



Essential Requirements for Quality Cancer Care: Glioma



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Abstract

European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCCs) are explanations of the organisation and actions necessary to provide high-quality care to patients with a specific cancer type. They are compiled by a working group of European experts representing disciplines involved in cancer care, and provide oncology teams, patients, policymakers and managers with an overview of the essential requirements in any healthcare system. The focus here is on adult glioma.

Gliomas make up approximately 80% of all primary malignant brain tumours. They are highly diverse and patients can face a unique cognitive, physical and psychosocial burden, so personalised treatments and support are essential.

However, management of gliomas is currently very heterogeneous across Europe and there are currently few formally-designated comprehensive cancer centres with brain tumour programmes.

To address this, the ERQCC glioma expert group proposes frameworks and recommendations for high quality care, from diagnosis to treatment and survivorship. Wherever possible, glioma patients should be treated from diagnosis onwards in high volume neurosurgical or neuro-oncology centres. Multidisciplinary team working and collaboration is essential if patients' length and quality of life are to be optimised. People in Europe equal access to high-quality care.

Preamble

European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCCs) are explanations of the organisation and actions necessary to provide high-quality care to patients with a specific cancer type. They are compiled by a working group of European experts representing disciplines involved in cancer care, and provide oncology teams, patients, policymakers and managers with an overview of the essential requirements in any healthcare system. The focus here is on adult glioma.

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European Cancer Organisation essential requirements for quality cancer care (ERQCC) are descriptions and explanations of challenges, organisation and actions that are necessary to give high quality care to patients with a specific tumour type.

Introduction

The Need for Quality Frameworks

Awareness of variations in cancer outcomes has resulted in a growing emphasis on quality by cancer organisations. The European Cancer Concord (ECC), a partnership of patients, advocates and cancer professionals, recognised major disparities in the quality of cancer management and funding in Europe in its European Cancer Patient's Bill of Rights.¹

This followed an assessment of the quality of cancer care in Europe as part of the European Partnership for Action Against Cancer initiative (EPAAC, <http://www.epaac.eu>), which reported important variations in service delivery between and within countries, with repercussions on care quality. Factors such as waiting times and provision of optimal treatment explain about a third of the differences in cancer survival among countries, while lack of a national cancer plan that promotes clinical guidelines, professional training and quality control measures may be responsible for a quarter of the survival differences.

The EU Joint Action on Cancer Control (CanCon), which replaced EPAAC from 2014, also focused on quality of cancer care and in 2017 published the European Guide on Quality Improvement in Comprehensive Cancer Control.² This recognised the need for comprehensive cancer centres (CCCs) and explored a model of comprehensive cancer care networks integrating expertise under a single governance structure. Further, research shows that care provided by multidisciplinary teams (MDTs) results in better clinical and organisational outcomes for patients.³ It is the core component in good quality cancer care.⁴

Countries have been concentrating expertise for certain tumour types in such networks and in dedicated centres or units, such as those for childhood and rare cancers, and all CCCs have teams for the main cancer types. However, with common adult tumours, only in breast and prostate cancer have there been efforts to establish dedicated, multidisciplinary units at European level. The view of the ERQCC expert group is that healthcare organisations must adopt the principles of such dedicated care for all tumour types.

Across Europe, there are currently few formally-designated CCCs with brain tumour programmes.⁵ This contrasts with the situation in the United States, where according to the American Brain Tumor Association there are nearly 50 CCCs with designated brain tumour programmes.⁵ There are hopes that European Reference Networks (ERNs) and specifically EURACAN (the ERN for rare adult solid tumours, including brain tumours) will improve access to expertise, support, information and clinical trials.⁶

Management of gliomas is very heterogeneous across Europe, so good international quality frameworks are essential. The European Association of Neuro-Oncology (EANO) publishes guidelines on specific aspects of care and specific brain tumour types,⁷ but more general care frameworks are required.

Glioma: Key Facts and Challenges

Key Facts

Central nervous system (CNS) cancer is responsible for substantial morbidity and mortality worldwide. In 2016, there were 330,000 incident cases of CNS cancer and 227,000 deaths globally, and age-standardised incidence rates increased globally by 17.3% between 1990 and 2016.⁸

Gliomas are tumours that originate in glial cells in the CNS. They make up approximately 30% of all brain and CNS tumours and 80% of all primary malignant brain tumours.⁹ They are classified according to the type of glial cell involved and the histological and genetic features, which can help predict how they will behave over time and the treatments most likely to work.

Glioblastoma, a fast-growing glioma, is the most common malignant primary brain tumour, with an incidence of 3.19 cases per 100,000 person years. It represents 45.2% of all malignant primary CNS tumours.

There are many glioma types. The 2016 World Health Organization Classification of Tumors of the Central Nervous System introduced an integrated diagnostic approach that incorporates both histopathological phenotype and molecular information.¹⁰ At time of writing, a fifth edition of the classification was in preparation, incorporating recommendations from cIMPACT-NOW (the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy).¹¹

The World Health Organization's integrated phenotypic-genotypic classification aims to:

- Improve diagnostic performance and reduce variability of histological interpretation¹²
- Provide more accurate prognostic stratification than former morphology-based methods¹⁰
- Further clinical applications of personalised medicine and the development of molecularly tailored therapies.¹³

Glioblastoma, a fast-growing glioma, is the most common malignant primary brain tumour, with an incidence of 3.19 cases per 100,000 person years.¹⁴ It represents 45.2% of all malignant primary CNS tumours.¹⁵

Gliomas have a propensity to diffusely infiltrate the brain, making complete surgical resection without significant neurological deficit challenging. Their inherent resistance to radiation and chemotherapy makes disease progression inevitable, and the lack of effective therapies is a clear unmet clinical need.

Risk Factors

The only known environmental risk factor for the development of malignant glioma is exposure to ionising radiation. No other environmental exposures including cell phone use, infection or trauma have yet been shown to have an effect.¹⁶ In rare cases, glioblastoma can occur in people with certain genetic syndromes.¹⁸ There are ongoing studies evaluating the genetic risk factors for developing glioma and the use of genome-wide association studies (GWAS) has identified to date seven genomic variants that confer increased glioma risk.

Diagnosis and Grading

The symptoms of glioma vary according to tumour size, location, growth rate and patient's age. The most common symptoms include headache, nausea or vomiting, personality changes, irritability, cognitive disorders, urinary incontinence, difficulty with balance, visual problems, speech difficulties, weakness on one side of the body and new onset of seizures.

Suspected cases require diagnostic imaging. Magnetic resonance imaging (MRI) is the preferred modality for characterising brain tumours, guiding surgical strategy and monitoring treatment response.

The detection of key molecular and genetic markers is critical to selecting treatment and predicting response (see Treatment and Outcomes below). Pathologists should now diagnose and grade CNS tumours according to 2016 WHO classification criteria, as they represent the gold standard for assuring adequate glioma management for every patient. Evaluation of glioma for IDH, ATRX and H3

K27M mutations and for 1p/19q co-deletion has expanded the number of diagnostic categories.¹⁰

Radiologists play a crucial role in the correct diagnosis of gliomas. One of the main challenges in glioma imaging is developing imaging protocols which reflect best practice but also take into account differences between institutions in equipment, expertise levels and financial limitations. Harmonising protocols could serve as a means of quality assurance and support multicentre research into new treatments.¹⁹

In the diagnostic phase, as well as in the follow-up, Response Assessment in Neuro-Oncology (RANO) guidance is currently used in most institutions. New methods for quantifying physiological parameters, such as ADC (Apparent Diffusion Coefficient) and especially rCBV (relative Cerebral Blood Volume) need to be standardised as soon as possible.

Treatment and Outcomes

This ERQCC recommends the EANO guidelines on specific aspects of care and specific brain tumour types.⁷

The standard of care for a patient with a suspected glioma is surgery followed by radiotherapy and chemotherapy using protocols tailored to the specific diagnosis. At a minimum, a stereotactic or open biopsy should be obtained. However, maximal safe resection should be attempted if the patient is fit with a good performance status. If radical surgery is undertaken it is imperative that every effort is made to avoid new neurological deficits, which can reduce survival and affect quality of life.

Pre-operative imaging is a mainstay for safe and effective surgical resection. Eloquent cortical and subcortical areas can be mapped with several different imaging techniques (including functional MRI, magnetoencephalography, navigated transcranial magnetic stimulation and diffusion tensor imaging fibre tracking) with the aim of improving surgical accuracy and safety.

It is also important to recognise that around one third of patients with high grade glioma do not enhance on MRI²⁰ and that low-grade gliomas can behave as aggressive cancers. For example, grade II and III gliomas with isolated TERT mutations behave as grade IV lesions.²¹

Median overall survival for patients with newly diagnosed glioblastoma is only 12 to 18 months.^{22,23}

Prognostic factors include the patient's age and neurological/performance status, tumour extension or molecular factor and extent of surgical resection.¹⁵ Recent studies suggest gender may be a further prognostic factor.²⁴ Outcomes for low-grade glioma patients depends on a number of factors (such as whether the tumour histology is astrocytic or oligodendroglial, the extent of resection, tumour pre-operative size, patient age) and are highly variable, with a median survival of between two and over 15 years reported.²⁵

Gliomas are highly diverse in their demographic and clinical characteristics, which means that personalised disease treatments and support are essential.²⁶ Some hope lies in individualising treatment based on the specific molecular abnormalities of a particular tumour. This demands a standard of care for diagnosis, molecular characterisation, treatment and follow-up.

There is an urgent need to improve survival and reduce potential complications of treatments such as neurological deficits and cognitive impairment which sometimes occur after surgery and radiotherapy (with or without chemotherapy).

Improving quality of life is a crucial aspect of treatment, embracing functional and physical status, emotional and social well-being. The importance of quality of life to patients has been increasingly recognised, as has the fact that its improvement may in turn improve overall survival.²⁷

Psychosocial Factors

Glioma patients are a heterogeneous and complex population. Because gliomas and their treatment directly affect the brain, patients can face a unique psychosocial burden, with progressive cognitive, psychological, behavioural and physical impairments. These in turn can lead to significant impacts on quality of life, relationships, working ability and activities of daily living.

Up to 74% of primary brain tumour patients experience some form of distress throughout their disease trajectory, with depression and anxiety common.

As a result of these profound and often permanent changes, and the stigma that can accompany them, glioma patients tend to depend more on family caregivers than patients with other cancers. Patients and caregivers can underestimate the negative impacts of the brain tumour on relationships, emotional and cognitive functioning and ability to cope. Patients are not always aware of their prognosis.²⁸

High rates of distress and psychological and psychiatric disorders are specific and distinct in neuro-oncology patients compared to other oncology groupings.^{29,30} Up to 74% of primary brain tumour patients experience some form of distress throughout their disease trajectory,³¹ with depression and anxiety common.^{32,33} Prevalence of psychosocial morbidity varies greatly depending on the measurement method and glioma location. It should be noted that caregivers and family members of brain tumour patients also have high rates of distress and psychological challenges.³⁴

Emotional concerns tend to be a more common source of distress for patients with brain tumours than physical concerns. Even today, cancer patients can be unwilling to communicate distress because of fear of stigmatisation. A quarter of glioma patients and 34% of their relatives are critical of healthcare systems' ability to deal with cancer distress.²⁸

Palliative Care

Palliative care can be introduced in parallel to neuro-oncological treatment as a means of providing symptom relief and supportive and psychosocial care for the patient and family. General palliative care consists of the medical, physical, psychological, spiritual, and social interventions that can sustain patients' functions while maintaining an acceptable quality of life and ensuring a dignified death.³⁵ This should be offered by all healthcare professionals treating patients with glioma. In the case of complex needs, early and continuing collaboration with palliative care specialists is necessary.

When clinical signs are present, collaboration between neurosurgical and neuro-oncology specialists and palliative care providers may have a positive impact on patients. The end-of-life phase involves progressive neurological deterioration and psychological, social and affective concerns.³⁶ In this phase, caregivers and family members may be involved in medical decision-making as proxies for

the patient.³⁷

In the face of the profound emotional and relationship issues that progression can bring, palliative care may also help relieve the distress of caregivers and relatives.³⁵ In high-grade glioma it is known that levels of distress in family members are often higher than in patients themselves.³⁸

Inequalities

There are clear disparities in cancer treatment and outcomes throughout Europe,³⁹ but authoritative data on inequalities is hard to find. There are geographic variations on the availability of diagnostics⁴⁰ and access to molecular markers.⁴¹ The International Brain Tumour Alliance (IBTA) with other brain tumour patient organisations around the world has published a patients' rights charter, aimed at addressing such inequalities.⁴² Under the Europe's Beating Cancer Plan⁴³, the European Commission will establish a Cancer Inequalities Registry to identify trends, disparities and inequalities between member states and regions.

One approach to inequalities is creating special task forces and linking low income countries with higher income countries providing education and technical support. However, overall, we recommend that inequalities should be fully addressed in each country's national cancer plan.

Research

Neuro-oncology is a challenging field for clinical studies because:

- Brain tumours are rare, making it difficult to accrue sufficient numbers of patients unless trials are performed at European or international level.⁴⁴
- Measuring quality of life over time has proved complicated⁴⁵ as demonstrated in the European Organisation for Research and Treatment of Cancer (EORTC) quality of life studies.⁴⁶ The SISAQOL consortium's work (led by EORTC with representation from brain tumour clinicians and patient advocates) on standardising analysis of patient reported outcomes and quality of life data in randomised trials will help address this challenge.⁴⁷

Every effort should be made to inform patients about opportunities to participate in research and clinical trials.

Specialism

The need for specialisation in glioma is becoming increasingly obvious. With many glioma subtypes having been identified in the 2016 World Health Organization Classification of Tumors of the Central Nervous System¹⁰ and the discovery of new druggable targets, sophisticated treatment strategies are now important. This means that the availability of specialist, experienced and highly qualified personnel is becoming even more of a priority.

Organisation of Care

Essential requirements for the organisation of glioma care are:

- Fast access to accurate diagnosis and a second opinion if required
- Timely treatment at all stages following diagnosis or identification of a lesion
- Effective care and survivorship planning centred on a multidisciplinary approach
- Care pathways that cover the entire patient journey
- Care in specialised neurosurgical and neuro-oncology centres that treat glioma patients on a daily basis
- Continuing multidisciplinary team working
- High quality palliative care spanning the entire patient journey
- A patient-centred approach, with information provided and patient involvement in shared decision-making at every stage
- Referral to brain tumour patient/caregiver support, information and advocacy organisation

Care Pathways and Timelines

Care for all glioma patients needs to be organised around key “decision nodes”. These are:

- Multidisciplinary team meetings (ideally before first surgery)
- First surgery
- Adjuvant therapy (radiotherapy or/and chemotherapy)
- Follow-up (involving the patient, allied healthcare professionals and primary care/general practitioner)
- Points at which patients return to “normal” life (e.g. re-entering society or workplace)
- Recurrence and subsequent MDT meeting
- End of life care (involving patient, caregivers/proxies, allied healthcare professionals specialising in palliative care and general practitioner)

Given the progressive nature of high-grade gliomas (WHO grades III-IV), surgery is recommended as soon as possible⁴⁸ to avoid neurological decline and facilitate earlier oncological adjuvant chemoradiotherapy. A pre-operative surgical planning scan and consent for surgery should ideally take place immediately after an MDT discussion.

EANO guidelines do not specify a time window for surgery because this should be personalised.⁷ Early radical resection of low-grade gliomas has been shown to significantly improve patient outcomes by delaying time to malignant transformation.⁴⁹ Indeed, radical resection of a radiologically-presumed low-grade gliomas is more likely to detect foci of early malignant transformation which push the tumour into the high-grade glioma category.

Timing of radiotherapy after surgery is also important. In glioblastoma, any delay in radiotherapy beyond 48 days after surgery may be associated with worse overall survival.⁵⁰

Radiological follow-up with contrast-enhanced MRI should be performed every 2-3 months in high-grade neoplasms and every 4-6 months in low-grade, depending on the presence of enhancement in the residual tumour.

There is some evidence from American studies that health disparities affect overall survival of patients with glioblastoma – not just because some people do not have access to specialist units, but because they cannot get access to treatment quickly enough. This may be because of issues such as lack of insurance coverage and cultural and language barriers. It is essential that all glioma patients are able to receive equal treatment regardless of ethnicity, geographic location, socioeconomic and insurance status.⁵¹

Care Planning

All newly diagnosed gliomas, both low- and high-grade, should be referred to the weekly neuro-oncology MDT meeting and a management plan proposed.

The type of surgical procedure and management plan should be based on the meeting's consensus recommendation, pre-operative anatomical and functional imaging, assessment of the patient and consultation with the patient and relatives about

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their wishes.

Pre-operative tumour volume planning is facilitated by volumetric FLAIR imaging for low-grade gliomas and volumetric contrast-enhanced MRI for high-grade gliomas.⁵²

Post-operative care should include: monitoring for surgical complications: wound and seizure management; an MRI within 72 hours; a discharge plan for review with pathology report when available; home community support from local general practitioner and other professionals, and referral to brain tumour patient organisations which can provide additional support and information.

Units and Centres

Wherever possible, glioma patients should be managed from diagnosis onwards in specialised neurosurgical or neuro-oncology centres that treat glioma patients on a daily basis.

Ideally, specialist clinicians (especially neurosurgeons and oncologists) should have at least 50% of their clinical practice devoted to brain cancer patients. There is evidence that patient outcomes, based on mortality and morbidity statistics, are superior in higher volume centres and when performed by neurosurgeons who perform high-volume intracranial tumour surgery.⁵³

Population-based studies indicate that overall survival of glioblastoma patients correlates significantly with treatment in a high-volume referral centre. Median survival following treatment at these centres has been found to be 24.1 months,

compared to 15.9 months in low-volume centres.⁵⁴ The benefits apply even if patients have to travel long distances to receive treatment at high-volume centres. They have superior post-operative outcomes compared to patients who receive treatment locally at low-volume centres.⁵⁵

There is also evidence that patients with low-grade gliomas treated in academic neuro-oncology units, or as part of research programmes, have increased survival and generally more favourable post-surgical outcomes.⁵⁶

Psychosocial Planning

International standards of quality cancer care recommend the integration of psychosocial support into routine care.⁵⁷ This should include systematic psychosocial distress screening and provision of evidence-based psychosocial services. Recent standards specifically for the management of adult gliomas from NICE, EANO and Cancer Council Australia have followed this inclusive approach.⁵⁸⁻⁶⁰

Mandatory, systemic and routinely assessed psychosocial distress screening should be part of the multidisciplinary management of patients with brain and other CNS tumours. This screening helps evaluate and monitor extent, sources, and practical consequences of psychosocial distress, and also identifies the social support needs of patients and family caregivers throughout the illness trajectory. The National Comprehensive Cancer Network's Distress Thermometer is a reliable psychological distress screening tool especially for patients with intracranial tumours.⁶¹

Psycho-oncology capacity needs to be built into neuro-oncology settings, with psychosocial services delivered by fully trained psycho-oncology staff such as clinical psychologists, neuropsychologists, psychiatrists and social workers or social care professionals.⁵⁸ Ongoing psycho-oncology core training should be provided for all members of multidisciplinary teams who are involved in communication, counselling and psychosocial support of patients and family caregivers.^{28, 62}

Evidence-based psychoeducational, supportive, cognitive and/or vocational rehabilitation interventions appropriate for neuro-oncological patients and their caregivers must be offered systematically across the cancer continuum.^{63, 64} Structured multidisciplinary interventions, including cognitive-behavioural strategies, have been proved to be effective in maintaining and enhancing

quality of life and existential well-being of brain tumour patients.⁶⁵

The Multidisciplinary Team

It is generally accepted that care quality for all glioma patients will benefit from MDT discussion, although evidence of this in the literature is limited.⁶⁶ It has been reported that, when managed through a regular MDT in a planned elective setting, patients with a newly diagnosed glioma have improved outcomes and a better experience of care, with cost savings for healthcare providers.⁴⁸ It has also been reported that MDT consideration substantially modifies earlier treatment plans in 35% of cases.⁶⁷

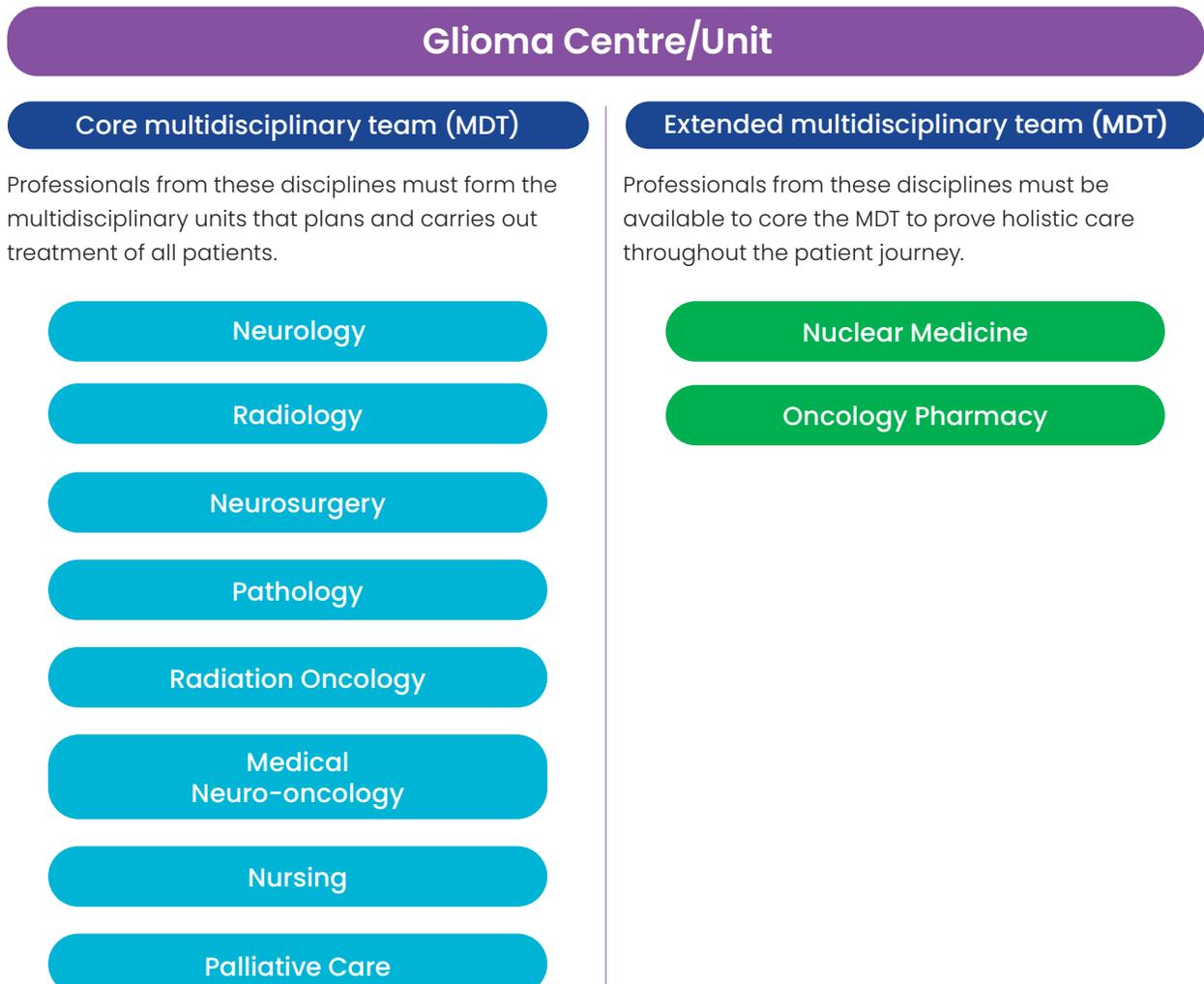
After initial treatment, the need for a multidisciplinary approach continues. In-depth interviews with patients who benefited from multidisciplinary clinics and brain scanning after radical radiotherapy ended revealed that they felt supported and reassured and that they appreciated individualised care with familiar staff.⁶⁸

We recommend that one member of the MDT should be designated a “key worker”, who creates a crucial link between the MDT and the patient. He or she should promote continuity of care by assessing patients’ needs, ensuring that care plans have been agreed with patients and making sure that assessments and care plans have been communicated to others involved in a patient’s care.⁵⁸

The dedicated members of the MDT currently vary significantly from unit to unit and country to country. This is partly a reflection of the human and financial resources available. So it has to be recognised that the “ideal” core team achievable in some settings is not realistic in others.

Below, in the core multidisciplinary team section, we describe the minimum skills requirement for a multidisciplinary team. In the recommended multidisciplinary team section, we list the skills that should be represented.

Figure 1. The Multidisciplinary Team for Glioma



Core multidisciplinary team members

The core multidisciplinary team should always include representation from: neurology, diagnostic radiology, neurosurgery, pathology, radiation oncology, medical oncology, nursing and palliative care. In some centres and in some countries, a neuro-oncologist – a neurologist who delivers antineoplastic drugs as well – may replace both neurologist and medical oncologist.

Note that in countries such as Germany where there are established specialisms in neurological radiology and neurological pathology (neuroradiology and neuropathology) these specialists should be represented on the core multidisciplinary team.

Neurology

The role of neurologists is to:

- Assess neurological symptoms and signs to be correlated with neuro-imaging findings (together with neurosurgeons)
- In cases of diagnostic uncertainty, perform specialised investigations such as a lumbar puncture for an examination of cerebrospinal fluid (when safe to do so)
- In conjunction with neurophysiology, perform and interpret neurophysiological examinations (electroencephalogram, evoked potentials, electromyography) when clinically needed
- Interpret neurocognitive tests when clinically needed
- Prescribe and monitor supportive medications, in particular antiepileptic drugs and steroids
- Monitor patients from a neurological point of view, during and after treatments, in cooperation with the other specialists involved

Neurologists might also be responsible for chemotherapy, targeted therapies and immunotherapy and are therefore often called neuro-oncologists.

Radiology

Radiology plays a major role in the diagnosis and follow-up of glioma and all patients with a clinical suspicion of brain neoplasm should undergo diagnostic imaging. The radiologist is responsible for the correct performance and interpretation of the diagnostic imaging, identifying the presence of a pathological lesion, describing its nature, location and anatomic relationships with the main structures.

After surgery, the radiologist must be able to identify the presence of any residual pathology differentiating it from normal post-surgical changes. During follow-up, the radiologist should be able to identify persistence or recurrence, using evidence-based guidelines to differentiate these from other conditions linked to therapy such as pseudo-progression and radiation necrosis. The use of standardised imaging protocols and standard response assessment criteria is essential for quality assurance and multicentre research into new treatments.¹⁹

Neurosurgery

Many glioma patients present acutely through emergency, stroke or less commonly acute neurology (for example a first fit clinic). However, entry to the specialist care pathway begins with neurosurgical intervention. This is because a diagnosis is essential in order for the plan of management to be tailored to the needs and performance status of the patient.

The role of the neurosurgeon is to:

- Provide tissue to establish histological/molecular diagnosis
- Achieve maximal safe resection when feasible

In some specialised centres, neurosurgeons can deliver locally therapeutic molecules such as gliadel wafers, immunotoxins and monoclonal antibodies – commonly within clinical trials.

Pathology

Pathologists play a key role in the MDT, providing timely diagnosis and prognostic/predictive assessment. Pathologists are needed for accurate diagnosis of gliomas given the large number of histotypes and the morphological overlap between low-grade and malignant cases. Pathologists also provide critical information about the molecular signature of gliomas that can help define the clinical management of these challenging patients. Since diagnosis drives treatment options, a dedicated and experienced pathologist must be in the core MDT from the start.

Radiation Oncology

Radiation oncologists play a central role in the staging and overall management of patients, helping define a personalised therapeutic strategy for each case.

They:

- Inform patients of the rationale of administering radiation and the evidence supporting it
- Include patients in clinical trials if patients qualify
- Discuss with patients the acute and long-term side effect of radiotherapy
- Simulate and plan the radiotherapy with the help of medical physicists, radiotherapists and dosimetrists
- Monitor the weekly performance of the patient and any side effects during radiotherapy
- Participate in the follow-up of patients treated with radiotherapy

Radiotherapy may be an option for palliation in patients with recurrent disease. Re-irradiation can be used in very selected cases of lower grade glioma or glioblastoma, especially when recurrence occurs a long time after the first line treatment and the dose delivered was sufficiently low to make a curative dose possible in the second treatment. Decision-making in such cases may be helped by using clinical prognostic scoring systems.⁶⁹

Medical Neuro-oncology

In European countries chemotherapy and targeted therapies are prescribed either by neurologists or medical oncologists or radiation oncologists for treatments concomitant with radiotherapy.

The role is to:

- Coordinate all aspects of multimodal drug treatment (chemotherapy, targeted therapies and immunotherapies) and monitor and treat adverse events
- Cooperate with other specialists in the management of neurological symptoms and monitor response to treatments
- Directly interact and share decision-making with glioma patients and their families about treatment options

Nursing

Glioma stands out from other cancers because of its impact on personality, autonomy and independence. It requires a specific type of care with multidimensional skills – relational, scientific and technical. Therefore, all patients affected by glioma should be assessed and supported by

a specialist cancer nurse, trained specifically in neuro-oncologic practices.

The unpredictability of symptoms means that it is fundamentally important to patients that nurses support them and act as case managers or key workers who can support patients with the challenges of, for example, fatigue, depression and fear.⁷¹ A neuro-oncology clinical nurse specialist, conversant with the wide-ranging effects of a brain tumour and its therapies, will aim to support and empower.

The value of cancer nurses, and their role as core members of the multidisciplinary team, needs greater recognition across Europe. This is being highlighted by the European Oncology Nursing Society (EONS) and supported by the European Cancer Organisation in their Recognising European Cancer Nursing (RECaN) project.

Palliative care

The involvement of palliative care specialists is very important for multidimensional management of care provision for patients with glioma. Decision-making should be shared with the patient and all specialists providing medical, physical, psychological, spiritual and social interventions to help the patient function while maintaining an acceptable quality of life and ensuring a dignified death.³⁵

The patient should be helped to set reasonable health and life goals, according to both functional and survival disease prognosis. EANO publishes guidelines for palliative care in adults with glioma, which this ERQCC recommends.⁷²

Recommended multidisciplinary team members

Nuclear Medicine

Current nuclear medicine techniques in glioma are based on PET/CT or PET/MRI scanning. PET with amino acid radiotracers such as [11C]MET, [18F]FET or [18F]FDOPA is superior to 2-[18F]FDG.^{73,74}

The role of the nuclear medicine physician is to oversee all aspects of PET scanning for patients who require this procedure, including indications, multidisciplinary algorithms and management protocols.

Clinical situations where PET scanning may have an impact on management are:

- Biopsy target planning, improving the probability of successfully extracting diagnostic tissue
- Differentiating between glioma recurrence and treatment-related changes in patients with equivocal MRI
- Response assessment in patients with equivocal MRI – for example, with non-contrast enhancing progression or during anti-angiogenic therapy
- Early prognostic evaluation

Oncology Pharmacy

The role of the oncology pharmacist as part of the extended MDT is to:

- Liaise with the medical oncologist and other members of the healthcare team to discuss cancer-specific pharmacotherapy, including interactions with concomitant treatments
- Contribute to assure efficacious, safe and cost-effective treatment
- Supervise the preparation and (if appropriate) dispensing of oncology drugs

In many cases, allied health professionals such as physiotherapists and speech and language therapists should also be represented on the MDT..

Essential Requirements in MDT Members

Neurology

The neurologist must have expertise in:

- Diagnosis of brain tumours, including in differential diagnosis between neoplastic and non-neoplastic lesions
- Interpreting cerebrospinal fluid findings, neurocognitive and neurophysiological tests
- Clinical and radiological monitoring and follow-up
- Antiepileptic drugs and steroids

Radiology

The radiologist must:

- Have expertise in neuroradiology
- Collaborate with the neurosurgeon, neurologist,

oncologist and radiotherapist and be aware of all information available during the therapeutic process

- Have access to MRI – the preferred method of diagnosis of gliomas
- Perform post-surgery follow-up by means of MRI within 72 hours of surgery to rule out post-surgical pitfalls
- Perform MRI later based on pathologic data, at specific time intervals, using clinical field strength units ($\geq 1.5T$), conventional imaging (T2w, volumetric T2w-FLAIR and T1w before and after administration of a gadolinium-based contrast agent) and advanced imaging (diffusion and perfusion weighted imaging)^{75, 76}
- Attempt to distinguish pseudo-progression and radiation necrosis from recurrence using conventional as well as advanced MR imaging (perfusion/spectroscopy)
- Help decide when to refer a patient to nuclear medicine (PET with amino acid radiotracers) in case of equivocal results.

Essential equipment requirements for MRI include clinical field strength units ($\geq 1.5T$), conventional imaging (T2w, volumetric T2w-FLAIR and T1w before and after administration of a gadolinium-based contrast agent) and advanced imaging (diffusion, perfusion).^{75, 76}

In selected cases, MR spectroscopy, susceptibility weighted and functional imaging with MRI (blood oxygen level dependent and tractography) is acquired for further diagnostic information and for surgical planning. However, these advanced imaging techniques cannot be considered essential.

Neurosurgery

Neurosurgeons must:

- Be dedicated to oncological neurosurgery in at least 50% of their practice
- Have access to an operating microscope to improve tumour visualisation
- Have access to high-dependency and intensive care facilities with specialist nursing and anaesthetic staff for peri-operative care when necessary
- Engage in regular audits of patient outcomes to facilitate improvements in service provision

- Be part of a multidisciplinary clinical team

They should:

- Have access to intra-operative electrophysiological mapping and monitoring of essential neurological function in order to minimise neurological deficits and enhance the extent of resection
- Have access to intra-operative image guidance such as navigation, ultrasound or intra-operative MRI⁷⁷
- Have access to 5-aminolevulinic acid (5-ALA) as an adjunct to maximise resection of suspected high-grade gliomas
- Have access to cavitating ultrasonic surgical aspirating devices to facilitate tumour removal with minimal collateral damage to neighbouring blood vessels and brain parenchyma
- Conduct follow-up examinations of patients, preferably throughout the course of the disease

Pathology

Pathologists must:

- Be aware of the type of tissue specimens and biopsies performed on gliomas and have access to clinical records, including patient history, neuroimaging and any prior or ongoing treatment⁷⁸
- Have expertise in reporting on gliomas, in order to establish a correct diagnosis, according to the specific tumour entities included in the WHO classification of CNS tumours⁷⁹
- Supply an integrated diagnosis that incorporates both tumour phenotype and molecular information according to the integrated diagnostic approach introduced by the 2016 WHO classification of CNS tumours¹⁰
- Apply national or (preferably) international evidence-based diagnostic algorithms on integration of molecular biomarkers such as that proposed by the European Organisation for Research and Treatment of Cancer (EORTC).⁸⁰ This integrated approach takes into account histopathologic and molecular differences between adult and pediatric gliomas⁸¹ and is subjected to a periodical update process⁸²
- Have access to an accredited laboratory for molecular testing, not necessarily on site⁸³
- Set aside and preserve material for molecular

testing according to guidelines⁸⁴

- Actively engage in quality control, harmonisation of standards and inter-laboratory comparisons by means of ring trials⁸⁵
- Provide a second opinion for patients with complex lesions⁷⁸

Radiation oncology

Patients who need to be irradiated for gliomas should have access to up to date radiotherapy equipment and radiation oncologists experienced in preparation, planning and administration of precision radiotherapy and stereotactic radiotherapy and radiosurgery.

Radiation oncologists must:

- Have expertise in all brain tumour types
- Participate in a multidisciplinary brain tumour/ neuro-oncology working group
- Work in close collaboration with board-certified radiologists for the delineation during the radiotherapy planning process
- Work in close collaboration with a board-certified neurosurgeon for the delineation during the radiosurgery planning process

Radiation oncologists should have access to:

- Intensity-modulated radiotherapy (IMRT) or volumetric arc therapy (VMAT), stereotactic fractionated radiotherapy (FSRT) and stereotactic radiosurgery (SRS)
- The basic bio-molecular analyses which contributes to the proper selection of patients for treatment

Radiation oncologists should participate in recruiting patients to prospective trials within the framework of institutional/national and/or international brain tumour studies.

The radiotherapy department should:

- Ensure that technical equipment in the radiotherapy department complies to the national regulation and guidelines and international advice (IAEA, AAPM)
- Implement protocol and quality assurance, for radiotherapy in general and for patient-specific care

- Implement daily online setup verification before the delivery of IMRT/FSRT or SRS
- Make available to radiotherapy department collaborators standard operating procedures for tumour delineation policies according to tumour types, target definitions (gross tumour volume, clinical target volume and planning target volumes with margins) and repositioning policy

Medical neuro-oncology

Medical oncologists or neuro-oncologists treating gliomas must:

- Have qualification and expertise in the medical treatment of gliomas and the management of side effects
- Have expertise in prescribing antineoplastic drugs, in particular for management of toxicity
- Have in-depth understanding of the prognostic and predictive value of clinical and molecular factors that are significant for deciding treatment indications
- Have expertise in managing neurological symptoms and preferably ability to understand neuroimaging findings
- Know the status of IDH 1-2 mutations, 1p/19q codeletion and MGMT methylation (especially for elderly patients with high-grade gliomas) before starting any treatment
- Participate in recruiting patients to clinical trials investigating novel systemic therapies

They should have access to:

- A central pharmacy for preparation of systemic/local treatments
- A dedicated outpatient service and clinical nurse specialists in neuro-oncology
- Fertility preservation facilities
- A neuro-psychologist for testing cognitive functions
- Radiologists, neurosurgeons and radiation oncologists locally, or within a regional network, in case of recurrence
- Molecular markers of prognostic/predictive value before starting treatments (such as IDH 1-2 mutations, 1p/19q codeletion, MGMT methylation, EGFR amplification), locally or within a regional network

- Centres of excellence, for patient access to clinical trials

Nursing

Specialist nurses must:

- Coordinate a personalised treatment and support plan, establishing a trustful relationship with the patient/family
- Ensure the plan incorporates the patient's physical, psychological, social, cultural, and spiritual needs, so they can provide the right support tailored to each patient and their family/caregiver
- Evaluate the safety of both patients and care providers at all stages of care
- Manage the symptoms of glioma and prevent or manage the side-effects of treatments, taking into account daily-life activities
- Enable flawless changeovers between different healthcare services (including primary care and rehabilitation), from active treatment through to survivorship and/or palliative and end of life, ensuring continuous and effective care

Palliative care

- Every healthcare professional involved in the care of patients with glioma should be able to:
 - Provide basic palliative care such as symptom management, communication and psychosocial support to patients and family
 - Provide end of life care
 - Detect patients with more complex needs who may benefit from specialised palliative care
- There should be close cooperation between these healthcare professionals and specialised palliative care teams
- In complex cases, early involvement of specialised palliative care is essential
- Specialised palliative care teams should be able to provide multidimensional support involving physicians, nurses and at least one supporting profession such as psychology, social work, physiotherapy, spiritual carer
- Palliative care teams should have glioma-specific expertise and experience

- Palliative care teams should foster and sustain regional networks of palliative care and hospice services.

Nuclear medicine

- A PET/CT or PET/MRI scanner must be available and PET imaging managed by nuclear medicine physicians with the appropriate expertise
- Nuclear medicine must be able to perform daily verification protocols and to react accordingly
- Quality-assurance protocols must be in place. An option for ensuring the high quality of PET/CT scanners is provided by the European Association of Nuclear medicine (EANM) through EARL (EANM Research Ltd) accreditation.

Oncology pharmacy

Oncology pharmacists must:

- Work closely with medical oncologists and other members of the core and the expanded MDT
- Have experience with antineoplastic treatments and supportive care
- Be experienced in applying specialised knowledge of the clinical use of medications (indication, dosing and adverse effects), the special requirements for oral chemotherapies and the adequate utilisation and monitoring of pharmacotherapy, patient counselling and pharmacovigilance

- Have knowledge about conditions influencing liberation, absorption, distribution, metabolism and excretion of drugs used for treatment
- Have knowledge of complementary and alternative medicines and how they might interfere with treatment
- Be able to manage interactions between the patient's pharmacotherapy and other drugs (for example, anti-seizure medicines and corticosteroids), radiation, food, and other diseases
- Be able to calculate dose adjustments based on a patient's physiological status (including age, liver and kidney function, pharmacogenetics or concurrent radiotherapy)
- Comply with the European Society of Oncology Pharmacy's QuapoS guidelines⁸⁶

Oncology drugs must be prepared in the pharmacy and dispensing must take place under the supervision of the oncology pharmacist.

Other Essential Requirements

Patient Involvement

Brain tumour patients and their families should be actively involved in all facets (and at all stages) of the decision-making process regarding their treatment and care. This involvement should not be tokenistic but should embrace meaningful patient input and shared decision-making at every stage. This involves healthcare professionals providing relevant, easily understood and reliable information and allowing time for detailed discussion and questions.

Because of the neurological deficits which can occur as a result of a brain tumour and its treatment, caregivers also play a crucial role in the lives of these patients and they too must be supported and encouraged to fully interact with healthcare teams.

Contact with Patient Organisations

Healthcare professionals should refer patients to brain tumour advocacy, support and information organisations from diagnosis. Patient advocacy organisations can support glioma patients and their families by:

- Providing information about glioma in lay language, and in the patient's mother tongue
- Helping patients and their families understand the treatment options available to them
- Providing support groups, either face-to-face, in hospital, online or via the telephone

Brain tumour patient organisations also:

- Campaign for better outcomes for brain tumour patients through health policy work
- Involve patients and their representatives in research projects, ethical committees, regulatory work and health technology assessment
- Help patients and families understand their rights
- Raise awareness of the challenges of brain tumours
- Support brain tumour research and advocate for improvements in trial design

- Help patients access information about clinical studies relevant to them
- Campaign for access to molecular testing
- Support the use of patient reported outcomes (PROs) to assess therapy benefit
- Contribute to clinical guidelines
- Work with international initiatives such as EURACAN (<http://euracan.ern-net.eu>) to improve outcomes for adult patients with rare solid tumours

The International Brain Tumour Alliance (IBTA) maintains an online list of brain tumour-relevant patient organisations around the world and encourages the establishment of new groups, in the hope that patient organisation services may be universally available to patients and families as part of the essential requirements for quality cancer care. Information can be accessed at <https://theibta.org>

Quality and Audit Measures

Pathology reporting

Pathology reporting is critical. A quality score incorporating critical parameters for clinical decision making – for example, type and grade of tumour, up-to-date classification, absence of equivocal language – should be introduced and adopted by national and international committees. Recently an audit conducted by Australian pathologists found that report quality was higher when pathologists subspecialised in neuropathology⁸⁷ and that only 24% of reports fulfilled all quality criteria.

A survey of members of the European Confederation of Neuropathological Societies⁴¹ found that neuropathologists uniformly rate molecular marker testing as highly relevant and already incorporate molecular information in their diagnostic assessments. However, there are substantial variations in access to crucial biomarkers and molecular techniques across geographic regions and within individual countries.

A recent international survey⁸⁸ on laboratory analyses for glioma flags up concerns regarding the validity of molecular test assays and finds that most respondents favour development of

international consensus guidelines.

Performance and quality

The ERQCC expert group recommends that centres develop:

- Performance measurement and quality indicators based on the essential requirements in this paper
- Operational policies to ensure coordinated clinical pathways based on published guidelines
- Accountability within the governance processes
- Systems to ensure safe and high-quality patient care and experience
- Effective data management and reporting systems
- Meaningful engagement with patients, caregivers and support groups to ensure reporting of patient outcomes and experience
- Involvement in national or international glioma studies

Three categories of outcomes should be measured and collected in databases:

- Clinical outcomes
- Process outcomes
- Patient-reported outcomes (PROs)

These approaches can be developed in the context of quality management systems (QMS) depending on the health economy of an individual country.

Outcomes audit

Data measured and collected varies among countries but it is recommended that these outcome metrics are measured and collected for audit:

- % of preoperative patients discussed in the MDT
- % of postoperative patients discussed in the MDT
- Proportion of patients according to clinical stage at time of diagnosis
- Proportion of patients receiving treatment with radical and palliative intent
- Complications
- 30 day mortality

- 30 day readmission
- 1 and 5 year overall survival rate

Multidisciplinary team performance

All MDT decisions should be documented and become part of patient records. All relevant patient data should meet quality standards and be available at the time of the MDT meeting.

MDT performance must be quality assured both internally and by external review, and MDT guidance must be promoted nationally and written into national cancer plans.

Further attention must be given to using PROs more systematically as part of discussions and evaluation within the MDT. The SISAQOL consortium, headed by the EORTC, is standardising the analysis of patient reported outcomes and quality of life endpoints data in cancer clinical trials.⁴⁷

Accreditation

The ERQCC expert group strongly recommends participation in national or international accreditation programmes such as those run by the Organisation of European Cancer Institutes (OECI) and European Cancer Centres.

ESMO's Designated Centres of Integrated Oncology and Palliative Care accreditation programme bestows special recognition for effectively integrating medical oncology and palliative care.⁸⁹

Education and Training

There are many teaching courses on glioma provided by national and international cancer societies, some specialising in neuro-oncology or neurosurgery.

The European Society of Medical Oncology (ESMO), the European School of Oncology (ESO) and Rare Cancers Europe (RCE) jointly run an annual clinical update course on rare adult solid cancers with a section on brain tumours. It runs alongside a course for rare cancer patient advocates.⁹⁰

The European Confederation of Neuropathological Societies (Euro-CNS) runs regular scientific and clinical courses to support European neuropathologists and the European Association of Neuro-Oncology (EANO) holds meetings and courses for all medical and scientific disciplines involved in the prevention, diagnosis and treatment of tumours of the CNS.

Registries and Research

Studying relatively rare diseases such as glioma is a significant scientific challenge. Traditionally, researchers use population- or hospital-based tumour registries to identify the large numbers of people required for studies. However, each registry will only include a small number of potential study subjects with glioma, making studies costly and labour intensive.

Across Europe, there are scattered CNS and brain tumour registries, both national and regional. For example, there are brain tumour registries in Austria and the UK, and there are CNS tumour registries in

the French department of Gironde and the Italian region of Piedmont. The International Low Grade Glioma (LGG) Registry allows for focused study of LGG, including quality of life.⁹¹ In 2018 it reported enrolment of 234 patients from nine countries (US, France, United Kingdom, Canada, Australia, Hong Kong, New Zealand, Belarus and Spain).⁹² Such initiatives should be supported and widened. It is important that brain tumour registries include registration of lower grade gliomas, not only glioblastomas.

Conclusions

Taken together, these recommendations compiled by an expert group constitute essential requirements for establishing a high-quality service for glioma. Recognising that services and capacity vary from country to country, the expert group has focused on defining realistic requirements within the reach of all. To meet European aspirations for comprehensive cancer control, national and local policy makers in healthcare across Europe must consider the requirements in this paper,

paying particular attention to multidisciplinary and patient-centred pathways from diagnosis, to treatment and survivorship. These requirements, alongside other Essential Requirements for Quality Cancer Care, should be reference points for Europe-wide initiatives to improve the quality of cancer care, such as Europe's Beating Cancer Plan and the EU Mission on Cancer. Together, they provide a vision of good practice and what the organisation of cancer care should be calibrated to achieve.

References

1. Højgaard L, Löwenberg B, Selby P, et al. The European Cancer Patient's Bill of Rights, update and implementation 2016. *ESMO Open*. 2017;1(6):e000127. Published 2017 Jan 6. doi:10.1136/esmoopen-2016-000127
2. Albrecht T, Kiasuma R, Van den Bulcke M. Cancon Guide – Improving cancer control coordination 2017. <https://cancercontrol.eu/archived/cancercontrol.eu/guide-landing-page/index.html>
3. Prades J, Remue E, van Hoof E, Borrás JM. Is it worth reorganising cancer services on the basis of multidisciplinary teams (MDTs)? A systematic review of the objectives and organisation of MDTs and their impact on patient outcomes. *Health Policy*. 2015;119(4):464-474. doi:10.1016/j.healthpol.2014.09.006
4. European Partnership Action Against Cancer consensus group, Borrás JM, Albrecht T, et al. Policy statement on multidisciplinary cancer care. *Eur J Cancer*. 2014;50(3):475-480. doi:10.1016/j.ejca.2013.11.012
5. Find a Brain Tumor Center, American Brain Tumour Association https://www.abta.org/about-brain-tumors/treatments-sideeffects/find-a-brain-tumor-center?_sft_treatment_center_category=nci-designated-comprehensive-cancer-centers-with-designated-brain-tumor-programs
6. Oliver K. Rare cancers: the landscape is changing. *Expert Opinion on Orphan Drugs*. 2018; 6: 509-511 <https://www.tandfonline.com/doi/pdf/10.1080/21678707.2018.1504676>
7. EANO guidelines. European Association of Neuro-Oncology. <https://www.eano.eu/publications/eano-guidelines/>
8. GBD 2016 Brain and Other CNS Cancer Collaborators. Global, regional, and national burden of brain and other CNS cancer, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2019;18(4):376-393. doi:10.1016/S1474-4422(18)30468-X
9. Goodenberger ML, Jenkins RB. Genetics of adult glioma. *Cancer Genet*. 2012 Dec;205(12):613-21. doi: 10.1016/j.cancergen.2012.10.009. Epub 2012 Dec 11. PMID: 23238284.
10. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131(6):803-820. doi:10.1007/s00401-016-1545-1
11. Louis DN, Wesseling P, Aldape K, et al. cIMPACT-NOW update 6: new entity and diagnostic principle recommendations of the cIMPACT-Utrecht meeting on future CNS tumor classification and grading. *Brain Pathol*. 2020;30(4):844-856. doi:10.1111/bpa.12832
12. Cimino PJ, Zager M, McFerrin L, et al. Multidimensional scaling of diffuse gliomas: application to the 2016 World Health Organization classification system with prognostically relevant molecular subtype discovery. *Acta Neuropathologica Communications*. 2017 May;5(1):39. doi: 10.1186/s40478-017-0443-7.
13. Le Rhun E, Preusser M, Roth P, et al. Molecular targeted therapy of glioblastoma. *Cancer Treat Rev*. 2019;80:101896. doi:10.1016/j.ctrv.2019.101896
14. Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005-2009 [published correction appears in *Neuro Oncol*. 2013 May;15(5):646-7]. *Neuro Oncol*. 2012;14 Suppl 5(Suppl 5):vi-v49. doi:10.1093/neuonc/nos218
15. Ostrom QT, Gittleman H, Stetson L, Virk SM, Barnholtz-Sloan JS. Epidemiology of gliomas. *Cancer Treat Res*. 2015;163:1-14. doi:10.1007/978-3-319-12048-5_1
16. Butowski NA. Epidemiology and diagnosis of brain tumors. *Continuum (Minneapolis, Minn)*. 2015;21(2 Neuro-oncology):301-313. doi:10.1212/01.CON.0000464171.50638.f0
17. Deltour I, Auvinen A, Feychting M, et al. Mobile phone use and incidence of glioma in the Nordic countries 1979-2008: consistency check. *Epidemiology*. 2012;23(2):301-307. doi:10.1097/EDE.0b013e3182448295
18. Rare Disease Database. National Organization for Rare Disorders. <https://rarediseases.org/rare-diseases/glioblastoma-multiforme/>
19. Thust SC, Heiland S, Falini A, et al. Glioma imaging in Europe: A survey of 220 centres and recommendations for best clinical practice. *Eur Radiol*. 2018;28(8):3306-3317. doi:10.1007/s00330-018-5314-5
20. Lasocki A, Gaillard F. Non-Contrast-Enhancing Tumor: A New Frontier in Glioblastoma Research. *AJNR Am J Neuroradiol*. 2019;40(5):758-765. doi:10.3174/ajnr.A6025
21. Eckel-Passow JE, Lachance DH, Molinaro AM, et al. Glioma Groups Based on 1p/19q, IDH, and TERT Promoter Mutations in Tumors. *N Engl J Med*. 2015;372(26):2499-2508. doi:10.1056/NEJMo1407279
22. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant

- temozolomide for glioblastoma. *N Engl J Med*. 2005;352(10):987-996. doi:10.1056/NEJMoa043330
23. Wen PY, Kesari S. Malignant gliomas in adults [published correction appears in *N Engl J Med*. 2008 Aug 21;359(8):877]. *N Engl J Med*. 2008;359(5):492-507. doi:10.1056/NEJMra0708126
 24. Franceschi E, Tosoni A, Minichillo S, et al. The Prognostic Roles of Gender and O6-Methylguanine-DNA Methyltransferase Methylation Status in Glioblastoma Patients: The Female Power. *World Neurosurg*. 2018;112:e342-e347. doi:10.1016/j.wneu.2018.01.045
 25. Hottinger AF, Hegi ME, Baumert BG. Current management of low-grade gliomas. *Curr Opin Neurol*. 2016;29(6):782-788. doi:10.1097/WCO.0000000000000390
 26. Rasmussen BK, Hansen S, Laursen RJ, et al. Epidemiology of glioma: clinical characteristics, symptoms, and predictors of glioma patients grade I-IV in the the Danish Neuro-Oncology Registry. *J Neurooncol*. 2017;135(3):571-579. doi:10.1007/s11060-017-2607-5
 27. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010; 363: 733-42
 28. Davies E, Higginson IJ. Communication, information and support for adults with malignant cerebral glioma : a systematic literature review. *Support Care Cancer*. 2003;11(1):21-29. doi:10.1007/s00520-002-0392-x
 29. Chambers SK, Grassi L, Hyde MK, Holland J, Dunn J. Integrating psychosocial care into neuro-oncology: challenges and strategies. *Front Oncol*. 2015;5:41. Published 2015 Feb 23. doi:10.3389/fonc.2015.00041
 30. Pace A, Villani V, Parisi C, et al. Rehabilitation pathways in adult brain tumor patients in the first 12 months of disease. A retrospective analysis of services utilization in 719 patients. *Support Care Cancer*. 2016; 24: 4801-4806. <https://doi.org/10.1007/s00520-016-3333-9>
 31. Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. *Psychooncology*. 2001;10(1):19-28. doi:10.1002/1099-1611(200101/02)10:1<19::aid-pon501>3.0.co;2-6
 32. Bao Y, Li L, Guan Y, et al. Prevalence and associated positive psychological variables of anxiety and depression among patients with central nervous system tumors in China: a cross-sectional study. *Psychooncology*. 2017;26(2):262-269. doi:10.1002/pon.4128
 33. Goebel S, Stark A, Kaup L, Von Harscher M, Mehdorn H. Distress in patients with newly diagnosed brain tumours. *Psychooncology* 2011a; 20(6), 623-630
 34. Applebaum AJ, Kryza-Lacombe M, Buthorn J, DeRosa A, Corner G, Diamond EL. Existential distress among caregivers of patients with brain tumors: a review of the literature. *Neurooncol Pract*. 2016;3(4):232-244. doi:10.1093/nop/npv060
 35. Giammalva GR, Iacopino DG, Azzarello G, et al. End-of-Life Care in High-Grade Glioma Patients. The Palliative and Supportive Perspective. *Brain Sci*. 2018;8(7):125. Published 2018 Jun 30. doi:10.3390/brainsci8070125
 36. Ostgathe C, Gaertner J, Kotterba M, et al. Differential palliative care issues in patients with primary and secondary brain tumours. *Support Care Cancer*. 2010;18(9):1157-1163. doi:10.1007/s00520-009-0735-y
 37. Pace A, Koekkoek JAF, van den Bent MJ, et al. Determining medical decision-making capacity in brain tumor patients: why and how?. *Neurooncol Pract*. 2020;7(6):599-612. Published 2020 Jul 16. doi:10.1093/nop/npaa040
 38. Seekatz B, Lukaszczik M, Löhr M, et al. Screening for symptom burden and supportive needs of patients with glioblastoma and brain metastases and their caregivers in relation to their use of specialized palliative care. *Support Care Cancer*. 2017;25(9):2761-2770. doi:10.1007/s00520-017-3687-7
 39. Challenging the Europe of Disparities in Cancer. European Cancer Patient Coalition. 2019. <https://ecpc.org/wp-content/uploads/2019/08/ECPC-White-Paper-Europe-of-disparities-EN-3.pdf>
 40. Andreiuolo F, Mazeraud A, Chrétien F, Pietsch T. A Global View on the Availability of Methods and Information in the Neuropathological Diagnostics of CNS Tumors: Results of an International Survey Among Neuropathological Units [published correction appears in *Brain Pathol*. 2017 Jan;27(1):120]. *Brain Pathol*. 2016;26(4):551-554. doi:10.1111/bpa.12383
 41. Woehrer A, Kristensen BW, Vital A, Hainfellner JA. Patterns of diagnostic marker assessment in adult diffuse glioma: a survey of the European Confederation of Neuropathological Societies (Euro-CNS). *Clin Neuropathol*. 2017;36 (2017)(1):5-14. doi:10.5414/NP301009
 42. The Brain Tumour Patients' Charter of Rights. International Brain Tumour Alliance. <https://theibta.org/charter>
 43. Europe's Beating Cancer Plan. The European Commission. 2021. https://ec.europa.eu/health/sites/health/files/non_communicable_diseases/docs/eu_cancer-plan_en.pdf

44. Lee EQ, Chukwueke UN, Hervey-Jumper SL, et al. Barriers to accrual and enrollment in brain tumor trials. *Neuro Oncol.* 2019;21(9):1100-1117. doi:10.1093/neuonc/noz104
45. van Leeuwen M, Husson O, Alberti P, et al. Understanding the quality of life (QOL) issues in survivors of cancer: towards the development of an EORTC QOL cancer survivorship questionnaire. *Health Qual Life Outcomes.* 2018;16(1):114. Published 2018 Jun 4. doi:10.1186/s12955-018-0920-0
46. Reijneveld JC, Taphoorn MJB, Coens C, et al. Health-related quality of life in patients with high-risk low-grade glioma (EORTC 22033-26033): a randomised, open-label, phase 3 intergroup study. *Lancet Oncol.* 2016;17(11):1533-1542. doi:10.1016/S1470-2045(16)30305-9
47. Coens C, Pe M, Dueck AC, et al. International standards for the analysis of quality-of-life and patient-reported outcome endpoints in cancer randomised controlled trials: recommendations of the SISAQOL Consortium. *Lancet Oncol.* 2020;21(2):e83-e96. doi:10.1016/S1470-2045(19)30790-9
48. Guilfoyle MR, Weerakkody RA, Oswal A, et al. Implementation of neuro-oncology service reconfiguration in accordance with NICE guidance provides enhanced clinical care for patients with glioblastoma multiforme. *Br J Cancer.* 2011;104(12):1810-1815. doi:10.1038/bjc.2011.153
49. Jakola AS, Myrmet KS, Kloster R, et al. Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. *JAMA.* 2012;308(18):1881-1888. doi:10.1001/jama.2012.12807
50. Katsigiannis S, Krischek B, Barleanu S et al. Impact of time to initiation of radiotherapy on survival after resection of newly diagnosed glioblastoma. *Radiat Oncol.* 2019; 14,73
51. Mandel JJ, Youssef M, Nam J, et al. Effect of health disparities on overall survival of patients with glioblastoma. *J Neurooncol.* 2019;142(2):365-374. doi:10.1007/s11060-019-03108-z
52. Rahman M, Abbatematteo J, De Leo EK, et al. The effects of new or worsened postoperative neurological deficits on survival of patients with glioblastoma. *J Neurosurg.* 2017;127(1):123-131. doi:10.3171/2016.7.JNS16396
53. Chernov MF. The impact of provider volume on mortality after intracranial tumor resection and outcome and cost of craniotomy performed to treat tumors in regional academic referral centers. *Neurosurgery.* 2004;54(4):1027-1028. doi:10.1227/01.neu.0000117120.32806.22
54. Brandes AA, Franceschi E, Ermani M, et al. Pattern of care and effectiveness of treatment for glioblastoma patients in the real world: Results from a prospective population-based registry. Could survival differ in a high-volume center?. *Neurooncol Pract.* 2014;1(4):166-171. doi:10.1093/nop/npu021
55. Lopez Ramos C, Brandel MG, Steinberg JA, et al. The impact of traveling distance and hospital volume on post-surgical outcomes for patients with glioblastoma. *J Neurooncol.* 2019;141(1):159-166. doi:10.1007/s11060-018-03022-w
56. Mahato D, De Biase G, Ruiz-Garcia HJ, et al. Impact of facility type and volume on post-surgical outcomes following diagnosis of WHO grade II glioma. *J. Clin. Neurosci.* 2018 Dec;58:34-41. doi: 10.1016/j.jocn.2018.10.078
57. Holland J, Watson M, Dunn J. The IPOS new International Standard of Quality Cancer Care: integrating the psychosocial domain into routine care. *Psychooncology.* 2011;20(7):677-680. doi:10.1002/pon.1978
58. Service guidance for improving outcomes for people with brain and other central nervous system tumours. National Institute for Health and Care Excellence. 2006. <http://www.nice.org.uk/csgbraincns>
59. Weller M, van den Bent M, Hopkins K, et al. EANO guideline for the diagnosis and treatment of anaplastic gliomas and glioblastoma [published correction appears in *Lancet Oncol.* 2014 Dec;15(13):e587]. *Lancet Oncol.* 2014;15(9):e395-e403. doi:10.1016/S1470-2045(14)70011-7
60. Clinical Practice Guidelines for the management of adult gliomas: astrocytomas and oligodendrogliomas. Cancer Council Australia/Australian Cancer Network/Clinical Oncological Society of Australia.
61. Goebel S, Mehdorn HM. Measurement of psychological distress in patients with intracranial tumours: the NCCN distress thermometer. *J Neurooncol.* 2011;104(1):357-364. doi:10.1007/s11060-010-0501-5
62. Davies E, Hopkins A. Good practice in the management of adults with malignant cerebral glioma: clinical guidelines. Working Group, Royal College of Physicians. *Br J Neurosurg.* 1997;11(4):318-330. doi:10.1080/02688699746104
63. Rummans TA, Clark MM, Sloan JA, et al. Impacting quality of life for patients with advanced cancer with a structured multidisciplinary intervention: a randomized controlled trial. *J Clin Oncol.* 2006;24(4):635-642. doi:10.1200/JCO.2006.06.209
64. Rusbridge SL, Walmsley NC, Griffiths SB, Wilford PA, Rees JH. Predicting outcomes of vocational rehabilitation in patients with brain tumours. *Psychooncology.* 2013;22(8):1907-1911. doi:10.1002/pon.3241
65. Kangas M. Psychotherapy Interventions for Managing Anxiety and Depressive Symptoms in Adult Brain Tumor Patients: A Scoping Review. *Front Oncol.* 2015;5:116. Published 2015 May 21. doi:10.3389/fonc.2015.00116

66. Croke JM, El-Sayed S. Multidisciplinary management of cancer patients: chasing a shadow or real value? An overview of the literature. *Curr Oncol*. 2012;19(4):e232–e238. doi:10.3747/co.19.944
67. Ameratunga M, Miller D, Ng W, et al. A single-institution prospective evaluation of a neuro-oncology multidisciplinary team meeting. *J Clin Neurosci*. 2018;56:127–130. doi:10.1016/j.jocn.2018.06.032
68. Catt SL, Anderson JL, Critchley GR. Patients' and staff's experiences of multidisciplinary follow-up for high-grade glioma after radical radiotherapy. *Psychol Health Med*. 2011;16(3):357–365. doi:10.1080/13548506.2011.554563
69. Chapman CH, Hara JH, Molinaro AM, et al. Reirradiation of recurrent high-grade glioma and development of prognostic scores for progression and survival. *Neurooncol Pract*. 2019;6(5):364–374. doi:10.1093/nop/npz017
70. EONS Cancer Nursing Education Framework (2018). European Oncology Nursing Society 2018
71. Komatsu H, Yagasaki K. The power of nursing: guiding patients through a journey of uncertainty. *Eur J Oncol Nurs*. 2014;18(4):419–424. doi:10.1016/j.ejon.2014.03.006
72. Pace A, Dirven L, Koekkoek JAF, et al. European Association for Neuro-Oncology (EANO) guidelines for palliative care in adults with glioma. *Lancet Oncol*. 2017;18(6):e330–e340. doi:10.1016/S1470-2045(17)30345-5. <https://www.eano.eu/publications/eano-guidelines/eano-guidelines-for-palliative-care-in-adults-with-glioma/>
73. Law I, Albert NL, Arbizu J, et al. Joint EANM/EANO/RANO practice guidelines/SNMMI procedure standards for imaging of gliomas using PET with radiolabelled amino acids and [¹⁸F]FDG: version 1.0. *Eur J Nucl Med Mol Imaging*. 2019;46(3):540–557. doi:10.1007/s00259-018-4207-9
74. Albert NL, Weller M, Suchorska B, et al. Response Assessment in Neuro-Oncology working group and European Association for Neuro-Oncology recommendations for the clinical use of PET imaging in gliomas. *Neuro Oncol*. 2016;18(9):1199–1208. doi:10.1093/neuonc/nov058
75. Boxerman JL, Quarles CC, Hu LS, et al. Consensus recommendations for a dynamic susceptibility contrast MRI protocol for use in high-grade gliomas. *Neuro Oncol*. 2020;22(9):1262–1275. doi:10.1093/neuonc/noaa141
76. Ellingson BM, Bendszus M, Boxerman J, et al. Consensus recommendations for a standardized Brain Tumor Imaging Protocol in clinical trials. *Neuro Oncol*. 2015;17(9):1188–1198. doi:10.1093/neuonc/nov095
77. Suero Molina E, Schipmann S, Stummer W. Maximizing safe resections: the roles of 5-aminolevulinic acid and intraoperative MR imaging in glioma surgery—review of the literature. *Neurosurg Rev*. 2019;42(2):197–208. doi:10.1007/s10143-017-0907-z
78. Weller M, van den Bent M, Tonn JC, et al. European Association for Neuro-Oncology (EANO) guideline on the diagnosis and treatment of adult astrocytic and oligodendroglial gliomas [published correction appears in *Lancet Oncol*. 2017 Nov;18(11):e642]. *Lancet Oncol*. 2017;18(6):e315–e329. doi:10.1016/S1470-2045(17)30194-8
79. Bruner JM, Louis DN, McLendon R, et al. The Utility of Expert Diagnosis in Surgical Neuropathology: Analysis of Consultations Reviewed at 5 National Comprehensive Cancer Network Institutions. *J Neuropathol Exp Neurol*. 2017;76(3):189–194. doi:10.1093/jnen/nlw122
80. Kros JM, Huizer K, Hernández-Laín A, et al. Evidence-Based Diagnostic Algorithm for Glioma: Analysis of the Results of Pathology Panel Review and Molecular Parameters of EORTC 26951 and 26882 Trials. *J Clin Oncol*. 2015;33(17):1943–1950. doi:10.1200/JCO.2014.59.0166
81. Sturm D, Pfister SM, Jones DTW. Pediatric Gliomas: Current Concepts on Diagnosis, Biology, and Clinical Management. *J Clin Oncol*. 2017;35(21):2370–2377. doi:10.1200/JCO.2017.73.0242
82. Louis DN, Aldape K, Brat DJ, et al. Announcing cIMPACT-NOW: the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy. *Acta Neuropathol*. 2017;133(1):1–3. doi:10.1007/s00401-016-1646-x
83. Back M, Rodriguez M, Jayamanne D, Khasraw M, Lee A, Wheeler H. Understanding the Revised Fourth Edition of the World Health Organization Classification of Tumours of the Central Nervous System (2016) for Clinical Decision-making: A Guide for Oncologists Managing Patients with Glioma. *Clin Oncol (R Coll Radiol)*. 2018;30(9):556–562. doi:10.1016/j.clon.2018.06.005
84. Cancer Genome Atlas Research Network. Comprehensive genomic characterization defines human glioblastoma genes and core pathways [published correction appears in *Nature*. 2013 Feb 28;494(7438):506]. *Nature*. 2008;455(7216):1061–1068. doi:10.1038/nature07385
85. Preusser M, Bent Mv. Clinical neuropathology practice news 2–2013: immunohistochemistry pins IDH in glioma - molecular testing procedures under scrutiny. *Clin Neuropathol*. 2013;32(2):82–83. doi:10.5414/np300622
86. Quality Standard for the Oncology Pharmacy Service (QuapoS 5). European Society of Oncology Pharmacy, 2018. <https://esop.li/quapos/>
87. White A, Fabian V, McDonald K, Nowak AK. Compliance with reporting guidelines by Australian

- pathologists: an audit of the quality of histopathology reporting in high-grade glioma. *Neurooncol Pract.* 2016;3(2):97-104. doi:10.1093/nop/npv033
88. Malmström A, Łysiak M, Kristensen BW, Hovey E, Henriksson R, Söderkvist P. Do we really know who has an MGMT methylated glioma? Results of an international survey regarding use of MGMT analyses for glioma. *Neurooncol Pract.* 2020;7(1):68-76. doi:10.1093/nop/npz039
 89. ESMO Accredited Designated Centres. European Society for Medical Oncology. 2020. <https://www.esmo.org/for-patients/esmo-designated-centres-of-integrated-oncology-palliative-care/esmo-accredited-designated-centres>
 90. ESO-ESMO-RCE Clinical Update on Rare Adult Solid Cancers. European School of Oncology. <https://www.eso.net/en/events/past-events/events-2019/4th-eso-esmo-rce-clinical-update-on-rare-adult-solid-cancers/3-4122-0->
 91. International Low Grade Cancer Registry. Yale School of Public Health. <https://lggregistry.wixsite.com/study>
 92. Benz L, Senders J, Wefel J, Claus E. QOLP-22. The International Low Grade Glioma Registry: Patient-Reported Quality of Life. *Neuro Oncol.* 2018;20(Suppl 6):vi219. doi:10.1093/neuonc/now148.908

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