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Interventions to help support caregivers of people with a brain or spinal cord tumour (Protocol)

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Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD012582.

DOI: 10.1002/14651858.CD012582.

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[Intervention Protocol]

Interventions to help support caregivers of people with a brain or spinal cord tumour

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Editorial group: Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group.

Publication status and date: New, published in Issue 3, 2017.

Citation: Boele FW, Bulbeck H, Browne C, Rooney AG, Sherwood P. Interventions to help support caregivers of people with a brain or spinal cord tumour. *Cochrane Database of Systematic Reviews* 2017, Issue 3. Art. No.: CD012582. DOI: 10.1002/14651858.CD012582.

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

Primary objective

To assess the effectiveness of supportive interventions at improving the well-being of caregivers of people with a brain or spinal cord tumour.

Secondary objectives

1. To assess the effects of supportive interventions for caregivers in improving the physical and emotional well-being of patients with a brain or spinal cord tumour
2. To assess the health economic benefits of supportive interventions for caregivers

BACKGROUND

Description of the condition

The diagnosis and treatment of a brain or spinal cord tumour can have a huge impact on the lives of patients and their families. Approximately 28 per 100,000 adults aged 20 and over are affected by central nervous system tumours, with the majority of tumours

(approximately 66%) being non-malignant (Ostrom 2014). In children and young adults under 19 years of age, central nervous system tumours are the most common tumour, with an annual age-adjusted incidence rate of 5.4 per 100,000 (Ostrom 2014). The treatment and expected outcome depend heavily on the tumour type, molecular markers, tumour grade, and location. Treatment generally consists of surgical intervention, radiotherapy, chemotherapy, or a combination of these treatment methods. In making treatment decisions, any benefit from treatment is weighed

against the expected quality of life (QoL) and symptom burden of patients.

Depending upon the tumour location and treatment side effects, patients can experience neurological symptoms such as weakness, sensory loss, and motor dysfunction, or visual-perceptual deficits and problems with speech and language (Mukand 2001). Cognitive deficits such as problems with memory and concentration occur in the majority of patients, and epilepsy is also common (Armstrong 2016; Durand 2015; van Loon 2015). Moreover, fatigue, depression and changes in personality and behaviour are frequently reported throughout the course of the disease (Armstrong 2016b; Cavers 2012; Rooney 2011). These symptoms can influence the degree to which patients can participate in vocational and social activities and can even prevent independence and affect QoL (Aaronson 2011; Klein 2001; Macartney 2014).

Patients commonly come to rely on their family caregivers (e.g. spouses, family members, or close friends) for both physical and emotional support. Consequently, many family caregivers experience considerable burden and distress, and consistently report feeling ill-prepared for their caregiving role (Choi 2012; Sterckx 2013). Therefore interventions to support caregivers are expected to help the caregiver, the patient and family unit.

Various studies have explored the needs of family caregivers in neuro-oncology, and show a need for clear information and communication with healthcare professionals: around symptoms, treatment, and available resources; health service needs and care coordination; and the need for psychological and social supportive care options (Moore 2013; Sterckx 2013).

Description of the intervention

Individual caregivers' needs can vary greatly depending on the time point in treatment, the person's social support system, expectations and experienced burden (i.e. the stress experienced as a result of the home care situation) (Ownsworth 2015). Therefore, any intervention programme aimed at improving the well-being of family caregivers in neuro-oncology will be considered for this review. Here, the term 'well-being' encompasses all aspects of QoL, psychological distress, coping and mastery, i.e. the feeling of being in control of the caregiving situation.

The interventions under investigation may include, but are not limited to, programmes aimed at empowering family caregivers through:

1. improving information provision; e.g. what to expect from their role as a family caregiver; teaching caregivers what the treatment options are; educating them on supportive care options;
2. caregiver skills training; e.g. how to recognise (changes in) patients' symptoms; how to manage symptoms or improve patients' everyday functioning; and
3. psychosocial support; e.g. psychosocial interventions to help caregivers cope better; therapeutic interventions to promote

a healthy relationship between the patient and caregiver;

bereavement support after the patient has passed.

It is not expected that effectiveness of interventions will vary within different subgroups of caregivers, e.g. grade of tumour, age of patient. The interventions are not expected to pose a risk to caregivers, however, length or complexity of intervention programmes may increase caregiver burden and could cause caregivers to feel overwhelmed instead of supported.

How the intervention might work

Supportive interventions for family caregivers in neuro-oncology may help in various ways.

Improving information provision and caregiver skills training may help prepare family members and friends for their caregiving role and activities. When caregivers learn more about the disease and its symptoms, they feel more confident in distinguishing between which (changes in) symptoms could be normal or expected and which may require medical follow-up. Through this mechanism, patient outcomes may be improved as better symptom management may be initiated sooner and new tumour activity may be detected earlier in the disease trajectory, allowing treatment to commence. Moreover, symptoms may be recognised and treated before becoming more serious and requiring inpatient treatment, thus potentially reducing healthcare costs. Finally, increasing caregivers' confidence in dealing with these medical issues can substantially improve their feelings of mastery. This may have a positive effect on their overall well-being, their QoL, and the quality of care they deliver in the home situation.

Psychosocial support may provide caregivers with the tools to improve coping strategies to deal with the psychological burden of being a caregiver to a person who has been diagnosed with a brain or spinal cord tumour. Many patients and caregivers struggle with maintaining a healthy relationship after changes in the patient's personality and behaviour, and psychological support to caregivers or patient-caregiver dyads can help couples work through these issues together. It is known that patients who go through divorce or separation are more likely to be hospitalised and less likely to complete treatment, become involved in clinical trials, or die at home (Glantz 2009). Promoting healthy patient-caregiver relationships may therefore also have a positive effect on long-term patient outcomes. This can help decrease caregivers' levels of distress and burden. As many caregivers will provide care for a longer period of time, up to many years on end, decreasing distress and burden may prove beneficial as the physical consequences of long-term high levels of stress may be prevented. Finally, maintaining good physical as well as emotional health in caregivers will allow them to continue their caregiving tasks, which will benefit patients as well.

Why it is important to do this review

Meeting the needs of family caregivers in neuro-oncology, by decreasing their distress and burden and improving their sense of mastery, is imperative in order to maintain their emotional and physical health. Protecting caregivers' QoL can enable them to continue their caregiving activities to maintain the best possible level of patients' well-being. Indeed, caregiver support is listed as a top research priority in neuro-oncology in the UK through the James Lind Alliance Neuro-Oncology Partnership (Grant 2015). Furthermore, the NHS has made a number of commitments to caregivers, including supporting caregivers' mental health and well-being alongside physical needs (NHS England 2014).

Information and support for caregivers of patients with brain and spinal cord tumours is becoming more widely available and caregiver programmes are becoming more common in clinical practice in some centres. However, large-scale implementation of caregiver support may be hindered by the lack of high-quality evidence for the effects of caregiver interventions in populations of brain and spinal tumour patients. Indeed, a recent report from Macmillan Cancer Support reveals that more than half of family caregivers in oncology do not receive support at present (Macmillan/You Gov 2016). This systematic review will provide an overview of caregiver interventions for those taking care of patients with a brain or spinal tumour, assessed in randomised controlled trials (RCTs). It will also provide a brief economic summary of the health economic benefits where these have been measured. It is expected that this will be useful to make recommendations for policy and practice.

OBJECTIVES

Primary objective

To assess the effectiveness of supportive interventions at improving the well-being of caregivers of people with a brain or spinal cord tumour.

Secondary objectives

1. To assess the effects of supportive interventions for caregivers in improving the physical and emotional well-being of patients with a brain or spinal cord tumour
2. To assess the health economic benefits of supportive interventions for caregivers

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs. Trials in which quasi-randomised methods are used will be included if there is sufficient evidence that the treatment and control groups are similar at baseline. If this is unclear, trial authors will be contacted to provide clarification.

Types of participants

We will include studies with adult caregivers (18 years or older) for people with a brain or spinal cord tumour. The people they provide care for can be of any age, suffering from any type of malignant or benign, primary or secondary brain or spinal cord tumour, at any time during the disease trajectory.

Types of interventions

Any type of intervention whose primary aim is to improve caregiver well-being will be considered. We will include trials which evaluate the effectiveness of individual and group-based interventions for caregivers, or for patient-caregiver dyads as long as caregiver outcomes are reported on. No restrictions will be placed on: the setting, e.g. in the hospital, clinic, psychologist office, at home or elsewhere; the facilitator of the intervention, e.g. a healthcare professional, social worker, or (guided) self-help; or the method of delivery of the intervention, e.g. delivered face-to-face, online, written, or by telephone. Any control condition is acceptable, e.g. wait list control groups, attention-only control groups, information-only control groups. Trial authors will be contacted if it is unclear whether a trial meets our inclusion criteria.

Types of outcome measures

For all primary outcomes we will accept recognised caregiver questionnaires or instruments measuring mood, caregiver burden, mastery, marital adjustment, quality of life and physical functioning. Where measured, the effect on patient emotional and physical well-being patient questionnaires will be assessed under [Secondary outcomes](#). Acceptable outcomes are detailed below.

Primary outcomes

Outcomes related to caregiver emotional or physical well-being

1. Psychological distress (depression and anxiety), e.g. Hospital Anxiety and Depression Scale (HADS; Crawford 2001), Center for Epidemiological Studies Depression Scale (CES-D; Radloff 1977)
2. Caregiver burden, e.g. Caregiver Reaction Assessment (CRA; Given 1992)

3. Caregiver mastery, e.g. Mastery Scale (Pearlin 1978)
4. Quality of patient-caregiver relationship, e.g. Locke-Wallace Short Marital Adjustment Test for spousal relationships (Jiang 2013)
5. Quality of life (QoL), either caregiver specific, e.g. Caregiver QoL index-cancer (CQOLC; Weitzner 1999), Caregiver oncology QoL questionnaire (CarGOQoL; Minaya 2012), or generic, e.g. Short Form Health Survey (SF-36; McHorney 1993), EuroQol (EQ-5D Brooks 1996)
6. Physical functioning, e.g. number of chronic conditions present, physical measures of stress levels (cytokines), physical subscales of QoL questionnaires

Secondary outcomes

Outcomes related to patient emotional or physical well-being

1. Psychological distress (depression and anxiety), e.g. Hospital Anxiety and Depression Scale (HADS; Crawford 2001), Center for Epidemiological Studies Depression Scale (CES-D; Radloff 1977)
2. Quality of life, e.g. European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30; Aaronson 1993); Functional Assessment of Cancer Therapy (FACT; Weitzner 1995), Short Form Health Survey (SF-36; McHorney 1993)
3. Symptom management, number and/or severity of symptoms measured with e.g. MD Anderson Symptom Inventory-Brain Tumor Module (MDASI-BT; Armstrong 2006), EORTC Brain Cancer Module (EORTC QLQ-BN20; Taphoorn 2010)
4. Number of visits to the emergency room, e.g. as detailed in medical records
5. Number and length of hospitalisations, e.g. as detailed in medical records

Outcomes related to the health economic effects

1. Caregiver and/or patient employment status, e.g. self-reported
2. Productivity loss at work of caregiver and/or patient, e.g. self-reported
3. Caregiver healthcare utilisation for acute and/or chronic conditions, e.g. self-reported or as detailed in caregiver's medical records

We will not exclude trials with different outcomes than those mentioned above, if they measure the same construct.

Search methods for identification of studies

No restrictions will be made based on type of publication, year of publication, or language. Papers published in languages other than English, Dutch or German will be translated. Both published and unpublished RCTs will be considered.

Electronic searches

We will search: the Cochrane Central Register of Controlled Trials (CENTRAL; latest issue), MEDLINE (1964 to date), Embase (1980 to date), and ClinicalTrials.gov (clinicaltrials.gov/). The MEDLINE search strategy is detailed in [Appendix 1](#).

Searching other resources

The references of identified studies will be handsearched for studies that were not identified through the electronic search.

Conference abstracts and proceedings from the last five years will be searched through the American Society of Clinical Oncology (ASCO; www.asco.org/ASCO/Meetings), the Society for Neuro-Oncology (SNO; supplements of *Neuro-Oncology*; neuro-oncology.oxfordjournals.org/conent/by/year), and the International Psycho-Oncology Society (IPOS; special issues of *Psycho-Oncology*;

The two main journals in the field of neuro-oncology, *Neuro-Oncology* and *Journal of Neuro-Oncology* will be handsearched for publications from the last year that were not identified through the electronic search.

We will contact the authors of publications known to focus on improving the well-being of caregivers of patients with a brain or spinal cord tumour, to enquire about unpublished or ongoing trials.

Data collection and analysis

Selection of studies

Two review authors will select studies for inclusion in this Cochrane review. All titles and abstract will be screened by the review authors independently. Discarded studies will be stored in a file as potentially relevant. The eligible studies will be subject to further independent assessment after full-text reports have been retrieved. Disagreements between review authors will be resolved by discussion and if disagreements persist, a third review author will be asked for their opinion. If the published report contains too little information to assess whether the trial should be included, we will contact the study authors for further details. EndNote will be used for database management.

Data extraction and management

Two review authors will examine each selected report and extract data using a piloted data collection form based on Cochrane Consumers and Communication's Group data extraction template (Cochrane CCG 2016). This data collection form will include participant characteristics (e.g. age, sex, group size, patients' tumour type, grade, disease stage, etc) and information about the supportive intervention, e.g. the method and duration, the time-points at which the outcomes were assessed, the results (continuous outcomes: mean difference and standard error; dichotomous outcome data: number of caregivers who show an improvement in terms of emotional or physical well-being as a proportion of the total number treated) and information on adherence and attrition (Chandler 2013).

If possible, we will assess the extent to which the following confounding factors may have influenced the results and the extent to which these were controlled for in the analysis: caregiver education, caregiver age, caregiver sex, caregiver income or socioeconomic status, caregiver use of psychotropic medication, nature of the relationship with the patient, patient diagnosis, patient age, patient sex. We will contact trial authors if these data are not reported on. Extracted data will be entered into Review Manager. Again, the two authors mentioned above will discuss and any uncertainties will be resolved by a third review author.

Assessment of risk of bias in included studies

The two review authors responsible for the selection of studies and data extraction will also assess the risk of bias in accordance with the Cochrane tool for assessing the risk of bias (Higgins 2011). This includes several domains: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; other sources of bias. The risk of bias will be categorised as high, low, or unclear. The assessments will be presented in a 'Risk of bias' table. The risk of bias in the included studies will be discussed and persisting disagreements between the review authors will be resolved by a third review author. The risk of bias will be incorporated in the interpretation of possible meta-analysis.

Measures of treatment effect

For dichotomous outcome data, we will present the number of caregivers who show an improvement in terms of emotional or physical well-being as a proportion of the total number treated. We will calculate and present risk ratios (RRs) with 95% confidence intervals (CIs).

For continuous outcome data from studies using the same instrument, we will estimate mean differences (MDs) between treatment groups. Where different instruments are used, we will calculate the standardised mean difference (SMD) by dividing the mean difference in post-intervention scores between the intervention and

control groups by the standard deviation of the outcome among participants. We will present both the MD and SMD with 95% CIs for individual outcomes in individual studies. If these data are unavailable, we will present the reported significance levels instead.

Unit of analysis issues

Different levels of randomisation (e.g. at the level of participants or groups) will be taken into account. When there are long-term follow-up assessments available within trials, we will analyse outcomes for two different follow-up categories: short term, i.e. 0 to 3 months; or medium to long term, i.e. 4 months and more. If studies with multiple intervention groups are identified, we will make pair-wise comparisons between all possible pairs of intervention groups. We will make sure that we do not double-count participants in the analysis.

Dealing with missing data

The corresponding authors of the trials will be contacted in writing (email, post, or both) to obtain missing data. We will evaluate the reporting of important numerical data such as the number of screened and randomised participants, and whether intention-to-treat or per-protocol analyses were done. Missing data will not be imputed (Higgins 2011).

Assessment of heterogeneity

The impact of the heterogeneity of included intervention studies will be assessed with the I^2 statistic for each outcome. Substantial heterogeneity will be defined as $I^2 > 50%$ and forest plots will be visually inspected for heterogeneity. A certain degree of heterogeneity is expected, therefore a random-effects model will be used for possible meta-analysis.

Assessment of reporting biases

If at least 10 studies are included, we will draw funnel plots of treatment effect versus precision with the data from all studies (Higgins 2011). The funnel plots will be visually inspected to assess whether there has been selective reporting of outcomes.

Data synthesis

If trials include different outcomes, we will pool outcomes that measure the same construct, or systematically report on outcomes that do not measure the same construct.

We will perform a meta-analysis if we find two or more RCTs with a low risk of bias in which study population, intervention and outcome measures are comparable. We will create a 'Summary of findings' table following the Cochrane template (see Appendix 2). This will include the primary and secondary outcomes as listed

above. For each outcome we will report the number of participants, the overall quality of the evidence according to the GRADE levels of evidence, and the effect size.

If a meta-analysis is not possible we will synthesise the findings of the included studies in a table, following the GRADE levels of evidence (Higgins 2011). The individual effect sizes of the studies and 95% CI will be reported.

Review Manager will be used for the analyses (tech.cochrane.org/revman).

Subgroup analysis and investigation of heterogeneity

If sufficient studies can be identified, i.e. at least two for each subgroup, we will perform subgroup analyses for the study design (RCT or quasi-RCT), the type of intervention, the type of control group, timing (e.g. shortly after the patient's diagnosis, during initial anti-tumour treatment, following initial treatment, in the palliative phase or during the bereavement phase), and patient tumour type.

Sensitivity analysis

If sufficient data are available, we will perform a sensitivity analysis to assess the robustness of results, e.g. excluding studies with high risk of bias.

ACKNOWLEDGEMENTS

We acknowledge Gail Quinn and Dr Robin Grant from Cochrane Gynaecological, Neuro-oncology and Orphan Cancers for their help with this protocol.

This project was supported by the National Institute for Health Research (NIHR), via Cochrane infrastructure funding to Cochrane Gynaecological, Neuro-oncology and Orphan Cancers. The views and opinions expressed herein are those of the review authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS), or the Department of Health.

We thank all of our external peer reviewers, including Charlotte Argyle and Kathy Oliver.

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* Indicates the major publication for the study

APPENDICES**Appendix I. MEDLINE search strategy**

1. exp Central Nervous System Neoplasms/
2. ((brain or cereb* or spinal cord or CNS or central nervous system) adj5 (cancer* or carcinoma* or tumor* or tumour* or malignan* or neoplas* or lymphoma* or hemangioma*)).mp.
3. exp Glioma/
4. (glioma* or astrocytoma* or meningioma* or oligodendroglioma* or glioblastoma* or ependymoma* or medulloblastoma* or craniopharyngioma* or pineal or pituitary or PNET* or DNET* or schwannoma*).mp.
5. 1 or 2 or 3 or 4
6. Caregivers/
7. exp Family/
8. (caregiver* or care giver* or carer*).mp.
9. ((family or families or spouse* or partner* or parent* or grandparent* or sibling* or relative* or friend* or husband* or wife or wives or close person* or significant other* or child or children) and (care or caring)).mp.
10. 6 or 7 or 8 or 9
11. 5 and 10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.
15. placebo.ab.
16. clinical trials as topic.sh.
17. randomly.ab.
18. trial.ti.
19. 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 11 and 19

Key:

mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, pt=publication type,ab=abstract, ti=title, sh=subject heading

Appendix 2. Example 'Summary of Findings' table

Title: Interventions to help support caregivers of people with a brain or spinal cord tumour						
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Patient or population: Adult caregivers of patients with a brain or spinal cord tumour Settings: Any Intervention: Any intervention aimed at improving caregiver well-being Comparison: Any control condition (e.g. waiting list control groups; attention only control groups; information only control groups)						
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Outcomes	Illustrative comparative risks*		Relative effect (95% CI)	No of participants (studies)	Quality of evidence (GRADE)	Comment
	Assumed risk	Corresponding risk				
1. Caregiver psychological distress						
2. Caregiver burden						
3. Caregiver mastery						
4. Quality of patient-caregiver relationship						
5. Caregiver quality of life						
6. Caregiver physical functioning						

(Continued)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
CI: confidence interval; HR: hazard ratio; MD: mean difference; RR: risk ratio; OR: odds ratio

*The basis for the (e.g. the median risk across studies in footnotes. The ing risk (and its dence interval) is assumed risk in the group and the re the intervention CI).
CI: confidence hazard ratio; MD ence; RR: risk ra ratio

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

GRADE Wor grades of evidence
High quality: Fu is very unlikely confidence in th effect.
Moderate qualit search is likely t portant impact dence in the esti and may change
Low quality: Fu is very likely to h tant impact on c in the estimate c likely to change
Very low quality uncertain about

CONTRIBUTIONS OF AUTHORS

FB drafted the protocol. The other review authors reviewed the protocol to improve its quality.

DECLARATIONS OF INTEREST

FB: involved in a RCT aimed at supporting informal caregivers of high-grade glioma patients through psycho-education and cognitive behavioural therapy.

PS: involved in an ongoing trial to support family caregivers of patients diagnosed with a primary brain tumour through a nurse-guided online programme.

HB: None known

CB: None known

AGR: None known

SOURCES OF SUPPORT

Internal sources

- New Source of support, Other.

External sources

- No sources of support supplied