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[Intervention Review]

Multidisciplinary rehabilitation after primary brain tumour treatment

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ABSTRACT

Background

Brain tumours can cause significant disability, which may be amenable to multidisciplinary rehabilitation. However, the evidence base for this is unclear. This review is an update of a previously published review in the Cochrane Database of Systematic Reviews [2013, Issue 1, Art. No. CD009509] on 'Multidisciplinary rehabilitation after primary brain tumour treatment'.

Objectives

To assess the effectiveness of multidisciplinary rehabilitation in people after primary brain tumour treatment, especially the types of approaches that are effective (settings, intensity).

Search methods

For this update, we searched the Cochrane Central Register of Controlled Trials (CENTRAL, the Cochrane Library up to Issue 12 of 12, 2014), MEDLINE (1950 to January week 2, 2015), EMBASE (1980 to January week 2, 2015), PEDro (1985 to January week 2 2015), and LILACS (1982 to January week 2, 2015). We checked the bibliographies of papers we identified and contacted the authors and known experts in the field to seek published and unpublished trials.

Selection criteria

Controlled clinical trials (randomised and non-randomised clinical trials) that compared multidisciplinary rehabilitation in primary brain tumour with either routinely available local services or lower levels of intervention, or studies that compared multidisciplinary rehabilitation in different settings or at different levels of intensity.

Data collection and analysis

Three review authors independently assessed study quality, extracted data, and performed a 'best evidence' synthesis based on methodological quality.

Main results

We did not identify any studies for inclusion in the previous version of this review. For this update, the literature search identified one low-quality controlled clinical trial involving 106 participants. The findings from this study suggest 'low-level' evidence to support high-intensity ambulatory (outpatient) multidisciplinary rehabilitation in reducing short- and long-term motor disability (continence, mobility and locomotion, cognition), when compared with standard outpatient care. We found improvement in some domains of disability (continence, communication) and psychosocial gains were maintained at six months follow-up. We found no evidence for improvement in overall

participation (quality of life and societal relationship). No adverse events were reported as a result of multidisciplinary rehabilitation. We found no evidence for improvement in quality of life or cost-effectiveness of rehabilitation. It was also not possible to suggest best 'dose' of therapy.

Authors' conclusions

Since the last version of this review, one new study has been identified for inclusion. The best evidence to date comes from this CCT, which provides low quality evidence that higher intensity ambulatory (outpatient) multidisciplinary rehabilitation reduces short- and long-term disability in people with brain tumour compared with standard outpatient care. Our conclusions are tentative at best, given gaps in current research in this area. Although the strength of evidence has increased with the identification of a new controlled clinical trial in this updated review, further research is needed into appropriate and robust study designs; outcome measurement; caregiver needs; evaluation of optimal settings; type, intensity, duration of therapy; and cost-effectiveness of multidisciplinary rehabilitation in the brain tumour population.

PLAIN LANGUAGE SUMMARY

Multidisciplinary rehabilitation after brain tumour treatment

People with brain tumours can experience a range of symptoms and disabilities, such as psychological problems, difficulties with mobility or self care, and relationship and work issues, which can substantially impact their quality of life. These symptoms and disabilities may be addressed through 'multidisciplinary rehabilitation' delivered by a team of different healthcare professionals (for example doctors, nurses, therapists) working in an organised manner.

We found one controlled clinical trial (poor quality) that compared multidisciplinary rehabilitation to standard outpatient care. The 106 people in this trial received treatment in the hospital outpatient clinic. Participants were in the multidisciplinary rehabilitation programme for up to eight weeks, and the results were measured at three and six months after completion of the programme.

There was some evidence to support the benefit of multidisciplinary rehabilitation in reducing disability in people with primary brain tumour. People in the multidisciplinary rehabilitation group showed improvement in their functional abilities (e.g. continence, mobility) and cognitive function compared to the group with standard care only. Multidisciplinary rehabilitation was not harmful. Current research gaps highlight the need for high-quality research to explore the effectiveness of various aspects of multidisciplinary rehabilitation and caregiver needs in this patient population.

The evidence in this review is up to date to January 2015.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

High-intensity multidisciplinary rehabilitation compared with wait-list control group with usual care for primary brain tumour

Patient or population: 106 participants with primary brain tumour

Settings: outpatient

Intervention: High-intensity multidisciplinary rehabilitation

Comparison: wait-list control group with usual care

Outcomes	Illustrative comparative risks*		Relative ef- fect* (Effect size 'R')#	No of Partici- pants (studies)	Quality of the evidence (GRADE) ¹	Comments
	Assumed risk	Corresponding risk				
	Usual care (control group)	High-intensity multidiscipli- nary rehabili- tation (inter- vention group)				
Short-term disability outcomes at 3-months postintervention						
Change in short-term disability (function) FIM motor	Median change = 8 points higher	Median change = 18 points higher	Z score: -3.13, P < 0.001 R: 0.32	106 (1 study)	⊕⊕⊕⊕ Low ¹	13 items with 4 subscales (self care, transfers, locomotion, sphincter control, assessing function (activity) and need for assistance, rated on a 7-point scale (1-7), with higher score indicating higher independence and lower need for assistance
Change in short-term disability (cognition) FIM cognition	Median change = 3 points higher	Median change = 6 points higher	Z score: -1.99, P < 0.05 R: 0.20	106 (1 study)	⊕⊕⊕⊕ Low ¹	3 items with 3 subscales (communication, psychological, cognition) assessing cognition, rated on a 7-point scale (1-7), with higher score indicating higher independence and lower need for assistance
Long-term disability outcomes at 6-months postintervention						
Change in long-term disability (function) FIM motor	Median change = 4 points higher	Median change = 12 points higher	Z score: -2.33, P < 0.05 R: 0.25	106 (1 study)	⊕⊕⊕⊕ Low ¹	13 items with 4 subscales (self care, transfers, locomotion, sphincter control, assessing function (activity) and need for assistance, rated on a 7-point scale (1-7),

with higher score indicating higher independence and lower need for assistance

Change in long-term disability (cognition) FIM cognition	Median change = 1.5 points higher	Median change = 6 points higher	Z score: -3.09, P < 0.001 R: 0.20	106 (1 study)	⊕⊕⊕⊕ Low ¹	3 items with 3 subscales (communication, psychological, cognition) assessing cognition, rated on a 7-point scale (1-7), with higher score indicating higher independence and lower need for assistance
Change in short-term participation outcomes at 3-months postintervention						
Change in short-term psychological outcomes DASS (total)	Median change = 12 points lower	Median change = 8 points lower	Z score: -0.53, P > 0.05 R: 0.05	106 (1 study)	⊕⊕⊕⊕ Low ¹	21 items with 3 subscales assessing depression, anxiety, and stress, rated on a 4-point scale, with higher score indicating higher level of impairment
Change in short-term participation PIPP (total)	Median change = 7 points lower	Median change = 6 points lower	Z score: -0.40, P > 0.05 R: 0.04	106 (1 study)	⊕⊕⊕⊕ Low ¹	23 items with 5 subscales assessing mobility, self care, relationships, participation, and psychological well-being, rated on a 6-point scale, with high scores indicating greater impact
Change in short-term QoL CARES-SF (global)	Median change = 0.2 points lower	Median change = 0.1 points lower	Z score: -0.10, P > 0.05 R: 0.01	106 (1 study)	⊕⊕⊕⊕ Low ¹	59-item global scale, with overall score indicating QoL and summary scores for the 5 domains (physical, psychosocial, medical interaction, marital and sexual function), assessing cancer-specific rehabilitation need and QoL, rated on a 4-point scale, with higher scores indicating more difficulty or lower QoL
Change in long-term participation outcomes at 6-months postintervention						
Change in long-term psychological outcomes DASS (total)	Median change = 10 points lower	Median change = 12 points lower	Z score: -0.98, P > 0.05 R: 0.11	106 (1 study)	⊕⊕⊕⊕ Low ¹	21 items with 3 subscales assessing depression, anxiety, and stress, rated on a 4-point scale, with higher score indicating higher level of impairment
Change in long-term participation PIPP (total)	Median change = 9.5 points higher	Median change = 5 points lower	Z score: -0.37, P > 0.05 R: 0.04	106 (1 study)	⊕⊕⊕⊕ Low ¹	23 items with 5 subscales assessing mobility, self care, relationships, participation, and psychological well-being, rated on a 6-point scale, with high scores indicating greater impact
Change in long-term QoL	Median change = 0.2 points lower	Median change = 0.2 points lower	Z score: -0.42, P < 0.05	106 (1 study)	⊕⊕⊕⊕ Low ¹	59-item global scale, with overall score indicating QoL and summary scores for the 5 domains (physical, psychosocial, medical interaction, marital and sexual function), assessing cancer-specific rehabilitation

CARES-SF (global) R: 0.05 need and QoL, rated on a 4-point scale, with higher scores indicating more difficulty or lower QoL

Change in other outcomes

Cost- effectiveness	See comment	See comment	Not estimable	106 (1 study)	See comment	Not measured
Serious adverse events	See comment	See comment	Not estimable	106 (1 study)	See comment	No serious adverse events attributed to the intervention

*Mann-Whitney U tests

Effect size statistics (R) were calculated and assessed against Cohen's criteria (0.1 = small, 0.3 = medium, 0.5 = large effect)

CARES-SF: Cancer Rehabilitation Evaluation System-Short Form; **DASS:** Depression Anxiety Stress Scales; **FIM:** Functional Independence Measure; **PIPP:** Perceived Impact of Problem Profile; **QoL:** quality of life

¹GRADE 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.

BACKGROUND

This review is an update of a previously published review in the Cochrane Database of Systematic Reviews [2013, Issue 1, Art. No. CD009509] on 'Multidisciplinary rehabilitation after primary brain tumour treatment'.

Description of the condition

Primary brain tumours are a diverse group of neoplasms that account for 2% of all cancers and affect approximately seven people per 100,000 population annually worldwide (Arber 2010; Parkin 2005). There is evidence to support the increasing overall incidence of primary brain tumours, with the highest increase noted in patients over 60 years of age (Flowers 2000). In 2009, there were an estimated 22,070 new cases of primary brain tumours in the United States (Jemal 2009). Three thousand new cases of primary brain tumours are reported each year in the United Kingdom, with approximately 2500 deaths per annum (Arber 2010). A similarly high incidence rate is also reported in Australia, with approximately 1400 new cases and more than 1200 deaths from malignant and benign brain tumours annually (Brain Foundation 2011).

Significant medical advances in the treatment of primary brain tumours have resulted in a marked increase in the number of survivors (Huang 2011; Poggi 2009). Surgery remains the primary treatment for the majority of people with brain tumours, with radiotherapy and chemotherapy or both as neoadjuvant, concomitant, or adjuvant treatment (Chandana 2008). However, the treatment regimens can produce significant adverse effects (Aziz 2003; Tang 2008). Despite these treatment options, brain tumours remain a significant source of functional and psychosocial impairment for this patient population, limiting them in everyday activity and participation due to many issues (Huang 2011; Tang 2008). Diagnosis of brain tumour can further have a distressing psychological impact, significant costs and socioeconomic implications, increased demand for health care, social, and vocational services, and caregiver burden (Tang 2008).

People with primary brain tumour can present with various combinations of problems, such as physical, cognitive, psychosocial, behavioural, and environmental issues. The World Health Organization (WHO) developed the International Classification of Functioning, Disability and Health (ICF), which defines a common language for describing the impact of disease at different levels: impairment (body structure and function), limitation in activity and participation (WHO 2001). Within this framework, primary brain tumour-related impairments can limit activity or function and participation in society and life situations, and reduce life span (Khan 2013b). Many people diagnosed with brain tumour may have ongoing concerns (such as relationship, employment, recurrence) (Ownsworth 2009). The limitation in function (disability) can have a cumulative effect over time and cause considerable distress to cancer survivors and their families, and reduce quality of life (QoL) (Ness 2010). Patients discharged back to the community are confronted by various adjustment issues, such as the person's perceptions of self worth, self image, and role reversal within the family. Families or caregivers or both often struggle to cope with the new demands associated with increased care needs, inability to drive and return to work, financial constraints, marital stress, and general limitation in the person's participation. A longitudinal study of people with brain tumours living in the community after treatment (median time

since diagnosis 2.1 years) found that over half still had pain (56%); 44% reported ataxia; 43% seizures; 37% paresis, 36% cognitive dysfunction; and 35% visual impairment (Khan 2013c). Ongoing monitoring, education, and counselling of the person (and family) are therefore important (Khan 2013d).

The care needs after treatment for primary brain tumour (surgery, chemotherapy, and radiotherapy) are varied given the complex, multifactorial nature of the condition and multiple disabilities (which may progress) in these people. These are best met with a coordinated, multidisciplinary, multifaceted approach that includes acute medical and surgical care, rehabilitation, palliative and other supportive interventions (Gabanelli 2005).

Description of the intervention

Rehabilitation has been defined as "a problem-solving educational process aimed at reducing disability and handicap (participation) experienced by someone as a result of disease or injury" (Wade 1992). In this review, multidisciplinary rehabilitation is defined as the coordinated delivery of multidimensional rehabilitation intervention provided by two or more disciplines (such as nursing, physiotherapy, occupational therapy, social work, psychology and other allied health), in conjunction with medical professionals (surgeon; oncologist; rehabilitation, palliative physician), which aims to improve patient symptoms and maximise functional independence and participation (social integration) using a holistic biopsychosocial model, as defined by the ICF (WHO 2001). A multidisciplinary approach provides patients with skills needed to manage their own care to improve their coping ability, knowledge base, and QoL (Corner 2007). It prioritises patient-centred care and focuses on a person's function and disability, using a goal-based, functionally oriented approach that is time based. The patients (and family or caregivers) are active participants in the goal-setting process. The content, intensity, and frequency of therapy in multidisciplinary rehabilitation can vary, as programmes are individualised based on clinical needs. The content can include physical reconditioning, task re-acquisition strategies, cognitive behavioural therapy, vocational and recreational programmes.

People after primary brain tumour treatment can present to rehabilitation settings with a range of difficulties that may be physical, emotional, psychosocial, and/or environmental (Khan 2013b). Multidisciplinary rehabilitation encompasses the framework and common language for describing the impact of disease at different levels using the ICF (WHO 2001). For example, in people after brain tumour treatment:

- 'impairments' are problems with body (anatomical) structures or function (headaches, seizures, neurocognitive dysfunction, muscle weakness, aphasia, visual impairments);
- 'activity limitations' (disabilities) are difficulties a person has executing everyday tasks (mobility or self care);
- 'restriction in participation' relates to problems a person has that limit involvement in societal participation and life situations (i.e. employment, family life, social re-integration);
- 'contextual factors' are:
 - 'environmental' issues, which make up the physical, social, and attitudinal environment in which a person lives their life (i.e. living condition, support and attitudes of friends and family); and

- 'personal' problems (such as gender, race, coping style, social and educational background) that may affect the person's experience of living with their condition.

Many systematic reviews support various treatment modalities for people with primary brain tumour such as chemotherapy and symptomatic pharmacological therapy (Stewart 2002), radiotherapy (Andrews 2004), or surgery (Pirzkall 1998). A number of reviews also address unidisciplinary rehabilitation for this population, such as psychological interventions (Ownsworth 2009; Sheard 1999). However, none address multidisciplinary rehabilitation in these people.

How the intervention might work

Multidisciplinary rehabilitation in people after primary brain tumour treatment can utilise various categories in domains comprising the structured framework outlined by the ICF, for targeted intervention and therapy. The ICF provides clinicians with specific categories within relevant domains for intervention, for example 'activity and participation' domain (relating to mobility, self care, domestic life, major life areas), and environmental factors (transport, access to places, relationships, attitudes).

Many impairments (hemiparesis, dysphasia, cognitive deficits) seen in the brain tumour population are also common in other neurological conditions such as acquired brain injury, stroke, and multiple sclerosis. There is strong evidence to support multidisciplinary rehabilitation in various neurological conditions, such as multiple sclerosis (Khan 2007), acquired brain injury (Turner Stokes 2005), Guillain-Barre syndrome (Khan 2010), motor neuron disease (Ng 2009), and stroke (SUTC 2007), as well as in oncological conditions, such as breast cancer (Khan 2012a; Khan 2012b). A number of studies have shown that people with brain tumours undergoing rehabilitation appear to make significant functional gains (Geler-Kulcu 2009; Greenberg 2006; Huang 2001a; Marciniak 2001; O'Dell 1998; Tang 2008), in line with those seen in people affected by other cerebral pathologies such as traumatic brain injury or stroke (Kirshblum 2001). Furthermore, there is strong evidence that unidisciplinary interventions such as exercise and physical therapies enhance physiological and functional outcomes and improve QoL in cancer survivors (MacVicar 1986; MacVicar 1989; Markes 2006; McNeely 2010).

Why it is important to do this review

There are no systematic reviews for multidisciplinary rehabilitation following primary brain tumour treatment to date. Other reasons to do this review include the following:

- Brain tumour rehabilitation is complex and challenging (Kirshblum 2001), and in light of recent initiatives as outlined in the United States National Coalition for Cancer Survivorship (NCCS 2009), which aims to produce evidence-based guidelines and implement survivorship care plans, there is a need to address the long-term requirements of cancer survivors. The previous version of this systematic review aimed to inform the implementation of a National Cancer Survivorship Initiative (Cancer Reform Strategy 2007). This initiative explored individualised approaches to survivorship care (education, nutrition, self management) and the provision of rehabilitation programmes, and was a national service framework in the United Kingdom. This updated review could also be useful for

the development of further rehabilitation programmes for those living with and beyond cancer, such as the Living With and Beyond Cancer Programme from United Kingdom (Department of Health 2013).

- Advances in medical care and increased life expectancy among people with disabilities mean that ongoing health and well-being become increasingly important and require longer-term planning (Campbell 1999; Turk 2001). From the rehabilitation perspective, the challenge is not just about helping the brain tumour survivor to overcome the symptoms and improving their performance status; it is also about helping them stay independent in the community in the face of changes associated with tumour progression/recurrence, as well as aging, and helping families to overcome the additional demands and stress.
- A better understanding of the optimal structure, function, and content of multidisciplinary rehabilitation (with clear delineation of the roles) would further guide improvement of service provision from an organisational and economic perspective.

A systematic review is therefore required to summarise the best available evidence to date. This review aimed to identify the existing evidence for multidisciplinary rehabilitation in people after primary brain tumour treatment, guide treating clinicians, and determine gaps in current knowledge.

OBJECTIVES

To assess the effectiveness of multidisciplinary rehabilitation in people after primary brain tumour treatment, and especially the types of approaches that are effective (settings, intensity).

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and controlled clinical trials (CCTs), including quasi-randomised and quasi-experimental designs with comparative controls (controlled before-and-after studies).

Types of participants

Inclusion criteria

- Adults (aged 18 years and older).
- Confirmed diagnosis of brain tumour, regardless of time of onset or disease stage according to the WHO classification of tumours of the central nervous system (CNS) (Louis 2007), which include: astrocytic tumours; oligodendroglial tumours; ependymal tumours; choroid plexus tumours; other neuroepithelial tumours; neuronal and mixed neuronal-glial tumours; tumours of the pineal region; embryonal tumours; tumours of the haemopoietic system; germ cell tumours; meningeal tumours; tumours of the sellar region.

We also included studies involving participants with a range of cancers or other diagnoses that reported data specifically for people with primary brain tumour.

Exclusion criteria

- Studies recruiting only participants with metastatic (i.e. non-primary) brain tumour.
- Studies involving participants with CNS cancers where data were not provided separately for primary brain tumour.

Types of interventions

As described above, multidisciplinary rehabilitation is defined as any intervention delivered by two or more disciplines (such as nursing, physiotherapy, occupational therapy, social work, psychology, and other allied health) in conjunction with medical input (surgeon, oncologist, rehabilitation and/or palliative physician), to maximise activity and participation, as defined by the ICF (WHO 2001).

Multidisciplinary rehabilitation interventions and programmes are broadly described in terms of settings and content (Khan 2007; Turner Stokes 2005). Rehabilitation settings may include "inpatient" settings, where care is delivered 24 hours a day in a hospital ward or specialist rehabilitation or palliative care unit; "ambulatory/outpatient settings", which may be within a hospital or in the community; and "home-based settings", which are set within the patient's own home and local community.

The content, intensity, and frequency of therapy provided in multidisciplinary rehabilitation programmes can vary based on individual needs. The content can include physical reconditioning, task re-acquisition strategies, environmental modification, cognitive behavioural therapy, vocational and recreational programmes.

We considered all studies that stated or implied multidisciplinary rehabilitation for inclusion in this review, provided they satisfied the definition above and compared multidisciplinary rehabilitation to some form of control condition. The control conditions included:

- lower-level or different types of interventions such as 'routinely available local services' (e.g. medical and nursing care);
- minimal interventions (such as 'information only');
- 'wait list' controls or no treatment, or usual care;
- interventions given in different settings and of lower intensity.

We excluded studies if they assessed the effect of therapy from a single discipline (for example physiotherapy only) or any unidisciplinary intervention or modality (for example physical exercise).

Types of outcome measures

Primary outcomes

Primary outcomes reflect the burden of disease on patients and on the services provided for them. We categorised these according to the ICF into those that focus on the following (WHO 2001).

1. Impairment, e.g. headache, seizures, muscle weakness, aphasia, visual impairments, pain.
2. Disability (limitation in activity), measured by validated tools such as the Functional Independence Measure (Granger 1998), Barthel Index (Mahoney 1965), Cancer Rehabilitation Evaluation System-short form (Ganz 1992; Schag 1991), Cancer Survivor

Unmet Needs measure (Hodgkinson 2007), and Perceived Impact of Problem Profile (Pallant 2006).

3. Restriction in participation and/or environmental or personal context, e.g. quality of life (SF-36; Ware 1993), fatigue (Fatigue Impacts Scale; Fisk 1994), psychological (Depression Anxiety Stress Scale; Lovibond 1995) and vocational outcomes (Work Instability Scale; Gilworth 2003), social re-integration and patient satisfaction measures, and others.
4. Any adverse events that may have resulted from the intervention, defined as those events that are life-threatening or requiring prolonged hospitalisation.

Secondary outcomes

Secondary outcomes included those that reflected service utilisation, such as the length of hospital stay in both acute and subacute settings, readmission, the cost of care, and the extent of services used at the time of discharge.

Timing of outcome measures

The time points for outcome assessments were: short term (immediately after intervention or up to three months) and long term (greater than three months) from the start of the intervention. We considered participant follow-up assessments similarly as short term (up to three months) and long term (greater than three months) after cessation of the intervention.

Search methods for identification of studies

We considered articles in all languages, with a view to translation if necessary.

Electronic searches

We searched the following databases:

- The Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library) Issue 12 of 12, 2014 (see Appendix 1)
- MEDLINE (via OvidSP) (from 1950 to January week 2, 2015) (see Appendix 2)
- EMBASE (via OvidSP) (from January 1980 to January week 2, 2015) (see Appendix 3)
- PEDro (from January 1985 to January week 2, 2015) (see Appendix 4)
- LILACS (from January 1982 to January week 2, 2015) (see Appendix 5)

The initial search strategy for this review also included searches of the Cochrane Cancer Network, CANCERLIT, BIOSIS, and Science Citation Index. We used the same principle to search each database. This included: (i) the terms and phrases identifying RCTs and CCTs combined using the Boolean "OR"; (ii) all the terms and phrases describing brain neoplasm combined with "OR", and (iii) all terms used to identify the interventions of interest, that is multidisciplinary rehabilitation, combined with "OR". We then grouped these terms with the Boolean operator "AND" and performed the final search of the articles from the displayed results. We used wild cards and truncation symbols to ensure that we did not miss terms with alternative spellings and endings. We exploded all MeSH terms.

Searching other resources

We searched the WHO International Clinical Trials Registry Platform (ICTRP) search portal (<http://apps.who.int/trialsearch/Default.aspx>), the metaRegister of Controlled Trials (<http://www.isrctn.com/>), and ClinicalTrials.gov (<https://clinicaltrials.gov/>) for all prospectively registered and ongoing trials. We checked the bibliographies of identified studies and contacted the study authors and known experts in the field seeking published and unpublished trials. We also handsearched the most relevant journals, which included (but were not limited to): *Brain*, *Cancer*, *Supportive Care in Cancer*, *Journal of Cancer Therapy*, *American Journal of Clinical Oncology: Cancer Clinical Trials*, *Annals of Cancer Research and Therapy*, *Journal of Surgical Oncology*, *Journal of Oncology*, *European Journal of Cancer and Clinical Oncology*, *Journal of the Cancer Institute*, *Neuro-oncology*, *Journal of Neuro-oncology*, *Journal of Neurology*, *Neurosurgery and Psychiatry*, *Physical Therapy*, *Archives of Physical Medicine and Rehabilitation*, and *Clinical Rehabilitation*.

We also undertook an expanded search using the related articles feature (via PubMed), ProQuest Dissertations & Theses, searching key authors (via Web of Science) and searching OpenGrey (System for Information on Grey Literature in Europe).

Data collection and analysis

Selection of studies

Two review authors (BA, LN) independently screened and short-listed all abstracts and study titles identified by the search strategy for appropriateness based on the selection criteria. The two review authors (BA, LN) independently evaluated each study from this short-list for inclusion or exclusion. We obtained the full text of all potential articles for further assessment to determine if the study met the inclusion/exclusion criteria. A consensus was met about the possible inclusion/exclusion of all studies, with the involvement of other review authors. Review authors were not masked to the name(s) of the author(s), institution(s), or publication source at any level of the review. As four authors of this review (FK, BA, KD, MG) are authors of the included study, one review author (LN) further screened the list of potential studies twice.

We had intended to contact trialists of eligible studies to further clarify details of their multidisciplinary rehabilitation if needed, however this was not necessary.

Data extraction and management

Three review authors (BA, LN, MG) independently extracted the data from each study that met the inclusion criteria using a standardised data collection form. We summarised all studies that met the inclusion criteria in the 'Characteristics of included studies' table provided in the Review Manager 5 (RevMan) software developed by The Cochrane Collaboration to include details on design, participants, interventions, and outcomes ([RevMan 2014](#)).

Assessment of risk of bias in included studies

Three review authors (BA, LN, MG) independently assessed the methodological quality of the included studies using Cochrane's 'Risk of bias' tool ([Higgins 2011](#)). This included the allocation sequence generation; allocation concealment; blinding of participants, therapists, and outcome assessors; incomplete outcome data; and selective outcome reporting. A judgement of

'low risk' indicated a low risk of bias, 'high risk' indicated a high risk of bias, and 'unclear' indicated either unclear or unknown risk of bias.

We considered studies to be of high methodological quality if the risk of bias for all domains was low. We termed these studies 'high-quality studies'. We rated studies as low methodological quality if there was unclear or high risk of bias for one or more domains, terming these 'low-quality studies'. Any disagreements or lack of consensus were resolved by consultation with a third review author (FK).

Measures of treatment effect

It was not possible to perform measures of treatment effect or to pool the data for meta-analysis, due to insufficient data and the type of data available and the diversity of methods in the studies. We entered and analysed all data in RevMan ([RevMan 2014](#)). We qualitatively summarised the studies in the 'Characteristics of included studies' table and presented the results of primary and secondary outcomes of included studies, categorised according to ICF framework, in the [Summary of findings for the main comparison](#). We described the results narratively in the [Discussion](#) section. If studies become available, and if meta-analyses are feasible in future updates, we will analyse treatment effects as described in the protocol version of this review ([Khan 2011](#)).

Unit of analysis issues

We anticipated that the appropriate unit of analysis would be by type, intensity, and setting of multidisciplinary rehabilitation.

Dealing with missing data

We would have attempted to contact the primary authors of potentially eligible studies to provide clarification of the data if necessary, however this was not required.

In addition, we excluded studies with 'fatal flaws' (for instance, withdrawals by more than 40% of the participants, nearly total non-adherence to the protocol, or very poor or non-adjusted comparability in the baseline criteria).

Assessment of heterogeneity

We followed the statistical analysis method as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). However, it was not possible to conduct a comprehensive quantitative analysis due to the variability of methods used and the type of available data reported in each study.

Assessment of reporting biases

We minimised publication bias by sourcing unpublished data where possible and would have contacted authors for the full data set or the reason for not publishing the data, however this was not required ([Egger 1998](#)).

Data synthesis

As mentioned above, we were unable to conduct a quantitative analysis due to lack of studies identified, clinical heterogeneity, and the variation in methods and available data in the included studies. If studies had been available, we would have attempted a quantitative analysis, provided there was clinical homogeneity and the data in each study allowed for such an analysis. We would

also have calculated a weighted treatment effect across trials using the RevMan and expressed the results as risk ratios with 95% confidence intervals (CIs) and risk differences with 95% CIs for dichotomous outcomes and mean differences and 95% CIs for continuous outcomes (RevMan 2014). We would have initially used a fixed-effect model and approximate Chi² tests for heterogeneity to assess outcome data for compatibility with the assumption of a uniform risk ratio ($P > 0.10$). In the presence of significant heterogeneity ($P < 0.10$), we would have used random-effects meta-analysis instead.

We used the GRADE approach to grade evidence quality, as described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We have highlighted the strength of study findings, discussed gaps in current literature, and identified future research directions in the Discussion section. If data becomes available in future updates, we will attempt a quantitative analysis, as described in the protocol version of this review (Khan 2011).

Subgroup analysis and investigation of heterogeneity

Due to lack of available data, it was not possible to perform subgroup analysis for the following:

1. type of multidisciplinary rehabilitation (i.e. inpatient, ambulatory care);
2. intensity of treatment (high-, low-intensity (usual outpatient care) multidisciplinary rehabilitation);
3. time from definitive treatment (surgery, radiotherapy, and chemotherapy) to commencement of multidisciplinary

rehabilitation (acute: less than six weeks, intermediate: six weeks to six months, and longer term: more than six months).

Factors considered in heterogeneity included: setting, type, and intensity of multidisciplinary rehabilitation.

Sensitivity analysis

We performed no sensitivity analysis. If studies had been available, and heterogeneity existed across trials, we would have conducted sensitivity analyses by omitting trials with a high risk of bias.

RESULTS

Description of studies

See the 'Characteristics of included studies' and 'Characteristics of excluded studies' tables for details.

Results of the search

The initial version of this review identified a total of 5410 references (CENTRAL = 957; MEDLINE = 1853; EMBASE = 2559; PEDro = eight; LILACS = 14; the Cochrane Neuromuscular Disease Group Specialized Register = 19) with our search criteria (up to 13 March 2013) (Khan 2013a). Of these references, 18 passed the first screening review and were selected for closer scrutiny. We also found two potentially relevant articles from bibliographies of papers identified. The updated electronic and manual search (up to 12 January 2015) yielded a further 1609 additional titles (CENTRAL = 103; MEDLINE = 888; EMBASE = 615; PEDro = two; LILACS = one). We finally screened titles and abstracts of 1543 articles after removal of duplicates. Of these, we scrutinised full-text of 24 potential articles and included one CCT. (See Figure 1 for the study flow chart.)

Figure 1. Study flow diagram.

Included studies

From the updated search we found one new CCT (Khan 2014), which compared a high-intensity multidisciplinary ambulatory (outpatient) rehabilitation programme with a standard outpatient care over six months. (See [Characteristics of included studies](#).) This study involved a total of 106 participants (with gliomas) recruited from a tertiary hospital in Melbourne, Australia. Participants were predominantly women (56%), with mean age of 51 years (standard deviation 13.6 years, range 21 to 77 years), and median time since diagnosis of 2.1 years. Participants were allocated to a treatment group (N = 53) for an individualised high-intensity multidisciplinary programme or a wait-list control group (N = 53).

The intensive multidisciplinary rehabilitation programme was an individualised, time-based, functional, goal-oriented treatment with active patient participation involving all relevant disciplines based on participant need and team consensus. The programme consisted of one-hour sessions of uninterrupted therapy two to three times per week for six to eight weeks or more (depending on the individual need). Each session was broken into half-hour therapy blocks (occupational, social, psychological, and physiotherapy).

The methods used included, for example, physiotherapy for strengthening, endurance, and gait training; occupational therapy to improve everyday function (domestic or community tasks), driving, and return to work; and clinical psychology for counselling and support as required.

The mean duration of the rehabilitation programme was 21 days (range 14 to 32 days). The control group were those people on

the wait-list for the rehabilitation programme, who continued with their usual activity in the community.

The primary outcome measured was change in the Functional Independence Measure (FIM), which assesses independence in daily activities including self care, continence, mobility, locomotion, and cognition. Secondary measures included measures of participation and psychosocial function: change in the Depression Anxiety Stress Scales (DASS), the Perceived Impact of Problem Profile (PIPP), and the Cancer Rehabilitation Evaluation System-Short Form (CARES-SF).

All outcome measures were assessed at baseline, three, and six months after programme completion.

Excluded studies

We excluded 23 studies for the reasons described in the '[Characteristics of excluded studies](#)' table. The primary reasons for exclusion were:

- not RCT or CCT (N = 17)
- unidisciplinary intervention (N = 5)
- data not specifically provided for brain tumour subgroup (N = 1)

Of the 17 studies excluded due to study design, 13 reported functional outcomes related to multidisciplinary rehabilitation and are described below in the [Discussion](#) section.

Risk of bias in included studies

See [Figure 2](#) and [Figure 3](#).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

The newly included CCT, [Khan 2014](#), comprehensively described details of the rehabilitation programme, and the trial investigators performed an a priori power calculation based on the primary

outcome. The study had several weaknesses that increased the risk of bias:

1. Participants were not randomised and allocation concealment procedure was not performed.
2. The trial tested a small convenience sample limited to one Australian metropolitan facility, limiting the external validity of the results.
3. The participants were not blinded, owing to the nature of the treatment.
4. Avoidance of co-interventions or their equal distribution throughout study groups was not reported. Reporting of co-interventions could have helped judgement of their division among study groups, and whether they would have significantly affected the outcome.
5. Loss of 21 participants (20%) at six-months follow-up.

Allocation

Allocation concealment of intervention assignment was not performed in this study.

Blinding

Participants were not blinded, as the rehabilitation intervention itself requires participants to be consented for treatment, hence making it difficult to blind participants. This could have influenced participant-reported outcomes. However, participants were asked not to discuss their involvement in the study with treating therapists and outcome assessors in order to reduce the risk of breaking blinding of the therapists and assessors. Treating therapists were blinded.

Incomplete outcome data

At three-months follow-up, eight participants (7%) dropped out: four in each group. At six-months follow-up, the overall dropout rate was 20%: 12 in the intervention group and nine in the control group.

Selective reporting

The authors of the study reported all prespecified (primary and secondary) outcomes in detail.

Other potential sources of bias

The study included a small selective cohort listed on a single database held at a single tertiary institution that agreed to participate in research projects, which may limit the generalisability of findings. Participant follow-up was short, that is only up to six months.

Avoidance of co-interventions or their equal distribution throughout study groups was not reported. Reporting of co-interventions could have helped judgement of their division among study groups, and whether they would have significantly affected the outcome.

Effects of interventions

See: [Summary of findings for the main comparison](#)

The CCT, [Khan 2014](#), addressed the effectiveness of outpatient (ambulatory) multidisciplinary rehabilitation for people with primary brain tumours. The findings for all outcomes are presented in [Table 1](#).

Short-term subjective outcomes (reduced disability and limitation in participation) at three-months postintervention

- The treatment group demonstrated a significantly greater gain in total FIM motor score in comparison with the control group (mean difference 3.5, 95% CI 0.8 to 6.2; $P = 0.012$). This difference was seen across all domains: self care, sphincter control, mobility, locomotion, and communication ($P < 0.01$ for all) and cognition subscale ($P < 0.05$) with small-to-moderate effect sizes (Cohen's $R = 0.2$ to 0.4).
- There were no significant short-term effects on other scores.

Longer-term subjective outcomes (reduced disability and limitation in participation) at six-months postintervention

- Significant improvement in the treatment group was maintained only for FIM 'sphincter', 'communication', and 'cognition' subscales ($P < 0.01$ for all).
- We noted no difference in groups on other scales.

Cost-effectiveness was not evaluated. The study reported no serious adverse events attributed to the rehabilitation intervention. P values are reported as they were stated in the study publications.

DISCUSSION

This review is an update of a previously published review in the Cochrane Database of Systematic Reviews [2013, Issue 1, Art. No. CD009509] on 'Multidisciplinary rehabilitation after primary brain tumour treatment'. The literature search for this update identified one low-quality controlled clinical trial (CCT) involving 106 participants.

Summary of main results

One small CCT, [Khan 2014](#), provided low-quality evidence that an individualised, high-intensity multidisciplinary ambulatory (outpatient) rehabilitation programme reduced disability (mobility, self care, continence, and cognition) when compared with the control group with usual outpatient care at three months. Improvement in some domains of disability (continence, communication) and psychosocial gains were maintained at six-months follow-up. The study demonstrated that the multidisciplinary rehabilitation programme positively impacted on participation when compared with usual outpatient care at six months ([Summary of findings for the main comparison](#)). The reported relative effect sizes were modest to large. This updated review increases the body of evidence for high-intensity multidisciplinary ambulatory (outpatient) rehabilitation, as previously no such studies had been identified.

Brain tumour is a complex and devastating condition that places many demands on patients, caregivers, and health professionals. People with brain tumour can have diverse presentations and a varied level of disability for rehabilitation, requiring an individualised approach. Rehabilitation itself is defined as a 'complex' intervention (when the active ingredient in the intervention is not easily identifiable) ([MRC 2000](#)).

For the overall completeness of this review, we have presented data from studies with other designs or observational studies in the section below, with the understanding that the contribution of such studies for best evidence synthesis is limited at best.

Overall completeness and applicability of evidence

The gaps in the evidence base in rehabilitation practice for people with brain tumour include:

1. limited high-quality evidence for overall effectiveness of multidisciplinary rehabilitation;
2. lack of agreement among treating clinicians with respect to the clinical approach and the most effective forms of intervention;
3. failure to incorporate the perspective of the person with brain tumour and their caregivers;
4. lack of common outcome measures to compare rehabilitation practice across different programmes and populations.

These are similar to evidence gaps that have been outlined previously for people with multiple sclerosis, motor neuron disease, and acquired brain injury (Khan 2007; Ng 2009; Turner Stokes 2005).

We identified one CCT, Khan 2014, evaluating the effectiveness of multidisciplinary rehabilitation in primary brain tumour survivors. Although randomised controlled trials (RCTs) and CCTs are the main scientific and rigorous approach to study comparative effectiveness of interventions and are widely considered as the 'gold standard' for high-level evidence, they are much less suited to studying 'complex' interventions such as rehabilitation (Horn 2012; Khan 2007; Turner Stokes 2005). The many challenges for traditional research designs (such as RCTs) in rehabilitation settings include: heterogeneous, interdependent components; different patient populations and contexts; treatments that are multifaceted, multilayered and involve organisational restructure; and individual intervention and ethical considerations (Horn 2012; Khan 2007; Khan 2010). Brain tumour survivors form a diverse group with a wide range of clinical presentations and varied levels of disability, requiring a customised and multifactorial approach to rehabilitation. Hence, such a rehabilitation approach does not lend itself well to RCTs, and as a result many vital questions remain unanswered (Horn 2012; Khan 2007; Whyte 2002).

Additional evaluation of observational studies

Given the paucity of clinical trials, we also evaluated observational studies (with 10 participants or more) in order to provide a more complete picture of the existing literature. The literature search identified 13 observational studies reporting various outcomes following multidisciplinary rehabilitation in people with brain tumours (Bartolo 2012; Fu 2010; Geler-Kulcu 2009; Greenberg 2006; Huang 1998; Huang 2000; Huang 2001a; Kim 2012; Marciniak 2001; O'Dell 1998; Pace 2007; Sherer 1997; Tang 2008). (See Table 1.) We have summarised the limited evidence from these studies below.

- Seven studies were conducted in the United States, two in Italy, and one each in Korea, Turkey, Israel, and Canada.
- Each study was conducted within a single institute/facility, with a total of 830 participants with various types of brain tumours.
- Eleven studies involved inpatient rehabilitation settings and two ambulatory settings (one outpatient setting, Sherer 1997, and one home based, Pace 2007).
- Seven studies were retrospective audits of hospital medical records (Fu 2010; Greenberg 2006; Huang 1998; Huang 2000; Marciniak 2001; O'Dell 1998; Tang 2008).

- Seven studies were case-control studies, of which six compared the rehabilitation outcomes of brain tumour participants with other non-oncological neurological condition cohorts (four compared with stroke survivors (Bartolo 2012; Geler-Kulcu 2009; Greenberg 2006; Huang 1998), two with traumatic brain injury (Huang 2000; O'Dell 1998). One study, Fu 2010, compared the functional outcomes between low- and high-grade astrocytomas.
- The content, duration, intensity, and nature of the multidisciplinary rehabilitation programmes were not well described.
- All studies had small sample sizes, making it difficult to detect a possible treatment effect.
- No adverse effects were reported.
- We rated all studies as very low quality due to lack of methodological robustness and unsystematic clinical observations (Table 1).

We have summarised the effects of interventions and results of these studies in Table 2.

Findings based on observational studies

Eleven studies addressed the efficacy of inpatient multidisciplinary rehabilitation (N = 696 participants) and reported significant reduction in disability (improvement in function) after a period of multidisciplinary rehabilitation as measured by various functional measurement tools (Functional Independence Measure (FIM), Barthel Index (BI), Modified Barthel Index (MBI), Karnofsky Performance Status Scale (KPS), Motricity Index (MI), Piper Fatigue Scale (PFS), Brief Fatigue Inventory (BFI); Table 2) (Bartolo 2012; Fu 2010; Geler-Kulcu 2009; Greenberg 2006; Huang 1998; Huang 2000; Huang 2001a; Kim 2012; Marciniak 2001; O'Dell 1998; Tang 2008). One study, Huang 2001a, reported continued functional improvements three months after discharge in a post-hoc analysis. Six studies compared multidisciplinary rehabilitation outcomes of people with brain tumours with people with other neurological conditions (stroke or traumatic brain injury). All six reported significantly greater gain in total FIM score when compared to stroke or traumatic brain injury (Bartolo 2012; Geler-Kulcu 2009; Greenberg 2006; Huang 1998; Huang 2000; O'Dell 1998). One study, Fu 2010, compared functional outcomes between different types of brain tumour and found no significant differences. Four studies noted shorter length of hospital stay (LOS) in people with brain tumour compared with people with either stroke or traumatic brain injury (Greenberg 2006; Huang 1998; Huang 2000; Huang 2001a), in contrast with findings of O'Dell 1998, which reported no difference in LOS between brain tumour and traumatic brain injury groups. The percentage of participants discharged to home/community environments was comparable or greater in the brain tumour group, compared with people with stroke or traumatic brain injury (Greenberg 2006; Huang 1998; Huang 2000; O'Dell 1998). Another study, Kim 2012, investigating fatigue severity and the relationship between fatigue and other associated factors in patients with brain tumours found that after four weeks of inpatient rehabilitation, both motor function (MI scores) and functional status (KPS, MBI scores) improved significantly, whereas there was no change in fatigue severity (PFS and BFI scores).

Two studies (N = 134 participants) evaluated the effectiveness of ambulatory multidisciplinary rehabilitation (Pace 2007; Sherer 1997). One study, Sherer 1997, reported favourable participation

outcomes (community independence and employment) after outpatient multidisciplinary rehabilitation in people with brain tumours. These gains were generally maintained at eight months after discharge. Another study, [Pace 2007](#), showed significant functional gain (BI, KPS scores) and improved quality of life after home-based multidisciplinary rehabilitation ([Table 2](#)).

These observational studies addressed a broad spectrum of outcomes with limited follow-up. The study participants were heterogeneous (disease severity, diagnostic criteria used) with varying rehabilitation practices across countries (United States, Turkey, Italy, Israel, Korea), limiting generalisability of findings.

Limitations of findings

This review highlighted a number of limitations in the existing literature for multidisciplinary rehabilitation in the brain tumour population. These include the following.

- Limited number of methodologically rigorous studies (RCTs or CCTs).
- Due to paucity of data, comparison of multidisciplinary rehabilitation in different settings or at different intensities was not possible.
- Only one low-quality study provided direct evidence for organised multidisciplinary rehabilitation in achieving better outcomes when compared with control conditions.
- No studies addressed cost benefits of multidisciplinary rehabilitation, nor information about caregiver burden or needs.

Issues for consideration in brain tumour multidisciplinary rehabilitation

Despite the lack of robust evidence for multidisciplinary brain tumour rehabilitation, significant progress in the management of cancer survivors has led to increased prominence for integrated multidisciplinary rehabilitation ([Franklin 2007](#); [Gabanelli 2005](#); [Kirshblum 2001](#)). Many issues need to be considered for improved care for brain tumour survivors, including those discussed below.

Brain tumours are complex and can be rapidly progressive, characterised by heterogeneous symptoms associated with increased intracranial pressure and focal symptoms related to tumour location ([Vargo 2011](#)). Brain tumours can present for rehabilitation with a diverse clinical picture, varying levels of disability ranging from cognitive impairment, alterations in functional status to the presence of neuropsychiatric symptoms, requiring an individualised approach ([Sherwood 2006](#)). It is often associated with a poor prognosis, particularly malignant tumours, which have a median overall survival of about 12 months ([Arber 2010](#)). In addition to optimising standard medical treatments (surgery, radiotherapy, chemotherapy) and minimising complications (pain, hemiparesis, dysphasia), these patients require comprehensive multidisciplinary rehabilitation, which goes beyond simple physical recovery ([Gabanelli 2005](#); [Kirshblum 2001](#)). The goals of multidisciplinary rehabilitation include post-acute psychosocial adjustment and participation (independence, economic stability, employment, leisure activities, education) and palliative care (if required), ultimately optimising quality of life of the person ([Huang 2011](#); [Kirshblum 2001](#)). Compared to other similar neurological impairments (such as traumatic brain injury, stroke), the time frames for intervention in people with brain tumour are shorter (due to high mortality rate), thus requiring

well-defined functional goals. Furthermore, detrimental effects of treatment in this population are significantly higher ([Kirshblum 2001](#)).

Despite advances in brain tumour treatment, rehabilitation has not gained similar momentum among treating healthcare professionals ([Kirshblum 2001](#); [Tang 2008](#)). A survey in the United States found that half of rehabilitation hospitals do not treat more than 10 people with brain tumours annually ([Boake 1993](#)). This may be due to either poor awareness of the extent of rehabilitation services available on the part of healthcare professionals (neurosurgeons, neurologists, neuro-oncologists), or lack of understanding of the principles/benefits of rehabilitation ([Kirshblum 2001](#); [Tang 2008](#)). There are well-defined conceptual frameworks and models for designing successful rehabilitation programmes for people with cancer diagnoses ([Dietz 1969](#); [Franklin 2007](#)). These serve as a tool for identification of issues, symptoms, and functional deficits that occur most frequently at each stage of the cancer journey (that is staging/pre-treatment, primary treatment, post-treatment, recurrence, end-of-life) and help formulate needs of patients to establish a framework for providing multidisciplinary rehabilitation over time ([Franklin 2007](#)). However, none of the observational studies identified in this review used this approach.

There is no optimal and universally accepted outcome measure that incorporates the full spectrum of problems for people with cancer ([Franklin 2007](#)). Generic measures used in brain tumour (and other cancer) populations in general rehabilitation settings (for example the FIM or BI) are not sensitive enough to capture the relevant gains following intervention, and have ceiling effects ([Franklin 2007](#); [Khan 2009](#)). The FIM constitutes an ordinal rating scale and therefore should not be summed to a single total score nor subjected to mathematical manipulation (such as division by LOS) to derive a measure of efficiency ([Khan 2009](#)). The KPS is frequently used in brain tumour research, but it does not provide sufficient/specific information to guide the selection of appropriate and timely rehabilitation interventions ([Franklin 2007](#)). More information is thus required to determine whether the functional efficiency reported in the identified observational studies has real implications for clinical practice.

The outcome measures used in the brain tumour population vary and need to reflect its complex constructs, with a focus on activity (disability) and especially restriction in participation, as advocated by the International Classification of Functioning, Disability and Health (ICF) ([WHO 2001](#)). The ICF provides a comprehensive framework and classification system for a universal language for health professionals, researchers, patients (and caregivers), and consumer organisations to facilitate communication and agreement among treating clinicians with respect to clinical approach ([Khan 2007](#); [Khan 2010](#); [Turner Stokes 2005](#)). An ICF 'core set' for head and neck cancers (lists of ICF categories selected by experts for targeted management) has been developed ([Tschiesner 2010a](#)) and validated ([Leib 2011](#); [Tschiesner 2010b](#)), and in the future can assist with scale development using ICF item-banking techniques ([Cieza 2008](#)). A prospective community cross-sectional survey used the ICF to evaluate patient-reported disability in primary brain tumours ([Khan 2013b](#)). The authors compared participants' responses with categories within core sets for stroke and traumatic brain injury and found the existing comprehensive stroke and traumatic brain injury core sets incorporated the

majority of issues relevant to brain tumour survivors in post-acute settings. The authors advocated that the findings not only assist in defining a future core set for brain tumour, but also have a potential of developing a single core set relevant to most long-term neurological conditions (Khan 2013b).

Cancer registries exist in many countries and contain data mainly for survival, medical, and treatment outcomes. However, data in post-acute settings that provide information about residual disability and restriction in participation after brain cancer treatment (including rehabilitation and palliative care input) is not routinely available, especially over a longer time period. In Australia, the Australasian Rehabilitation Outcomes Centre (AROC), the national rehabilitation data set, collates inpatient and ambulatory data from 182 accredited public and private rehabilitation facilities across the country (AROC 2011). The AROC data set provides a national benchmarking system to improve clinical rehabilitation outcomes and produce information on the efficacy of interventions through the systematic collection of outcomes information in both inpatient and ambulatory settings. It currently provides generic measures of global disability and essential rehabilitation outcome data only (such as the degree of reduction in disability, length of hospital stay, and discharge destinations) (AROC 2011). A review is underway to refine and collect information in specific domains over time, relevant to brain cancer survivors in the AROC, so that information obtained on outcomes will make this data set more clinically relevant in the future.

Quality of the evidence

One low-quality CCT provides support for outpatient (ambulatory) multidisciplinary rehabilitation in the brain tumour population, including:

1. low-quality evidence for the effectiveness of outpatient multidisciplinary rehabilitation in reducing longer-term disability (at six-months postintervention);
2. low-quality evidence for short-term reduction of disability (at three-months postintervention);
3. no evidence for improvement in quality of life or participation or both following multidisciplinary rehabilitation or cost-effectiveness of such programmes;
4. no adverse effects attributable to multidisciplinary rehabilitation;
5. no evidence for caregiver burden, cost, or vocational outcomes (such as return to work, education, etc.).

In addition, we evaluated 13 observational studies (with methodological limitations) in order to provide a more complete picture of the existing literature. The best evidence synthesis from these observational studies provides 'very-low-level' evidence, suggesting that multidisciplinary rehabilitation (both inpatient and home based) may improve function and that ambulatory programmes may improve vocational outcomes and quality of life in people with brain tumour in the short term.

Potential biases in the review process

The conclusions from this review are limited by the lack of robust clinical trials and 'observational' studies of poor methodological quality with diverse approaches to multidisciplinary rehabilitation as described above. In addition, the review authors recognise a

number of limitations in the methodology of the review itself and the completeness of the retrieved literature.

1. The possibility of selection bias from the literature search (van Tulder 2003). Our search strategy principally encompassed cited literature. However, we used an extended range of terms to capture the widest possible selection of the relevant literature.
2. Publication bias cannot be ruled out as we cannot exclude the possibility of negative trials that have not reached the published literature (Egger 1998).
3. Similarly, reference bias is a further possible confounder (Goetzsche 1987), although our search strategy included searching of reference lists within the relevant articles for other possible articles missed in our electronic searches.
4. Searches on the foreign language databases (LILACS) were limited mainly to English language terms, so it is possible that we missed relevant studies in other languages.

We therefore welcome contact from any readers who are aware of important high-quality studies that would meet the criteria for this review, but are so far not included. We did not find or were not aware of any ongoing studies.

Agreements and disagreements with other studies or reviews

The findings of this review highlight the existing gaps in the literature and emphasise the lack of robust evidence to support multidisciplinary rehabilitation for people with brain tumours. These findings are consistent with other reviews in this field (Huang 2001b; Huang 2011; Vargo 2011).

AUTHORS' CONCLUSIONS

Implications for practice

People with brain tumour

We found low-quality evidence that multidisciplinary rehabilitation improves functional abilities and cognitive function in people with brain tumour.

Clinicians

Evidence from one controlled clinical trial provided low-level evidence on the effectiveness of multidisciplinary rehabilitation in reducing short- and long-term disability in people with primary brain tumours. The gap in current research should not be interpreted as proof that multidisciplinary care is ineffective; in clinical settings multidisciplinary rehabilitation can address various functional, behavioural, and cognitive difficulties in brain tumour survivors that compromise their ability to perform everyday living activities and participation. Rehabilitation integrated with neuro-oncology and palliative care services can provide appropriate treatment for each phase of the cancer survivor's journey.

Policymakers

The findings of this review highlight the existing gaps in the literature and emphasise the need for robust evidence to support multidisciplinary rehabilitation for people with brain tumours.

Funders

We found no studies evaluating the cost of rehabilitation programmes, and cost-effectiveness analysis was not undertaken.

Implications for research

General

We found that the current evidence base for multidisciplinary rehabilitation in people with brain tumour is based on one low-quality controlled clinical trial with a small number of participants (53 in each treatment arm) with a significant dropout rate (20%). This highlights the need for more evidence to support specific multidisciplinary rehabilitative interventions in this patient population. Future studies should incorporate neuro-oncology, rehabilitation, and palliative care models to guide treating clinicians. Patient and caregiver perspective, caregivers' burden and their involvement in rehabilitation programmes, research on specific rehabilitation modalities for evidence-based practices, and cost-effectiveness of multidisciplinary rehabilitation need to be explored further. Future studies also need to put more emphasis on psychological care over the longer term.

Design

There is an urgent need for methodologically robust studies in multidisciplinary rehabilitation in the brain tumour population. Well-designed research methodology using randomised controlled trials and controlled clinical trials, and also using 'clinical practice

trials' where data are routinely gathered without disrupting the natural milieu of treatment, is needed to provide valuable information about outcomes in real-life clinical settings in future.

Measurement (endpoints)

A sensitive and appropriate outcome measurement tool, targeting participatory domains in particular, needs to be developed for future brain tumour trials. Longitudinal and longer-term data evaluating the impact of rehabilitation interventions are still lacking.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Khan 2014

Methods	Controlled clinical trial
Participants	<p>Australia. N = 106 (with gliomas): treatment group = 53, control group= 53</p> <p>Demographic characteristics:</p> <p>Intervention group: age: mean 53.1 +/- 13.3, range 21 to 77 years; female 59%; married/partner: 77%; disease duration (median 2.3, interquartile range:- 0.8, 5.5 years)</p> <p>Control group: age: mean 50.0 +/- 13.8, range 28 to 74 years; female 57%; married/partner: 76%; disease duration (median 1.9, interquartile range:- 0.8, 3.8 years)</p> <p><i>Inclusion criteria:</i> aged ≥ 18 years; fulfilled criteria for BT grading system (grade I to IV) for gliomas as outlined by the WHO for Central Nervous System Tumours; stable medical course, post BT surgery, radiotherapy, and/or chemotherapy, assessed by a rehabilitation physician/neurosurgeon for presence of neurological deficits and ability to participate in therapy up to 2.5 hours of interrupted therapy/day; and the clinical judgement of the assessing rehabilitation team; resided in the community (area of greater Melbourne < 60 km radius); able to communicate in English</p> <p><i>Exclusion criteria:</i> those diagnosed with benign or metastatic BTs, significant comorbidities or medically unstable, or psychiatric disorders (such as uncontrolled schizophrenia, actively suicidal/self harm, or physically aggressive (based on clinical judgement)) limiting participation in rehabilitation, those bed-bound or institutionalised in nursing homes or both</p>
Interventions	<p><i>Treatment group:</i> individualised high-intensity outpatient multidisciplinary rehabilitation programme, up to 3 one-hour sessions of interrupted therapy/week, comprising half-hour blocks of therapy sessions (occupational, social, psychological, and physiotherapy), 2 to 3 times per week for 6 to 8 weeks</p>

Khan 2014 (Continued)

Control group: wait-list with usual outpatient care (offered treatment poststudy)

Outcomes	Measures for activity: FIM Measures for participation: DASS, CARES-SF, PIPP Assessment time points: baseline, 3 months, and 6 months
Notes	Single-centre study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants not randomised to the treatment or control group
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants were not blinded, as the rehabilitation intervention itself requires participants to be consented for treatment, hence making it difficult to blind participants. This could have influenced participant-reported outcomes. However, participants were asked not to discuss their involvement in the study with treating therapists and outcome assessors in order to reduce the risk of breaking blinding of the therapists and assessors. Treating therapists were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded. See row above for further explanation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Overall, 21 participants (20%) dropout at 6-months follow-up: 12 in the intervention group and 9 in the control group (8 participants (7%) dropout at 3-months follow-up: 4 in each group)
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported.
Other bias	Unclear risk	<ul style="list-style-type: none"> Poor generalisability: single institution, not representative of all Australian people Potential source of bias related to the study design No long-term follow-up Avoidance of co-interventions or their equal distribution throughout study groups was not reported. Reporting of co-interventions could have helped judgement of their division among study groups, and whether they would have significantly affected the outcome Size of study: unclear risk (50 to 199 participants)

BT: brain tumour

CARES-SF: Cancer Rehabilitation Evaluation System-Short Form

DASS: Depression Anxiety Stress Scales

FIM: Functional Independence Measure

PIPP: Perceived Impact of Problem Profile

WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bartolo 2012	Not RCT or CCT
Chan 2013	Not RCT or CCT. Details of brain tumour subgroup not provided
Cohen 2002	Uni-disciplinary - physical therapy
Fu 2010	Not RCT or CCT
Gehring 2009	Unidisciplinary - psychological intervention
Geler-Kulcu 2009	Not RCT or CCT
Greenberg 2006	Not RCT or CCT
Huang 1998	Not RCT or CCT
Huang 2000	Not RCT or CCT
Huang 2001a	Not RCT or CCT
Jensen 2014	Unidisciplinary - physical therapy
Kawahira 2004	Not RCT or CCT
Kim 2012	Not RCT or CCT
Marciniak 1996	Not RCT or CCT
Marciniak 2001	Not RCT or CCT
O'Dell 1998	Not RCT or CCT
Pace 2007	Not RCT or CCT
Piil 2013	Not RCT or CCT
Rummans 2006	Details of brain tumour subgroup not provided
Sherer 1997	Not RCT or CCT
Tang 2008	Not RCT or CCT
Vereeck 2008	Unidisciplinary - physical therapy
Zucchella 2013	Unidisciplinary - psychological intervention

CCT: controlled clinical trial

RCT: randomised controlled trial

ADDITIONAL TABLES

Table 1. Characteristics of observational studies

Bartolo 2012	
Methods	Case-control study, Italy
Participants	<p>N = 150; Intervention: N = 75 with brain tumours (meningioma and glioblastoma), control: N = 75 with stroke</p> <p><i>Inclusion:</i> all admitted patients to an inpatient neurorehabilitation unit after surgery for brain tumours (meningiomas or glioblastomas) over a 2-year period (2007-2009). Control participants were stroke patients (ischaemic or haemorrhagic), matched one-to-one for age, sex, and side of lesion</p> <p><i>Exclusion:</i> people with oligoastrocytoma, oligodendroglioma, and ependymomas in order to obtain homogenous group</p>
Interventions	Inpatient multidisciplinary rehabilitation administered by experienced physical therapists, 60-min session, 6 days/week for 4 consecutive weeks, which included passive/assisted stretching exercises, strengthening exercises, balance exercises, ground-floor walking (including step control), and 4 weeks of speech therapy (individual 60-min sessions, once daily, 6 days/week) when aphasia was diagnosed
Outcomes	Sitting balance, standing balance, Hauser Index: gait disorders, MGHFAC: severity of gait disorders, FIM
Assessment time points	Before and after the intervention
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: case-control study • Intervention did not include input from other disciplines, apart from speech pathologists. Also unclear if all the participants in the intervention group and control group received a similar programme • No sample size calculation performed
Quality rating of the study	Very low
Fu 2010	
Methods	Retrospective case-control study, USA
Participants	<p>N = 42; Intervention: N = 21 with low-grade gliomas, control: N = 21 with high-grade gliomas</p> <p><i>Inclusion:</i> all patients admitted to an inpatient acute rehabilitation programme between 1996 and 2008. 21 of 443 with high-grade and 21 of 24 with low-grade astrocytoma were selected</p>

Table 1. Characteristics of observational studies (Continued)

Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; LOS; discharge-to-home rate
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> N/A</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: retrospective (medical records) case-control • Contents, duration, and nature of multidisciplinary rehabilitation programme not described • Unclear selection criteria. Selected patients reported to have "adequate medical records", with the implication that patients who were not selected may not have had "adequate medical records"
Quality rating of the study	Very low
Geler-Kulcu 2009	
Methods	Case-control study, Turkey
Participants	<p>N = 42; Intervention: N = 21 with brain tumours (benign and malignant), control: N = 21 with stroke</p> <p><i>Inclusion:</i> all admitted patients to an inpatient neurorehabilitation unit, control participants were stroke patients (ischaemic or haemorrhagic), matched by side of lesion</p> <p><i>Exclusion:</i> people with oligoastrocytoma, oligodendroglioma, and ependymomas in order to obtain homogenous group</p>
Interventions	Inpatient "conventional" rehabilitation programme, single 60-min sessions, 5 days/week for 4 consecutive weeks, which included physiotherapy and occupational therapy (if needed). Physiotherapy focused on positioning, postural control, range of motion, and progressive resistive exercises together with endurance and gait. Patients were discharged when their functional level was considered sufficient to allow them to participate in outpatient rehabilitation
Outcomes	PAS for Stroke, BBS, MAS, FIM (mobility)
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p>

Table 1. Characteristics of observational studies (Continued)

- Study design: case-control study
- Intervention not adequately described and did not include input from other disciplines apart from PT and OT
- No sample size calculation performed

Quality rating of the study	Very low
Greenberg 2006	
Methods	Retrospective case-control study, Israel
Participants	N = 1828; Intervention N = 168 with brain tumours (128 meningiomas, 40 gliomas), control: N = 1660 with stroke (ischaemic or haemorrhagic) <i>Inclusion:</i> all admitted patients to an inpatient neurorehabilitation unit over an 11-year period (1993-2004)
Interventions	Inpatient multidisciplinary rehabilitation provided by PT, medical staff, OT, and speech pathologist. Details of the multidisciplinary rehabilitation not provided
Outcomes	FIM, FIM efficiency, LOS days, discharge destination (rate discharge to home)
Assessment time points	Admission and discharge
Risk of bias	<i>Adequate sequence generation:</i> No <i>Adequate allocation concealment:</i> No <i>Blinding:</i> No <i>Incomplete outcome data addressed:</i> No <i>Free of selective reporting:</i> Yes Other bias: <ul style="list-style-type: none"> • Study design: retrospective, case-control, compared with unmatched control cohort • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined • No sample size calculation performed
Quality rating of the study	Very low
Huang 2001a	
Methods	Prospective case series, USA
Participants	N = 10 (brain tumour) <i>Inclusion:</i> all admitted patients to an inpatient neurorehabilitation unit over a 1-year period (1999-2000)
Interventions	Inpatient multidisciplinary rehabilitation that included: OT, rehabilitation therapy, recreational therapy, speech therapy, PT, rehabilitation nursing and case management

Table 1. Characteristics of observational studies (Continued)

Outcomes	FIM, DRS, KPS, FACT-BR
Assessment time points	Admission and discharge, post hoc analysis at 3-month postdischarge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: case-series study, no control group • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined • Small sample size
Quality rating of the study	Very low
Huang 2000	
Methods	Retrospective case-control, USA
Participants	<p>N = 156; Intervention: N = 78 with primary or metastatic brain tumours (benign and malignant), control: N = 78 with traumatic brain injury matched by age and side of lesion</p> <p><i>Inclusion:</i> evaluation by a physiatrist for the following criteria: medical stability, need for therapy from more than one discipline, demonstration of gains with acute-care therapies, potential to tolerate 3 hours of therapy, willingness and motivation to participate in a rehabilitation programme</p> <p><i>Exclusion:</i> patients who did not complete rehabilitation due to medical complications or death</p>
Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; FIM efficiency; LOS; discharge destination to community rate
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: retrospective case-control • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined • Unclear selection criteria: medically stable, motivated, and interested candidates only were selected by a single physiatrist for multidisciplinary rehabilitation with support arrangements for discharge to the community

Table 1. Characteristics of observational studies (Continued)

Quality rating of the study	Very low
Huang 1998	
Methods	Retrospective case-control study, USA
Participants	N = 126; Intervention: N = 63 with primary or metastatic brain tumours (benign and malignant), control: N = 63 with stroke, case matched by age, gender, and side of lesion <i>Inclusion:</i> all patients admitted to an inpatient rehabilitation centre
Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; FIM efficiency; LOS; discharge destination to community rate
Assessment time points	Admission and discharge
Risk of bias	<i>Adequate sequence generation:</i> No <i>Adequate allocation concealment:</i> No <i>Blinding:</i> No <i>Incomplete outcome data addressed:</i> Unclear <i>Free of selective reporting:</i> Yes Other bias: <ul style="list-style-type: none">• Study design: retrospective case-control study• Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined
Quality rating of the study	Very low
Kim 2012	
Methods	Cohort study without control, Korea
Participants	N = 25 with brain tumours <i>Inclusion:</i> all admitted patients to an inpatient neurorehabilitation unit after surgery (resection) for brain tumours (benign or malignant) over a 1-year period (1 July 2008 to 30 June 2009), able to follow simple commands, as determined by scores ≥ 24 on the Korean version of the Mini-Mental State Examination <i>Exclusion:</i> those unable to complete a questionnaire because of a severe aphasia or a cognitive deficit, or who were clinically unstable, either medically or surgically
Interventions	Inpatient rehabilitation (4 weeks); details not provided
Outcomes	Fatigue severity: PFS, BFI Mood status: BDI Motor impairment: MI Functional status: KPS, MBI QoL: EORTC QLQ-C30

Table 1. Characteristics of observational studies (Continued)

Assessment time points	Before and after the intervention
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: cohort study without control group • Contents, duration, and nature of rehabilitation intervention not described • Small sample size and no sample size calculation • High dropout rate: 9/25 participants (36%)
Quality rating of the study	Very low
Marciniak 2001	
Methods	Retrospective case series, USA
Participants	<p>N = 132 participants divided into 4 groups: astrocytomas 26%, meningiomas 33%, metastatic tumours 16%, other tumours 25%. Participants also grouped into those with tumour recurrence and those with initial tumour presentation</p> <p><i>Inclusion:</i> all patients > 18 years, inpatient rehabilitation within a 3-year period (1993-1996)</p>
Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; FIM efficiency; LOS; discharge destination to home rate
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: retrospective case series without control • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined
Quality rating of the study	Very low
O'Dell 1998	
Methods	Retrospective case-control, USA

Table 1. Characteristics of observational studies (Continued)

Participants	<p>N = 80; Intervention: N = 40 participants with brain tumours (benign and malignant), control: N = 40, case matched by admission FIM score, age, and gender to 40 participants with traumatic brain injury</p> <p><i>Inclusion:</i> all patients admitted to an inpatient acute rehabilitation programme over a 2-year period (1994-1996)</p>
Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; LOS; discharge destination to home rate
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: retrospective case-control • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined
Quality rating of the study	Very low
Pace 2007	
Methods	Prospective case series (before and after) study, Italy
Participants	<p>N = 121 with malignant brain tumours</p> <p><i>Inclusion:</i> all patients discharged from hospital over 3-year period (2000-2003) with neurological deficits</p>
Intervention	Home neurorehabilitation programme including physiotherapy 1 hour/3 times a week for 3 months, neurologist evaluation, psychological assistance, nursing and palliative care team if needed (further details not provided)
Outcomes	BI, KPS, EORTC QLQ-C30
Assessment time points	Before and 3 months after rehabilitation
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Patients who completed only basal questionnaire were excluded</p> <p><i>Free of selective reporting:</i> Yes</p>

Table 1. Characteristics of observational studies (Continued)

Other bias:	
<ul style="list-style-type: none"> • Study design: prospective before-after study without control • Contents, duration, and nature of multidisciplinary rehabilitation (intervention) not clearly defined 	
Quality rating of the study	Very low
Sherer 1997	
Methods	Retrospective case series, USA
Participants	N = 13 (primary malignant brain tumours with a history of surgical resection, radiation, and chemotherapy)
	<i>Inclusion:</i> all patients receiving outpatient rehabilitation who had a diagnosis of malignant brain tumour and adequate medical records to characterise their tumour and courses of therapy
Intervention	Outpatient rehabilitation with input from psychologists, speech/language pathologists, OT, and vocational specialists. Participants received an average of 2.6 ± 1.9 months of therapy (duration of 5 hours/day) (further details not provided)
Outcomes	Level of independence, vocational (productivity) outcomes
Assessment time points	Admission, discharge, and 8-months follow-up
Risk of bias	<i>Adequate sequence generation:</i> No <i>Adequate allocation concealment:</i> No <i>Blinding:</i> No <i>Incomplete outcome data addressed:</i> Yes <i>Free of selective reporting:</i> Yes Other bias: <ul style="list-style-type: none"> • Study design: retrospective case series without control • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined • Small sample size • No validated measures used
Quality rating of the study	Very low
Tang 2008	
Methods	Retrospective case series, Canada
Participants	N = 63 with primary and metastatic brain tumours, divided into 3 groups: glioblastoma multiforme 29%; metastatic tumours 40%; and various other primary brain tumours 31%
	<i>Inclusion:</i> all patients admitted to an inpatient rehabilitation ward over a 3-year period (2003-2006)
	<i>Exclusion:</i> patients with meningiomas

Table 1. Characteristics of observational studies (Continued)

Intervention	Inpatient multidisciplinary rehabilitation (details not provided)
Outcomes	FIM; FIM efficiency; LOS; discharge destination to home rate; survival
Assessment time points	Admission and discharge
Risk of bias	<p><i>Adequate sequence generation:</i> No</p> <p><i>Adequate allocation concealment:</i> No</p> <p><i>Blinding:</i> No</p> <p><i>Incomplete outcome data addressed:</i> Unclear</p> <p><i>Free of selective reporting:</i> Yes</p> <p>Other bias:</p> <ul style="list-style-type: none"> • Study design: retrospective case series without control • Contents, duration, and nature of multidisciplinary rehabilitation not clearly defined
Quality rating of the study	Very low

BBS: Berg Balance Scale

BDI: Beck Depression Inventory

BFI: Brief Fatigue Inventory

BI: Barthel Index

DRS: Disability Rating Scale

EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30

FACT-BR: Functional Assessment of Cancer Therapy–Brain

FIM: Functional Independence Measure

KPS: Karnofsky Performance Status Scale

LOS: length of stay

MAS: Motor Assessment Scale

MBI: Modified Barthel Index

MGHFAC: Massachusetts General Hospital Functional Ambulation Classification

MI: Motricity Index

N: total number

N/A: not applicable

OT: occupational therapist

PAS: Postural Assessment Scale

PFS: Piper Fatigue Scale

PT: physiotherapist

QoL: quality of life

USA: United States of America

Table 2. Results of observational studies
Bartolo 2012

Statistical analysis	Student's t test, Chi ² test, Wilcoxon matched-pairs signed-rank test, Mann-Whitney U test, Kruskal–Wallis ANOVA
Results	<ul style="list-style-type: none"> • All the measures of outcome (FIM: mobility, ADL, cognition; balance tests, MGHFAC) were indicative of substantial improvements for brain tumour and stroke patients ($P = 0.000$ for all). • The values of functional gain in all scores were comparable between brain tumour and stroke groups.

Table 2. Results of observational studies (Continued)

	<ul style="list-style-type: none"> Analysis of subgroups showed that people affected by meningioma achieved better results (in efficiency terms) as regards independence in ADL ($P = 0.02$) and mobility ($P = 0.04$) compared with people affected by glioblastoma or stroke. No statistically significant differences were found on other clinical scales.
Author's conclusions	Rehabilitation after surgery can improve functional outcome, justifying the delivery of rehabilitation services, even during the acute phase, to brain tumour inpatients, irrespective of tumour type
Fu 2010	
Statistical analysis	Descriptive analysis, Chi ² test, Kruskal-Wallis test, Mann-Whitney U test
Results	<ul style="list-style-type: none"> Both groups made statistically significant functional gains in their total FIM scores, ADL, and mobility FIM score from admission to discharge ($P < 0.05$ for all). Significantly greater gains were noted in high-grade astrocytoma for total FIM (22 vs. 13, $P = 0.02$) and cognition FIM subscores (4.6 vs. 1.7, $P = 0.04$) compared with low-grade astrocytoma. FIM efficiency was comparable between groups (1.9 high-grade astrocytoma vs. 1.8 low-grade astrocytoma, $P = 0.8$). Mean length of stay in the rehabilitation unit for people with high-grade astrocytoma was significantly longer than for low-grade (13 vs. 9 days, $P = 0.04$). Discharge to home rate was also comparable between groups: 90% in both groups.
Author's conclusion	All participants made significant functional gains from admission to discharge. Compared with people with low-grade astrocytoma, people with high-grade astrocytoma had higher total FIM gain but also longer LOS. FIM efficiencies were comparable between the groups
Geler-Kulcu 2009	
Statistical analysis	Freidman test, Chi ² test, Mann-Whitney U test, ANOVA
Results	<ul style="list-style-type: none"> Both groups improved significantly in terms of PASS, BBS, MAS, and FIM mobility scores (all $P < 0.05$). There was no statistically significant difference between the two groups with respect to any of the four outcome measures. There was no statistically significant difference between the groups in any of the four outcome measures when compared between people with different forms of brain tumours and people with stroke.
Author's conclusions	People with brain tumour progressed as well as people with stroke in a post-acute inpatient rehabilitation programme
Greenberg 2006	
Statistical analysis	Descriptive statistics, analysis of variance
Results	<ul style="list-style-type: none"> Functional variables during inpatient multidisciplinary rehabilitation were found to be similar in all the groups: average FIM rating at admission was 80.07 in the meningioma group, 68.2 in the glioma group, and 70.4 in the stroke group ($P = 0.16$); average discharge FIM rating was 90.3 for people with meningiomas, 80.7 for people with gliomas, and 87.8 for people with stroke ($P = 0.76$). There was no significant difference in functional gain among groups: functional gain was 17.9 for people with meningioma, 17.2 for people with glioma, and 21.8 for people with stroke ($P = 0.4$). FIM efficiency analysis showed that both brain tumour groups had similar efficacy and that people with stroke had the lowest efficiency ($P = 0.001$). Average LOS was 24 days for the meningioma group, 23 days for the glioma group, and 75.4 days for the stroke group.

Table 2. Results of observational studies (Continued)

- 88.1% of people with stroke, 91.7% of people with meningioma, and 82.7% of people with glioma were discharged to their homes, and 5.4%, 3.4%, and 8.6%, respectively, were discharged to nursing homes.

Author's conclusions	Both people with gliomas and people with meningiomas hospitalised for inpatient rehabilitation improved their FIM ratings after a short inpatient multidisciplinary rehabilitation. Both groups had high rates of discharge to the community
Huang 2001a	
Statistical analysis	ANOVA, Spearman's correlation analysis, Bonferroni statistical test
Results	<ul style="list-style-type: none"> • Improvement in total functional outcome was indicated by all 3 functional measures (FIM: $P < 0.05$; DRS: $P < 0.05$; KPS: $P < 0.05$). • Significant improvements were found between admission and discharge scores for the FIM and DRS. • KPS revealed significant improvement between admission and 3-months follow-up scores. • All admission and discharge functional scales (FIM, DRS, KPS) correlated significantly with each other. • No significant change was noted in the FACT-BR between admission and discharge scores, but FACT-BR scores did improve at 1- and 3-months postdischarge relative to admission. • FIM, KPS, and DRS did not show significant correlation with FACT-BR. • 90% of participants were initially discharged to a home environment.
Author's conclusion	Although participants made functional gains during and after inpatient multidisciplinary rehabilitation, gains in QoL were not significant until 1-month postdischarge. QoL does not appear to correlate well with functional outcomes. Furthermore, the KPS is less sensitive than the FIM and DRS in detecting change in functional status
Huang 2000	
Statistical analysis	ANOVA, Chi ² test
Results	<ul style="list-style-type: none"> • Both groups improved significantly for FIM score at discharge ($P < 0.01$). • Change in FIM score was significantly greater in the traumatic brain injury group for total FIM score ($P < 0.01$), ADL FIM score ($P < 0.01$), and mobility FIM score ($P < 0.01$). • No differences were noted for change in cognitive FIM between groups ($P = 0.06$). • FIM efficiency was similar between groups (FIM change per week: 10 tumour vs. 11.3 traumatic brain injury, $P = 0.3$). • LOS was significantly shorter in tumour group (22 days vs. 32 days, $P < 0.01$). • Discharge community rate was significantly greater in tumour group (87%) vs. traumatic brain injury group (74%) ($P < 0.05$).
Author's conclusion	People with brain tumour can achieve comparable functional outcome and have a shorter rehabilitation length of stay and greater discharge to community rate than people with traumatic brain injury
Huang 1998	
Statistical analysis	ANOVA, Chi ² test
Results	<ul style="list-style-type: none"> • Both groups improved significantly for FIM score at discharge. • FIM change was comparable between groups (23.6 brain tumour vs. 29.1 stroke, $P = 0.08$) • Change in ADL FIM score was significantly greater in stroke group (10.8 vs. 8.3, $P = 0.03$). No differences were noted for change in motor and cognitive FIM between groups.

Table 2. Results of observational studies (Continued)

	<ul style="list-style-type: none"> FIM efficiency was comparable between groups (FIM change/week: 8.4 brain tumour vs. 7.2 stroke, $P = 0.29$). LOS was significantly shorter in brain tumour group (25 days vs. 34 days, $P < 0.01$). Discharge to community rate was comparable between groups (86% for brain tumour vs. 94% for stroke) ($P = 0.06$).
Author's conclusion	People with brain tumour can achieve comparable functional outcome and discharge to community rate, and have a shorter rehabilitation length of stay than people with stroke
Kim 2012	
Statistical analysis	Mann–Whitney test, Spearman's correlation analysis, Wilcoxon signed-rank tests
Results	<ul style="list-style-type: none"> Fatigue correlated significantly with the KPS, MBI, and EORTC QLQ-C30 physical functioning and insomnia scales. Insomnia was a significant predictor of fatigue before rehabilitation ($P = 0.004$). Baseline fatigue scales, MBI, MI, and EORTC QLQ-C30 physical functioning scale were the important independent predictors of fatigue after rehabilitation. After 4 weeks rehabilitation, there was significant improvement in KPS (50.0 ± 11.5 vs. 59.4 ± 13.4, $P = 0.04$), MBI (47.2 ± 27.0 vs. 72.2 ± 28.1, $P < 0.01$), MI (56.2 ± 20.6 vs. 63.4 ± 14.0, $P < 0.01$), whereas total PFS and BFI scores did not change. Participants with a moderate level of fatigue showed significant improvement in the PFS (5.2 ± 0.5 vs. 3.1 ± 1.6, $P = 0.02$), KPS (47.1 ± 9.5 vs. 64.3 ± 11.3, $P = 0.02$), MBI (45.7 ± 28.8 vs. 69.1 ± 37.8, $P = 0.04$), MI scores (64.1 ± 11.7 vs. 70.6 ± 9.2, $P = 0.03$), and participants with a mild level of fatigue significantly improved in the MBI score (56.3 ± 29.6 vs. 77.9 ± 24.4, $P = 0.04$).
Author's conclusion	The findings suggest that people with brain tumours commonly complain of a moderate level of fatigue, which may reduce daily functioning and quality of life, with sleep disturbance being a significant predictor of fatigue. During rehabilitation, functional outcomes and motor power showed improvements in those people, not aggravating fatigue
Marciniak 2001	
Statistical analysis	Descriptive analysis, analysis of variance
Results	<ul style="list-style-type: none"> All groups made significant functional gains in their FIM score, and motor and cognitive FIM subscores from admission to discharge. Total FIM change was comparable between tumour groups. The change in FIM motor subscores was significantly smaller for those with metastasis (8.6) and astrocytomas (16.2) when compared with meningiomas (20) and other tumours (21). The tumour recurrence group had significantly lower motor FIM gains (13.4 vs. 21.4), and FIM efficiency (0.55 vs. 0.98), lower discharge motor FIM scores (50.1 vs. 63.1) compared to those receiving rehabilitation after initial tumour treatment. Participants who received radiation during rehabilitation had significantly greater motor efficiency score (1 ± 0.79) than those who did not ($P < 0.05$). Participants in the metastatic disease group had significantly shorter LOS than other tumour groups ($P = 0.03$). Overall, 65% of the 132 admissions were discharged home. People with meningiomas were less likely to be discharged home (47%) than those with metastatic tumours (71%), astrocytic tumours (71%), or those in the other tumours group (79%) ($P = 0.01$).
Author's conclusion	Metastatic or primary brain tumour type does not affect the efficiency of functional improvement during inpatient multidisciplinary rehabilitation. People receiving concurrent radiation therapy make greater functional improvement per day than those not receiving radiation. People with recurrent tumours make significantly smaller functional motor gains than those completing inpatient multidisciplinary rehabilitation after the initial diagnosis of the tumour

Table 2. Results of observational studies (Continued)

O'Dell 1998

Statistical analysis	Descriptive analysis, Chi ² test, Kruskal-Wallis test, Mann-Whitney U test
Results	<ul style="list-style-type: none"> Both groups made significant functional gains in their FIM scores: total FIM, ADL and mobility sub-scores from admission to discharge. Total FIM change was significantly greater in the traumatic brain injury group compared to the brain tumour group (35 vs. 25, $P < 0.02$). FIM efficiency was comparable between groups: 1.9 for traumatic brain injury vs. 1.5 for brain tumour. LOS was comparable between groups: 22 days for traumatic brain injury vs. 18 days for brain tumour. Discharge to home rate was also comparable between groups: 93% for traumatic brain injury vs. 83% for brain tumour.
Author's conclusion	Daily functional gains made by people with brain tumour undergoing multidisciplinary rehabilitation were similar to those made by people with traumatic brain injury matched by age, gender, and admission functional status

Pace 2007

Statistical analysis	Chi ² test, Student t test (paired or not, as appropriate)
Results	<p>At 3-months follow-up:</p> <ul style="list-style-type: none"> BI improved in 47 participants (39%), was stable in 20 (16%), and worsened in 54 (44%). In those with clinical improvement, BI score increased significantly from baseline (median 15 points, $P < 0.001$). KPS scores were better in only 24% of participants by median 10 points ($P < 0.001$). No significant difference was observed between various subgroups of brain tumour and between those with initial diagnosis and those treated for reoccurrence. Only 54 participants completed the QoL questionnaire before and after treatment: 72% were found to have an improvement in at least one domain score compared with their baseline QoL scores. In those with improved BI scores, physical and social scores increased in 67%, emotional functional score increased in 39%, and global QoL score increased in 44%.
Author's conclusion	Multidisciplinary rehabilitation at home in people with brain tumour was associated with significant functional gain measured both with BI and KPS. The benefit of multidisciplinary rehabilitation may influence patient's perception of quality of life

Sherer 1997

Statistical analysis	Descriptive analyses only
Results	<ul style="list-style-type: none"> At the time of discharge from the programme, 6 participants had increased independence, 6 were unchanged, and 1 had decreased independence. At discharge, 8 participants had increased productivity (increased/improved/maintained the previous vocational status), 4 were unchanged, and 1 had decreased productivity. At 8-months follow-up after discharge all the treatment gains were maintained. At follow-up, compared with admission status, 7 participants had increased independence, 4 were unchanged, 1 had decreased independence, and 1 had died.
Author's conclusion	People with primary malignant brain tumours achieved increased community independence and vocational outcomes (such as employment, education) after individualised outpatient multidisciplinary rehabilitation.

Table 2. Results of observational studies (Continued)

plinary rehabilitation. Such treatment programme appears to be an attractive, relatively low-cost option for these patients, however additional investigation is needed.

Tang 2008

Statistical analysis	ANOVA, Chi ² test, Kruskal-Wallis and post-hoc tests using Mann-Whitney U test with Bonferroni adjustment, Wilcoxon signed-ranks test, logistic regression, Kaplan-Meier analyses
Results	<ul style="list-style-type: none"> • All groups made significant improvement in their FIM scores from admission to discharge. Motor FIM, but not cognitive FIM scores, improved significantly in all 3 groups. • FIM efficiency was comparable between groups (0.33 GBM, 0.4 metastatic, 0.2 other). • None of the independent variables (age, length of rehabilitation, concurrent radiation therapy, concurrent chemotherapy, type of tumour, hemispheric location, or number of brain lesions) were significant predictors of high or low FIM gain for all people with brain tumours. • Discharge-to-home rate was comparable between groups (76% GBM, 72% metastatic, 70% other). • Estimated median survival was 141 days for brain metastases, 214 days for GBM, and 439 days for other tumours.
Author's conclusion	People with primary and metastatic brain tumours achieved functional gains after multidisciplinary rehabilitation. High functional improvement is a significant predictor of longer survival in brain metastases and GBM.

ADL: activities of daily living

ANOVA: analysis of variance

BBS: Berg Balance Scale

BFI: Brief Fatigue Inventory

BI: Barthel Index

DRS: Disability Rating Scale

EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30

FACT-BR: Functional Assessment of Cancer Therapy-Brain

FIM: Functional Independence Measure

GBM: glioblastoma multiforme

KPS: Karnofsky Performance Status Scale

LOS: length of stay

MAS: Motor Assessment Scale

MBI: Modified Barthel Index

MGHFAC: Massachusetts General Hospital Functional Ambulation Classification

MI: Motricity Index

OT: occupational therapist

PASS: Postural Assessment Scale for Stroke

PFS: Piper Fatigue Scale

PT: physiotherapist

QoL: quality of life

USA: United States of America

APPENDICES

Appendix 1. The Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 MESH DESCRIPTOR Central Nervous System Neoplasms EXPLODE ALL TREES

#2 MESH DESCRIPTOR Neoplasms, Neuroepithelial EXPLODE ALL TREES

#3 MESH DESCRIPTOR Neoplasms, Germ Cell and Embryonal EXPLODE ALL TREES

#4 (((central nervous system or CNS or brain or glioma* or astrocyt* or oligodendrogl* or ependy* or choroid plexus or neuro-epitheli* or neuroepitheli* or neuronal* or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening* or sellar) adj5 (neoplasm* or tumour* or tumor* or malignan* or carcinoma* or cancer*))) :TI,AB,KY

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#5 #1 OR #2 OR #3 OR #4

#6 MESH DESCRIPTOR Rehabilitation EXPLODE ALL TREES

#7 MESH DESCRIPTOR Ambulatory Care EXPLODE ALL TREES

#8 MESH DESCRIPTOR Physical Therapy Modalities EXPLODE ALL TREES

#9 MESH DESCRIPTOR Home Care Services EXPLODE ALL TREES

#10 MESH DESCRIPTOR Inpatients

#11 MESH DESCRIPTOR Outpatients

#12 MESH DESCRIPTOR Behavior Therapy EXPLODE ALL TREES

#13 MESH DESCRIPTOR Social Work EXPLODE ALL TREES

#14 MESH DESCRIPTOR Dietary Services EXPLODE ALL TREES

#15 MESH DESCRIPTOR Counseling EXPLODE ALL TREES

#16 MESH DESCRIPTOR Patient Care Team EXPLODE ALL TREES

#17 ((multidisciplinary or multi-disciplinary or integrated or interdisciplinary or inter-disciplinary)):TI,AB,KY

#18 ((rehabilitat* or physiotherap* or physical therap* or speech or occupation* or social work*)):TI,AB,KY

#19 ((cognitive therap* or behavior therap* or counseling or nutrition* or diet* or food)):TI,AB,KY

#20 ((outpatient* or inpatient* or hospital* or home)):TI,AB,KY

#21 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20

#22 #5 AND #21

#23 18/04/2012 TO 31/12/2014:DL

#24 #22 AND #23

Appendix 2. MEDLINE search strategy

1. exp Central Nervous System Neoplasms/

2. exp Neoplasms, Neuroepithelial/

3. exp "Neoplasms, Germ Cell and Embryonal"/

4. ((central nervous system or CNS or brain or glioma* or astrocyt* or oligodendrogl* or ependy* or choroid plexus or neuro-epitheli* or neuroepitheli* or neuronal* or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening* or sellar) adj5 (neoplasm* or tumour* or tumor* or malignan* or carcinoma* or cancer*)).mp.

5. or/1-4

6. rehabilitation.fs.

7. exp Rehabilitation/

8. exp Ambulatory Care/

9. exp Physical Therapy Modalities/

10. exp Home Care Services/

11. Inpatients/

12. Outpatients/

13. exp Behavior Therapy/

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14. exp Social Work/
15. Dietetics/
16. exp Dietary Services/
17. exp Counseling/
18. exp Patient Care Team/
19. (multidisciplinary or multi-disciplinary or integrated or interdisciplinary or inter-disciplinary).mp.
20. (rehabilitat* or physiotherap* or physical therap* or speech or occupation* or social work*).mp.
21. (cognitive therap* or behavio?r therap* or counsel?ing or nutrition* or diet* or food).mp.
22. (outpatient* or inpatient* or hospital* or home).mp.
23. or/6-22
24. 5 and 23
25. randomized controlled trial.pt.
26. controlled clinical trial.pt.
27. randomized.ab.
28. placebo.ab.
29. drug therapy.fs.
30. randomly.ab.
31. trial.ab.
32. groups.ab.
33. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. exp animals/ not humans.sh.
35. 33 not 34
36. 24 and 35

key:

mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier

pt=publication type

ab=abstract

sh=subject heading

Appendix 3. EMBASE search strategy

1. exp central nervous system tumor/
2. neuroepithelioma/
3. exp germ cell tumor/
4. ((central nervous system or CNS or brain or glioma* or astrocyt* or oligodendrogl* or ependy* or choroid plexus or neuro-epitheli* or neuroepitheli* or neuronal* or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening* or sellar) adj5 (neoplasm* or tumour* or tumor* or malignan* or carcinoma* or cancer*)).mp.

5. or/1-4
6. rh.fs.
7. exp rehabilitation/
8. exp ambulatory care/
9. exp physiotherapy/
10. exp home care/
11. exp hospital patient/
12. outpatient/
13. behavior therapy/
14. cognitive therapy/
15. social work/
16. dietetics/
17. nutrition service/
18. exp counseling/
19. exp patient care/
20. (multidisciplinary or multi-disciplinary or integrated or interdisciplinary or inter-disciplinary).mp.
21. (rehabilitat* or physiotherap* or physical therap* or speech or occupation* or social work*).mp.
22. (cognitive therap* or behavio?r therap* or counsel?ing or nutrition* or diet* or food).mp.
23. (outpatient* or inpatient* or hospital* or home).mp.
24. or/6-23
25. 5 and 24
26. random\$.tw.
27. factorial\$.tw.
28. crossover\$.tw.
29. cross over\$.tw.
30. cross-over\$.tw.
31. placebo\$.tw.
32. (doubl\$ adj blind\$).tw.
33. (singl\$ adj blind\$).tw.
34. assign\$.tw.
35. allocat\$.tw.
36. volunteer\$.tw.
37. Crossover Procedure/
38. double-blind procedure.tw.
39. Randomized Controlled Trial/

40. Single Blind Procedure/

41. or/26-40

42. (animal/ or nonhuman/) not human/

43. 41 not 42

44. 25 and 43

key:

mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword

Appendix 4. PEDro search strategy

Abstract + Title = (brain cancer) OR (brain tumour) AND (rehabilitation) + Method = Clinical Trial

Appendix 5. LILACS search strategy

(Mh Brain Neoplasms) OR (brain cancer\$ or brain tumor\$ or brain tumour\$ or brain carcinoma\$ or brain neoplasm\$) OR (glioma\$ or astrocyte\$ or oligodendrogl\$ or ependy\$ or choroid plexus or neuroepitheli\$ or neuroepitheli\$ or neuronal\$ or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening\$ or sellar)

AND (Mh Ambulatory Care) OR (Mh Rehabilitation) OR (Mh Hospitalization) OR (Mh Physical Therapy Modalities) OR (Mh Home Care Services, Hospital-Based) OR (Mh Home Care Services) OR (Mh Inpatients) OR (Mh Outpatients) OR (Mh Cognitive Therapy) OR (Mh Behavior Therapy) OR (Mh SocialWork) OR (Mh Dietetics) OR (Mh Dietary Services) OR (Mh Counseling) OR (Mh Patient Care Team) OR (multidisciplinary) OR (intergrated) OR rehabilitat\$ OR (home health care) OR (physiotherap\$) OR (physical therap\$) OR (speech) OR (occupation\$) OR (social work) OR (cognitive therap\$) OR (behavior therap\$) OR (counseling) OR (nutrition) OR (diet\$) OR (food) OR (outpatient\$) OR (inpatient\$) OR (hospital\$)

AND (((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)))

WHAT'S NEW

Date	Event	Description
15 July 2019	Amended	Contact details updated.
4 June 2019	Review declared as stable	See Published notes .

HISTORY

Protocol first published: Issue 12, 2011

Review first published: Issue 1, 2013

Date	Event	Description
11 April 2017	Review declared as stable	See Published notes .
3 February 2015	New search has been performed	This review has been updated; new searches were conducted in January 2015.
13 January 2015	New citation required and conclusions have changed	One new controlled clinical trial is included; five additional studies were excluded. 'Summary of findings' table and 'Risk of bias' tables added. The conclusions have changed, and we recommend that readers of the previous version re-read this update.

Date	Event	Description
21 September 2012	Amended	Change of title

CONTRIBUTIONS OF AUTHORS

Fary Khan (FK) and Bhasker Amatya (BA) were involved in all aspects of the review.

FK, BA, and Louisa Ng (LN) screened, identified, and analysed all relevant studies. LN provided independent evaluation and drafted the results of the controlled clinical trial, as she was not involved in the included study. BA and FK reviewed the results and drafted the discussion. Comments from all review authors, including Kate Drummond and Mary Galea, were in the updated final review.

FK and BA will be responsible for updating the review in the future.

DECLARATIONS OF INTEREST

The review authors are clinicians in the field of Physical and Medical Rehabilitation who wish to provide the best possible service to their patients.

F Khan has no relevant personal or financial conflicts of interest to declare.

B Amatya has no relevant personal or financial conflicts of interest to declare.

L Ng has no relevant personal or financial conflicts of interest to declare.

K Drummond has no relevant personal or financial conflicts of interest to declare.

M Galea has no relevant personal or financial conflicts of interest to declare. F Khan, B Amatya, K Drummond, and M Galea are authors of the included study ([Khan 2014](#)).

SOURCES OF SUPPORT

Internal sources

- Department of Rehabilitation Medicine, Royal Melbourne Hospital, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

2012: The title of the review has been amended and a new author (M Galea) added.

2015: We have included a 'Summary of findings' table in the updated review; key outcomes identified, which the authors deemed to be the most relevant to decision-makers including patients, clinicians, and policymakers.

NOTES

2017

A search in February 2017 did not identify any potentially relevant studies, although we are aware of some relevant ongoing studies that we will assess once published. Therefore, this review has now been stabilised following discussion with the authors and editors. If appropriate, we will update the review if new evidence likely to change the conclusions is published, or if standards change substantially which necessitate major revisions.

2019

A restricted search in May 2019 did not identify any potentially relevant studies likely to change the conclusions. Therefore, this review has now been stabilised following discussion with the authors and editors. We will reassess the review for updating in five years. If appropriate, we will update the review sooner if new evidence likely to change the conclusions is published, or if standards change substantially which necessitate major revisions.

INDEX TERMS**Medical Subject Headings (MeSH)**

Anal Canal; Brain Neoplasms [*rehabilitation] [therapy]; Combined Modality Therapy [methods]; Controlled Clinical Trials as Topic; Locomotion; Quality of Life; Social Participation

MeSH check words

Adult; Humans