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Abstract

Glioma patients are not only confronted with the diagnosis and treatment of cancer, but often experience disease-specific symptoms that greatly affect everyday life. Common symptoms among patients include motor dysfunction, sensory loss, seizures, cognitive deficits, changes in behaviour and personality, mood issues, and fatigue. This review focuses on family caregivers, for whom dealing with the diagnosis and treatment of a brain tumour in their loved one while managing disease-specific symptoms can be challenging. Supportive interventions to assist caregivers have been reported, but high quality scientific evidence for the effectiveness of these programs is largely lacking. Further research is needed to determine how we can best support family caregivers to manage glioma patients' symptoms while maintaining their own health as a caregiver. Research is also required in evaluating the health economic benefits of support programs for caregivers, as better care for caregivers may potentially reduce overall healthcare costs.

Keywords

Family caregiving; informal caregiving; glioma; brain tumour; supportive care

Key points

- Psychological distress is reported in approximately half of family caregivers in neuro-oncology;
- Providing assistance for family caregivers may prevent them from developing emotional or physical problems themselves;
- Research shows that family caregivers of glioma patients can benefit from information and concrete advice on dealing with everyday difficulties;
- More research is needed as large-scale implementation of caregiver support may be hindered by the lack of high quality scientific evidence for the beneficial effects of caregiver interventions in neuro-oncology.

Background

Gliomas

In 2016, an estimated 24,790 people in the United States alone will be diagnosed with a primary malignant brain tumour, 80% of which will be gliomas (Ostrom et al. 2015a). The most common gliomas are astrocytomas and oligodendrogliomas (Ostrom et al. 2015b). The prognosis and treatment are primarily based on the malignancy grade of the tumour, although tumours with an oligodendroglial component generally have a more favourable prognosis than astrocytic tumours (Ostrom et al. 2015b). Patients diagnosed with a World Health Organization (WHO) grade I glioma may be cured after surgical intervention, but WHO grade II gliomas almost always recur after treatment. The median survival of patients suffering from a low-grade glioma is 5-15 years (Van den Bent et al. 2005). Anaplastic gliomas (WHO grade III) and glioblastomas (WHO grade IV) are generally rapidly progressive tumours and are typically associated with a poor prognosis (Wen and Kesari 2008), with median survival ranging from 2-3 years for patients with a grade III glioma (Ohgaki and Kleihues 2005; van den Bent et al. 2013) to 12-14 months for patients with grade IV gliomas (Stupp et al. 2013). Treatment usually consists of a combination of surgery, radiotherapy and chemotherapy.

Depending upon the location of the tumour and the treatment side-effects, patients can experience various neurological and cognitive symptoms that may affect patients' ability to function independently (Mukand et al. 2001). Irrespective of the level of functioning or disability, the consequences of glioma can hinder patients in participating fully in vocational and social activities, affecting the quality of life (QOL) of both patients and their family members to a great extent (Janda et al. 2007; Taphoorn et al. 2010; Aaronson et al. 2011). As the disease progresses, patients rely more heavily on their loved ones for physical and emotional support. Consequently, spouses, family members or close friends assume the role of family caregiver.

Family caregivers

In the glioma patient context, spouses most frequently take up the role of family caregiver, although parents, children, siblings, other family members, or close friends and neighbours can also provide care. Caregivers can help patients deal with physical and emotional symptoms of the disease and treatment, they can help express more subtle changes in the patient's symptoms in clinic, and they

may assist in making health and treatment decisions. The latter becomes most relevant after disease progression, as a patient's mental capacity may decline. Providing practical support (e.g., taking over household chores, arranging services for the patient, providing transportation, managing financial affairs) is also often part of their experience. Adapting to their new role as caregiver can be difficult for family members and friends. In neuro-oncology caregiving research, the adapted Pittsburgh Mind Body Center Model (PMBC Model) has been suggested as a useful framework (Sherwood et al. 2008). Caregivers' psychological and behavioural responses to their new role are influenced by both the patient's disease characteristics (e.g. tumour type, treatment trajectory, specific symptom burden) and caregivers' personal characteristics (e.g. sociodemographic characteristics, personality traits, social support). Depending on the level of distress experienced by the caregiver, this can trigger biologic responses (e.g. stress hormones, cardiac response) which may on the longer term lead to a change in overall physical health of the caregiver. Thus, this model takes not only the emotional, but also the physical consequences of caregiving in neuro-oncology into account.

Many of the previously published reviews have primarily focused on describing the needs of neuro-oncology caregivers (e.g., Ford et al. 2012; Sterckx et al. 2013). In this article, we will instead focus on support for the management of glioma from the family caregivers' perspective following the adapted PMBC model. We included studies with a focus on managing symptoms, medications and side-effects, and support for caregivers or patient-caregiver dyads.

Consequences of family caregiving

Family caregivers can experience positive sentiments toward their new role (Newberry et al. 2012), but negative emotional responses are more frequently reported (Newberry et al. 2012; Sterckx et al. 2013). The acute distress following diagnosis and uncertainty regarding immediate effects of treatment and overall prognosis place major and multifactorial stresses on patient and family. Continuous caregiving, poor sleep and exhaustion (Kim and Rose 2011), and disrupted daily activities contribute to poor emotional health in caregivers (Cochrane et al. 1997). In fact, psychological distress is reported in approximately half of family caregivers in neuro-oncology (Choi et al. 2012; Trad et al. 2015). This is not limited to caregivers but extends to the family situation. Although sometimes, a cancer diagnosis may bring families and friends closer together, it is also common for caregivers experience social isolation (Janda et al. 2006; Arber et al. 2013). Talking with children about the

disease can be stressful, and often, parents will welcome advice on how to initiate this difficult conversation (Madsen and Poulsen 2011). Changes in the spousal relationship commonly occur with caregiving (Li and Loke 2014). If present, changes in the patient's personality and behaviour can complicate the marital relationship and everyday family life (Pinquart and Sorensen 2007; Andrewes et al. 2013). In the long term, women with brain tumours are more likely to go through divorce or separation than men with brain tumours (Glantz et al. 2009). After separation, patients are more likely to be hospitalized and less likely to complete treatment, become involved in clinical trials, or die at home (Glantz et al. 2009). Consequences of the disease and caregiving extend beyond this, with caregiver burden having an impact on the financial situation of the family as well (Bayen et al. 2016). The chronic stress experienced by caregivers may contribute to the development of chronic illness. In various caregiver populations, increased levels of pro-inflammatory cytokines have been found (Gouin et al. 2008; Roepke et al. 2011), and recent efforts focusing on brain tumour caregivers specifically, report elevated cytokine levels as well (Miller et al. 2014; Sherwood et al. 2016). This suggests an association between neuro-oncology caregivers' long-term physical health and chronic stress. Evidently, these far-reaching consequences of taking care of a patient with a brain tumour put caregivers at risk for diminished quality of life. Especially the quality of life of those caregivers of patients with more aggressive, high-grade tumours appears to be vulnerable compared with both the normative population (Flores et al. 2014; Janda et al. 2007) and other caregiver populations (Boele et al. 2013a). While this negative effect may be attenuated by personality traits and coping strategies (Baumstarck et al. 2016), the physical and emotional consequences of caregiving are often hypothesized to influence the quality of care delivered to glioma patients in the home. This may influence patient health and functioning in a negative way (Grunfeld et al. 2004; Vrettos et al. 2012). Indeed, the level of caregiver mastery, i.e. the feeling of being in control of the care situation, has been associated with patient survival in neuro-oncology (Boele et al. 2016). Supporting family caregivers perform their tasks while maintaining their own physical and emotional health, is therefore vital.

Challenges in family caregiving

Below, findings will be discussed for 1) the early treatment phase (i.e., the period following diagnosis through initial treatment); 2) the post-treatment phase (i.e., after initial treatment, disease may be stable); and 3) the end-of-life phase and beyond (i.e., treatment options have been exhausted;

progressive disease, followed by death). During each phase, new challenges may present, although we acknowledge that these phases may overlap and do not always occur sequentially. 'Challenges' represent any issues or concerns reported by neuro-oncology caregivers, whereas 'support' refers to any formal or informal support they may have or should have access to. As evidence-based supportive programs are rare, we included information and practical advice that could be useful for caregivers and those health care professionals supporting them, based on our expert opinions, online resources from patient organisations, and supported by systematic reviews of evidence from caregiver studies in progressive cognitive conditions or at end of life (Candy et al. 2011; Huis In Het Veld et al. 2015).

Early treatment phase

Managing symptoms, medications and side-effects is a complicated task, especially for family caregivers who have not had a medical education. A systematic review shows that this may be increasingly stressful if the caregiver is not well informed (Moore et al. 2012). Information provision should be tailored to the individual patient and caregiver, as symptoms are largely dependent upon the location of the tumour and treatment side effects. The more common symptoms may be covered in routine information efforts. A retrospective study among brain tumour patients admitted for inpatient rehabilitation shows that in terms of physical symptoms, many glioma patients experience motor dysfunction, sensory loss, visual-perceptual deficits, cognitive problems, fatigue, and seizures (Mukand et al. 2001). Although evidence-based supportive programs are rare (see '*supportive care and interventions for family caregivers*' below), caregivers may nevertheless benefit from information and practical advice. Informing caregivers on 1) the possible causes of these symptoms; 2) how to recognise (changes in) symptoms; 3) possible treatments including medication, physical therapy or (cognitive) rehabilitation, and finally; 4) ways to manage everyday life in a safe way, can help patient-caregiver dyads feel better prepared. In the case of motor or sensory loss, for example, caregivers may be informed that this may depend on the location of the tumour and the treatment the patient underwent, and that it can present as numbness, tingling, sometimes a burning feeling or a change in the perception of temperature. Caregivers should be advised to contact health care professionals when changes in symptoms occur (American Brain Tumor Association 2016). To help manage these symptoms, a home safety evaluation can be performed by a home care agency. Moreover, everyday tips such as checking the patient's skin for cuts or bruises or setting the maximum water temperature

so that the patient can't inadvertently burn him- or herself can be useful. Furthermore, caregivers may want to be advised on making adjustments in the house to improve safety, e.g. by removing rugs or adding handrails to the bathroom (American Brain Tumor Association 2016).

Motor or sensory loss is one of the more straightforward examples. Dealing with seizures can be more challenging. Caregivers can help patients by reminding them to take their medications, obtaining routine blood tests for drug levels, and promoting healthy behaviours that may minimize seizure frequency (e.g., getting enough sleep, limiting alcohol intake, reducing stress). Both patient and caregiver should be educated to recognise unsafe situations such as bathing alone or driving (American Brain Tumor Association 2016). Caregivers can also benefit from education and training in how to manage a seizure, and how to be prepared for status epilepticus. Here, the caregiver may feel better supported when advised on when to call an ambulance, and they may be trained in administering AEDs in buccal or intranasal form. This was found feasible in a multicentre pilot study ($N=25$), providing caregivers with more confidence to manage seizures (Koekkoek et al. 2015).

For other common issues such as communication difficulties or emotional symptoms, the same principles of education on the possible causes, recognising (changes) in symptoms, possible treatments, and managing symptoms in everyday life apply. Examples of tips on how to manage common symptoms such as motor and sensory loss, seizures, communication deficits, changes in cognition, behaviour and personality, and fatigue are presented in Box 1 – although it should be noted that this is by no means an exhaustive overview. These tips are only suggested as an addition to formal supportive and psychological care options.

Post-treatment phase

After treatment, a relatively stable period may follow that comes with new challenges. In qualitative interviews, caregivers describe that it can be difficult to adjust to the new 'normal situation' after the acute phase - the realisation that interpersonal roles have changed for good, from family member to caregiver, is often difficult to accept (Coolbrandt et al. 2015). Dealing with the loss of the person the patient used to be can be difficult (Sterckx et al. 2013), and can trigger a grief response. A difficult balance between fear and hope has been described (Coolbrandt et al. 2015). In a longitudinal qualitative study some caregivers report that it helps them to maintain a positive outlook on the future through promoting healthy lifestyle choices and maintaining hope (Piil et al. 2015a).

Financial issues that result from the costs of treatment and lost hours at work are a common concern in cancer, as e.g. two large-scale prospective studies show (Yun et al. 2005; Longo et al. 2006), and often become more pressing during this phase. Moreover, fatigue, mood, and changes in behaviour may become more prominent after initial anti-tumour treatment. We believe that support through education and training should therefore be ongoing. For example, to improve a patient's cognitive functioning, cognitive rehabilitation could be initiated at this post-treatment stage. As this is a relatively quiet period in their disease trajectory, it is thought that patients may be better able to handle the often quite high demands of cognitive rehabilitation programs. Moreover, the months between surgery and treatment have allowed patients' cognitive functioning to improve spontaneously, as often occurs (Stein and Hoffman 2003; Munoz-Cespedes et al. 2005). As cognitive rehabilitation is generally a combination of psycho-education, compensatory strategies and training of cognitive skills (Gehring et al. 2010), the family caregiver's role in successful rehabilitation is key. They can encourage the patient by helping to make the necessary adjustments around the home, and supporting the implementation of compensatory strategies in everyday life (American Brain Tumor Association 2016).

Often, cognitive functioning eventually deteriorates as the disease progresses. Indeed, cognitive deficits are known to precede disease progression in glioma patients, with tests of executive functions and attention being most closely associated with prognosis after controlling for functional status and age in a sample of 91 patients (Johnson et al. 2012). Initiating conversation with the patient and caregiver early in the disease trajectory regarding their preferred treatment plan during advanced disease and even the end-of-life phase, is important. This so-called advance care planning (ACP) is discussed in more detail below.

End of life phase and beyond

The end of life (EOL) phase is defined as the period when the patient starts to deteriorate and anti-tumour treatment is no longer possible (Dirven et al. 2015). Studies show that certain symptoms may emerge or become more evident only in the EOL phase as detailed in a systematic review (Sizoo et al. 2013). Common disease-specific symptoms in the EOL phase include a reduced consciousness, dysphagia, headaches, epilepsy, motor dysfunction, and an increase in cognitive and behavioural symptoms (Sizoo et al. 2013; Dirven et al. 2015). Additional difficulties with symptom management may arise as medication administration may become more difficult with swallowing difficulties.

Sometimes alternative administration methods can be considered. For example, buccal and intranasal anticonvulsants proved feasible in glioma patients and improved caregiver satisfaction, as tested in a pilot study (Koekkoek et al. 2015). However, despite these advances, many bereaved caregivers explain that they felt ill-prepared for the final phase of the patients' life (Schubart et al. 2008; Sizoo et al. 2013), highlighting the EOL phase as a very distressing period for family caregivers. Indeed, an Austrian study among 52 bereaved caregivers of GBM patients shows that caregivers rate their own QOL only slightly better than the patients' QOL in the last three months of life (Flechl et al. 2013). In the EOL phase, specifically, caregivers suffer from sadness, fear, burnout, a decreased interest in others, and irritation, as well as financial difficulties (Flechl et al. 2013).

As the disease progresses, important medical decisions should be made. According to expert opinion these can include ceasing life-prolonging treatment, managing symptoms with medications that have or could have a life-shortening effect, or starting palliative sedation (Dirven et al. 2015). It is especially relevant to have patients participate in future decisions regarding the EOL phase early on in the disease trajectory (i.e., ACP), as patients often become unable to participate in decision-making as time progresses. Retrospectively, physicians rated 20% of their patients incompetent in the last months before death, which increased to 52% and 88% in the last weeks and days before death, respectively (Sizoo et al. 2012). However, early discussion might be complicated by the need expressed by caregivers to sustain hope throughout the disease trajectory (Piil et al. 2013; Sterckx et al. 2013). A conversation on EOL, if ill-executed or poorly timed, could hinder this. However, in hindsight, many caregivers would have liked to be better informed as reported in a retrospective qualitative study (Collins et al. 2014). The optimal timing to initiate conversation on EOL may be different for each patient-caregiver dyad, and is largely up to the treatment team to determine. In general, health care providers bring this topic up relatively close to the death of high-grade glioma patients (Sizoo et al. 2013), and referral to palliative care often only occurs when all treatment options have been exhausted (Walbert and Chasteen 2015). Experts suggest that earlier involvement of the palliative care team may facilitate the initiation of conversation on EOL and ACP (Greer et al. 2013), and may lead to better information provision on the available palliative care services (Walbert and Chasteen 2015). These include but are not restricted to hospice care (both in- and outpatient), hospital services, community based nursing, and social services (Faithfull et al. 2005). This support can

potentially reduce patient and caregiver distress in the EOL phase, as bereaved caregivers suggested in qualitative interviews more than a decade ago (Sherwood et al. 2004).

After the patient dies, caregivers often report feeling alone in dealing with their grief (Collins et al. 2014). It is particularly difficult to transition from an active caregiver to a grieving family member after the patient dies (Sherwood et al. 2004). At 18 months after the patient's death, caregivers' ($N=51$) QOL had improved when compared to a time of active caregiving, but still had significantly worse levels of QOL than the normative population (Petruzzi et al. 2015). In general, bereaved caregivers express gratitude for being able to talk about their experiences during qualitative studies (Lipsman et al. 2007; Flechl et al. 2013). This emphasizes the need to support caregivers even after the death of the patient. Any truly holistic treatment approach should continue to support family caregivers in the bereavement phase.

Supportive care and interventions for family caregivers

Bereaved caregivers speaking from experience indicate that health care providers can potentially decrease caregiver burden by informing family caregivers on what they can expect of their new role, and by educating them on where to find both formal and informal support (Sherwood et al. 2004). In a systematic review it was suggested that promoting healthy family dynamics through psychosocial treatment of both patient and caregiver helps caregivers cope, and may also be beneficial for the patient's (emotional) health (Hopkinson et al. 2012). In providing support, it is important to realise that the needs of caregivers may differ from patients' needs at various time points (Collins et al. 2014). Maintaining good emotional and physical health is not only dependent upon the patient's physical functioning and need for care. Each individual caregiver may have their own set of strengths and weaknesses leading to different supportive care needs (Ownsworth et al. 2015). Just like patient care, we believe caregiver support should therefore be tailored to each family's needs.

Efforts have been undertaken to develop neuro-oncology specific caregiver interventions, relevant to the stage of disease, although systematic reviews conclude that especially high-quality evidence of benefit remains rare (Piil et al. 2014; Langbecker and Janda 2015). An overview is presented in Table 1. The outcomes of only one randomized controlled trial for family caregivers of adult glioma patients have been reported on. This psychological intervention consisting of psycho-education and cognitive behavioural therapy was effective in improving caregiver mastery (Boele et al.

2013b). 56 caregivers of high-grade glioma patients were randomized to either the intervention or a care as usual control group. Those in the intervention group received 6 one-hour sessions with a psychologist, aimed at helping them cope better with their changed situation and caregiving tasks. Eight months after the intervention, caregivers' mental health remained more stable and their feelings of mastery improved compared with the control group. Major difficulties were experienced in this trial with regard to dropout – 43% of the sample did not complete the final assessment, mostly due to experienced burden, lack of time, and patient death.

Two other randomized controlled studies aimed specifically at improving neuro-oncology caregiver wellbeing are still underway. One is an internet-based program paired with nurse support (R01NR013170; PIs Sherwood and Donovan). The goal of this 8 week program is to teach caregivers effective problem-solving techniques which they can use throughout the patient's disease trajectory. Evidence-based guides for over 30 common caregiver issues and links to neuro-oncology resources are provided as well. Nurse interventionists provide telephone support to individualise strategies and teach caregivers how to best use the program to meet their needs. Another intervention called Care-IS is being tested in Australia (Halkett et al. 2015), aiming to recruit 240 caregivers of high-grade glioma patients undergoing chemoradiation to be randomly allocated to the intervention or a care as usual group. This intervention consists of a telephone needs assessment by a nurse interventionist followed by a home visit. Caregivers will have access to a personalised resource file. Follow-up will consist of regular telephone calls from the nurse.

Other, non-controlled interventions have been reported on. A qualitative study showed that a specialist nurse proved useful in providing information and support, increasing the family's autonomy and facilitating decision-making within the family (Spetz et al. 2005; Spetz et al. 2008). In this study, support was continued during the bereavement phase. Moreover, a comprehensive caregiver training program aimed at developing practical care skills and providing information through an 8-hour workshop delivered by neuro-oncology nurses seems promising, although results of the evaluation are not yet published (Patterson and Lovely 2007). Nevertheless, a caregiver program has been implemented at the same institution in San Francisco, with a handbook that is freely available to download (Goodman et al. 2013). Similarly, a pilot program aiming to educate caregivers about compensatory strategies, which consisted of a half day workshop delivered by a psychologist, a nurse consultant and a radiation oncologist, yielded positive results in a pre- post-test design (Whiting et al.

2012). After the intervention, caregivers' knowledge increased and caregivers rated the intervention 'good' to 'very good'. A psycho-educative group intervention supported by a psychologist and a physician was evaluated as helpful to discuss emotional aspects, changes in everyday life, and medical queries (Schratter-Sehn et al. 2011). Most interventions described above rely heavily on specialist nurse support. However, in clinical practice it might not be feasible for them to attend to every dyads' needs due to time restraints and costs. A different approach might be to install a care coordinator or patient navigator to help patients and families find their way to the support they need. A recent qualitative study described the implementation of patient navigation for neuro-oncological patients specifically, arguing that it could improve access to health services and that developing a relationship in itself could have supportive value (Bailey et al. 2015). Although promising, the benefit to patients and caregivers remains to be evaluated.

A different approach to provide family caregivers with information and support includes a telephone hotline for disease and treatment-related questions (Spezeski et al. 2007). This was widely accessed by both patients (35%) and family caregivers (52%). The provision of hard copy and digitally provided information sheets on common symptoms and problems in neuro-oncology was evaluated positively (Wright et al. 2015). Similarly, caregivers appreciated a brain tumour website, and the possibility to ask health care professionals questions through the website (Piil et al. 2015b). Although this appreciation certainly highlights the usefulness of these information provision interventions, it remains difficult to objectively estimate the benefit to caregivers and patients in terms of mental or physical wellbeing.

Discussion

This review was aimed at providing an overview of the challenges and supportive care options for caregivers of people suffering from a brain tumour. Studies of mixed methodology as well as various systematic reviews highlight the multifactorial stresses that neuro-oncology caregivers and patients face throughout the disease trajectory and for caregivers, extending into the bereavement phase. According to the adapted PMBC Model, this does not only have a negative effect on caregivers' emotional health, but also on their physical functioning. These negative consequences can, in turn, influence the quality of care delivered to the patient in the home situation. The need for support is

evident, and studies are emerging to develop and test different ways to provide this support to both caregivers and patients.

To summarise findings, regardless of the method of delivery, family caregivers of glioma patients can benefit from information and concrete advice on dealing with everyday difficulties. This may include learning how to ask for help from both formal and informal resources for everyday or more complex issues (e.g., financial matters; talking with children), compensatory strategies, relaxation techniques and psychological techniques to help put issues in perspective, advice on nutrition, physical exercise, paying attention to one's own health problems, and encouraging a healthy sleep hygiene. Support from the palliative care team earlier on in the disease trajectory may facilitate ACP. After the patient has passed, family caregivers may benefit from bereavement support.

This expert review has clear methodological limitations. The search strategy, in- and exclusion criteria, and the process of selecting articles was not pre-specified nor documented in detail. As a result, it may be difficult for a reader to assess the quality of the publications discussed in this review. As literature focused on supporting caregivers in neuro-oncology is scarce, we have supplemented recommendations based on our expert opinion, which could not always be supported by references. Therefore this review may reflect our opinions more clearly than a systematic approach would have done. Nevertheless, the present review could provide useful pointers to help guide and support family members of glioma patients.

In conclusion, providing assistance for caregivers may prevent them from developing emotional or physical problems themselves. Although caregiver programs are becoming more common in neuro-oncological practice, the information and support provided could become more widely available. However, large-scale implementation of caregiver support may be hindered by the lack of high quality scientific evidence for the beneficial effects of caregiver interventions in neuro-oncology. As caregiver support is listed as one of the top research priorities in neuro-oncology in the United Kingdom (Grant et al. 2015), it is expected that new studies will be conducted to evaluate the benefits of caregiver support, so that we may support family caregivers better as they adjust to their new role. Evaluating any health economic benefit of caregiver programs should be included in future research, as better care for caregivers may potentially reduce overall healthcare costs of the dyad.

Disclosure

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Box 1. Tips on how to help caregivers manage patients' common disease specific symptoms.

<p>Supporting caregivers in clinical practice</p>	<ol style="list-style-type: none"> 1. Provide information on the possible cause of symptoms 2. Help caregivers recognise how to spot (changes in) symptoms 3. Inform them on possible treatments or symptom management solutions 4. Provide tips on ways to manage everyday life in a safe way
<p>Examples</p>	
<p>Symptom or issue</p>	<p>Tips to manage everyday life at home</p>
<p>Motor and sensory loss</p>	<ul style="list-style-type: none"> -Check for cuts and bruises -Limit maximum water temperature -Make adjustments to the house to avoid falls (e.g., add handrails, remove rugs)
<p>Seizures</p>	<ul style="list-style-type: none"> -Remind patient to take medications -Promote healthy behaviour: enough sleep; limit alcohol intake; reduce stress -Avoid unsafe situations: bathing alone or driving -Training on how to manage a seizure and when to call an ambulance
<p>Communication deficits</p>	<ul style="list-style-type: none"> -Limit distractions at home -Be patient, allow plenty of time -Set a positive mood -Use pictures/pictograms or technology to facilitate communication
<p>Cognition, behaviour, personality</p>	<ul style="list-style-type: none"> -Promote the use of compensatory strategies such as calendars, audible reminders, checklists -Try to distract the patient if they persevere in behaviours or feel anxious -Create calm, structured home environment and daily routine

Fatigue	<ul style="list-style-type: none"> -Allow patient plenty of time to avoid frustration -Divide tasks or activities into smaller steps -Limit choices to make it easier to make decisions -Identify triggers and patterns that cause problem behaviour, avoid if possible -Limit hazards in the home (e.g., store car keys, medicines and alcohol in a safe place) -Promote a slow increase in physical activity -Encourage patient to invest energy in rewarding rather than unrewarding activities -Create calm, structured home environment and daily routine -Plan daily activities: set small goals; mornings are often best for important activities -Allow enough time for rest and relaxation -Promote healthy sleep hygiene; e.g. limit daytime naps and avoid caffeine at night
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Table 1. Overview of neuro-oncology specific caregiver interventions.

Type of study	Reference	Intervention	Study population	Main results
Randomized controlled trials	Boele et al., 2013	Cognitive behavioural therapy, psycho-education	56 spousal caregivers of high-grade glioma patients	Improved feelings of mastery at 8-months post intervention
	Halkett et al., 2015	Needs assessment followed by resource package and home visit. Regular phone calls from nurse.	Family caregivers of high-grade glioma patients undergoing chemoradiation, aimed inclusion N=240	Not yet published

	Sherwood et al., ongoing	Web-based intervention with nurse support	Family caregivers of patients with primary brain tumours; recruitment ongoing	Not yet published
Quantitative evaluations of interventions	Whiting et al., 2012	3 interventions to manage challenging behaviours after brain tumour: (1) single case pilot of skill-based training; (2) half-day workshop with compensatory strategies; (3) 1-day workshop for health care professionals	(1) One patient with low-grade glioma; (2) 7 family members of brain tumour patients; (3) 43 health care professionals	(1) Decrease in problem behaviour; (2,3) both workshops resulted in increased perceived knowledge of strategy use.
	Wright et al., 2015	Hard copy and digitally provided information	N/a: implementation in neuro-oncology practice	Only results on utilization: 100 hard copies requested within 1 month; digitally provided information accessed hundreds of times in 3 months
Qualitative evaluations of interventions	Schratter-Sehn et al., 2011	Group-based psycho-education by psychologist and a physician	104 patients with high-grade glioma and their relatives	Participants reported to find the meetings helpful to discuss mental aspects and medical questions
	Spetz et al., 2005; 2008	Specialist nurse support	16 brain tumour patients and their next-of-kin	Participants reported to find nurse support a helpful resource

Both qualitative and quantitative evaluations of interventions	Pill et al., 2015	Brain tumour website to provide information	All visitors of the website; 9 high-grade glioma patients (7 non-users) and 8 caregivers (5 non-users) were interviewed	Website was accessed by 637 individuals; interview participants described barriers to use of technology but felt website was a positive development
	Spezeski et al., 2007	Telephone hotline	75 brain tumour patients/caregivers	Participants reported to find the hotline useful in asking for information and support
Interventions without formal evaluations	Bailey et al., 2015	Care coordination/ patient navigation	N/a: implementation in neuro-oncology practice	N/a
	Goodman et al., 2013	A handbook to provide easily accessible and accurate information for caregivers in neuro-oncology	N/a: handbook is freely available	N/a
	Patterson et al., 2007	8-hour workshop aimed to train caregivers, delivered by neuro-oncology nurses	N/a: implementation in neuro-oncology practice	N/a