Considerations of Care for the Adult Patient with a Brain Tumor

A Clinical Practice Guideline

By Robin Saiki, Jean Arzbaecher, Molly Baker, Rory Breslin-Sani, Karl Cristie Figuracion, Angela Starkweather, and Kiffon Keigher

AANN
American Association of Neuroscience Nurses

1061 American Lane, Suite 310
Schaumburg, IL 60173-4973
888.557.2266
International phone: 847.375.4733
Fax: 847.375.6430
info@aann.org | www.AANN.org

Lead Author
Robin Saiki, DNP ACNP-BC

Content Authors
Jean Arzbaecher, MS APN CNRN
Molly Baker, MSPAS PA-C
Rory Breslin-Sani, DNP ACNP-BC CCRN CNRN CSRN
Karl Cristie Figuracion, PhD ARNP A-GNP AOCNP
Angela Starkweather, PhD RN ACNP-BC FAANP FAAN

Senior Author
Kiffon Keigher, DNP MSN ACNP-BC FAHA

Clinical Practice Guideline Board Liaisons
Kiffon Keigher, DNP MSN ACNP-BC FAHA
Angela Starkweather, PhD RN ACNP-BC FAANP FAAN

Clinical Practice Guideline Series Editor
Joan Censullo, PhD FAHA

Content Reviewers
Ashley Higgins, MSN APRN ACCNS-AG CCRN CNRN SCRN
Sarah Beam, MSN APRN ACNP-BC CNRN

Librarian
Jennifer C. Westrick, MSLIS AHIP, Library Research Information Specialist, Rush University Medical Center

AANN National Office
Leah Zamora, Executive Director
Katie James, Managing Editor

Acknowledgments
The nursing profession and AANN are indebted to the volunteers who have devoted their time and expertise to this valuable resource, which was created for those who are committed to excellence in the care of patients with brain tumors.

Disclaimer of Liability/Publisher's Note
The authors, editors, and publisher of this document neither represent nor guarantee that the practices described herein will, if followed, ensure safe and effective patient care. The authors, editors, and publisher further assume no liability or responsibility in connection with any information or recommendations contained in this document. These recommendations reflect judgment of the American Association of Neuroscience Nurses (AANN) regarding the state of general knowledge and practice in their field as of the date of publication and are subject to change based on the availability of new scientific information.

Conflict of Interest Disclosures
There are no relevant financial relationships with ineligible companies for any individuals with the ability to control content of the activity.

Introduction

The purpose of this document is to provide an evidence-based review and best practice recommendations related to topics that will assist the registered nurse in the care of the adult patient with a brain tumor. Adult patients with brain tumors require expert nurses to help manage the phases of care once they receive their diagnosis. The care of patients with neuro-oncologic disease is complex and requires management across the spectrum of the disease state, including surgical and nonsurgical treatment options, symptom management, and palliative considerations. Patients and families experience fear and anxiety surrounding the diagnosis, treatment, and recovery from this group of diseases. Nurses caring for this patient population require evidence-based recommendations for guidance when dealing with multiple phases of the patient experience. These include acceptance of the diagnosis, anxiety, fear of potential complications with surgery, being educated on adjuvant therapies, and understanding symptom management. In response to these needs, the American Association of Neuroscience Nurses (AANN) appointed a writing group to conduct a critical review of the literature to determine best practice recommendations for the nursing care of patients with a brain tumor diagnosis. The writing group formulated the population, intervention, comparison, and outcome (PICO) questions, performed the literature review, and identified relevant studies published between 2012 and 2022. The evidence was critically analyzed and is summarized in the evidence tables (Appendix). The methodology used for this clinical practice guideline (CPG) and all of AANN's CPGs and evidence-based clinical reviews is described in the AANN CPG methodology manuscript.[1]

Results

Diagnosis

In 2021, the World Health Organization (WHO) revised the classification system for tumors of the central nervous system (CNS; Table 1).[2-4] These changes reflect advances in the understanding of the histopathology and molecular pathology of brain tumors. Central nervous system tumors are categorized in a manner that reflects their collective prognosis as it pertains to their molecular pathology. This new classification system provides more guidance to clinicians with regard to both optimal therapy and prognosis.[4]

In patients with high-grade glioma, what is the nurse's role in understanding the presence of an IDH1 mutation compared to IDH1 wild type (no IDH mutation) for brain tumor in terms of prognostication and patient outcome?

Recommendation: Nursing professionals caring for individuals with brain tumors should be well-versed in molecular profiling of glioma, in particular isocitrate dehydrogenase 1 (IDH1) status, as this informs diagnosis, prognostication, and patient education. Understanding survival and prognostication helps nurses in management and support of the patient with IDH1 mutation (strong recommendation, high level of evidence).

Rationale: In the 2021 WHO CNS tumor classification update, the distinction was made between the diagnosis of glioblastoma (GBM; WHO grade 4 [IDH wild type]) and astrocytoma (WHO grade 4 [IDH mutant]) based on IDH1 status.[2] Prior to this reclassification of GBM as IDH wild type, a meta-analysis (N=3,464) that examined the association of IDH1/2 mutations with overall survival and progression-free survival in patients with GBM described that the IDH1 mutation is associated with a decreased mortality rate (relative risk [RR]=0.43, 95% CI 0.35-0.54, $P<.001$).[5] Another meta-analysis of 24 studies evaluated the hazard ratio (HR); the pooled HR of 0.358 (95% CI 0.264-0.487, $P<.001$) indicated that IDH mutations were associated with better overall survival, and the pooled HR of 0.322 (95% CI 0.24200.455, $P<.001$) indicated that IDH mutations were associated with better progression-free survival.[6]

It is imperative that nurses caring for patients with gliomas understand these data to appropriately advise and educate patients and families. This knowledge may help guide patients and families in planning for the future and may lead to difficult discussions related to advance care planning (ACP) and palliative care. The research described above was robust and rigorous in examining the association of IDH mutation status with health outcomes, in particular overall survival and progression-free survival. However, further research is necessary to examine how supportive interventions such as early integration of palliative care impact the quality of health and symptom burden among these patients.

Risk Factor Assessment and Mitigation

Risk factors for the development of brain tumors have been studied through large epidemiological studies, clinical trials, and meta-analyses. This section covers environmental factors, such as exposure to mobile phones and environmental pollutants.

What is the impact of environmental risk factors on brain tumor development in adults?

Recommendation: There is insufficient evidence to support a practice recommendation related to nursing interventions focused on risk prevention measures involving exposure to cell phones or environmental pollutants (weak recommendation, low level of evidence).

Exposure to Mobile Phones

Rationale: Five studies were reviewed: three meta-analyses,[7-9] one case-control study,[10] and one retrospective data registry review.[11] None of the studies revealed high-quality evidence that mobile phone use is a risk factor impacting tumor growth or outcome after diagnosis with brain tumor. The relationship between meningioma, acoustic neuroma, or glioma growth and mobile phone exposure was assessed using a large data registry. There was a low correlation between tumor growth (n=447) and regular use of mobile phones compared with nonusers (n=892).[10] This study also reported a positive association between both high-volume users (at least weekly for 6 months continuously) and lifetime users (cumulative duration for more than 10 years) and ipsilateral use of mobile device for glioma development. Two meta-analyses demonstrated a positive correlation between glioma development and mobile phone use.[8,9] However, the evidence was determined to be of low quality due to identified limitations. For one, the primary effect for each of these included predominantly case-controlled studies consisting of questionnaires and surveys. Additionally, there

Table 1. 2021 WHO Classification of Central Nervous System Tumors: Gliomas, Glioneuronal and Neuronal Tumors, and Ependymal Tumors

Adult-Type Diffuse Gliomas	
Astrocytoma, IDH mutant	Glioblastoma, IDH wild type
Oligodendroglioma, IDH mutant and 1p/19q codeleted	
Circumscribed Astrocytic Gliomas	
Pilocytic astrocytoma	Subependymal giant cell astrocytoma
High-grade astrocytoma with piloid features	Chordoid glioma
Pleomorphic xanthoastrocytoma	Astroblastoma, MN1 altered
Glioneural and Neuronal Tumors	
Ganglioglioma	Diffuse leptomeningeal glioneuronal tumor
Desmoplastic infantile ganglioglioma/desmoplastic infantile astrocytoma	Gangliocytoma
Dysembryoplastic neuroepithelial tumor	Multinodular and vacuolating neuronal tumor
Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters	Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)
Papillary glioneuronal tumor	Central neurocytoma
Rosette-forming glioneuronal tumor	Extraventricular neurocytoma
Myxoid glioneuronal tumor	Cerebellar liponeurocytoma
Ependymal Tumors	
Supratentorial ependymoma	Posterior fossa ependymoma, group PFB
Supratentorial ependymoma, ZFTA fusion positive	Spinal ependymoma
Supratentorial ependymoma, YAP1 fusion positive	Spinal ependymoma, MYCN amplified
Posterior fossa ependymoma	Myxopapillary ependymoma
Posterior fossa ependymoma, group PFA	Subependymoma

YAP1, yes1-associated transcriptional regulator; ZFTA, zinc finger translocation associated.

Modified from Berger TR, Wen PY, Lang-Orsini M, Chukwueke UN. World Health Organization 2021 classification of central nervous system tumors and implications for therapy for adult-type gliomas. *JAMA Oncol*. 2022;8(10):1493-1501. https://doi.org/10.1001/jamaoncol.2022.2844.

was heterogeneity within the case and control groups in both reviews, and there are insufficient data defining high-volume mobile phone usage. Lastly, a risk of bias exists given the nature of questionnaires and surveys and potential for inaccurate recall as well as lifestyle changes after receiving a brain tumor diagnosis.

Although three meta-analyses were included in this review, the quality of the evidence was low. When educating patients on a link between the development of brain tumors and the use of mobile phones, nursing professionals can report that there is no high-level evidence demonstrating a correlation. There continues to be a lack of evidence that the use of mobile phones is a cause of brain tumor growth or progression. More study is needed in this area, as mobile phone usage starts earlier in life and spans decades.

Exposure to Environmental Pollutants and Toxins

Rationale: There is low-quality evidence indicating that brain tumor growth, specifically gliomas, is influenced by exposure to environmental factors that include air pollution,[12] allergic conditions,[13] lead exposure,[14] or fish intake.[15] Review of the literature revealed very few high-quality studies that evaluated the risk of exposure to environmental toxins or pollutants and development or growth of brain tumors. Jorgenson et al.[12] found weak evidence that ambient air pollution was associated with brain tumor development in women over 44 years of age. One meta-analysis found evidence suggesting a correlation between lead exposure and meningioma development.[14] This same study found that lead exposure may have a protective role against glioma development and recommended more robust investigation of these findings.

Overall, the studies evaluated for this review were not targeted to one tumor type, to a homogenous population, or to defined measures of the toxin or pollutant of concern. This contributed to poor quality of evidence in detailing any true risk of environmental exposures for development of any type of brain tumor. More targeted and defined measures are needed to determine this risk to patients.

Obesity

Do patients with obesity and brain tumors have increased mortality outcomes compared to patients without obesity?

Recommendation: Nurses should evaluate and coach patients with obesity on weight loss interventions and educate on the possible risk of association with brain tumor growth, excluding gliomas (weak recommendation, low level of evidence).

Rationale: There are limited studies evaluating the mortality risk of patients with brain tumors and obesity, increased body mass index (BMI), and body type association. A prospective study[16] and a systematic review with a dose-response meta-analysis[17] looking at the association of BMI to glioma growth demonstrated a weak association. Additionally, there was low-level evidence to suggest correlation between obesity, diabetes mellitus, and hyperlipidemia in development of GBM.[18] In the studies reviewed, there is no evidence that obesity has a direct impact on mortality outcomes for patients with meningioma or glioma. Cote et al.[16] determined there was no correlation between weight or BMI with glioma risk in adults (N=508). Specifically, they found that waist circumference and adult BMI posed no increased risk of glioma. This group did find a moderate association between the risk of developing a glioma and having a higher measured BMI at 21 years of age in a pooled cohort of men and for women over 18 years with a taller height. Both prospective studies had small sample sizes and yielded low-quality evidence.

Zhang and colleagues[17] found a positive correlation between higher BMI and meningiomas but not gliomas in the adult population. This systematic review and dose response meta-analysis included 16 publications looking at an association of BMI and brain tumor type with a nonlinear association. They reported that obesity was linked with a 34% increment risk of brain tumors and 48% increment risk of meningiomas but with a weakening effect in subgroup analysis of confounding relationship such as sex. Significant results were noted for possible positive correlation between brain tumors and females (P=.001 for obesity and P=.004 for overweight) but not for males.[17] This suggests a possible correlation between hormones, particularly estrogen, and brain tumor risks. Many limitations were identified with the systematic review, including publication bias with a possible overstated positive correlation between BMI and brain tumor and reporting bias with the identified mixed parameters study designs, which include different BMI category measurements and different brain tumor criteria.[17] Barami et al.[18] found that the presence or absence of diabetes was less important in survival than glycemic control in the patient with GBM. Further investigation is needed to determine what type of relationship, if any, exists between brain tumor development, obesity, and other associative risk factors such as diabetes and circulating hormones.

Diet and Nutrition

Do certain dietary patterns impact glioma risk for patients with brain tumors, requiring targeted nursing education interventions, compared to patients without?

Recommendation: There are no recommended nursing interventions targeting dietary management for patients

with brain tumors. Nursing assessments and education should focus on the importance of healthy and balanced diets for the patient diagnosed with a brain tumor (weak recommendation, low level of evidence).

Rationale: Dietary habits have long been a concern for risk to many chronic and acute disease states. An evaluation of fifteen food groups, three dietary patterns, and fourteen nutrients across three large prospective studies showed no increased incidence of glioma risk with dietary patterns.[19] While this large cohort meta-analysis evaluated mixed populations of both individuals with cancer diagnosis and those without who had been living in either the U.K. or U.S. for an extended time frame (mean 12.2 years/participant), it failed to quantify or define the components of a healthy dietary pattern, did not have a mechanism to validate the studied control state of standardized calories at 1,600 per day (females) and 2,000 per day (males), and relied on patient self-reported intake, which is likely to include some risk of bias and poor recall. While previous case reports and small observational studies suggest diets high in cured meats and nitrites contribute to a higher incidence of tumor development, there is no clear evidence that diet has any significant impact on the risk of glioma in adults.[19]

Diagnostic Tools

It is essential to understand the reasoning behind—and the importance of—diagnostic imaging and other assessment tools used in the care of the adult patient with brain tumor. This knowledge guides the nurse in understanding treatment choices and educating patients.

Does the use of advanced imaging and specialized interpretation of magnetic resonance imaging increase the sensitivity of diagnosis of brain tumor, recurrence, and evaluation of treatment effect?

Recommendation: Nurses should be aware of the different imaging modalities used for the diagnosis of a brain tumor and treatment effect and know that the use of these modalities may differ from institution to institution. This knowledge may help impact patient outcomes due to earlier diagnosis and treatment through the nurse's advocacy for timely and appropriate diagnostic testing (good practice recommendation).

Rationale: Maia and colleages[20] described the association between relative cerebral blood volume (rCBV) derived from perfusion-weighted imaging and high-grade gliomas (HGGs), given these tumors are highly angiogenic and tend to form large, tortuous microvessels. In regard to differentiating recurrence and treatment effect, a meta-analysis of 28 articles demonstrated that the pooled sensitivities and specificities for detecting tumor recurrence with mean rCBV and maximum rCBV were 88% and 88% (95% CI: 0.81-0.94; 0.78-0.95) and 93% and 76% (95% CI: 0.86-0.98; 0.66-0.85), respectively.[21] Though this meta-analysis highlights the increasing clinical use of advanced imaging to differentiate between tumor progression and treatment effect, it does not detail the standard technique in capturing these advanced images. Thus, despite promising benefits in diagnosis and differentiating recurrence vs treatment effect, there is variability between institutions with regard to technique, thresholding, and postprocessing of the images, and further investigation and standardization are needed in future research. The use of advanced imaging techniques such as dynamic susceptibility contrast perfusion magnetic resonance imaging (MRI) can help in differential diagnosis between HGG and low-grade glioma (LGG) and may help to differentiate tumor recurrence from posttreatment effects.[20,21] Nurses can help facilitate timely, appropriate diagnostic testing and patient education to promote early identification of patients who may require cancer treatment or goals-of-care discussions.

Neuropsychological Evaluation

In nursing care and management of adults diagnosed with brain tumors, how does formal neuropsychological assessment compare to symptom-only assessment?

Recommendation: Though the reviewed evidence is weak and further research is needed, AANN recommends objective, formal neuropsychological testing as well as standard symptom assessment for patients diagnosed with primary brain tumors when clinically feasible and appropriate. When cognitive deficits and symptoms are identified, nurses can help identify resources such as vocational counseling, speech, and other neurocognitive rehabilitation, as well as other services that can support the patient and their family members during and after treatment. Specific subgroups of adult patients with brain tumors that may benefit include patients with larger tumors, patients with tumors in frontal locations, and patients with dominant hemisphere tumors (moderate recommendation, low level of evidence).

Rationale: Two articles matched this PICO question.[22,23] As a result of tumor location and treatment effects, patients with brain tumors may often have some neurocognitive decline. One prospective study evaluated neurocognitive function in patients newly diagnosed with a brain tumor (n=46 patients with a brain tumor, n=46 healthy controls).[22] Larger tumor volume, frontal location, and left-dominant hemisphere were associated with worse executive functioning and verbal fluency ($P<.05$).

Additionally, larger tumors and left-dominant location correlated with impairments in perceptual speed tasks (P<.05). Frontal tumor location was related to worse performance in visual-spatial and short- and long-term memory (P<.05). The study demonstrates the significant neurocognitive issues that are experienced among patients newly diagnosed with a brain tumor despite reliable performance status. Of the 46 participants with brain tumors, the median Karnofsky Performance Status score was 90 (range 60-100).

A cross-sectional study (N=40) assessed the discrepancy of formal, objective neurocognitive testing with subjective patient-reported cognitive function and found discordance between objective and subjective measures in 50% of their participants.[23] Thirteen of their participants scored normal in performance-based neurocognitive testing while reporting worsened cognitive symptoms. Six participants had impaired neurocognitive testing while reporting no change in cognitive symptoms. The greatest discordance was observed in the domains of attention and memory.[23] Though the study was a cross-sectional design with a small sample size, it illustrated the discrepancy in neurocognitive testing and subjective patient reports, highlighting the fact that a comprehensive approach is warranted to better characterize cognitive function among patients with brain tumors.

Research remains limited when examining the optimal strategy for assessing cognitive function among patients with brain tumors. Though numerous studies highlight the cognitive impairment that arises from brain tumors and treatment, future studies should also include the timing of assessment, frequency, and use of subjective reporting. Identification of cognitive issues can facilitate early identification of resources and services to patients and their family members. Nurses can play an integral role in educating patients and families on the potential cognitive issues that may occur as well as providing standard nursing care through ongoing symptom assessment.

Radiation Treatment

Brain tumors may require radiation therapy as a primary or adjunctive modality of treatment. Adult patients may develop symptoms related to treatment depending on the type of radiation used, the volume of irradiated tissue, and the location of the tissue. Symptoms caused by any type of cranial radiation are related to multiple factors. Location and volume of irradiated brain, radiation dose, fractionation, and concurrent therapies such as chemotherapy or immunotherapy all play important roles in the development of acute or chronic symptoms related to brain irradiation.[24]

In the adult patient undergoing brain irradiation for primary or metastatic brain tumors, compared to those patients who do not receive this treatment, what are the common symptoms experienced and the influence on quality of life that nursing care can impact?

Recommendation: Neurocognitive decline and other symptoms can impair quality of life (QOL) in patients diagnosed with a brain tumor. AANN recommends conducting symptom and QOL assessments over time to examine the impact of ongoing treatment on these outcomes. Patients with a higher number of brain metastases (≥3) or with neurocognitive impairment have worse symptoms and QOL and may benefit from referral to palliative care for specialized management of symptoms. Telehealth supportive care can offer greater accessibility at less cost and time for transportation in follow-up during receipt of radiation therapy (weak recommendation, low level of evidence).

General Symptoms

Rationale: A case-control study demonstrated that patients with brain metastases report significantly greater distress than patients without brain metastases (P=.029).[25] Patients (n=217) with brain metastases receiving whole brain radiation therapy (WBRT) reported a significant increase in nausea, pain, and depression from the initiation of radiation therapy to month 3 (P=.033, .037, .002, respectively), and patients experiencing more symptoms over time had worse QOL.[26] A similar observational study in patients with brain metastases found no significant difference in QOL scores from the start of WBRT to the end of treatment; however, physical functioning scores worsened after radiotherapy (P=.015).[27] In spite of this, WBRT improved Karnofsky Performance Status scores and did not worsen sleep quality or mood, even in patients with poor performance status. In patients with single or multiple brain metastases (N=122) undergoing stereotactic radiosurgery (SRS), mean QOL preservation was 79%.[28] However, patients with more than three brain metastases were at significantly greater risk for QOL decline (P<.01).[28] In patients with brain metastases who underwent a single session of gamma knife radiosurgery, the incidence of new symptomatic lesions was low, and most patients had improvements in symptoms.[29] This study supports the importance of follow-up MRIs and symptom assessments in evaluating QOL.

Neurocognitive Symptoms

Rationale: Neurocognitive symptoms including problems with short-term memory, attention, processing speed, and executive function can occur as a result of radiation-induced changes to the brain. These symptoms may be temporary or permanent and can start within the first 6

months after radiation or later in a more delayed fashion.[24] In patients with primary or metastatic brain tumors at least 6 months postradiation therapy (≥30 gray [Gy] of fractionated, partial, or whole brain radiation), one study found that 66% of patients met criteria for mild cognitive impairment (MCI), suggesting that assessment of MCI using standardized criteria may help identify patients experiencing neurocognitive dysfunction and facilitate planning with family.[30]

The optimal treatment for survival among older adults newly diagnosed with GBM was investigated in a systematic review and network meta-analysis.[31] Using data from 7 randomized controlled trials (RCTs) including 1,569 patients, the authors concluded that, in terms of overall survival, moderately hypofractionated radiation therapy (3 weeks) with concurrent and adjuvant temozolomide was the best and second-best adjuvant therapy option with 81% and 99.1% probability, respectively. In patients with HGG (N=229), most developed cognitive impairment over an 18-month follow-up period, and risk factors of cognitive impairment included genomic factors, tumor type (GBM), and residual tumor volume.[32] An observational study involving patients who underwent proton beam therapy for a brain tumor (N=62) and were recurrence-free over a mean period of 22.5 months found that cognitive function was stable over time, although those with cognitive impairment had lower global health status and higher symptom scores.[33] A systematic review of 16 studies found that telehealth supportive care among patients with a primary brain tumor and their caregivers was feasible and acceptable, while adherence and clinical gains were greater when interventions involved real-time interactions as opposed to self-guided interventions.[34]

General symptoms and neurocognitive decline vary during and after radiation treatment depending on many factors, including tumor type and location; treatment type and intensity; and demographics, such as age. Prior research in this area has been primarily observational but suggests that routine assessment of symptoms, QOL, and neurocognitive decline using standardized measures are important for guiding nursing care in symptom management strategies and support for patients and their families.

In adult patients undergoing brain irradiation for primary or metastatic brain tumors, what nursing interventions may be used to prevent or improve symptoms?

Recommendation: Memantine may be an option for patients receiving WBRT or who are at risk of progressive cognitive dysfunction as a result of radiation therapy. Hippocampal avoidance during WBRT can significantly reduce cognitive symptoms (strong recommendation, moderate to high level of evidence). Exercise therapy may also be an option for patients and caregivers who are willing and able to participate, as it can provide improvements in strength and function (weak recommendation, low level of evidence). Nurses caring for patients receiving WBRT as part of their treatment plan should be aware of these interventions and advocate for their use when appropriate.

Rationale: A randomized, double-blind, placebo-controlled trial involving 508 adult patients with brain metastases who were receiving WBRT was conducted to determine whether memantine could prevent cognitive dysfunction. Memantine blocks the effects of the excitatory neurotransmitter glutamate, which can be present in excessive amounts after WBRT. In doing so, it regulates glutamate activity, which ultimately reduces the potential for further damage to brain cells.[35] Participants were randomized to receive memantine (20 mg/day; n=256) or placebo (n=252) within 3 days of starting radiotherapy for 24 weeks. The memantine arm had significantly longer time to cognitive decline (HR 0.78, 95% CI 0.62-0.99, *P*=.01); the probability of cognitive function failure at 24 weeks was 53.8% in the memantine arm and 64.9% in the placebo arm. Superior results were seen in the memantine arm for executive function at 8 (*P*= .008) and 16 weeks (*P*=.0041) and for processing speed (*P*=.0137) and delayed recognition (*P*=.0149) at 24 weeks.[35]

Radiation to the hippocampi via conventional WBRT is associated with cognitive side effects, with deficits in learning, memory, and executive function. Hippocampal avoidance WBRT is meant to circumvent this issue by limiting the dose of radiation to this region.[36] In a Phase 3 randomized trial of adult patients with brain metastases randomized to hippocampal avoidance WBRT with memantine or WBRT with memantine, it was found that hippocampal avoidance significantly reduced cognitive symptoms over time (*P*=.043).[36] In addition, patients receiving hippocampal avoidance WBRT reported less symptom burden at 6 months (*P*<.001) and 12 months (*P*=.026) compared to the WBRT group.

In a qualitative study involving patients with GBM (n=19) and their caregivers (n=15), the researchers found that both patients and caregivers identified benefits of exercise during chemoradiotherapy including achieving improvements in health, regaining a sense of control, interacting with people, and keeping active.[37] Subsequently, a feasibility study was conducted with 30 patients to examine the safety and preliminary efficacy of a supervised, autoregulated multimodal exercise program during chemoradiation.[38] Only 50% of patients were willing or able to commence exercise, indicating it may not be feasible for a sizable proportion of this patient population. However, for patients willing and able to complete the intervention, it was found to be safe and effective for improving strength and function.

Surgical Treatment

How does the adoption of enhanced recovery after surgery strategies in adult patients with brain tumors improve pain control, postoperative nausea and vomiting, length of stay, and patient satisfaction?

Recommendation: Among adult patients with brain tumors, the adoption of enhanced recovery after surgery (ERAS) protocols is safe and effective in terms of preoperative optimization, discharge instructions, pain control, and postoperative nausea and vomiting (PONV) control. Further study is needed when it comes to standardizing more controversial areas such as venous thromboembolism (VTE) prophylaxis (moderate recommendation, low to moderate level of evidence).

Rationale: Four articles (N=468 unique patients)[43,44,46,47] correspond to the subject of this PICO question. Two studies' populations were restricted to brain tumors. The other studies included patients after elective craniotomy with diagnoses ranging from brain tumor to trigeminal neuralgia to cavernous malformation. Review of the literature revealed few high-quality studies evaluating the use of ERAS programs in cranial neurosurgery for patients with brain tumors.

The use of ERAS protocols in adult patients recovering from craniotomy is an emerging field of study and not yet a widely adopted tool in the management of patients with brain tumors. ERAS protocols typically include evidence-based recommendations for care in the pre-, intra-, and postoperative periods. Though in general neurosurgery experts agree on some aspects of ERAS protocols, such as preoperative education and postoperative instructions, there is less agreement on other features, such as postoperative VTE prophylaxis.[39,40]

Two systematic reviews determined that the benefits of ERAS protocols following craniotomy in patients with brain tumors included reduced length of stay (LOS) and cost, with no resulting increase in complications.[41,42] They concluded that ERAS protocols for patients recovering from craniotomy for brain tumor were likely advantageous but recommended more research in the form of prospective studies. One of the systematic reviews[41] noted that some evidence-based interventions were readily implemented, such as preoperative screening and optimization, if appropriate, as well as the use of formal criteria for discharge from the hospital after craniotomy. ERAS components that were least likely to be used in patients undergoing craniotomy included presurgical carbohydrate loading and postoperative thromboprophylaxis.

Pain Control

Rationale: Multiple articles in this review discussed pain control as an important feature or secondary outcome of an ERAS program in cranial neurosurgery.[39,40,42-45] The single RCT reviewed used multiple modalities to achieve pain control in patients recovering from craniotomy.[43] These modalities were described in several of the other papers as well and include scalp blocks and local infiltration of the incision, selective COX-2 inhibitors, gabapentin, and dexmedetomidine. The consensus was to limit the use of opioids in favor of nonopioid analgesia when at all possible.[43]

Postoperative Nausea and Vomiting

Rationale: All the articles in this review examined the prevention of PONV as an aspect of an ERAS protocol for patients who underwent craniotomy. The strongest recommendations were for the use of dexamethasone and serotonin antagonists (ondansetron). Other recommendations included preoperative identification of patients at higher-than-average risk for PONV using different scoring systems such as the Apfel simplified risk score.[43] This score is calculated from four questions inquiring after gender, smoking status, history of motion sickness or PONV, and use of postoperative opioids. A score of 0 equates to a 24-hour risk of PONV of 10%, and a score of 4 equates to a 24-hour risk of PONV of 79%.[43]

Length of Stay

Rationale: Length of stay was a primary outcome for most of the studies reviewed.[43,45-47] The single RCT revealed a statistically significant reduction in the LOS of patients undergoing elective craniotomy when following an ERAS protocol, from 4 days to 3 days ($P<.0001$).[43] Both systematic reviews reported reductions in LOS in patients following ERAS protocols postcraniotomy.[41,42] Complication and readmission rates were similar in both ERAS and conventional groups.[41,42]

Patient-Reported Outcomes

Rationale: One secondary analysis of an RCT studied the patient experience as it related to ERAS protocols after craniotomy.[44] The primary outcome was patient satisfaction and was measured using a questionnaire covering multiple topics at discharge (information, medical care, nursing care, enhanced recovery, and comfort). Patient satisfaction scores were higher in the ERAS group compared to the control group (92.2 vs 86.8, range 85-100). Significant predictors of patient satisfaction included shorter LOS, reducing PONV, and using absorbable sutures for closure.[44] Incorporating standardized ways of measuring patient satisfaction and other patient-reported outcomes will be critical moving forward for the development of cranial neurosurgery ERAS protocols.[41]

There is a dearth of systematic research looking at all aspects of an ERAS protocol in craniotomy for tumors. The populations studied often include a more generalized group and are not specific to patients with brain tumors. In addition, many ERAS protocols for cranial neurosurgery cherry-pick parts of the ERAS protocol,

while leaving other critical aspects on the table due to wide variations in practice. Further study is needed with systematic implementation of ERAS protocols to specific subgroups of patients.

Although there is robust evidence demonstrating the effectiveness of ERAS protocols in other surgical specialties, including spinal surgery and general surgery, cranial neurosurgery has yet to adopt a standard approach to ERAS protocols in patients who are postcraniotomy for resection of brain tumor.[41] There is evidence that ERAS protocols implemented in patients after craniotomy help reduce LOS and improve patient satisfaction.[41-47] Overall, the evidence for ERAS in cranial neurosurgery is currently at a low level. More study is needed to determine if other postoperative parameters could be improved with ERAS.

Nursing support is critical to the success of ERAS protocols. Many of the components of an ERAS protocol are heavily nursing-driven and require nurses for implementation (eg, patient education, pain control, nausea control). Outstanding nursing care will only enhance patient care as ERAS protocols become more common in cranial neurosurgery.

Complementary Therapies

Complementary therapies are additional therapies used in conjunction with traditional medical approaches and can include acupuncture, massage, dietary supplements, hypnosis, and meditation, among others.

What is nursing's impact on education about common complementary therapies used by adults with brain tumors? Is there any evidence of their efficacy compared to no complementary therapy intervention?

Recommendation: At every visit, nurses and other healthcare professionals should review the use of complementary treatments and self-help practices to monitor the possible risks and benefits and interaction with standard treatment. Nurses should be aware of what complementary therapies their patients are using so they can appropriately educate them regarding the pros and cons (moderate recommendation, low level of evidence).

Rationale: Two studies reported on the use of complementary therapies in the brain tumor population. One study was a retrospective chart review of 845 subjects,[48] with 63% reporting the use of complementary treatment in the past year. The most common complementary treatments were vitamins (58%), massage/body work (10%), herbs (7%), spiritual healing (7%), and osteopathic/chiropractic manipulation (7%). Use of self-help practices were reported by 51%. The most common were prayer (45%), special diet (10%), meditation (9%), relaxation (8%), and yoga (7%). There were no associations between QOL and use of complementary therapies.

The second study reported complementary and alternative medicine use in France with 227 subjects.[49] Complementary therapies were reported in 66% of the subjects and included dietary changes (45%), vitamins (23%), food supplements (22%), phytotherapy (15%), and homeopathy (15%). The subjects self-reported a positive impact on their QOL as well as the efficacy of treatments. Studies that looked at efficacy of complementary treatments or interactions with other therapies were severely lacking. Given the high percentage of patients who report use of these treatments, further research is needed. No studies examining nursing's impact on education related to complementary therapies existed.

Exercise

Exercise is often recommended as a way to improve overall health and well-being. Nurses must have the knowledge to educate adult patients with brain tumors on the potential positive impact of consistent exercise on their health-related QOL.

Does a regular exercise program improve the health-related quality of life for patients with brain tumors compared to patients without a standard exercise regimen?

Recommendation: Nurses and other healthcare professionals caring for individuals with brain tumors should promote and encourage physical activity and exercise in the care of this population (good practice recommendation).

Rationale: The number of studies on this topic is limited, and the evidence is weak. One small study (N=20) revealed clinically significant improvements in overall cancer symptoms' severity, symptom interference, depressive symptoms, and mental QOL in subjects participating in a yoga program during radiotherapy.[50] Subsequently, this study team also pilot tested a dyadic yoga intervention for patients with brain tumors and their caregivers and found this to be a reasonable intervention for QOL and symptom management (N=20).[51] A qualitative study[37] looked at a tailored exercise program for individuals during chemoradiotherapy. Identified themes included benefitting from improved health, regaining a sense of control, interacting with people, and keeping active. Another study looked at compliance and safety of a home exercise program.[52] The small sample size (N=15) showed a trend toward increased quality-of-life scores, and the exercise program was safe and feasible. One study found no change in QOL, pain, and depression after participating in an outpatient rehabilitation program.[53] Although the level of evidence is insufficient, it suggests that it is appropriate to promote and encourage physical activity in adult patients with brain tumors.

Reducing Complications

Complications in patients with brain tumors can occur for a wide variety of reasons, such as from the risks associated with treatments, the natural history of the particular disease, and the nature of hospitalization and recovery.

Intracranial Hemorrhage and Anticoagulation

Is the patient with a brain tumor who requires anticoagulation at increased risk of intracranial hemorrhage, compared to the patient with a brain tumor who does not require anticoagulation therapy?

Recommendation: The risks and benefits of starting prophylactic or therapeutic anticoagulation (AC) must be weighed for individual patients with brain tumors. Factors such as history of coagulopathy, timing of surgery, hemostasis during surgery, and vascularity of the tumor all must be considered. In addition, the probability of VTE must be considered and can be assessed with risk scales such as the Caprini score (weak recommendation, low level of evidence).

Rationale: Certain types of brain tumors are more susceptible to intracranial hemorrhage (ICH) than others, with or without AC therapy. Brain tumors can disrupt the integrity of blood vessels, making patients more susceptible to ICH. Anticoagulation, age, history of prior ICH, coagulopathies, recent craniotomy and longer operative times, tumor location (vascular components or nearby eloquent structures), certain therapies (such as bevacizumab), and comorbidities can place patients with brain tumors at further risk of ICH.[54,55]

Making things more complicated, the use of anticoagulant medication is often warranted in patients with brain tumors due to elevated risk for VTE secondary to hypercoagulable states, limited physical mobility, surgical procedures, and treatments for both primary and metastatic brain tumors. While AC alone is not the only risk factor for ICH, the use of AC does heighten the risk of ICH in patients with brain tumors.[55]

The question of when to initiate VTE prophylaxis remains contentious among neurosurgeons. Given the lack of high-level evidence around recommendations for timing to initiate VTE prophylaxis after surgery, it is often decided on a case-by-case basis, taking into consideration factors such as the tumor type, vascular supply, risk factors for ICH and VTE, and intraoperative findings.[55,56] Most often, chemical VTE prophylaxis is initiated on postoperative day 1, though further research is needed around the risks and benefits of perioperative VTE prophylaxis to provide more concrete recommendations.[57] Despite a known higher risk of VTE in patients with GBM and cancer, there is currently insufficient evidence to support prophylactic AC outside the surgical or acute hospital setting.[58]

The presence of a brain tumor and risk of ICH is not a contraindication for therapeutic AC. Patients with brain tumors and known VTE or atrial fibrillation may require therapeutic doses of AC with direct oral anticoagulants (DOACs), low-molecular weight heparin (LMWH), or warfarin. Literature suggests that from an overall safety perspective, DOACs are the preferred choice of anticoagulant for patients with brain tumors.[54,59,60] There are currently no randomized trials comparing LMWH and DOACs as it relates to the incidence of ICH. The risks and benefits should be weighed when considering starting AC on patients with brain tumors with acute ICH and VTE. When deemed clinically stable, in efforts to prevent recurrent ICH, studies support reviewing tumor pathology and size of ICH before reinitiation of AC.[60]

While not part of the anticoagulant class of medications, bevacizumab is part of the treatment arsenal for recurrent malignant gliomas, other recurrent brain tumors, and, at times, for treatment of cerebral edema from treatment changes. Some data have indicated that bevacizumab can increase the risk of VTE and bleeding. Much research has been done around the risk of bevacizumab and the risk of hemorrhage. There is no conclusive evidence to suggest the risk of ICH outweighs the benefit of bevacizumab in recurrent brain tumors. Risk-to-benefit analysis should be undertaken for each individual patient, specifically including any previous history of ICH and tumor pathology for those being considered for treatment with bevacizumab.[61]

Patients with brain tumors are at an increased risk of developing an ICH due to a multitude of factors. Careful consideration of risks and benefits is necessary prior to initiation of AC. When therapeutic AC is indicated due to preexisting or acute onset of comorbidities such as VTE or atrial fibrillation, the risk-to-benefit ratio must be reviewed as well as alternative treatment options.[62] Patient and caretaker education and close monitoring by healthcare providers are critical to the safety of patients if AC is started.

Leptomeningeal Carcinomatosis

Leptomeningeal carcinomatosis (LMC), also known as leptomeningeal metastases or leptomeningeal disease, is cancer involving the pia mater and arachnoid mater. Studies have shown that solid tumors, including brain tumors and hematological cancers, can metastasize to involve the leptomeninges. It is an uncommon and late complication seen in 5% to 8% of cases of solid tumors. While treatments for LMC exist, the diagnosis is considered fatal, with a median survival of 2 to 4 months.

Clinical practice guidelines for management of leptomeningeal metastasis have been published.[63]

In the adult patient undergoing surgical resection for primary or metastatic brain tumors, what are the predictors of leptomeningeal carcinomatosis that may lead to worse outcomes?

Recommendation: In patients who are undergoing surgical resection of a brain tumor, screening for risk factors of LMC should be considered to guide discussions on potential complications, treatment options, possible outcomes, and patient preferences (weak recommendation, low level of evidence).

Rationale: A retrospective analysis involving 212 patients who underwent surgery for brain metastases found that patients treated with localized radiotherapy had an increased risk of new lesions (P<.001) and LMC (P=.04) compared to WBRT or intraoperative radiotherapy, although there was no significant difference in median survival.[64] In a retrospective analysis of patients diagnosed with GBM (N=321), both younger age and initial tumor size were related to more frequent incidence of LMC.[65] The median age of the LMC group was 46.5 years compared to 53.9 years in the group without LMC (P=.001). More patients in the LMC group had an initial tumor size larger than 30 mm compared to patients without LMC (P<.001). In a retrospective study (N=413) aimed at identifying risk factors that may predispose patients to LMC, it was found that prior surgical resection of brain metastases before SRS was associated with 6.5 times higher odds (95% CI 1.45-29.35, P=.01) of developing LMC after radiosurgery compared to those with no prior resections of brain metastases.[66] Another retrospective study looking at 129 patients with resected brain metastases receiving postoperative SRS and immunotherapy or postoperative SRS alone showed that postoperative fractionated SRS with immunotherapy significantly decreased the incidence of LMC and distant brain parenchymal failure (9% vs 18%, respectively).[67]

In a systematic review and meta-analysis of risk factors for LMC after surgical resection for brain metastases, 18 unique risk factors were identified that were significantly associated with LMC occurrence.[68] These included larger tumor size, infratentorial brain metastasis location, proximity of brain metastases to cerebrospinal fluid spaces, ventricle violation during surgery, subtotal or piecemeal resection, and postoperative SRS. Breast cancer as primary tumor location (HR=2.73, 95% CI 2.12-3.52) and multiple brain metastases (HR=1.37, 95% CI 1.18-1.58) were significantly associated with a higher risk of LMC occurrence. Machine learning was used to examine the risk factors of LMC after brain tumor resection using data from 1,054 patients.[68] The most important predictors of LMC occurrence and time to LMC were lymph node metastasis of the primary tumor at brain tumor diagnosis and a cerebellar brain tumor location.

Although the quality of the evidence is low due to study design and smaller sample sizes, the research reveals that predictors of the development of LMC in patients undergoing surgical resection of brain metastases include primary tumor type, location of brain metastases, size of brain metastases, type of treatment, and sequencing of treatments. Screening for patients at risk for LMC may guide discussions on surgical risks, complications, and treatment options.

Radiation Necrosis

Radiation-induced brain necrosis is a serious complication and occurs in approximately 25% of patients after radiation therapy. Symptoms of radiation necrosis vary depending upon the area of the brain involved but can include headache, drowsiness, memory loss, personality changes, and seizures. Once thought to be progressive and irreversible, it has been shown that some cases of radiation necrosis are repairable; therefore, early detection is paramount. Recommendations for the management of symptomatic brain radiation necrosis after SRS have been published.[69]

In adult patients undergoing brain irradiation for primary or metastatic brain tumors, what are the predictors of radionecrosis that nurses need to be aware of in order to appropriately educate patients and caregivers?

Recommendation: Patients may have a higher risk of radiation necrosis depending upon several factors including—but not limited to—the type of tumor (oligodendroglioma vs astrocytoma), higher dosage of radiation, larger mean target volume, single fraction treatment, diabetes, uncontrolled systemic disease, melanoma histology, increasing number of brain metastases, and an age of at least 59 years. These criteria can be used by nurses for screening patients at higher risk of radiation necrosis and guide routine assessment of symptoms as well as patient and caregiver reporting of worsening symptoms (weak recommendation, low level of evidence).

Rationale: A retrospective analysis of 99 patients with large brain metastases undergoing postoperative SRS found that uncontrolled systemic disease (P=.03), melanoma histology (P=.04), and increasing number of brain metastases (P<.001) were significant predictors of radiation necrosis and distant brain failure.[70] In a retrospective analysis with 319 patients diagnosed with oligodendroglioma or astrocytoma, risk factors of radiation necrosis were identified.[71] Patients with oligodendroglioma were at higher risk compared to patients with astrocytoma (P<.001), with the risk increasing with higher doses of radiation (>54 Gy).[71] In a systematic review and meta-analysis including 335 patients who received stereotactic

reirradiation for local failure of brain metastases following previous radiosurgery, a higher risk of radiation necrosis was found with a median patient age of at least 59 years old (P=.004) and lower use of WBRT (P=.004).[72] In another retrospective study involving 170 patients treated with SRS for brain metastases, it was found that 4% of patients developed symptomatic radiation necrosis with a median time of 8.3 months after SRS.[73] Risk factors of symptomatic radiation necrosis included a larger mean target volume (P<.0001) and thus larger radiation dose. Single fraction treatment (P=.0025) and diabetes (P=.019) were also significantly associated with symptomatic radiation necrosis.

Prior research on the predictors of radiation necrosis has primarily been retrospective. Therefore, to strengthen this evidence-base, prospective validation studies are needed to determine whether the proposed predictors can identify patients early in the development of necrosis. For all patients receiving radiation and especially those with risk factors, routine assessment and instructing family and caregivers to report symptoms of radiation necrosis can inform the need for diagnostic testing and follow-up.

Symptom Management

Patients with brain tumors experience a variety of symptoms. The most common symptoms include fatigue, headaches, neurocognitive deficits, depression, and anxiety.

Can the use of standardized symptom assessment tools by nurses improve symptom management in patients with brain tumors?

Recommendation: Research suggests that the use of standardized symptom assessment tools for patients with brain tumors will assist with earlier identification of symptoms. The use of standardized tools, including physical and psychological screening used routinely at clinic visits, can assist with earlier intervention and support for these symptoms. This will improve the overall QOL of patients with brain tumors and their caregivers (moderate recommendation, moderate quality of evidence).

Rationale: Five articles matched the aims of this PICO question.[74-78] The most common symptoms experienced by patients with a brain tumor diagnosis are fatigue, sleep disturbances, headaches, neurological and cognitive impairments, seizures, headaches, depression, and anxiety. Patients with gliomas often report that supportive care needs including physical, psychological, daily living (fatigue, pain), sexuality, and health system needs are not being met. Failure to address symptoms can lead to distress and worse outcomes for patients with brain tumors.[74,75] Fatigue has been noted to be multifactorial and has negative effects on other symptoms that may develop, while lack of recognition of depression has been shown to lead to increased complications and shorter survival.[76-78]

It is recommended that specific attention be given to all symptoms patients with brain tumors experience. Once these are identified, healthcare providers can offer coping strategies and support. Currently there is no specific standardized assessment tool that is widely recommended. This is an area where nursing research is needed. Literature suggests that the use of practice guidelines, symptom assessment tools, and educational resources for symptoms and for their disease can better support the QOL of patients and their caretakers. In addition, these resources can assist patients in overcoming their negative beliefs and distress around their diagnosis and understanding the rationale for interventions.[76,79]

Impact of Tumor Type

Does tumor type impact the symptoms of patients with brain tumors and require nursing assessment and care on outcome?

Recommendation: There is low quality of evidence highlighting the importance of tumor type and associated prognosis when prioritizing symptom management. There is low to moderate quality of evidence to support the identification of symptoms that patients with brain tumors may experience throughout the course of their disease and treatment. Nurses must focus attention on the symptoms causing the most concern for patients at a given time (moderate recommendation, moderate quality of evidence).

Rationale: Research shows that the most common symptoms associated with brain tumors are similar whether the tumors are primary or metastatic in nature.[80] Symptoms may fluctuate throughout the course of each individual's life, as there is variation in the disease course and treatment for each patient. In addition, the course of the disease varies in benign vs malignant tumor types.

Eleven articles were reviewed on patients with primary and metastatic brain tumors.[27,30,33,74,77,80-85] Symptoms associated with brain tumors present a challenge to the patient's QOL. There is consistency among the type of symptoms experienced by patients with both primary and metastatic brain tumors. Symptoms correlate more with the size, location, and infiltrative properties of the tumor itself, though may also be secondary to the concomitant medications, treatments, and comorbidities. Both the disease itself and its treatment affect symptom burden. Given this, the difference in symptoms among different brain tumor types can vary in severity and timing of occurrence.[80] For patients with LGG, the most common symptom presentation is seizures.[81] Patients

with metastatic brain tumors have been shown to have a higher degree of negative emotions and fatigue that may be in part from the disease course thus far.[80] Higher grade or recurrent brain tumors can cause a larger range of symptoms and neurocognitive effects due to the rapid tempo of development or the amount of brain affected.[82] It is necessary for nurses to be aware of the most common symptoms or side effects that often cluster during various stages of the course of brain tumors.

Symptoms can wax and wane depending on where a patient is in the course of their disease. Lack of standardized assessment tools and time limitations of healthcare providers have led to limited thorough symptom assessment.[77] Healthcare providers must not discount that most patients with brain tumors have a baseline of underlying symptoms that may fluctuate in severity or priority over time.[74,83] Use of assessment tools can assist in addressing patients' concerns and target the symptoms of that particular tumor, at that particular time, in the course of their disease.[80]

The goals of symptom management will vary depending on disease progression, which dictates phase of care. There is a difference in symptom treatment options for a patient with a recently resected low-grade meningioma who is returning to full-time work compared to a patient with recurrent HGG who has elected to transition to hospice care. During active treatment with chemotherapy, radiation, or progression of disease, patients may experience worsening neurological function and more apparent systemic symptoms; however, longer life expectancy may lead to an increase in health-related QOL and neurocognitive function.[27,84] Patients with HGG with shorter life expectancies may consider palliative radiation therapy to alleviate some of the current symptoms affecting their QOL. Research suggests certain radiation doses may improve some of these symptoms while also leading to delayed cognitive decline in adult patients with brain tumors.[30,33,85] This must be weighed for patients with longer recurrence-free periods, longer life expectancies, and often lower grade tumors and should have a strong focus on maintaining neurocognitive function and long-term QOL.[33,86]

Several factors influence symptom development in adult patients with brain tumors. Size, location, tempo of growth, and other neurologic comorbidities affect the extent and severity of symptoms. In addition, the treatments used for control or cure may lead to adverse effects or complications that cause symptoms. It is essential for nurses to understand how the above factors influence symptoms and be well versed in adverse effects and potential complications resulting from surgery or other treatments.

Advance Care Planning and Palliative Care

Advance care planning offers significant benefits to patients with brain tumors and their families. It creates an integrative approach from diagnosis to death and empowers patients with express end-of-life (EOL) wishes.[87,88] Advance care planning promotes patient-centered care and facilitates a dignified, compassionate approach to EOL decision making. Research shows that when addressed early in the disease course, ACP can more positively impact the trajectory of coping and the well-being of patients and caregivers as the disease advances and more complex decisions are presented.[79,89]

In adult patients with brain tumors, how does advance care planning impact end-of-life decision making compared to lack of advance care planning in the setting of the patient's reduced decision-making capacity?

Recommendation: It is strongly recommended that nurses have early and consistent discussions related to ACP in all patient populations, including adult patients with brain tumors. Regular assessments of the psychological well-being of patients with brain tumors and their caretakers are essential to their QOL. This includes discussion about prognosis, goals of care, future wishes, and EOL care (strong recommendation, moderate level of evidence).

Rationale: Nine articles were reviewed as pertaining to this PICO question regarding ACP in patients with cancer and brain tumors. Advance care planning is a process of discussion, reflection, and communication of a person's EOL or future healthcare preferences or wishes. Given the recurrent and progressive nature of brain tumors, the short length of survival of higher-grade brain tumors, and the cognitive and physical limitations these patients can experience, ACP has been shown to be beneficial in this population.[90] Psychotherapy in patients with cancer shows that ACP can assist in confronting death while still finding meaning in the life that remains ahead.[91] Early introduction of ACP in patients with brain tumors allows for early discussions of options and considerations of clinical trials and wishes around treatment interventions. Advance care planning assists with effective decision-making when faced with sudden or difficult choices between high-risk clinical trials vs more comfort-focused care. Patients with brain tumors often experience cognitive impairments as the disease advances, impacting their QOL, disability, and caretakers. A patient's goals of care may change as symptoms and the disease progress.[79]

Nurses for patients with brain tumors play a crucial role in psychosocial care and support. Quality of life for

patients with brain tumors is impacted by the psychological domains. Fear and worry are some of the highest unmet needs in patients with brain tumors.[25] Patients and families cope better when they have a general understanding of the prognosis and courses of treatment beyond the first line of treatment. It is recommended that routine assessment of the psychological needs of patients and caretakers be reviewed, including assessment of demographics and global health assessment scales. Combining these assessments with ACP can further support patients' needs in times of high distress.[92]

The burden on caretakers for patients with brain tumors evolves over time. Caretakers are affected by the neurological, psychological, and cognitive challenges in patients with brain tumors. Furthermore, there may be changes to the dynamics of the previous relationship between the now-caretaker and the patient with a brain tumor that can lead the caretaker to social isolation, financial restrictions, and full-time caretaking, thereby affecting the caretaker's ability to cope. The quality of care and support that patients receive does directly correlate to the coping and well-being of the caregivers. This support around ACP can alleviate some of the burden of care and decision making from the caretaker and healthcare systems.[87,92,93] Advance care planning further supports caretakers and alleviates some of the distress of making decisions on behalf of the patient.[93]

Prior studies have indicated there is a benefit of ACP in patients with cancer and brain tumors.[87,92,93] Further prospective studies are needed to define what specific quality measures and guidelines are essential to ACP for the brain tumor population. Clinician-led discussion on ACP may be tailored based on tumor type given the wide variations in prognosis and survival.[94] Advance care planning for patients with brain tumors is beneficial to both the patient and caretakers. It can alleviate stressors associated with EOL decisions as well as the QOL patients with brain tumors may experience at the end of one's life.

In adults with brain tumors, how do patient care teams that refer to palliative care, compared to patient teams that do not refer to palliative care, affect quality of life and control of symptoms within the first year of survivorship?

Recommendation: AANN recommends referral to palliative care for adult patients with brain tumors. This recommendation is based on the known benefits of palliative care with its exceptional ability to manage chronic symptoms and the resulting impact on QOL (good practice recommendation).

Rationale: There is insufficient research to answer this PICO question. In the review of 11 articles, data are limited that specifically compare those who had palliative care team involvement and those who did not. However, general conclusions can be drawn from related principles and studies that indicate palliative care involvement can lead to better symptom management for patients with cancer.

Palliative care teams focus on managing complex symptoms in addition to pain, depression, anxiety, distress, and overall QOL. Palliative care providers assist with discussions on prognosis, goals of treatment, suffering, and conflict resolution. Unfortunately, palliative care is often not introduced to patients and families early on in the course of disease.[95-97]

The introduction of palliative care services at the time of diagnosis of advanced cancer has repeatedly been shown to provide more meaningful experiences for patients and caretakers through symptom management, QOL improvements, and treatment planning. Early involvement of palliative care teams can assist with navigating tough decisions, exploring coping strategies, and adjusting to changes in functional status throughout the disease course. Preservation of QOL has been shown to be a priority for all patients with brain tumors. Palliative care teams can help guide symptom control and share the role of supporting unmet needs that exist in this population.

There is evidence to suggest that cancer incidence, progression, and mortality are associated with depression.[98] Resilience and coping strategies can be vital to prevent treatment interference and emotional struggles while dealing with the physical symptoms and manifestations of the disease.[99] Some research suggests that patients with more optimism or resilience may fare better in adjusting to the mental distress from their cancer or progressive disease, which can improve their overall survival.[99] Palliative care teams foster a more comprehensive approach to care to better meet the needs of patients.

The involvement of palliative care for patients with brain tumors is beneficial throughout the course of their disease process. Palliative care should be introduced to patients early in the course of treatment for brain tumors to assist with managing symptoms, setting realistic expectations, and ensuring patient wishes are being met throughout the course of their disease and, most especially, at the end of life. Nursing's role is to advocate for palliative care involvement in patients with brain tumors experiencing chronic symptoms related to their diagnosis or treatment.

Summary

This evidence-based guideline of a systematic literature review is limited to the scope of the predetermined PICO questions addressed. It is intended as a comprehensive review and does not fully address the continuity of care practices for all adult patients with brain tumors. The recommendations put forth in this guideline lay a foundation for clinical practice to improve patient outcomes following diagnosis of a brain tumor. Critical to neuroscience nursing science, this guideline identifies knowledge gaps, reinforcing the need for research scholars to study nursing care interventions to improve outcomes and practice scholars to implement the evidence in clinical care across settings.

References

1. Censullo JL, Tran DS, Starkweather A. Methods for developing neuroscience nursing clinical practice guidelines. *J Neurosci Nurs*. 2024;56(6):236-238. doi:10.1097/JN.0000000000000795.
2. WHO Classification of Tumours Editorial Board (ed). *Central Nervous System Tumours: WHO Classification of Tumours*. 5th ed. Vol 6. Lyon, France: International Agency for Research on Cancer; 2021.
3. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. *Neuro Oncol*. 2021:23(8):1231-1251. doi:10.1093/neuonc/noab106.
4. Berger TR, Wen PY, Lang-Orsini M, Chukwueke UN. World Health Organization 2021 classification of central nervous system tumors and implications for therapy for adult-type gliomas. *JAMA Oncol*. 2022;8(10):1493-1501. doi:10.1001/jamaoncol.2022.2844.
5. Dai Y, Ning X, Han G, Li W. Assessment of the association between isocitrate dehydrogenase 1 mutation and mortality risk of glioblastoma patients. *Mol Neurobiol.* 2016;53(3):1501-1508. doi:10.1007/s12035-015-9104-7.
6. Chen JR, Yao Y, Xu H-Z, Qin Z-Y et al. Isocitrate dehydrogenase (IDH)1/2 mutations as prognostic markers in patients with glioblastomas. *Medicine (Baltimore)*. 2016;95(9):e2583. doi:10.1097/MD.0000000000002583.
7. Wang Y, Guo X. Meta-analysis of association between mobile phone use and glioma risk. *J Cancer Res Ther*. 2016;12(8):C298-C300. doi:10.4103/0973-1482.200759.
8. Wang P, Hou C, Li Y, Zhou D. Wireless phone use and risk of adult glioma: evidence from a meta-analysis. *World Neurosurg*. 2018;115:e629-e636. doi:10.1016/j.wneu.2018.04.122.
9. Yang M, Guo W, Yang C, et al. Mobile phone use and glioma risk: a systematic review and meta-analysis. *PLoS One*. 2017;12(5):e0175136. doi:10.1371/journal.pone.0175136.
10. Coureau G, Bouvier G, Lebailly P, et al. Mobile phone use and brain tumours in the CERENAT case-control study. *Occup Environ Med*. 2014;71(7):514-522. doi:10.1136/oemed-2013-101754.
11. Chapman S, Azizi L, Luo Q, Sitas F. Has the incidence of brain cancer risen in Australia since the introduction of mobile phones 29 years ago? *Cancer Epidemiol*. 2016;44:109. doi:10.1016/j.canep.2016.04.010.
12. Jørgensen JT, Johansen MS, Ravnskjær L, et al. Long-term exposure to ambient air pollution and incidence of brain tumours: the Danish Nurse Cohort. *Neurotoxicology*. 2016;55:122-130. doi:10.1016/j.neuro.2016.06.003.
13. Pouchieu C, Raherison C, Piel C, et al. Allergic conditions and risk of glioma and meningioma in the CERENAT case-control study. *J Neurooncol*. 2018;138(2):271-281. doi:10.1007/s11060-018-2816-6.
14. Meng Y, Tang C, Yu J, Meng S, Zhang W. Exposure to lead increases the risk of meningioma and brain cancer: a meta-analysis. *J Trace Elem Med Biol*. 2020;60:126474. doi:10.1016/j.jtemb.2020.126474.
15. Quach P, El Sherif R, Gomes J, Krewski D. A systematic review of the risk factors associated with the onset and progression of primary brain tumours. *Neurotoxicology*. 2016;61:214-232. doi:10.1016/j.neuro.2016.05.009.
16. Cote DJ, Downer MK, Smith TR, Smith-Warner SA, Egan KM, Stampfer MJ. Height, waist circumference, body mass index, and body somatotype across the life course and risk of glioma. *Cancer Causes Control*. 2018;29(8):707-719. doi:10.1007/s10552-018-1052-x.
17. Zhang D, Chen J, Wang J, et al. Body mass index and risk of brain tumors: a systematic review and dose–response meta-analysis. *Eur J Clin Nutr*. 2016;70(7):757-765. doi:10.1038/ejcn.2016.4.
18. Barami K, Lyon L, Conell C. Type 2 diabetes mellitus and glioblastoma multiforme—assessing risk and survival: results of a large retrospective study and systematic review of the literature. *World Neurosurg*. 2017;106:300-307. doi:10.1016/j.wneu.2017.06.164.
19. Kuan AS, Green J, Kitahara CM, et al. Diet and risk of glioma: combined analysis of 3 large prospective studies in the UK and USA. *Neuro Oncol*. 2019;21(7):944-952. doi:10.1093/neuonc/noz013.
20. Maia Jr ACM, Malheiros SM, da Rocha AJ, et al. MR cerebral blood volume maps correlated with vascular endothelial growth factor expression and tumor grade in nonenhancing gliomas. *AJNR Am J Neuroradiol.* 2005;26(4):777-783.
21. Patel P, Baradaran H, Delgado D, et al. MR perfusion-weighted imaging in the evaluation of high-grade gliomas after treatment: a systematic review and meta-analysis. *Neuro Oncol.* 2017;19(1):118-127. doi:10.1093/neuonc/now148.
22. Hendrix P, Hans E, Griessenauer CJ, Simgen A, Oertel J, Karbach J. Neurocognitive status in patients with newly diagnosed brain tumors in good neurological condition: the impact of tumor type, volume, and location. *Clin Neurol Neurosurg.* 2017;156:55-62. doi:10.1016/j.clineuro.2017.03.009.
23. Allen D, Carlson BW, Carlson JR, Raynor RH, Neelon VJ. Assessing discrepancies in neurocognitive and patient-reported measures of brain tumor survivors. *Oncol Nurs Forum.* 2020;47(1):E1-E12. doi:10.1188/20.ONF.E1-E12.

24. Shaaban SG, LeCompte MC, Kleinberg LR, Redmond KJ, Page BR. Recognition and management of the long-term effects of cranial radiation. *Curr Treat Options Oncol*. 2023;24(7):880-891. doi:10.1007/s11864-023-01078-z.

25. Cordes M-C, Scherwath A, Ahmad T, et al. Distress, anxiety, and depression in patients with brain metastases before and after radiotherapy. *BMC Cancer*. 2014;14:731. doi:10.1186/1471-2407-14-731.

26. Wong E, Zhang L, Rowbottom L, et al. Symptoms and quality of life in patients with brain metastases receiving whole-brain radiation therapy. *Support Care Cancer*. 2016;24(11):4747-4759. doi:10.1007/s00520-016-3326-8.

27. Teke F, Bucaktepe P, Kıbrıslı E, Demir M, Ibiloglu A, Inal A. Quality of life, psychological burden, and sleep quality in patients with brain metastasis undergoing whole brain radiation therapy. *Clin J Oncol Nurs*. 2016;20(5):AE-2. doi:10.1188/16.cjon.ae-02.

28. Miller JA, Kotecha R, Barnett GH, et al. Quality of life following stereotactic radiosurgery for single and multiple brain metastases. *Neurosurgery*. 2017:81(1):147-155. doi:10.1093/neuros/nyw166.

29. Nakazaki K, Nishigaki M. Evaluation of new lesions and symptoms after gamma knife radiosurgery for brain metastases: a retrospective cohort study. *Acta Neurochir (Wien)*. 2018:160(7):1461-1471. doi:10.1007/s00701-018-3524-x.

30. Cramer CK, McKee, N, Case LD, et al. Mild cognitive impairment in long-term brain tumor survivors following brain irradiation. *J Neurooncol*. 2019;141(1):235-244. doi:10.1007/s11060-018-03032-8.

31. Kalra B, Kannan S, Gupta T. Optimal adjuvant therapy in elderly glioblastoma: results from a systematic review and network meta-analysis. *J Neurooncol*. 2020;146(2):311-320. doi:10.1007/s11060-019-03375-w.

32. Wang Q, Xiao F, Qi F, Song X, Yu Y. Risk factors for cognitive impairment in high-grade glioma patients treated with postoperative radiochemotherapy. *Cancer Res Treat*. 2019;52(2):586-593. doi:10.4143/crt.2019.242.

33. Dutz A, Agolli L, Butof R, et al. Neurocognitive function and quality of life after proton beam therapy for brain tumour patients. *Radiother Oncol*. 2020;143:108-116. doi:10.1016/j.radonc.2019.12.024.

34. Ownsworth T, Chan RJ, Jones S, Roberston J, Pinkham MB. Use of telehealth platforms for delivering supportive care to adults with primary brain tumors and their family caregivers: a systematic review. *Psychooncology*. 2021;30(1):16-26. doi:10.1002/pon.5549.

35. Brown PD, Pugh S, Laack NN, et al. Memantine for the prevention of cognitive dysfunction in patients receiving whole-brain radiotherapy: a randomized, double-blind placebo-controlled trial. *Neuro Oncol*. 2013;15(10):1429-1437. doi:10.1093/neuonc/not114.

36. Gondi V, Deshmukh S, Brown PD, et al. Sustained preservation of cognition and prevention of patient-reported symptoms with hippocampal avoidance during whole-brain radiation therapy for brain metastases: final results of NRG Oncology CC001. *Int J Radiat Oncol Biol Phys*. 2023;117(3):571-580. doi:10.1016/j.ijrobp.2023.04.030.

37. Halkett GKB, Cormie P, McGough S, et al. Patients and carers' perspectives of participating in a pilot tailored exercise program during chemoradiotherapy for high grade glioma: a qualitative study. *Eur J Cancer Care (Engl)*. 2021;30(5):e13453. doi:10.1111/ecc.13453.

38. Nowak AK, Newton RU, Cruickshank T, et al. A feasibility, safety, and efficacy evaluation of supervised aerobic and resistance exercise for patients with glioblastoma undertaking adjuvant chemoradiotherapy. *Neurooncol Pract*. 2023;10(3):261-270. doi:10.1093/nop/npad006.

39. Hagan K, Bhavsar S, Raza S, et al. Enhanced recovery after surgery for oncological craniotomies. *J Clin Neurosci*. 2016;24:10-16. doi:10.1016/j.jocn.2015.08.013.

40. Greisman J, Olmsted Z, Crorkin PJ, et al. Enhanced recovery after surgery (ERAS) for cranial tumor resection: a review. *World Neurosurg*. 2022;163:104-122. doi:10.1016/j.wneu.2022.03.118.

41. Peters EJ, Robinson M, Serletis D. Systematic review of enhanced recovery after surgery in patients undergoing cranial surgery. *World Neurosurg*. 2022;158;279-289. doi:10.1016/j.wneu.2021.10.176.

42. Stumpo V, Staartjes VE, Quddusi A, et al. Enhanced recovery after surgery strategies for elective craniotomy: a systematic review. *J Neurosurg*. 2021;135(6):1-25. doi:10.3171/2020.10.JNS203160.

43. Wang L, Cai H, Wang Y, et al. Enhanced recovery after elective craniotomy: a randomized controlled trial. *J Clin Anesth*. 2022;76:110575. doi:10.1016/j.jclinane.2021.110575.

44. Liu B, Liu S, Wang Y, et al. Neurosurgical enhanced recovery after surgery (ERAS) programme for elective craniotomies: are patients satisfied with their experiences? A quantitative and qualitative analysis. *BMJ Open*. 2019;9(11):e028706. doi:10.1136/bmjopen-2018-028706.

45. Liu B, Liu S, Zheng T, et al. Neurosurgical enhanced recovery after surgery for geriatric patients undergoing elective craniotomy: a review. *Medicine (Baltimore)*. 2022;101(33):e30043. doi:10.197/MD.0000000000030043.

46. Hughes M, Culpin E, Darley R, et al. Enhanced recovery and accelerated discharge after endoscopic transsphenoidal pituitary surgery: safety, patient feedback, and cost implications. *Acta Neurochir (Wien)*. 2020;162(6):1281-1286. doi:10.1007/s00701-020-04282-0.

47. Elayat A, Jena SS, Nayak S, Sahu RN, Tripathy S. Enhanced recovery after surgery: ERAS in elective craniotomies—a non-randomized controlled trial. *BMC Neurol*. 2021;21(1):127. doi:10.1186/s12883-021-02150-7.

48. Randazzo DM, McSherry F, Herndon JE, et al. Complementary and integrative health interventions and their association with health-related quality of life in the primary brain tumor population. *Complement Ther Clin Pract*. 2019;36:43-48. doi:10.1016/j.ctcp.2019.05.002.

49. Le Rhun E, Devos P, Bourg V, et al. Complementary and alternative medicine use in glioma patients in France. *J Neurooncol*. 2019;145(3):487-499. doi:10.1007/s11060-019-03315-8.

50. Milbury K, Mallaiah S, Mahajan A, et al. Yoga program for high-grade glioma patients undergoing radiotherapy and their family caregivers. *Integr Cancer Ther*. 2017;17(2):332-336. doi:10.1177/1534735417689882.

51. Milbury K, Li J, Weathers S-P, et al. Pilot randomized, controlled trial of a dyadic yoga program for glioma patients undergoing radiotherapy and their family caregivers. *Neurooncology Pract*. 2018;6(4):311-320. doi:10.1093/nop/npy052.

52. Baima J, Omer ZB, Varlotto J, Yunus S. Compliance and safety of a novel home exercise program for patients with high-grade brain tumors, a prospective observational study. *Support Care Cancer*. 2017;25(9):2809-2814. doi:10.1007/s00520-017-3695-7.

53. McCarty S, Eickmeyer SM, Kocherginsky M, et al. Health-related quality of life and cancer-related symptoms during interdisciplinary outpatient rehabilitation for malignant brain tumor. *Am J Phys Med Rehabil*. 2017;96(12):852-860. doi:10.1097/PHM.0000000000000756.

54. Giustozzi M, Proetti G, Becattini C, Roila F, Agnelli G, Mandalà M. ICH in primary or metastatic brain cancer patients with or without anticoagulant treatment: a systematic review and meta-analysis. *Blood Adv*. 2022;6(16):4873-4883. doi:10.1182/bloodadvances.2022008086.

55. Rinaldo L, Brown DA, Bhargav AG, et al. Venous thromboembolic events in patients undergoing craniotomy for tumor resection: incidence, predictors, and review of literature. *J Neurosurg*. 2019;132(1):10-21. doi:10.3171/2018.7.jns181175.

56. Cote DJ, Dubois HM, Karhade AV, et al. Venous thromboembolism in patients undergoing craniotomy for brain tumors: a U.S. nationwide analysis. *Semin Thromb Hemost*. 2016;42(8):870-876. doi:10.1055/s-0036-1592306.

57. Salmaggi A, Simonetti G, Trevisan E, et al. Perioperative thromboprophylaxis in patients with craniotomy for brain tumours: a systematic review. *J Neurooncol*. 2013;113(2):293-303. doi:10.1007/s11060-013-1115-5.

58. Yust-Katz S, Mandel JJ, Wu J, et al. Venous thromboembolism (VTE) and glioblastoma. *J Neurooncol*. 2015;124(1):87-94. doi:10.1007/s11060-015-1805-2.

59. Diaz M, Schiff D. Vascular complications in patients with brain tumors. *Curr Opin Oncol*. 2022;34(6):698-704. doi:10.1097/cco.0000000000000875.

60. Carney BJ, Uhlmann EJ, Puligandla M, et al. Anticoagulation after intracranial hemorrhage in brain tumors: risk of recurrent hemorrhage and venous thromboembolism. *Res Pract Thromb Haemost*. 2020;4(5):860-865. doi:10.1002/rth2.12377.

61. Yang L, Chen C-J, Guo X, et al. Bevacizumab and risk of intracranial hemorrhage in patients with brain metastases: a meta-analysis. *J Neurooncol*. 2018;137(1):49-56. doi:10.1007/s11060-017-2693-4.

62. Yang J, He Z, Li M, Hong T, Ouyang T. Risk of intracranial hemorrhage with direct oral anticoagulation versus low molecular weight heparin in the treatment of brain tumor–associated venous thromboembolism: a meta-analysis. *J Stroke Cerebrovasc Dis*. 2023;32(8):107243. doi:10.1016/j.jstrokecerebrovasdis.2023.107243.

63. Le Rhun E, Weller M, van den Bent M, et al. Leptomeningeal metastasis from solid tumours: EANO-ESMO Clinical Practice Guideline for diagnosis, treatment, and follow-up. *ESMO Open*. 2023;8(5):101624. doi:10.1016/j.esmoop.2023.101624.

64. Hsieh J, Elson P, Otvos B, et al. Tumor progression in patients receiving adjuvant whole-brain radiotherapy vs localized radiotherapy after surgical resection of brain metastases. *Neurosurgery*. 2015;76(4):411-420. doi:10.1227/NEU.0000000000000626.

65. Noh J-H, Lee MH, Kim WS, et al. Optimal treatment of leptomeningeal spread in glioblastoma: analysis of risk factors and outcome. *Acta Neurochir (Wien)*. 2015;157:569-576. doi:10.1007/s00701-015-2344-5.

66. Ma R, Levy M, Gui B, et al. Risk of leptomeningeal carcinomatosis in patients with brain metastases treated with stereotactic radiosurgery. *J Neurooncol*. 2018;136(2):395-401. doi:10.1007/s11060-017-2666-7.

67. Minniti G, Lanzetta G, Capone L, et al. Leptomeningeal disease and brain control after postoperative stereotactic radiosurgery with or without immunotherapy for resected brain metastases. *J Immunother Cancer*. 2021:9(12):e003730. doi:10.1136/jitc-2021-003730.

68. Tewarie IA, Jessurun CAC, Hulsbergen AFC, Smith TR. Mekary RA, Broekman MLD. Leptomeningeal disease in neurosurgical brain metastases patients: a systematic review and meta-analysis. *Neurooncol Adv*. 2021;3(1):vdab162. doi:10.1093/noajnl/vdab162.

69. Vellayappan B, Lim-Fat MJ, Kotecha R, et al. A systematic review informing the management of symptomatic brain radiation necrosis after stereotactic radiosurgery and International Stereotactic Radiosurgery Society recommendations. *Int J Radiat Oncol Biol Phys*. 2024:118(1):14-28. doi:10.1016/j.ijrobp.2023.07.015.

70. Ling DC, Vargo JA, Wegner RE, et al. Postoperative stereotactic radiosurgery to the resection cavity for large brain metastases: clinical outcomes, predictors of intracranial failure, and implications for optimal patient selection. *Neurosurgery*. 2015;76(2);150-157. doi:10.1227/NEU.0000000000000584.

71. Ahmad H, Martin D, Patel SH, et al. Oligodendroglioma confers higher risk of radiation necrosis. *J Neurooncol*. 2019;145(2):309-319. doi:10.1007/s11060-019-03297-7.

72. Loi M, Caini S, Scoccianti S, et al. Stereotactic reirradiation for local failure of brain metastases following previous radiosurgery: systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2020:153:103034. doi:10.1016/j.critrevonc.2020.103043.

73. Sayan M, Sahin B, Mustafayev TZ, et al. Risk of symptomatic radiation necrosis in patients treated with stereotactic radiosurgery for brain metastases. *Neurocirugia (Engl Ed)*. 2021;32(6):261-267. doi:10.1016/j.neucir.2020.08.009.

74. Renovanz M, Hechtner M, Janko M, et al. Factors associated with supportive care needs in glioma patients in the neuro-oncological outpatient setting. *J Neurooncol*. 2017;133(3):653-662. doi:10.1007/s11060-017-2484-y.

75. Giesinger JM, Kuijpers W, Young T, et al. Thresholds for clinical importance for four key domains of the EORTC QLQ-C30: physical functioning, emotional functioning, fatigue, and pain. *Health Qual Life Outcomes*. 2016;14:87. doi:10.1186/s12955-016-0489-4.

76. Huang Y, Jiang Z-J, Deng J, Qi Y-J. Sleep quality of patients with postoperative glioma at home. *World J Clin Cases*. 2020;8(20):4735-4742. doi:10.12998/wjcc.v8.i20.4735.

77. Jeon MS, Dhillon HM, Koh E-S, Nowak AK, Hovey E, Agar MR. Sleep disturbance in people with brain tumours and caregivers: a survey of healthcare professionals' views and current practice. *Support Care Cancer*. 2021;29(3):1497-1508. doi:10.1007/s00520-020-05635-2.

78. Pranckeviciene A, Tamasauskas S, Deltuva VP, Bunevicius R, Tamasauskas A, Bunevicius A. Suicidal ideation in patients undergoing brain tumor surgery: prevalence and risk factors. *Supportive Care Cancer*. 2016;24(7):2963-2970. doi:10.1007/s00520-016-3117-2.

79. Kluger BM, Ney DE, Bagley SJ, et al. Top ten tips palliative care clinicians should know when caring for patients with brain cancer. *J Palliative Med*. 2020;23(3):415-421. doi:10.1089/jpm.2019.0507.

80. Acquaye AA, Payén SS, Vera E, et al. Identifying symptom recurrences in primary brain tumor patients using the MDASI-BT and qualitative interviews. *J Patient Rep Outcomes*. 2019;3(1):58. doi:10.1186/s41687-019-0143-0.

81. Yu B, Ji N, Ma Y, Yang B, Kang P, Luo F. Clinical characteristics and risk factors for headache associated with non-functioning pituitary adenomas. *Cephalalgia*. 2016;37(4):348-355. doi:10.1177/0333102416648347.

82. Maitre P, Gupta T, Maitre M, et al. Prospective longitudinal assessment of quality of life and activities of daily living as patient-reported outcome measures in recurrent/progressive glioma treated with high-dose salvage re-irradiation. *Clin Oncol (R Coll Radiol)*. 2021;33(3):e155-e165. doi:10.1016/j.clon.2020.08.011.

83. Kim S-H, Byun Y. Trajectories of symptom clusters, performance status, and quality of life during concurrent chemoradiotherapy in patients with high-grade brain cancers. *Cancer Nurs*. 2018;41(1):E38-E47. doi:10.1097/ncc.0000000000000435.

84. Shin JY, Kizilbash SH, Robinson S, Uhm JH, Aminah Jatoi. Incidence, characteristics, and implications of seizures in patients with glioblastoma. *Am J Hosp Palliat Care*. 2017;34(7):650-653. doi:10.1177/1049909116647405.

85. Osoba D, Aaronson NK, Muller M, et al. Effect of neurological dysfunction on health-related quality of life in patients with high-grade glioma. *J Neurooncol*. 1997;34(3). doi:10.1023/a:1005790632126.

86. Dutz A, Agolli L, Bütof R, et al. Neurocognitive function and quality of life after proton beam therapy for brain tumour patients. *Radiother Oncol*. 2020;143:108-116. doi:10.1016/j.radonc.2019.12.024.

87. Alturki A, Gagnon B, Petrecca K, Scott SC, Nadeau L, Mayo N. Patterns of care at end of life for people with primary intracranial tumors: lessons learned. *J Neurooncol*. 2014;117(1):103-115. doi:10.1007/s11060-014-1360-2.

88. Diamond EL, Russell D, Kryza-Lacombe M, et al. Rates and risks for late referral to hospice in patients with primary malignant brain tumors. *Neuro Oncol.* 2016;18(1):78-86. doi:10.1093/neuonc/nov156.

89. Philip J, Collins A, Panozzo S, Staker J, Murphy M. Mapping the nature of distress raised by patients with high-grade glioma and their family caregivers: a descriptive longitudinal study. *Neurooncol Pract*. 2020;7(1):103-110. doi:10.1093/nop/npz032.

90. Song K, Amatya B, Voutier C, Khan F. Advance care planning in patients with primary malignant brain tumors: a systematic review. *Front Oncol*. 2016;6:223 doi:10.3389/fonc.2016.00223.

91. Loughan AR, Aslanzadeh FJ, Brechbiel J, et al. Death-related distress in adult primary brain tumor patients. *Neurooncol Pract*. 2020;7(5):498-506. doi:10.1093/nop/npaa015.

92. Renovanz M, Maurer D, Lahr H, et al. Supportive care needs in glioma patients and their caregivers in clinical practice: results of a multicenter cross-sectional study. *Front Neurol*. 2018;9:763. doi:10.3389/fneur.2018.00763.

93. Halkett GKB, Lobb EA, Shaw T, et al. Do carer's levels of unmet needs change over time when caring for patients diagnosed with high-grade glioma and how are these needs correlated with distress? *Support Care Cancer*. 2018;26(1):275-286. doi:10.1007/s00520-017-3846-x.

94. Hemminger LE, Pittman CA, Korones DN, et al. Palliative and end-of-life care in glioblastoma: defining and measuring opportunities to improve care. *Neurooncology Pract*. 2016;4(3):182-188. doi:10.1093/nop/npw022.

95. Quill TE, Abernethy AP. Generalist plus specialist palliative care—creating a more sustainable model. *N Engl J Med*. 2013;368(13):1173-1175. doi:10.1056/nejmp1215620.

96. Parikh RB, Kirch RA, Smith TJ, Temel JS. Early specialty palliative care—translating data in oncology into practice. *N Engl J Med*. 2013;369(24):2347-2351. doi:10.1056/NEJMsb1305469.

97. Greer JA, Jackson VA, Meier DE, Temel JS. Early integration of palliative care services with standard oncology care for patients with advanced cancer. *CA Cancer J Clin*. 2013;63(5):349-363. doi:10.3322/caac.21192.

98. Shi C, Lamba N, Zheng LJ, et al. Depression and survival of glioma patients: a systematic review and meta-analysis. *Clin Neurol Neurosurg* . 2018;172:8-19. doi:10.1016/j.clineuro.2018.06.016.

99. Liang S-Y, Liu H-C, Lu Y-Y, Wu S-F, Chien C-H, Tsay S-L. The influence of resilience on the coping strategies in patients with primary brain tumors. *Asian Nurs Res (Korean Soc Nurs Sci)*. 2020;14(1):50-55. doi:10.1016/j.anr.2020.01.005.

Appendix: Evidence Tables

Diagnosis

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Dai, Ning, Han, et al., 2016	Meta-analysis	3,464	Patients diagnosed with GBM	Reach a reliable assessment of the association between IDH1 mutation and mortality of GBM patients.	Patients with IDH1 mutation had decreased risk of mortality compared to those patients without IDH1 mutation (RR=0.43, 95% CI 0.35-0.54, *P*<.001). GBM patients with IDH1 mutation from European countries also had decreased mortality risk compared to those patients without IDH1 mutation (RR=0.35, 95% CI 0.25–0.49, *P*<.001), but GBM patients with IDH1 mutation from Asia only had 32% decreased mortality risk compared with those patients without IDH1 mutation (RR=0.68, 95% CI 0.49-0.94, *P*=.018). The findings from the meta-analysis provide strong evidence for the association between IDH1 mutation and decreased mortality risk of GBM patients.
Chen, Yao, Xu, et al., 2016	Meta-analysis	N/A (24 studies)	Patients with a malignant brain tumor	Examine the association of IDH1/2 mutations with overall survival and progression-free survival in patients with GBMs.	When patients were stratified by surgery vs no surgery or IDH1 vs IDH1/2 mutations, the results indicated that the presence of IDH mutations was associated with better overall survival and progression-free survival. The IDH mutations are associated with improved survival in patients with GBMs.
Wang, Guo, 2016	Meta-analysis	N/A (11 studies)	Case-control or cohort studies of adults, documented cell phone frequency of use (>1yr and >5yr); diagnosis of glioma with MRI	Evaluate the association between mobile phone use and glioma risk through pooling the published data for patients' cell phone use at >1 year and >5 years.	• Combined data showed that there was no association between mobile phone use and glioma: odds ratio (OR)=1.08 (95% CI 0.91-1.25, *P*>.05). • A significant association was found between mobile phone use more than 5 years and glioma risk: OR=1.35 (95% CI 1.09-1.62, *P*<.05).
Wang, Huo, Li, et al., 2018	Meta-analysis	4,655 (10 studies)	Adults older than 16 years of age, identified cell phone use	Determine the association between wireless phone use and risk of adult gliomas.	• Combined OR of adult gliomas associated with ever use of wireless phones was 1.03 (95% CI 0.92-1.16) with high heterogeneity (I^2=54.2%, *P*=.013). • In subgroup analyses, no significant association was found between tumor location in the temporal lobe and adult glioma risk, with ORs of 1.26 (95% CI 0.87-1.84), 0.93 (95% CI 0.69-1.24), and 1.61 (95% CI 0.78-3.33). • Significant association with risk of glioma was found in long-term users (≥10 years) with OR of 1.33 (95% CI 1.05-1.67).
Yang, Guo, Yang, et al., 2017	Meta analysis	6,028 cases; 11,488 controls	Adult brain tumor patients with documented cell phone use for at least 6 continuous months	Investigate potential association between mobile phone use and glioma risk	• Significant positive association between long-term mobile phone use (minimum 10 years) and glioma (OR=1.44, 95% CI=1.08-1.91) • Significant positive association between long-term ipsilateral mobile phone use and the risk of glioma (OR=1.46, 95% CI=1.12-1.92) • Long-term mobile phone use was associated with 2.22 times greater odds of LGG occurrence (OR=2.22, 95% CI=1.69-2.92). • Mobile phone use of any duration was not associated with the odds of HGG (OR=0.81, 95% CI=0.72-0.92). • Contralateral mobile phone use was not associated with glioma regardless of the duration of use. • An association was not observed when the analysis was limited to HGG.

Diagnosis (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Coureau, Bouvier, Lebailly, et al., 2014	Multicenter, population-based, case-control study	253 patients with gliomas, 194 patients with meningiomas, 832 matched controls	Subjects ≥16 yo with benign or malignant CNS tumor, diagnosed between 2004 and 2006, living in France	Analyze the association between mobile phone exposure and primary central nervous system tumors (gliomas and meningiomas) in adults.	• No association with brain tumors when comparing regular mobile phone users with nonusers (OR=1.24, 95% CI 0.86-1.77 for gliomas; OR=0.90, 95% CI 0.61-1.34 for meningiomas) • Positive association, statistically significant, in the heaviest users when considering life-long cumulative duration (≥896h: OR=2.89, 95% CI 1.41-5.93 for gliomas; OR=2.57, 95% CI 1.02-6.44 for meningiomas) and number of calls for gliomas (≥18,360 calls: OR=2.10, 95% CI 1.03-4.31) • Higher risk, not statistically significant, for gliomas, temporal tumor, urban use, and heavy mobile phone use (defined as >1,640 hours and/or longer than 10 years)
Chapman, Azizi, Luo, et al., 2016	Retrospective, observational, trend analysis, epidemiologic study	19,858 males; 14,222 females	National Cancer Registry data; diagnosed with a brain tumor in Australia between 1982 and 2012	Assess the association between brain cancer incidence and mobile phone use.	• Observed stability of brain cancer incidence over the time span between 1982 and 2012 except in people over the age of 70 years, suggesting mobile phone use unlikely source of risk for brain tumor
Jorgensen, Johansen, Ravnskjaer, et al., 2016	Retrospective review	28,731	Female Danish nurses, over 44 yo, without brain tumor at time of enrollment where particulate matter (PM) could be measured	Examine associations between long-term exposure to ambient air pollution and risk for development of brain tumors.	• 121 developed brain cancer during 15.7 years of follow-up. • Weak positive association between total brain tumors and PM2.5 (1.06; 0.80-1.40 per 3.37 mg/m3), NO2 (1.09; 0.91-1.29 per 7.5 mg/m3), and NOx (1.02; 0.93-1.12 per 10.22 mg/m3), and none with PM10 (0.93; 0.70–1.23 per 3.31 mg/m3) • Associations with PM2.5 and NO2 were stronger for tumors located in meninges than in brain, and for benign than for malignant tumors • Association of total brain tumors with PM2.5 was modified by BMI and was statistically significantly enhanced in obese women (2.03; 1.35-3.05)
Pouchieu, Raherison, Piel, et al., 2018	Case control	273 patients with glioma, 218 patients with meningioma, 982 matched controls	Subjects ≥16 yo with benign or malignant CNS tumor, diagnosed between 2004 and 2010, living in France	Examine the association between allergy history and risk of glioma and meningioma in adults using data from the CERENAT (CEREbral tumors: a NATional study) multicenter case-control study carried out in four areas in France in 2004-2010.	A significant inverse association was found between glioma and a history of any allergy (OR 0.52, 95% CI 0.36-0.75), with a dose-effect relationship with the number of allergic conditions reported (*P*-trend=.001) and a particularly strong association with hay fever/allergic rhinitis (OR 0.46, 95% CI 0.30-0.72). Associations with glioma risk were more pronounced in women. For meningioma, no association was observed with overall or specific allergic conditions.
Meng, Tang, Yu, et al., 2020	Meta-analysis	N/A (12 studies)	Adult patients, reported lead exposure, brain tumor diagnosis	Analyze the relationship between environmental lead exposure and various types of brain tumors.	• In case-control studies, lead exposure was associated with gliomas (OR 0.82, 95% CI 0.69-0.95) and meningiomas (OR 1.06, 95% CI 0.65-1.46). • In the cohort study, lead exposure was associated with brain cancer (OR 1.07, 95% CI 0.95-1.19) and meningiomas (OR 1.06, 95% CI 0.94-1.17). • The risk of childhood brain tumors associated with parental lead exposure was OR 1.17 (95% CI 0.99-1.34). • Lead may be a risk factor for meningiomas and brain cancers. However, the glioma results suggest that lead may be a protective factor, which needs to be further studied.

Diagnosis (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Quach, El Sherif, Gomes, et al., 2017	Systematic review	N/A	77 observational studies and 38 systematic reviews published between 2010 and 2013 including adult and pediatric patients with primary brain tumors	Identify risk factors for onset and natural progression of primary brain tumors, which were shown to increase, decrease, or have a null association with risk of primary brain tumor.	• Based on this review, various genetic variants, pesticide exposures, occupational farming/hairdressing, cured meat consumption, and personal hair dye use appear to be associated with increased risk of onset among adults. • The specific epidermal growth factor polymorphism 61-A allele within Caucasian populations and having a history of allergy was associated with a decreased risk. For progression, M1B-1 antigen was shown to increase the risk. • High birth weight, pesticide exposure (childhood exposure, and parental occupational exposure), and maternal consumption of cured meat during pregnancy may also increase the risk of onset of childhood brain tumors. • Conversely, maternal intake of prenatal supplements (folic acid) appeared to decrease risk. • Children with neurofibromatosis 2 were considered to have worse overall and relapse free survival compared to neurofibromatosis 1, as were those children who had grade III tumors compared to lesser grades.
Cote, Downer, Smith, et al., 2018	Prospective, observational, 2-arm cohort study	508	121,696 women from the Nurses' Health Study and 51,400 men from the Health Professionals Follow-up Study that reported height and weight in questionnaires	Evaluate the association between body habitus and risk of glioma.	• Adult BMI and waist circumference were not associated with glioma. • Higher BMI at age 21 for men and at age 18 for women was modestly associated with risk in the pooled cohort. • Based on body somatotypes, however, women with heavier body types during childhood and young adulthood may be at lower risk of glioma, although this association was not observed later in life with measurements of BMI. • Greater height was associated with increased risk, and the trend was more pronounced in women.
Zhang, Chen, Wang, et al., 2016	Meta-analysis	11,614 patients with a brain tumor, 3,887,156 controls	Adult brain tumor patients with reported BMI in US, Asia, and Europe	Evaluate the relationship, if any, of a patient's BMI and development of a brain tumor.	Excess weight (obesity) was associated with increased risk of brain tumors and meningiomas but not with gliomas.
Barami, Lyon, and Conell, 2017	Retrospective study	1,074	Patients with GBM diagnosis, identified in one healthcare system cancer registry, with diabetes mellitus type 2 (DM2)	Determine if DM2 or DM2-associated factors were associated with risk of developing GBM and if DM2 affected survival of GBM patients.	• No association was seen between DM2, hyperlipidemia, obesity, and GBM. • DM2 was associated with poorer survival in univariate testing, yet not in multivariate testing.
Kuan, Green, Kitahara, et al., 2019	Prospective review	1,262,104	Glioma patients	Evaluate any association between diet and development of gliomas.	The largest prospective evidence to date suggests little, if any, association between major food groups, nutrients, or common healthy dietary patterns and glioma incidence.
Maia, Malheiros, da Rocha, et al., 2005	Cross-sectional study	20	Patients with a primary brain tumor	Evaluate if rCBV is correlated with vascular endothelial growth factor (VEGF) expression in presumed supratentorial LGGs.	In patients with heterogeneous tumors on perfusion-weighted images, the high rCBV focus had areas of oligodendroglioma or anaplastic astrocytoma on stereotactic biopsy, whereas the surgical specimens were predominantly astrocytomas. Anaplastic gliomas had high rCBV ratios and positive VEGF immunoreactivity. Diffuse astrocytomas had negative VEGF expression and mean rCBV values significantly lower than those of the other two groups. Three diffuse astrocytomas had positive VEGF immunoreactivity and high rCBV values.

Diagnosis (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Patel, Baradaran, Delgado, et al., 2017	Meta-analysis	937 cases of tumor progression and 806 cases of treatment effect (28 studies)	High-grade gliomas WHO grade 3 and 4	Evaluate whether dynamic susceptibility contrast-enhanced (DSC) and dynamic contrast-enhanced (DCE) PWI metrics can effectively differentiate between recurrent tumor and posttreatment changes within the enhancing signal abnormality on conventional MRI.	The pooled sensitivities and specificities for detecting tumor recurrence using the two most commonly evaluated parameters, mean rCBV (threshold range, 0.9-2.15) and maximum rCBV (threshold range, 1.49-3.1), were 88% and 88% (95% CI 0.81-0.94, 0.78-0.95) and 93% and 76% (95% CI 0.86-0.98, 0.66-0.85), respectively.
Hendrix, Hans, Griessenauer, et al., 2017	Prospective cohort design	92	Primary and metastatic brain tumors	Identify risk factors for neurocognitive dysfunction in patients suffering from common supratentorial brain tumors with minor neurological deficits.	A total of 46 patients and 46 healthy controls underwent neurocognitive testing. Overall, neurocognitive performance was significantly worse in patients compared to healthy controls. Larger tumor volume, frontal location, and left-dominant hemisphere were associated with worse executive functioning and verbal fluency. Additionally, larger tumors and left-dominant location correlated with impairments on perceptual speed tasks. Frontal tumor location was related to worse performance in visual-spatial and short- and long-term memory. Tumor type, clinical presentation, and patient self-awareness were not associated with specific neurocognitive impairments.
Allen, Carlson, Carlson, et al., 2020	Cross-sectional study	40	Primary brain tumor	Examine the association between performance-based neurocognitive and patient-reported cognitive function tests and identify characteristics that may explain observed discrepancies as a means to advance intervention development.	Neurocognitive impairments included executive control, memory, and attention. Age, time since diagnosis, and tumor- or treatment-specific variables were not associated with neurocognitive or patient-reported cognitive function. Those reporting worse cognitive impairment tended also to report greater severity of primary brain tumor-specific and depressive symptoms

Radiation Treatment

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Cordes, Scherwath, Ahmad, et al., 2014	Prospective	94 (67 patients with brain tumor and 32 controls)	Adult patients with brain metastases who were treated with WBRT or hypofractionated stereotactic radiotherapy	Prospectively assess distress, anxiety, and depression in patients with brain metastases from different solid primary tumors treated with radiotherapy to the brain.	Before radiotherapy, the treatment group experienced higher distress than the control group (P=.029). Using a cut-off ≥5, 70% of the treatment group was suffering from significant distress (66% of the control group). No significant time-by-group interaction on distress, anxiety, and depression was observed. At all time points, a high proportion of patients reported psychological stress, which featured more prominently than most of the somatic problems. Global distress correlated strongly with the hospital anxiety score before radiotherapy, but only moderately or weakly with both anxiety and depression scores after radiotherapy, with the weakest association 6 months after radiotherapy.
Wong, Zhang, Rowbottom, et al., 2016	Descriptive	217	Adult patients with brain metastases who were treated with WBRT	Determine the symptom experience and overall QOL in patients with brain metastases before and after WBRT.	Following WBRT, certain symptoms may influence overall QOL to a greater extent than others, which may fluctuate with time.
Teke, Bucaktepe, Kibrisli, et al., 2016	Descriptive	33	Adult patients with brain metastases treated with WBRT	Evaluate QOL, anxiety, depression, and sleep characteristics in patients with brain metastases at the beginning and end of WBRT and 3 months after treatment.	Overall survival was better in those who reported better sleep. Whole brain radiation therapy improves Karnofsky Performance Status scores and does not worsen sleep quality or mood, even in patients with poor performance status. When changes in mood and sleep quality are observed, survival and QOL may improve in patients with BM; consequently, nurses should be responsive to these changes.
Miller, Kotecha, Barnett, et al., 2017	Descriptive	67	Adult patients with brain metastases undergoing SRS as upfront or adjuvant treatment	Examine the impact of the number of brain metastases upon QOL preservation following SRS.	Among patients with brain metastasis, QOL preservation must remain paramount as multimodality therapy continues to improve. In the present investigation, 12-month QOL preservation was 79%. However, patients with more than three brain metastases were at significantly greater risk for QOL decline.
Nakazaki and Nishigaki, 2018	Retrospective review	238	Adult patients who underwent gamma knife radiosurgery (GKRS) for brain metastases without whole brain radiotherapy or surgery	Determine the symptoms of new lesions after GKRS, including the outcomes of salvage GKRS.	The incidence of symptomatic new lesions that appeared after GKRS was low, and more than half of the patients showed improvements in their symptoms after salvage GKRS. However, careful MRI-based assessments and salvage GKRS are critical for the QOL.
Cramer, McKee, Case, et al., 2019	Retrospective analysis	198	Brain tumor survivors post radiation therapy (RT)	Evaluate cognitive impairment for post-RT brain tumor adults.	Two-thirds of post-RT brain tumor survivors met the National Institute on Aging and the Alzheimer's Association criteria for MCI. This taxonomy may be useful when applied to brain tumor survivors because it defines cognitive phenotypes that may be differentially associated with course, treatment response, and risk factor profiles.
Kalra, Kannan, Gupta, 2020	Meta-analysis	1,569 (7 studies)	Elderly patients with GBM who were randomly assigned to any adjuvant therapy regimen	Identify the most optimal adjuvant therapy regimen in elderly GBM patients through systematic review and network meta-analysis.	Moderately hypofractionated radiation therapy (3 weeks) with concurrent and adjuvant temozolomide is the most optimal and preferred adjuvant therapeutic regimen in elderly GBM.
Wang, Xiao, Qi, et al., 2020	Longitudinal	229	Patients with HGG who underwent surgery	Identify risk factors for cognitive impairment in patients with HGG.	At the end of follow-up among the 229 patients, 147 patients (67%) developed cognitive impairment and 82 patients (36%) remained in normal cognitive condition. In multivariate analysis, unmethylated MGMT promoter (HR 1.679, 95% CI 1.212-2.326, P=.002), GBM (HR 1.550, 95% CI 1.117-2.149, P=.009), and residual tumor volume more than 5.58 cm^3 (HR 1.454, 95% CI 1.047-2.020, P=.026) were independent risk factors for cognitive impairment.

Radiation Treatment (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Ownsworth, Chan, Jones, et al., 2021	Feasibility study	N/A	Adult patients with a primary brain tumor	Evaluate the feasibility, acceptability, and efficacy of delivering supportive care via telehealth platforms to adults with primary brain tumor and family caregivers.	Seventeen articles, reporting on 16 studies, evaluated telephone-based support (5 studies), videoconferencing (3 studies), web-based programs and resources (7 studies), and combined use of videoconferencing and web-based modules (1 study) to deliver supportive care remotely. Caregivers were involved in 31% of interventions. Mean rates of accrual (68%) and adherence (74%) were moderate, whereas acceptability or satisfaction for those completing the interventions was typically high (satisfied or very satisfied=81%). Adherence rates were generally higher, and clinical gains were more evident for interventions involving real-time interaction as opposed to self-guided interventions. Telehealth delivery of supportive care is feasible and acceptable to a high proportion of individuals with primary brain tumor and their caregivers. It is recommended that future research focuses on implementation outcomes, including factors influencing the uptake and sustainability of telehealth platforms in practice.
Brown, Pugh, Laack, et al., 2013	Randomized	508	Adult patients with brain metastases who received WBRT and were randomized to receive placebo or memantine (20mg/d) within 3 days of initiating radiotherapy for 24 weeks	Determine the protective effects of memantine on cognitive function in patients receiving WBRT.	Memantine was well tolerated and had a toxicity profile very similar to placebo. Although there was less decline in the primary endpoint of delayed recall at 24 weeks, this lacked statistical significance, possibly due to significant patient loss. Overall, patients treated with memantine had better cognitive function over time; specifically, memantine delayed time to cognitive decline and reduced the rate of decline in memory, executive function, and processing speed in patients receiving WBRT.
Halkett, Cormie, McGough, et al., 2021	Single arm, prospective, qualitative	19 patients, 15 caregivers	Newly diagnosed HGG patients and caregivers	Describe GBM patients' and carers' perspectives of participating in a tailored exercise intervention during chemoradiotherapy.	Two themes identified were benefits and challenges of participating in the tailored exercise intervention during chemoradiation. Benefits included improvements in health, regaining a sense of control, interacting with people, keeping active, and benefits for carers. Challenges included managing symptoms associated with diagnosis and treatment while participating in the program, juggling treatment and exercise, and difficulties engaging in the program.

Surgical Treatment

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Hagan, Bhavsar, Raza, et al., 2015	Review	67 references reviewed	28 RCT, 16 systematic reviews or meta-analyses, 8 prospective studies, 9 review articles, 6 retrospective studies	Discuss ERAS interventions in the setting of craniotomy and delve into innovative concepts specific to enhanced recovery after craniotomy (eg, scalp blocks, minimally invasive craniotomies).	Recommendations for multiple guidelines for the perioperative care of the patient after craniotomy, including recommendations related to preoperative counseling, preoperative smoking and alcohol consumption, VTE prophylaxis, pain relief, and PONV
Greisman, Olmsted, Crorkin, et al., 2022	Literature review	Not indicated	Retrospective and prospective cohort analyses, case series, expert reviews, systematic reviews, and meta-analyses	Provide narrative, comprehensive, and current recommendations for craniotomy for tumor resection patients across the perioperative period.	Summarization of the current state of ERAS protocols in cranial neurosurgery
Peters, Robinson, Serletis, 2022	Systematic review	9 studies included	A total of 1,287 cranial surgery patients with diagnoses ranging from pituitary tumor to malignant brain tumors to intracranial aneurysm and trigeminal neuralgia	Perform a systematic review evaluating the use of ERAS in cranial surgery patients to determine the extent of integration of ERAS in this population and to assess the effectiveness of ERAS protocols in this population.	Primary: incidence of postoperative complications, LOS, and patient satisfaction Secondary: readmission rates, hospitalization costs, duration of urinary catheterization, postoperative pain, analgesia use, PONV, functional recovery, sleep quality, and anxiety
Stumpo, Staartjes, Quddusi, et al., 2021	Systematic Review	27 studies reviewed	Elective craniotomy patients	Perform a systematic review and summary of the literature examining ERAS strategies for elective craniotomy patients.	There are many evidence-based interventions that can be used during the pre-, intra-, and postoperative periods to improve recovery after elective craniotomy, and the use of ERAS protocols in this population is feasible.
Wang, Cai, Wang, et al., 2021	RCT	151	18-70 years old, American Society of Anesthesiologists (ASA) class I or II, a single intracranial lesion, elective craniotomy	Evaluate safety and effectiveness of ERAS protocol in elective craniotomy.	ERAS group patients had significantly shorter LOS and lower hospital costs than the control group. Patients in the ERAS group also had reduced PONV, lower postoperative pain scores, and less opioid use in the perioperative period.
Liu, Liu, Wang, et al., 2019	Single center, prospective, RCT	140	Adults 18-65 years old with a single intracranial lesion and medically stable for an elective craniotomy	Evaluate patient satisfaction and experience associated with ERAS protocols for elective craniotomy patients.	Higher overall satisfaction was reported by the ERAS group. The ERAS group also had higher satisfaction with information, medical and nursing care, and enhanced recovery.
Liu, Liu, Zheng, et al., 2022	Literature review	Not indicated	Adults 65 years of age or older	Development of ERAS protocol for patients over 65 years undergoing elective craniotomy.	The authors' proposal for ERAS development for this population is feasible. The implementation of this protocol was not discussed.
Hughes, Culpin, Darley, et al., 2020	Retrospective review of consecutive cohorts	107	Adult patients with pituitary tumor after endoscopic transsphenoidal pituitary surgery	Develop and assess enhanced recovery protocol for elective pituitary surgery with evaluation of safety, impact on LOS, and patient feedback.	LOS mean reduced from 4.5 to 1.7 days, with no difference in readmission rates. High (9.7/10) patient satisfaction in the ERAS group as well.
Elayat, Jena, Nayak, et al., 2021	Non-randomized controlled trial	70	Adult patients (ASA status I and II) 18 years and older with a single supratentorial space–occupying lesion requiring elective craniotomy.	Prospectively analyze the effect of an ERAS protocol on patient outcomes in this population.	An ERAS protocol is feasible in this neurosurgery population and resulted in a statistically significant reduction of ICU stays for the ERAS group compared with the control group.

Complementary Therapies

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Randazzo, McSherry, Herndon, et al., 2019	Retrospective review	845	Primary brain tumor patients	Identify the percentage of patients using complementary and integrative health interventions in the primary brain tumor population and explore the impact on QOL.	Use of these interventions showed no association between intervention and QOL.
Le Rhun, Devos, Bourg, et al., 2019	Descriptive cohort and comparative analysis; prospective multicenter study	277	Adult patients with glioma	Explore complementary and alternative medicine (CAM) use in adult glioma patients in France to determine whether CAM use may affect QOL, familial organization, or leisure activities, and to estimate the cost and the financial consequences of different CAM approaches, with the goal to better understand needs, motivations, and expectations of patients and their caregivers.	Complementary and alternative medicine are frequently used by glioma patients in France. Underlying needs and expectations, potential interactions with tumor-specific treatments, and financial and QOL burden should be discussed with patients and caregivers.
Milbury, Malliah, Mahajan, et al., 2018	Formative single-arm trial	10	Adults with HGG undergoing at least 5 weeks of radiotherapy, and their family caregivers	Establish the feasibility and acceptability of a 12-week dyadic yoga (DY) intervention.	The DY intervention consisting of breathing exercises, gentle movements, and guided meditations was safe, feasible, and acceptable, with clinically significant reductions in patient sleep disturbance and improvement in patient and family caregiver mental quality of life.
Milbury, Li, Weathers, et al., 2018	RCT	20	Glioma patients undergoing radiotherapy and their caregivers randomized to 12-session DY or waitlist control group	Examine the feasibility and preliminary efficacy of a DY intervention as a supportive care strategy.	A DY intervention appears to be a feasible and beneficial symptom and QOL management strategy for glioma patients undergoing radiotherapy and their caregivers. An efficacy trial with a more stringent control group is warranted.
Baima, Omer, Varlotto, et al., 2017	Single-arm, prospective	15	Patients with HGG	Evaluate compliance with and safety of a novel independent home exercise program for patients with HGG tumors.	Fourteen of 15 started the exercises during the course of the month, 5 did the exercises 4 or more times per month, 9 of the 14 continued the exercises throughout the month on a regular basis.
McCarty, Eickmeyer, Kocherginsky, et al., 2017	Prospective, observational	49	Malignant brain tumor patients participating in outpatient therapies	Determine the relationships between functional outcomes, clinical symptoms, and health-related QOL among patients with malignant brain tumors receiving interdisciplinary outpatient rehabilitation.	Health-related QOL, pain, and depression did not worsen. Patients who reported less depression and pain had better reported health-related QOL. Level of function was also associated with health-related QOL and pain, but not depression.

Reducing Complications

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Cote, Dubois, Karhade, et al., 2016	Retrospective review	19,409 craniotomies	Patients who develop VTE after craniotomies for brain tumor	Identify risk factors for postoperative VTE for patients undergoing craniotomy for brain tumor between 2006-2014.	Venous thromboembolism occurs in approximately 3% of patients undergoing craniotomy for brain tumor resection. Independent predictors for developing VTE include older age, higher BMI, recent steroid use, and total operative time.
Yust-Katz, Mandel, Wu, et al., 2015	Retrospective review	64 from 440 patient volume	Patients with GBM treated at MD Anderson during the years 2005-2011	Estimate the frequency of VTE in GBM patients and identify potential risk factors for the development of VTE during adjuvant chemotherapy. Furthermore, examine whether the Khorana score accurately predicts the risk of VTE in GBM patients.	Of the 64 patients who developed a VTE, 36 were treated with AC, 2 with an inferior vena cava filter, and 21 with both. Complications (ICH, bleeding in other organs, and thrombocytopenia) secondary to AC were reported in 16% (n=10). Venous thromboembolism is common in patients with GBM. Results did not validate the Khorana score in GBM patients. Additional studies identifying which GBM patients are at highest risk for VTE are needed to enable further evaluation of VTE preventive measures in this selected group.
Hsieh, Elson, Otvos, et al., 2015	Retrospective review	212	Patients who underwent resection of brain metastases	Examine the effect of postsurgical WBRT or localized radiotherapy, including SRS and intraoperative radiotherapy, on the rate of recurrence both local and distal to the resection site in the treatment of brain metastases.	Localized radiotherapy as adjuvant treatment to surgical resection of brain metastases is associated with an increased rate of development of new distant metastases and leptomeningeal disease compared with WBRT, but not with recurrence at the resection site or of unresected lesions treated with radiation.
Noh, Lee, Kim, et al., 2015	Retrospective review	321	Patients diagnosed with GBM	Report the risk of leptomeningeal spread (LMS) and the prognosis between treatment modalities in GBM patients.	Treatment of LMS is mainly palliative. IT-MTX is generally the first-line treatment modality of LMS. Prediction and prevention of LMS is crucial because its treatment has been limited. Further approaches to improve the therapeutic effect should be established.
Ma, Levy, Gui, et al., 2018	Retrospective review	413	Patients with brain metastases who received SRS	Evaluate risk factors that may predispose patients to LMC after SRS treatment in this case–control study of patients with brain metastases who underwent single-fraction SRS between 2011 and 2016.	Prior surgical resection of brain metastases before SRS was associated with 6.5 times higher odds (95% CI 1.45-29.35, *P*=.01) of developing LMC after radiosurgery compared to those with no prior resections of brain metastases. Additionally, adjuvant WBRT may help to reduce the risk of LMC and can be considered in decision making for patients who have had brain metastasectomy.
Ahmad, Martin, Patel, et al., 2019	Retrospective review	319	Adults with grade II and grade III glioma seen at the authors' institution	Determine if patients with oligodendroglioma have a higher risk of radiation necrosis, compared to patients with astrocytoma.	Identified radiation necrosis in 41 patients (12.9%): 28 patients (21.3%) with oligodendroglioma and 13 (6.9%) with astrocytoma (HR 3.42, *P*<.001). Patients with oligodendroglioma who received more than 54 Gy had a higher incidence (31.2%) than those receiving 54 Gy or less (14.3%; HR 6.9, *P*=.002). There was no similar correlation among patients with astrocytoma. There was no difference in incidence based on use of concomitant temozolomide. Radiation necrosis appeared within 24 months from radiation in 80.5% of patients. The study suggests that patients with oligodendroglioma are at higher risk of developing radiation necrosis. The incidence increases with increasing radiation dose in patients with oligodendroglioma but not with astrocytoma. Radiation necrosis usually appears within 24 months from radiation therapy. Patients with oligodendroglioma receiving more than 54 Gy are at highest risk.

Reducing Complications (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Loi, Caini, Scoccianti, et al., 2020	Systematic review and meta-analysis	11 studies	Patients with recurrent brain metastases receiving stereotactic reirradiation	Identify studies reporting local failure, overall survival, and radiation necrosis rates following a second round of SRS (SRS2). Meta-analysis was performed to identify predictors of radiation necrosis.	Cumulative crude rate of radiation necrosis was 13%, with subgroup analysis showing higher radiation necrosis incidence in studies with the median patient age >59 years and lower incidence following prior WBRT. In patients with in-site recurrence of brain metastases following upfront SRS, a second course of SRS (SRS2) is an effective strategy.
Sayan, Sahin, Mustafayev, et al., 2021	Retrospective review	170	Patients with brain metastases treated with SRS	Examine the risk factors associated with the development of symptomatic radiation necrosis in patients treated with SRS for brain metastases.	SRS is an effective treatment option for patients with brain metastases; however, a subset of patients may develop symptomatic radiation necrosis. The study found that patients with larger tumor size and larger plan V100%, V50%, V12 Gy, or V10 Gy who received single-fraction SRS or who had diabetes were all at higher risk of symptomatic radiation necrosis.

Symptom Management

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Huang, Jiang, Deng, et al., 2020	Prospective	549	Adult glioma patients who underwent surgery more than 3 months before the survey	Investigate the sleep quality of patients with postoperative glioma.	The sleep quality of patients with postoperative glioma at home is worse than that of normal adults. Moreover, difficulty falling asleep and sleep disorders are common complications among these patients, and age, postoperative duration, and postoperative chemoradiotherapy could affect sleep quality.
Jeon, Dhillon, Koh, et al., 2021	Prospective survey	73	Healthcare professionals	Explore perceptions of healthcare professionals actively engaged in neuro-oncology care toward sleep disturbance in adults with primary or secondary brain tumor and identify facilitators and barriers to assessment and management of sleep disturbance.	Overall, participants perceived sleep disturbance as highly prevalent in neuro-oncology and positively viewed the importance of managing this symptom. Practical barriers to management were reported that future interventions can target.
Pranckeviciene, Tamasauskas, Deltuva, et al., 2016	Prospective observational	211	Brain tumor patients to undergo surgery	Investigate the prevalence rate and correlates of preoperative suicidal ideation (SI) in brain tumor patients admitted for elective brain tumor surgery.	Suicidal ideation was self-reported by 6% of brain tumor patients before surgical intervention and was associated with a past history of psychiatric disorders and worse perceived health status. Poor mental health was an independent correlate of SI. The perception of health status by a patient should be considered as an important determinant of poor mental health in brain tumor patients.
Baima, Omer, Varlotto, et al., 2017	Prospective observational	15	High-grade brain tumor patients	Evaluate compliance with and safety of a novel independent home exercise program for patients with high-grade brain tumor.	The small group of subjects with high-grade brain tumors demonstrated compliance with and safety of a novel independent strength and balance exercise program in the home setting. Higher frequency of exercising was associated with life quality parameters as well as marriage and income.
Acquaye, Payén, Vera, et al., 2019	Qualitative interviews, use of MD Anderson Symptom Inventory-Brain Tumor (MDASI-BT) instrument compared to confirm the validity	23	Adult glioma patients	Compare qualitative interviews with MDASI-BT results to confirm validity of the instrument.	Completion of the MDASI-BT found that patients reported, on average, 6.8 symptoms, with 14% of reported symptoms (mean=3) rated as moderate to severe. The findings demonstrate how applicable the MDASI-BT is in capturing significant symptoms experienced and how important it is to use throughout ones' care to manage symptoms effectively.
Yu, Ji, Ma, et al., 2017	Prospective observational	97	Chinese adult patients with pituitary adenomas	Investigate the prevalence and clinical characteristics of, and the risk factors for, nonfunctioning pituitary adenoma (NFPA)–associated headaches in Chinese patients with normal endocrine activity.	Migraine-like headaches are a common clinical manifestation in patients with NFPAs. A family history of primary headaches and cavernous sinus invasion are risk factors for NFPA-associated headaches.
Shi, Lamba, Nayan, et al., 2018	Systematic review and meta-analysis	6 articles included of 619 identified	Adult patients with glioma and depression	Study the effect of depression on glioma patients' survival.	Depression was associated with significantly worsened survival regardless of time of diagnosis, especially among patients with HGG.
Maitre, Gupta, Maitre, et al., 2021	Nonrandomized, prospective, longitudinal	49	Adults with malignant brain tumors	Evaluate QOL and activities of daily living (ADL) longitudinally in patients treated with salvage reirradiation for recurrent or progressive glioma. Secondary end points included post-reirradiation survival.	High-dose salvage reirradiation in carefully selected patients with recurrent or progressive glioma is associated with stable QOL (preserved functional domains and reduced symptom burden) and improvement in ADL (greater functional independence) over time, with encouraging survival outcomes.

Symptom Management (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Kim and Byun, 2018	Prospective longitudinal study	51	Adults newly diagnosed with primary malignant brain tumor	Identify symptom clusters in patients with high-grade brain cancers and determine the relationship of each cluster with the performance status and QOL during concurrent chemoradiotherapy (CCRT).	Differences were observed in symptom clusters in patients with high-grade brain cancers during CCRT. In addition, the symptom clusters were correlated with the performance status and QOL of patients, and these effects could change during CCRT.
Dutz, Agolli, Bütof, et al., 2020	Retrospective exploratory study	42	Adult patients with HGG	Study the impact of clinical factors and dosimetric parameters on neurocognitive function and QOL during recurrence-free follow-up after proton beam therapy is investigated.	Self-reported and objectively measured neurocognition and most other QOL domains remained largely stable over time during recurrence-free follow-up for brain tumor patients treated with proton beam therapy. The association between reduced cognitive function and irradiated volume of the anterior cerebellum requires validation in larger studies and comparison to patients treated with photon therapy.
Renovanz, Hechtner, Janko, et al., 2017	Prospective analysis questionnaire study	173	Adult patients with diagnosis of glioma (any grade)	Assess glioma patients' supportive care needs in a neurosurgical outpatient setting and identify factors that are associated with needs for support.	Glioma patients in neuro-oncological departments report unmet supportive care needs, especially in the psychological domain. Distress is the factor most consistently associated with unmet needs requiring support and could serve as an indicator for clinical neuro-oncologists to initiate support.

Advance Care Planning and Palliative Care

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Diamond, Russell, Kryza-Lacombe, et al., 2016	Retrospective cohort study	160	Patients with primary malignant brain tumor (PMBT) admitted to the home hospice program of a large, urban, not-for-profit home healthcare agency between 2009 and 2013	Compare early vs late referrals to hospice for patients with PMBT.	Of 160 patients with PMBT followed to death in hospice care, 32 (22.5%) were enrolled within 7 days of death. When compared with patients referred to hospice more than 7 days before death, a greater proportion of those with late referral were bedbound at admission (97.2% vs 61.3%, OR=21.85, 95% CI 3.42-919.20, *P*<.001), aphasic (61.1% vs 20.2%, OR=6.13, 95% CI 2.59-15.02, *P*<.001), unresponsive (38.9% vs 4%, OR=14.76, 95% CI 4.47-57.98, *P*<.001), or dyspneic (27.8% vs 9.7%, OR=21.85, 95% CI 3.42-10.12, *P*=.011). In multivariable analysis, male patients who were receiving Medicaid or charitable care and were without a healthcare proxy were more likely to enroll in hospice within 1 week of death. Late hospice referral in PMBT is common. Patients with PMBT enrolled late in hospice are severely neurologically debilitated at the time hospice is initiated and therefore may not derive optimal benefit from multidisciplinary hospice care. Men, patients with lower socioeconomic status, and those without a healthcare proxy may be at risk for late hospice care and may benefit from proactive discussion about EOL care in PMBT, but prospective studies are needed.
Philip, Collins, Panozzo, et al., 2020	Prospective longitudinal study	63 (32 patients and 31 caregivers)	People with HGG and their caregivers	Describe the severity and content of key concerns raised by patients and their caregivers in the 3 months following a diagnosis of HGG.	This prospective longitudinal descriptive study revealed that, following a new diagnosis of HGG, patients and caregivers had changing needs for support and fluctuating distress, mirroring the illness trajectory. Palliative care needs were apparent from diagnosis, and early integration of palliative care should be considered.
Loughan, Aslanzadeh, Brechbiel, et al., 2020	Cross-sectional study	105	Primary brain tumor patients	Examine the prevalence of death-related distress and its correlates in primary brain tumor patients.	Patients with primary brain tumors appear to have a high prevalence of death-related distress, particularly death anxiety. Further, four distinct profiles of distress were identified, supporting the need for tailored approaches to addressing death-related distress. A shift in clusters of distress based on time since diagnosis also suggests the need for future longitudinal assessment.
Alturki, Gagnon, Bruno, et al., 2014	Retrospective analysis	1,623	Adult patients with primary brain tumors	Determine the variability in processes of care in the last 6 months of life experienced by patients dying of primary intracranial tumors and potential predictors of place of death.	An integrative approach for this patient population, from diagnosis to death, could potentially reduce the care burden in the final period on the healthcare system and patient's family and improve access to a better place of death.
Renovanz, Maurer, Lahr, et al., 2018	Prospective analysis, questionnaire study	232	Patients with HGG	Assess the needed support using a simple structured questionnaire. Investigate the psychosocial burden and support requested from caregivers.	Data showed that glioma patients and their caregivers were both highly burdened. The Patients' Perspective Questionnaire allowed researchers to evaluate the psychosocial support requested and perceived by patients, detect supportive care needs, and provide information at a glance. Patients in poorer clinical condition are at risk of having unmet needs. The caregivers' burden and unmet needs are not congruent with the patients' need for support. In particular, caregivers of patients on chemotherapy were more highly burdened than patients themselves.
Halkett, Lobb, Shaw, et al., 2018	Prospective longitudinal study via survey	234 (116 patients, 118 carers)	Patients and family carers of patients diagnosed with HGG	Determine how carer needs changed longitudinally and understand associations between unmet needs and distress.	Carers of people with HGG remain highly distressed and their needs evolve over time, indicating a requirement for ongoing evaluation of unmet needs and interventions to address carer psychological morbidities.

Advance Care Planning and Palliative Care (continued)

Reference	Study Design	Sample Size	Population	Study Aims	Findings
Renovanz, Hechtner, Janko, et al., 2017	Prospective multicenter questionnaire analysis	173	Adult patients with diagnosis of glioma (any grade)	Assess glioma patients' supportive care needs in a neurosurgical outpatient setting and identify factors that are associated with needs for support.	Glioma patients in neuro-oncological departments report unmet supportive care needs, especially in the psychological domain. Distress is the factor most consistently associated with unmet needs requiring support and could serve as an indicator for clinical neuro-oncologists to initiate support.
Song, Amatya, Voutier, et al., 2016	Literature, retrospective review (19 studies were included: [1 RCT, 17 cohort studies, 1 qualitative study])	4,686	Adult patients with PMBT	Present an evidence-based overview of ACP in patients with PMBT.	This review found some beneficial effects of ACP in PMBT. The literature remains limited in this area, with a lack of intervention studies, making it difficult to identify superiority of ACP interventions in PMBT. More robust studies with appropriate study design, outcome measures, and defined interventions are required to inform policy and practice. Positive effects of ACP included lower hospital readmission rates and intensive care unit utilization. None of the studies assessed mortality outcomes associated with ACP.
Hemminger, Pittman, Korones, et al., 2016	Retrospective analysis	117	Deceased GBM patients	Evaluate adherence to five palliative care quality measures and explore associations with patient outcomes in GBM.	Late advance directive documentation, minimal early palliative care involvement, and the association of early hospice enrollment with death in a home setting underscore the need to improve care and better define palliative care quality measures in GBM.