glioma	1,980	1999–2010	Prognostic factors: frontal lobe location, EOR, age	Alattar ⁵
SEER	Grade II glioma	4,113	1999–2010	Prognostic factors: EOR	Schupper ⁶
CSP	HGG	2,743	1990–2000	5-year OS 6%; median OS 6.6 months; improved survival over time; prognostic factors: age, WHO grade, tumor site, primary treatment, year of treatment, academic hospital	Tsao-Wei ⁴⁵
PMSI	HGG	1,659	2010–2018	Median OS was 1.4 years; prognostic factors: carmustine wafer, age, gender, recurrent disease	Champeaux ⁴⁶
MarketScan and Medicare supplemental health claims database	HGG	2,157	2009–2015	No significant association between use of BEV and occurrence of thromboembolic events	Lee ⁵³

(Continued)

Table 1 (Continued)

Database used	Patient pathology	Sample size	Study year	Study findings	Reference
SEER	HGG	154	1973–2013	Median OS 10 months; prognostic factors: non-brainstem location, RT	Maxwell ⁴⁷
SEER	HGG	353	1973–2015	Prognostic factors: age; no tumor-related characteristics were associated with survival	Yang ⁴⁹
SEER	HGG	14,461	1998–2007	Prognostic factor: WHO grade, RT	Rusthoven ⁴⁸
SEER	HGG	3,706	2000–2013	Median OS 14.3 month; 5-year OS 6.2%; prognostic factor: age, location (unilateral), EOR, RT	Xia ¹²⁷
ACS-NSQIP	Mix of malignant brain tumor	4,407	2007–2012	Perioperative steroid use associated with shorter hospitalization and increased readmission; no adverse events with steroid use	Alan ⁵⁴
CBTRUS	Oligodendroglioma		2000–2013	OD and AOD showed decreased incidence over time	Achey ⁷
SEER	Oligodendroglioma	762	1973–2012	Prognostic factors: age, gender, race; improved survival over time	Furst ¹²
SEER	Oligodendroglioma	7,001	1973–2013	Prognostic factor age	Lau ¹¹
SEER	Oligodendroglioma	3,406	1999–2010	Prognostic factors: EOR; limited benefit for GTR in OG compared to AA or GBM	Alattar ⁸
SEER	Oligodendroglioma	3,880	1999–2012	Improved survival over time	Brandel ⁹
SEER	Oligodendroglioma	3,135	2004–2013	Prognostic factors: EOR	Kinslow ¹⁰

Abbreviations: AA anaplastic astrocytoma; AO, anaplastic oligodendroglioma; ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program database; BZM, bevacizumab; CA, California; CBTRUS, Central Brain Tumor Registry of the United States; CAD, coronary artery disease; CCR, California Cancer Registry; CHF, congestive heart failure; CSP, Cancer Surveillance Program; EOR, extent-of-resection; FCDS, Florida Cancer Data Registry; GBM, glioblastoma multiforme; GTR, gross total resection; HGG, high-grade glioma; LGG, low-grade glioma; NCDB, National Cancer Database; NIS, National Inpatient Sample; OS, overall survival; PMSI, French medico-administrative national database; RT, radiotherapy; RTOG, Radiation Therapy Oncology Group; SEE, Southern and Eastern Europe Tumor Registry; SEER, Surveillance, Epidemiology and End Results Database; TCGA, The Cancer Genome Atlas; TMZ, temozolomide; UCSF, University of California - San Francisco.

AO via the NCDB database between 2004 and 2013.⁴¹ An overall 5-year of 59.8% was seen and significant benefits in survival were seen from RCT or single-agent chemotherapy. Patients were more likely to receive adjuvant RCT if treated in later time epochs, were male, had private insurance, or had \geq \$63,000 median income. While the survival benefit from AOs compared with AAs were not unexpected, differences in treatment with RCT often depended on socioeconomic factors.

HGG also represent a diverse group of studied pathologies commonly aggregated in database studies. Tsao-Wei et al showed improved survival in HGG in Los Angeles County over time between 1990 and 2000.⁴⁵ In addition, this study showed relative improvement in survival of GBM compared with grade III gliomas over the same time period despite an OS of 6% at 5-years for the study group. Several other studies regarding HGG have studied several prognostic factors including age, gender, recurrent disease, tumor location, WHO grade, primary treatment, RT, and EOR.^{28,45–52} Another study by Lee et al showed no association between bevacizumab use and thromboembolic events.⁵³ One study evaluated 4,407 patients via the NSQIP database who underwent resection of a malignant brain tumor between 2007 and 2012. This study included metastatic tumors ($n=1611$) and malignant gliomas ($n=2796$).⁵⁴ Steroid use

was found to decrease hospital length of stay but increase risk of readmission in an unmatched case-control analysis; however, these findings were not confirmed on a propensity matched analysis.

Glioblastoma

Studies on GBM encompass the largest topic of database analysis in gliomas. A total of 68 studies were published between 2002 and 2020 (► **Table 1**). Studies evaluating prognostic factors showed that age, tumor histology, molecular markers, race, sex, education, marital status, treatment in high-volume and/or urban centers, insurance status, EOR, RCT, and tumor location impacted outcomes.^{52,55–111} Although a few studies simply described general demographic changes of GBMs,^{112,113} most studied specific questions.^{52,55–91,93–110,114–116} Most studies also demonstrated improved survival over time, which was likely associated with an increased use of RCT, temozolomide, and adjuvant treatments, such as bevacizumab, but could not deliver more granular specifics.

The impact of facility type and location on outcome after GBM treatment has been evaluated by several studies. Aulakh et al⁵⁵ evaluated 60,672 patients in the NCDB from 2004 to 2013, demonstrating that treatment in a high-volume facility, along with temozolomide treatment,

improved survival. In fact, treatment in a high-volume center conferred a 2-month OS benefit. Another study by Hauser et al⁶⁴ evaluating 89,839 patients in the NCDB from 2004 to 2013 suggested better outcomes for patients treated in academic centers, and a study by Delavar et al.¹⁰³ evaluating 37,581 patients between 2001 and 2011 showed a 3-month improvement in OS for patients living in metropolitan areas compared with nonmetropolitan areas. Other studies support the impact of institution type on treatment accessibility and outcome.^{65,68} Nuno et al¹¹⁷ evaluated 1,273 patients in the SEER database between 1991 and 2007 to compare hospitals with low and high rates of readmission after GBM treatment. No differences were seen in patient outcomes such as complications, nonroutine discharge, length of stay, EOR, or OS. Thus, facility characteristics, such as patient volume and facility location, seemed to impact outcome.

Several studies have evaluated the impact on outcome of socioeconomic factors, namely, marital status, race/ethnicity, and insurance status. Several studies have shown the positive impact of marriage on outcome after GBM.^{52,56,68,69,75,78,87,89,104,110,118} Several studies have shown the impact of race on outcome, primarily demonstrating that non-White races fared worse.^{52,69,71,74,87,89,95,100,101,104,118,119} Aizer et al⁶⁹ studied 22,777 patients between 1998 and 2007 via the SEER database and showed that factors associated with omission of RT included African-American and Asian-American races, unmarried status, and lower annual income. Other factors associated with reduced likelihood of RT included older age and subtotal resection/biopsy. Forst et al¹⁰⁴ evaluated 12,437 patients via the SEER database between 2002 and 2011, showing that hospice enrollment was associated with higher education, White race, and lower median income among other factors. Studying 13,665 patients in the SEER database between 2007 and 2012, Rong et al¹¹⁰ showed that insurance status highly affected prognosis. Patients who were uninsured or had Medicaid coverage were likely to be younger and unmarried and to present with larger tumors. In addition, incremental survival benefits from 2007 through 2011 were seen in insured patients but not uninsured patients.

Discussion

An evaluation of the use of administrative databases and big data in the study of gliomas demonstrated 122 studies across a wide range of pathologies and clinical questions. While we aimed to characterize the important prognostic factors seen across various geographic locales and significant time frames, there remained limitations in the granular study details important to clinical applicability. Several factors, including age, tumor grade and histology, as well as surgical EOR and adjuvant therapies, were reliably impactful on patient survival which were unsurprising. More specific patient situations or treatments that offer insight to treatment could often not be determined based on the database structure. Other prognostic factors often were

not reproducible among different studies. Numerous studies show improvement in survival rates over time and loosely attribute this to improved surgical technique and optimal timing of adjuvant RCT. But the impact of specific treatment changes could not be identified from these databases. The incorporation of molecular diagnostics in the discussion of these patients was commonly lacking and multiple studies combined different pathologies or WHO grade tumors to report findings.

One of the major advantages of large databases is the ability to compare across variation of socioeconomic factors, such as race, marital status, and insurance status, which would not be possible for many individual centers which have more homogeneous patient populations. This allows tracking of outcomes in disadvantaged patients and raises awareness for the patient management. In addition, some studies have shown the improvement of survival for patients in high-volume centers or metropolitan areas, suggesting variation in care delivery. However, the major disadvantage of large databases involves higher level of detail regarding patients and tumor types. These group of studies also did not indicate avenues to improve on health care disparities despite detecting them multiple times.

Improved analysis of large administrative databases is still needed. Despite some reported benefits, large databases are generally not designed to address all clinically relevant study questions with precision. One example of this is that different studies can show contradictory results for various prognostic factors. This may be likely a result of patient heterogeneity or the statistical analysis performed. Use of traditional statistical methods have the potential to identify statistically significant but not clinically relevant findings. Improvements are needed in our ability to analyze data from large administrative databases to ensure we can answer impactful questions and recognize reproducible epidemiologic patterns. Use of uniform reporting criteria for these studies, such as the STROBE criteria, is also necessary to improve the quality of these studies.

Conclusions

This study helped identify databases involved in the understanding of treatment for various gliomas. Descriptive information regarding the involved databases is provided. Consistent prognostic factors included age, tumor grade, histology, and EOR. While improvement in survival was seen over time, it was unclear which treatments specifically impacted this. In addition, marked socioeconomic, and racial disparities in health care persisted over time for a variety of pathologies. Administrative databases were also limited in integrating updates in molecular tumor subtypes. The application of insights from research databases to impact patient care remains inadequate.

Funding
None.

Conflict of Interest

None declared.

References

- 1 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(09):1254–1262
- 2 Karsy M, Neil JA, Guan J, Mahan MA, Colman H, Jensen RL. A practical review of prognostic correlations of molecular biomarkers in glioblastoma. *Neurosurg Focus* 2015;38(03):E4
- 3 Oravec CS, Motiwala M, Reed K, et al. Big data research in neurosurgery: a critical look at this popular new study design. *Neurosurgery* 2018;82(05):728–746
- 4 Jhaveri J, Liu Y, Chowdhary M, et al. Is less more? Comparing chemotherapy alone with chemotherapy and radiation for high-risk grade 2 glioma: an analysis of the National Cancer Data Base. *Cancer* 2018;124(06):1169–1178
- 5 Alattar AA, Carroll KT, Bryant AK, et al. Prognostic importance of age, tumor location, and tumor grade in grade II astrocytomas: An Integrated Analysis of the Cancer Genome Atlas and the Surveillance, Epidemiology, and End Results Database. *World Neurosurg* 2019;121:e411–e418
- 6 Schupper AJ, Hirshman BR, Carroll KT, Ali MA, Carter BS, Chen CC. Effect of Gross Total Resection in World Health Organization Grade II Astrocytomas: SEER-Based Survival Analysis. *World Neurosurg* 2017;103:741–747
- 7 Achey RL, Khanna V, Ostrom QT, Kruchko C, Barnholtz-Sloan JS. Incidence and survival trends in oligodendrogliomas and anaplastic oligodendrogliomas in the United States from 2000 to 2013: a CBTRUS Report. *J Neurooncol* 2017;133(01):17–25
- 8 Alattar AA, Brandel MG, Hirshman BR, et al. Oligodendroglioma resection: a Surveillance, Epidemiology, and End Results (SEER) analysis. *J Neurosurg* 2018;128(04):1076–1083
- 9 Brandel MG, Alattar AA, Hirshman BR, et al. Survival trends of oligodendroglial tumor patients and associated clinical practice patterns: a SEER-based analysis. *J Neurooncol* 2017;133(01):173–181
- 10 Kinslow CJ, Garton ALA, Rae AI, et al. Extent of resection and survival for oligodendroglioma: a U.S. population-based study. *J Neurooncol* 2019;144(03):591–601
- 11 Lau CS, Mahendraraj K, Chamberlain RS. Oligodendrogliomas in pediatric and adult patients: an outcome-based study from the Surveillance, Epidemiology, and End Result database. *Cancer Manag Res* 2017;9:159–166
- 12 Furst T, Hoffman H, Chin LS. All-cause and tumor-specific mortality trends in geriatric oligodendroglioma (OG) patients: A surveillance, epidemiology, and end results (SEER) analysis. *J Clin Neurosci* 2020;73:94–100
- 13 Dubrow R, Darefsky AS. Demographic variation in incidence of adult glioma by subtype, United States, 1992–2007. *BMC Cancer* 2011;11:325
- 14 Mezencev R. Epidemiology of gliomas in women diagnosed with breast cancer supports the protective role of estrogenic exposure. *Bratisl Lek Listy* 2018;119(08):463–468
- 15 Persaud-Sharma D, Burns J, Trangle J, et al. Demographic variation in the frequency of gliomas in Florida. *Medicina (Kaunas)* 2019;55(01):E5
- 16 Hess KR, Broglio KR, Bondy ML. Adult glioma incidence trends in the United States, 1977–2000. *Cancer* 2004;101(10):2293–2299
- 17 Jhaveri J, Cheng E, Tian S, et al. Proton vs. Photon Radiation Therapy for Primary Gliomas: An Analysis of the National Cancer Data Base. *Front Oncol* 2018;8:440
- 18 Li K, Lu D, Guo Y, et al. Trends and patterns of incidence of diffuse glioma in adults in the United States, 1973–2014. *Cancer Med* 2018;7(10):5281–5290
- 19 Plascak JJ, Fisher JL. Area-based socioeconomic position and adult glioma: a hierarchical analysis of surveillance epidemiology and end results data. *PLoS One* 2013;8(04):e60910
- 20 Gittleman H, Ostrom QT, Stetson LC, et al. Sex is an important prognostic factor for glioblastoma but not for nonglioblastoma. *Neurooncol Pract* 2019;6(06):451–462
- 21 Samaan MC, Akhtar-Danesh N. The impact of age and race on longevity in pediatric astrocytic tumors: A population-based study. *Pediatr Blood Cancer* 2015;62(09):1567–1571
- 22 Zhao YY, Chen SH, Hao Z, Zhu HX, Xing ZL, Li MH. A nomogram for predicting individual prognosis of patients with low-grade glioma. *World Neurosurg* 2019;130:e605–e612
- 23 Deb S, Pendharkar AV, Schoen MK, Altekruze S, Ratliff J, Desai A. The effect of socioeconomic status on gross total resection, radiation therapy and overall survival in patients with gliomas. *J Neurooncol* 2017;132(03):447–453
- 24 Dong X, Noorbakhsh A, Hirshman BR, et al. Survival trends of grade I, II, and III astrocytoma patients and associated clinical practice patterns between 1999 and 2010: A SEER-based analysis. *Neurooncol Pract* 2016;3(01):29–38
- 25 Iwamoto FM, Reiner AS, Nayak L, Panageas KS, Elkin EB, Abrey LE. Prognosis and patterns of care in elderly patients with glioma. *Cancer* 2009;115(23):5534–5540
- 26 Long S, Li M, Ou S, Li G. The effect of marital status on glioma patient survival: analysis of 617 cases: A SEER-based study. *Medicine (Baltimore)* 2018;97(52):e13900
- 27 Wu J, Neale N, Huang Y, et al. Comparison of Adjuvant Radiation Therapy Alone and Chemotherapy Alone in Surgically Resected Low-Grade Gliomas: Survival Analyses of 2253 Cases from the National Cancer Data Base. *World Neurosurg* 2018;112:e812–e822
- 28 Xie JC, Yang S, Liu XY, Zhao YX. Marital status is associated with survival of patients with astrocytoma. *J Clin Neurosci* 2018;56:79–87
- 29 Zhu P, Du XL, Blanco AI, et al. Impact of facility type and volume in low-grade glioma outcomes. *J Neurosurg* (e-pub ahead of print). Doi: 10.3171/2019.6.JNS19409
- 30 Claus EB, Black PM. Survival rates and patterns of care for patients diagnosed with supratentorial low-grade gliomas: data from the SEER program, 1973–2001. *Cancer* 2006;106(06):1358–1363
- 31 Claus EB, Walsh KM, Wiencke JK, et al. Survival and low-grade glioma: the emergence of genetic information. *Neurosurg Focus* 2015;38(01):E6
- 32 Jairam V, Kann BH, Park HS, et al. Defining an Intermediate-risk Group for Low-grade Glioma: A National Cancer Database Analysis. *Anticancer Res* 2019;39(06):2911–2918
- 33 Lehrer S. Glioma and Alzheimer's disease. *J Alzheimers Dis Rep* 2018;2(01):213–218
- 34 Nguyen HS, Best B, Doan NB, et al. Glioblastoma in the setting of prior lower grade gliomas - insights from SEER database. *Oncotarget* 2018;9(70):33271–33277
- 35 Smoll NR, Gautschi OP, Schatlo B, Schaller K, Weber DC. Relative survival of patients with supratentorial low-grade gliomas. *Neuro-oncol* 2012;14(08):1062–1069
- 36 Youssef I, Lee A, Garay EL, Becker DJ, Schreiber D. Patterns of care and outcomes of postoperative radiation for low-grade gliomas in United States hospitals. *J Clin Neurosci* 2018;58:124–129
- 37 Missios S, Kalakoti P, Nanda A, Bekelis K. Craniotomy for glioma resection: a predictive model. *World Neurosurg* 2015;83(06):957–964
- 38 Mukherjee D, Sarmiento JM, Nosova K, et al. Effectiveness of radiotherapy for elderly patients with anaplastic gliomas. *J Clin Neurosci* 2014;21(05):773–778
- 39 Padwal JA, Dong X, Hirshman BR, Hoi-Sang U, Carter BS, Chen CC. Superior efficacy of gross total resection in anaplastic astrocytoma patients relative to glioblastoma patients. *World Neurosurg* 2016;90:186–193

- 40 Shin JY, Diaz AZ. Anaplastic astrocytoma: prognostic factors and survival in 4807 patients with emphasis on receipt and impact of adjuvant therapy. *J Neurooncol* 2016;129(03):557–565
- 41 Shin JY, Diaz AZ. Utilization and impact of adjuvant therapy in anaplastic oligodendroglioma: an analysis on 1692 patients. *J Neurooncol* 2016;129(03):567–575
- 42 Shin JY, Yoon JK, Diaz AZ. Racial disparities in anaplastic oligodendroglioma: An analysis on 1643 patients. *J Clin Neurosci* 2017;37:34–39
- 43 Smoll NR, Hamilton B. Incidence and relative survival of anaplastic astrocytomas. *Neuro-oncol* 2014;16(10):1400–1407
- 44 Zhao YY, Wan QS, Hao Z, Zhu HX, Xing ZL, Li MH. Clinical nomogram for predicting the survival of patients with cerebral anaplastic gliomas. *Medicine (Baltimore)* 2020;99(10):e19416
- 45 Tsao-Wei DD, Hu J, Groshen SG, Chamberlain MC. Conditional survival of high-grade glioma in Los Angeles County during the year 1990–2000. *J Neurooncol* 2012;110(01):145–152
- 46 Champeaux C, Weller J. Implantation of carmustine wafers (Gliadel) for high-grade glioma treatment. A 9-year nationwide retrospective study. *J Neurooncol* 2020;147(01):159–169
- 47 Maxwell R, Luksik AS, Garzon-Muvdi T, et al. Population-based study determining predictors of cancer-specific mortality and survival in pediatric high-grade brainstem glioma. *World Neurosurg* 2018;119:e1006–e1015
- 48 Rusthoven CG, Carlson JA, Waxweiler TV, et al. The impact of adjuvant radiation therapy for high-grade gliomas by histology in the United States population. *Int J Radiat Oncol Biol Phys* 2014;90(04):894–902
- 49 Yang W, Xu T, Garzon-Muvdi T, Jiang C, Huang J, Chaichana KL. Survival of Ventricular and Periventricular High-Grade Gliomas: A Surveillance, Epidemiology, and End Results Program-Based Study. *World Neurosurg* 2018;111:e323–e334
- 50 Barnholtz-Sloan JS, Williams VL, Maldonado JL, et al. Patterns of care and outcomes among elderly individuals with primary malignant astrocytoma. *J Neurosurg* 2008;108(04):642–648
- 51 Sun Y, Xiong ZY, Yan PF, Jiang LL, Nie CS, Wang X. Characteristics and prognostic factors of age-stratified high-grade intracranial glioma patients: a population-based analysis. *Bosn J Basic Med Sci* 2019;19(04):375–383
- 52 Xie JC, Yang S, Liu XY, Zhao YX. Effect of marital status on survival in glioblastoma multiforme by demographics, education, economic factors, and insurance status. *Cancer Med* 2018;7(08):3722–3742
- 53 Lee I, Adimadhyam S, Nutescu EA, et al. Bevacizumab use and the risk of arterial and venous thromboembolism in patients with high-grade gliomas: a nested case-control study. *Pharmacotherapy* 2019;39(09):921–928
- 54 Alan N, Seicean A, Seicean S, Neuhauser D, Benzel EC, Weil RJ. Preoperative steroid use and the incidence of perioperative complications in patients undergoing craniotomy for definitive resection of a malignant brain tumor. *J Clin Neurosci* 2015;22(09):1413–1419
- 55 Aulakh S, DeDeo MR, Free J, et al. Survival trends in glioblastoma and association with treating facility volume. *J Clin Neurosci* 2019;68:271–274
- 56 Dressler EV, Liu M, Garcia CR, et al. Patterns and disparities of care in glioblastoma. *Neurooncol Pract* 2019;6(01):37–46
- 57 Glaser SM, Dohopolski MJ, Balasubramani GK, Flickinger JC, Beriwal S. Glioblastoma multiforme (GBM) in the elderly: initial treatment strategy and overall survival. *J Neurooncol* 2017;134(01):107–118
- 58 Mak KS, Agarwal A, Qureshi MM, Truong MT. Hypofractionated short-course radiotherapy in elderly patients with glioblastoma multiforme: an analysis of the National Cancer Database. *Cancer Med* 2017;6(06):1192–1200
- 59 Malakhov N, Lee A, Garay E, Becker DJ, Schreiber D. Patterns of care and outcomes for glioblastoma in patients with poor performance status. *J Clin Neurosci* 2018;52:66–70
- 60 Lee A, Malakhov N, Sheth N, Wang A, Han P, Schreiber D. Patterns of care and outcomes of chemoradiation versus radiation alone for MGMT promoter unmethylated glioblastoma. *Clin Neurol Neurosurg* 2018;170:127–131
- 61 Lee A, Youssef I, Osborn VW, Safdieh J, Becker DJ, Schreiber D. The utilization of MGMT promoter methylation testing in United States hospitals for glioblastoma and its impact on prognosis. *J Clin Neurosci* 2018;51:85–90
- 62 Buszek SM, Al Feghali KA, Elhalawani H, Chevli N, Allen PK, Chung C. Optimal Timing of Radiotherapy Following Gross Total or Subtotal Resection of Glioblastoma: A Real-World Assessment using the National Cancer Database. *Sci Rep* 2020;10(01):4926
- 63 Haque W, Thong Y, Verma V, Rostomily R, Brian Butler E, Teh BS. Patterns of management and outcomes of unifocal versus multifocal glioblastoma. *J Clin Neurosci* 2020;74:155–159
- 64 Hauser A, Dutta SW, Showalter TN, Sheehan JP, Grover S, Trifiletti DM. Impact of academic facility type and volume on post-surgical outcomes following diagnosis of glioblastoma. *J Clin Neurosci* 2018;47:103–110
- 65 Rhome R, Fisher R, Hormigo A, Parikh RR. Disparities in receipt of modern concurrent chemoradiotherapy in glioblastoma. *J Neurooncol* 2016;128(02):241–250
- 66 Kole AJ, Park HS, Yeboa DN, et al. Concurrent chemoradiotherapy versus radiotherapy alone for “biopsy-only” glioblastoma multiforme. *Cancer* 2016;122(15):2364–2370
- 67 Trifiletti DM, Alonso C, Grover S, Fadul CE, Sheehan JP, Showalter TN. Prognostic implications of extent of resection in glioblastoma: analysis from a large database. *World Neurosurg* 2017;103:330–340
- 68 Wegner RE, Abel S, Horne ZD, et al. National trends in radiation dose escalation for glioblastoma. *Radiat Oncol J* 2019;37(01):13–21
- 69 Aizer AA, Ancukiewicz M, Nguyen PL, Shih HA, Loeffler JS, Oh KS. Underutilization of radiation therapy in patients with glioblastoma: predictive factors and outcomes. *Cancer* 2014;120(02):238–243
- 70 Al-Husseini MJ, Saad AM, El-Shewy KM, et al. Prior malignancy impact on survival outcomes of glioblastoma multiforme: population-based study. *Int J Neurosci* 2019;129(05):447–454
- 71 Barnholtz-Sloan JS, Maldonado JL, Williams VL, et al. Racial/ethnic differences in survival among elderly patients with a primary glioblastoma. *J Neurooncol* 2007;85(02):171–180
- 72 Bartek J Jr, Alattar AA, Dhawan S, et al. Receipt of brachytherapy is an independent predictor of survival in glioblastoma in the Surveillance, Epidemiology, and End Results database. *J Neurooncol* 2019;145(01):75–83
- 73 Siker ML, Wang M, Porter K, et al. Age as an independent prognostic factor in patients with glioblastoma: a Radiation Therapy Oncology Group and American College of Surgeons National Cancer Data Base comparison. *J Neurooncol* 2011;104(01):351–356
- 74 Thumma SR, Fairbanks RK, Lamoreaux WT, et al. Effect of pretreatment clinical factors on overall survival in glioblastoma multiforme: a Surveillance Epidemiology and End Results (SEER) population analysis. *World J Surg Oncol* 2012;10:75
- 75 Walker GV, Li J, Mahajan A, et al. Decreasing radiation therapy utilization in adult patients with glioblastoma multiforme: a population-based analysis. *Cancer* 2012;118(18):4538–4544
- 76 Yusuf MB, Gaskins J, Amsbaugh MJ, Woo S, Burton E. Survival impact of prolonged postoperative radiation therapy for patients with glioblastoma treated with combined-modality therapy. *Neurooncol Pract* 2019;6(02):112–123
- 77 Zinn PO, Colen RR, Kasper EM, Burkhardt JK. Extent of resection and radiotherapy in GBM: A 1973 to 2007 surveillance, epidemiology and end results analysis of 21,783 patients. *Int J Oncol* 2013;42(03):929–934

- 78 Chang SM, Barker FG II. Marital status, treatment, and survival in patients with glioblastoma multiforme: a population based study. *Cancer* 2005;104(09):1975–1984
- 79 Chen JH, Huang CY, Lee YC, et al. Comparative cost analysis for the surgical and endovascular treatment of ruptured intracranial aneurysms in Taiwan: a nationwide population-based cohort study. *World Neurosurg* 2018;116:e485–e490
- 80 Darefsky AS, King JT Jr, Dubrow R. Adult glioblastoma multiforme survival in the temozolomide era: a population-based analysis of Surveillance, Epidemiology, and End Results registries. *Cancer* 2012;118(08):2163–2172
- 81 Iwamoto FM, Reiner AS, Panageas KS, Elkin EB, Abrey LE. Patterns of care in elderly glioblastoma patients. *Ann Neurol* 2008;64(06):628–634
- 82 Adams H, Adams HH, Jackson C, Rincon-Torroella J, Jallo GI, Quiñones-Hinojosa A. Evaluating extent of resection in pediatric glioblastoma: a multiple propensity score-adjusted population-based analysis. *Childs Nerv Syst* 2016;32(03):493–503
- 83 Johnson DR, Ma DJ, Buckner JC, Hammack JE. Conditional probability of long-term survival in glioblastoma: a population-based analysis. *Cancer* 2012;118(22):5608–5613
- 84 Johnson DR, O'Neill BP. Glioblastoma survival in the United States before and during the temozolomide era. *J Neurooncol* 2012;107(02):359–364
- 85 Lam S, Lin Y, Zinn P, Su J, Pan IW. Patient and treatment factors associated with survival among pediatric glioblastoma patients: A Surveillance, Epidemiology, and End Results study. *J Clin Neurosci* 2018;47:285–293
- 86 Noorbakhsh A, Tang JA, Marcus LP, et al. Gross-total resection outcomes in an elderly population with glioblastoma: a SEER-based analysis. *J Neurosurg* 2014;120(01):31–39
- 87 Pan IW, Ferguson SD, Lam S. Patient and treatment factors associated with survival among adult glioblastoma patients: A USA population-based study from 2000–2010. *J Clin Neurosci* 2015;22(10):1575–1581
- 88 Porter AB, Lachance DH, Johnson DR. Socioeconomic status and glioblastoma risk: a population-based analysis. *Cancer Causes Control* 2015;26(02):179–185
- 89 Shah BK, Bista A, Sharma S. Survival trends in elderly patients with glioblastoma in the United States: a population-based study. *Anticancer Res* 2016;36(09):4883–4886
- 90 Tian M, Ma W, Chen Y, et al. Impact of gender on the survival of patients with glioblastoma. *Biosci Rep* 2018;38(06):BSR20180752
- 91 Wachtel MS, Yang S. Odds of death after glioblastoma diagnosis in the United States by chemotherapeutic era. *Cancer Med* 2014;3(03):660–666
- 92 Zhu P, Du XL, Lu G, Zhu JJ. Survival benefit of glioblastoma patients after FDA approval of temozolomide concomitant with radiation and bevacizumab: A population-based study. *Oncotarget* 2017;8(27):44015–44031
- 93 Aneja S, Khullar D, Yu JB. The influence of regional health system characteristics on the surgical management and receipt of post operative radiation therapy for glioblastoma multiforme. *J Neurooncol* 2013;112(03):393–401
- 94 Koshy M, Villano JL, Dolecek TA, et al. Improved survival time trends for glioblastoma using the SEER 17 population-based registries. *J Neurooncol* 2012;107(01):207–212
- 95 Shabihkhani M, Telesca D, Movassaghi M, et al. Incidence, survival, pathology, and genetics of adult Latino Americans with glioblastoma. *J Neurooncol* 2017;132(02):351–358
- 96 Shu C, Yan X, Zhang X, Wang Q, Cao S, Wang J. Tumor-induced mortality in adult primary supratentorial glioblastoma multiforme with different age subgroups. *Future Oncol* 2019;15(10):1105–1114
- 97 Smoll NR, Schaller K, Gautschi OP. The cure fraction of glioblastoma multiforme. *Neuroepidemiology* 2012;39(01):63–69
- 98 Arvold ND, Cefalu M, Wang Y, Zigler C, Schrag D, Dominici F. Comparative effectiveness of radiotherapy with vs. without temozolomide in older patients with glioblastoma. *J Neurooncol* 2017;131(02):301–311
- 99 Arvold ND, Wang Y, Zigler C, Schrag D, Dominici F. Hospitalization burden and survival among older glioblastoma patients. *Neuro-oncol* 2014;16(11):1530–1540
- 100 Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Racial differences in survival after diagnosis with primary malignant brain tumor. *Cancer* 2003;98(03):603–609
- 101 Bohn A, Braley A, Rodriguez de la Vega P, Zevallos JC, Barengo NC. The association between race and survival in glioblastoma patients in the US: a retrospective cohort study. *PLoS One* 2018;13(06):e0198581
- 102 Davies J, Reyes-Rivera I, Pattipaka T, et al. Survival in elderly glioblastoma patients treated with bevacizumab-based regimens in the United States. *Neurooncol Pract* 2018;5(04):251–261
- 103 Delavar A, Al Jammal OM, Maguire KR, Wali AR, Pham MH. The impact of rural residence on adult brain cancer survival in the United States. *J Neurooncol* 2019;144(03):535–543
- 104 Forst D, Adams E, Nipp R, et al. Hospice utilization in patients with malignant gliomas. *Neuro-oncol* 2018;20(04):538–545
- 105 Johnson DR, Leeper HE, Uhm JH. Glioblastoma survival in the United States improved after Food and Drug Administration approval of bevacizumab: a population-based analysis. *Cancer* 2013;119(19):3489–3495
- 106 Ladomersky E, Scholtens DM, Kocherginsky M, et al. The coincidence between increasing age, immunosuppression, and the incidence of patients with glioblastoma. *Front Pharmacol* 2019;10:200
- 107 Marcus LP, McCutcheon BA, Noorbakhsh A, et al. Incidence and predictors of 30-day readmission for patients discharged home after craniotomy for malignant supratentorial tumors in California (1995–2010). *J Neurosurg* 2014;120(05):1201–1211
- 108 Pendharkar AV, Rezaii PG, Ho AL, Sussman ES, Li G, Desai AM. Functional mapping for glioma surgery: a propensity-matched analysis of outcomes and cost. *World Neurosurg* 2020;137:e328–e335
- 109 Rahmani R, Tomlinson SB, Santangelo G, et al. Risk factors associated with early adverse outcomes following craniotomy for malignant glioma in older adults. *J Geriatr Oncol* 2020;11(04):694–700
- 110 Rong X, Yang W, Garzon-Muvdi T, et al. Influence of insurance status on survival of adults with glioblastoma multiforme: A population-based study. *Cancer* 2016;122(20):3157–3165
- 111 Huang J, Samson P, Perkins SM, et al. Impact of concurrent chemotherapy with radiation therapy for elderly patients with newly diagnosed glioblastoma: a review of the National Cancer Data Base. *J Neurooncol* 2017;131(03):593–601
- 112 Nguyen HS, Doan NB, Gelsomino M, et al. Management and survival trends for adult patients with malignant gliomas in the setting of multiple primary tumors: a population based analysis. *J Neurooncol* 2019;141(01):213–221
- 113 Zada G, Bond AE, Wang YP, Giannotta SL, Deapen D. Incidence trends in the anatomic location of primary malignant brain tumors in the United States: 1992–2006. *World Neurosurg* 2012;77(3–4):518–524
- 114 Huang LE, Cohen AL, Colman H, Jensen RL, Fulst DW, Couldwell WT. IGFBP2 expression predicts IDH-mutant glioma patient survival. *Oncotarget* 2017;8(01):191–202
- 115 Chen LF, Yang Y, Ma XD, et al. Optimizing the extent of resection and minimizing the morbidity in insular high-grade glioma surgery by high-field intraoperative MRI guidance. *Turk Neurosurg* 2017;27(05):696–706
- 116 Li X, Li Y, Cao Y, et al. Risk of subsequent cancer among pediatric, adult and elderly patients following a primary diagnosis of glioblastoma multiforme: a population-based study of the SEER database. *Int J Neurosci* 2017;127(11):1005–1011

- 117 Nuño M, Ly D, Mukherjee D, Ortega A, Black KL, Patil CG. Quality of surgical care and readmission in elderly glioblastoma patients. *Neurooncol Pract* 2014;1(02):33–39
- 118 Wang W. Increased incidence of second primary malignancy in patients with malignant astrocytoma: a population-based study. *Biosci Rep* 2019;39(06):BSR20181968
- 119 Xu H, Chen J, Xu H, Qin Z. Geographic variations in the incidence of glioblastoma and prognostic factors predictive of overall survival in US adults from 2004–2013. *Front Aging Neurosci* 2017;9:352
- 120 Bin Abdulrahman AK, Bin Abdulrahman KA, Bukhari YR, Faqihi AM, Ruiz JG. Association between giant cell glioblastoma and glioblastoma multiforme in the United States: A retrospective cohort study. *Brain Behav* 2019;9(10):e01402
- 121 Lai R, Hershman DL, Doan T, Neugut AI. The timing of cranial radiation in elderly patients with newly diagnosed glioblastoma multiforme. *Neuro-oncol* 2010;12(02):190–198
- 122 Chen YR, Sole J, Ugiliweneza B, et al. National trends for reoperation in older patients with glioblastoma. *World Neurosurg* 2018;113:e179–e189
- 123 Chen YR, Ugiliweneza B, Burton E, Woo SY, Boakye M, Skirboll S. The effect of postoperative infection on survival in patients with glioblastoma. *J Neurosurg* 2017;127(04):807–811
- 124 Zhou X, Zhang S, Niu X, et al. Risk factors for early mortality among patients with glioma: a population-based study. *World Neurosurg* 2020;136:e496–e503
- 125 Haque W, Verma V, Butler EB, Teh BS. Patterns of care and outcomes of multi-agent versus single-agent chemotherapy as part of multimodal management of low grade glioma. *J Neurooncol* 2017;133(02):369–375
- 126 Diaz-Aguilar D, ReFaey K, Clifton W, et al. Prognostic factors and survival in low grade gliomas of the spinal cord: A population-based analysis from 2006 to 2012. *J Clin Neurosci* 2019;61:14–21
- 127 Xia Y, Liao W, Huang S, et al. Nomograms for Predicting the Overall and Cancer-Specific Survival of Patients with High-Grade Glioma: A Surveillance, Epidemiology, and End Results Study. *Turk Neurosurg* 2020;30(01):48–59