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Multidisciplinary rehabilitation after primary brain tumour treatment (Review)

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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.

Objectives

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

Search methods

We searched the Cochrane Neuromuscular Disease Group Specialized Register (March week 2, 2012), The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library Issue 3, 2012), MEDLINE (1966 to March week 2, 2012), EMBASE (1980 to March week 2, 2012), PEDro (1982 to March 2012) and LILACS (1982 to March week 2, 2012). We checked the bibliographies of papers identified and contacted the authors and known experts in the field to seek published and unpublished trials.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

No randomised controlled trials (RCTs) or controlled clinical trials (CCTs) were identified.
Authors’ conclusions

No RCTs or CCTs were available for synthesis of ‘best evidence’ for multidisciplinary rehabilitation after treatment for brain tumour patients. However, this does not suggest the ineffectiveness of multidisciplinary rehabilitation but rather highlights the challenges in trial design and rigour, outcome measurement and complexities of care in this population. For completeness of literature, 12 observational studies (with high risk of bias) involving patients with brain tumours were included. These studies provided ‘very low level’ evidence suggesting that multidisciplinary rehabilitation (inpatient, home-based) may improve functional outcomes, and ambulatory programmes (outpatient and home-based) may improve vocation and quality of life. These conclusions are tentative at best, given gaps in current research in this area. 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 for brain tumours

People with brain tumours may experience a range of symptoms and disabilities such as psychological problems, difficulties with mobility or self-care, and relationship and work issues, which can have a substantial impact on 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.

This review did not find any high quality studies that evaluated the effectiveness of such multidisciplinary care. The evidence from twelve poor quality studies suggested that multidisciplinary rehabilitation may improve disability and quality of life. Multidisciplinary rehabilitation does not appear to be harmful and gaps in current research should not be interpreted as proof that multidisciplinary rehabilitation for brain tumours is ineffective. There is a need for high quality research to explore the effectiveness of multidisciplinary rehabilitation in people with brain tumours.

Background

Description of the condition

Primary brain tumours are a diverse group of neoplasms that account for 2% of all cancers (Arber 2010) and affect approximately seven persons per 100,000 population annually worldwide (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 22,070 estimated new cases of primary brain tumours in the United States (Jemal 2009). In the United Kingdom, 3000 new cases of primary brain tumours are reported each year, 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). Radiation therapy remains the primary treatment for brain tumours; adjuvant chemotherapy and surgical treatment have recently gained more support as a means of prolonging survival (Huang 2011). 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). Furthermore, diagnosis of brain tumour can have a distressing psychological impact, significant costs and socioeconomic implications, increased demand for health care, social and vocational services, and caregiver burden (Tang 2008).

Persons 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. Many people diagnosed with brain tumour may have ongoing concerns (relationship, employment, recurrence) (Ownsworth 2009). The limitation in function (disability) can have a cumulative effect over time and cause considerable distress to the cancer survivor 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 patient’s perceptions of self worth, self image and role reversal within the family. Families and/or carers often struggle to cope with new demands associated with increased care needs, inability to drive and return to work, financial constraints, marital stress and general limitation in patients’ participation. Ongoing monitoring, education and counselling of the patient (and family) are therefore important. The care needs after treatment for primary brain tumours (surgery, chemotherapy and radiotherapy) are varied, given the complex, multifactorial nature and multiple disabilities (which may progress) in these persons. These are best met with a coordinated multidisciplinary, multifaceted approach, which includes acute medical and surgical care, rehabilitation, palliative and other supportive interventions (Gabanelli 2005).

### Description of the intervention

Rehabilitation is 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 (which encompasses physical and psychosocial aspects) of care, 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 carer) 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 reacquisition strategies, cognitive and behavioural therapy, vocational and recreational programmes, and psychological (and counselling) input.

Persons after primary brain tumour treatment can present to rehabilitation settings with a range of difficulties which may be physical, emotional, psychosocial and/or environmental. 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 persons after brain tumour treatment:

- ‘impairments’ are problems with body (anatomical) structures or function (headaches, seizures, neurocognitive dysfunction, muscle weakness, aphasia, visual impairments);
- ‘activity limitation’ (disability) are difficulties faced by a person executing everyday tasks (mobility or self care);
- ‘restriction in participation’ relates to problems experienced by a person which limit involvement in societal participation and life situations (that is, employment, family life, social reintegration);
- ‘contextual factors’ are:
  - ‘environmental’ issues, which make up the physical, social and attitudinal environment in which a person lives their life (construction the same as above); and
  - ‘personal’ problems (such as gender, race, coping style, social and educational background) which may affect the person’s experience of living with their condition.

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

### How the intervention might work

Multidisciplinary rehabilitation in persons after primary brain tumour treatment can utilise various categories in domains comprising the structured framework outlined by the ICF, for targeted intervention and therapy. It 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 2011), acquired brain injury (Turner Stokes 2011) and stroke (SUTC 2007). A number of studies show that patients with brain tumours undergoing rehabilitation appear to make significant functional gains (Geler-Kulcu
To assess the effectiveness of multidisciplinary rehabilitation in persons after primary brain tumour treatment, and specifically to explore the following areas:

- Does organised multidisciplinary rehabilitation achieve better outcomes than the absence of such services in persons after primary brain tumour treatment?
- Which type of programmes are effective and in which setting?
- Does a greater intensity (time and expertise, or both) of rehabilitation programmes lead to greater gains?
- Which specific outcomes are influenced (survival, dependency, social integration, mood, quality of life)?

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

All randomised controlled trials (RCTs) and controlled clinical trials (CCTs), which included 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; oligodendrogial 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.

Studies involving participants with a range of cancers or other diagnoses where data specifically for persons with primary brain tumour were reported, were also included.
**Exclusion criteria**
- Studies recruiting only participants with metastatic (i.e. non-primary) brain tumour.
- Studies involving participants with CNS cancers, where data were not separately provided 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 (Turner Stokes 2011; Khan 2011). 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/ out-patient 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 of such programmes can include physical reconditioning, task reacquisition strategies, environmental modification, cognitive and behavioural therapy, vocational and recreational programmes, and psychological (and counselling) input.

All studies that stated or implied multidisciplinary rehabilitation were considered for inclusion in this review provided they satisfied the definition above and compared it to some form of control condition. The control conditions included:
- lower level or different types of interventions such as ‘routinely available local services’ (for example, medical and nursing care);
- minimal interventions (such as ‘information only’);
- ‘wait list’ controls or no treatment;
- interventions given in different settings and lower intensity of interventions.

Studies were excluded 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. These were categorised according to the ICF (WHO 2001) into those that focus on:
- impairment, for example, headache, seizures, muscle weakness, aphasia, visual impairments, pain;
- disability (limitation in activity), measured by validated tools such as the Functional Independence Measure (FIM) (Granger 1998), Barthel index (BI) (Mahoney 1965), Cancer Rehabilitation Evaluation System- short form (CARES-SF) (Ganz 1992; Schag 1991), Cancer Survivor Unmet Needs (CaSUN) measure (Hodgkinson 2007) and Perceived Impact of Problem Profile (PIPP) (Pallant 2006);
- restriction in participation and/or environmental or personal context, for example, quality of life (QoL) (SF-36; Ware 1993), fatigue (Fatigue Impacts Scale; Fisk 1994), psychological (Depression Anxiety Stress Scale; Lovibond 1995) and vocational outcomes (Work Instability Scale; Gilbowth 2003), social reintegration and patient satisfaction measures and others.
- 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 (LOS) in both acute and subacute settings, readmission, the cost of care and the extent of services used at the time of discharge.

**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 sources.
- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library) (see Appendix 1)
- MEDLINE (via OvidSP) (from 1950 to March week 2, 2012) (see Appendix 2)
- EMBASE (via OvidSP) (from January 1980 to March week 2, 2012) (see Appendix 3)
- PEDro (from January 1985 to March week 2, 2012)
- LILACS (from January 1982 to March week 2, 2012)
- The WHO International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/Default.aspx) for all prospectively registered and ongoing trials

The search strategy also included searches of: the Cochrane Cancer Network (CCN), CancerLit, Biosis and Science Citation Index. We used the same principle to search each database. This included:
(i) the terms and phrases identifying randomised controlled trials and controlled clinical trials 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, i.e. 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 terms with alternative spellings and endings were not missed. We exploded all MeSH terms.

**Searching other resources**

We checked the bibliographies of studies identified 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 by using the related articles feature (via PubMed), Proquest Dissertations and Theses, searching key authors (via Web of Science) and searching SIGLE (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 titles of studies identified by the search strategy for appropriateness based on the selection criteria. The two review authors (BA, LN) independently evaluated each study from the short-list of potentially appropriate studies for inclusion or exclusion. We obtained the full text of the article 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, hence it was not necessary to involve other review authors in this process. Authors were not masked to the name(s) of the author(s), institution(s) or publication source at any level of the review.

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**

Review authors (FK, BA, LN) independently extracted the data from each study that met the inclusion criteria, using a standardised data collection form. All studies that met the inclusion criteria were to be summarised in the 'Characteristics of Included Studies' table provided in the Review Manager 5 software developed by The Cochrane Collaboration (RevMan 5) to include details on design, participants, interventions and outcomes.

**Assessment of risk of bias in included studies**

Two review authors (BA, LN) 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 (see Table 1). 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 and termed these ‘low-quality studies’ (see Table 2). Any disagreements or lack of consensus were resolved by a third review author (FK).

**Measures of treatment effect**

It was not possible to perform measures of treatment effect or pool the data for meta-analysis, due to insufficient data and type of data available, and the diversity of methods in the studies. If studies had been available, we would have calculated risk ratios (RR) with 95% CIs for dichotomous data and differences in means or standardised differences in means (SMD) with 95% confidence intervals (CIs)) for continuous data. We would also have calculated for each outcome of interest, summary estimates of treatment effect (with 95% CIs for each comparison).

**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 patients or 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 (Egger 1998) by sourcing unpublished data where possible and we would have contacted authors for the full data set or the reason for not publishing the data, however this was not required.

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 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 Cochrane statistical package Review Manager 5 (RevMan 5) and expressed the results as risk ratios (RRs) with 95% CIs and risk differences (RDs) with 95% CIs for dichotomous outcomes and mean differences (MDs) and 95% CIs for continuous outcomes. 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), random-effects meta-analysis would have been used instead.

We used the GRADE approach to grade the quality of evidence, 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.

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-intensity, low-intensity multidisciplinary rehabilitation);
3. time from definitive treatment (surgery, radiotherapy and chemotherapy) to commencement of multidisciplinary rehabilitation (acute: < six weeks, intermediate: six weeks to six months, and longer term: > six months). We reviewed participants randomised in the acute stages following definitive treatment (< six weeks) as a separate group from participants randomised in the later or convalescent stages (> six weeks following treatment).

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

Sensitivity analysis

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

RESULTS

Description of studies

See: Characteristics of excluded studies.

See the ‘Characteristics of excluded studies’ table for further details on exclusions.

Results of the search

Electronic and manual searches identified 5410 references (MEDLINE = 1853; EMBASE = 2559; CENTRAL = 957; PEDro = eight; LILACS = 14; Cochrane Neuromuscular Disease Group Specialized Register = 19) with our search criteria. Of these, 18 passed the first screening review and were selected for closer scrutiny. Two potentially relevant articles were also identified from bibliographies of papers identified.

Included studies

No RCTs or CCTs were identified that compared multidisciplinary rehabilitation in people with brain tumours with either routinely available local services or lower levels of intervention; nor were there trials that compared multidisciplinary rehabilitation in different settings or at different levels of intensity.

Excluded studies

We excluded 18 studies for the reasons shown in the ‘Characteristics of excluded studies’ table. The primary reasons for exclusion were:

- not RCT or CCT (N = 14)
- uni-disciplinary intervention (N = 3)
- data not specifically provided for brain tumour subgroup (N = 1)

Of the 14 studies excluded due to study design, 12 reported functional outcomes related to multidisciplinary rehabilitation and are described below in the ‘Discussion’ section.
Risk of bias in included studies
No RCTs or CCTs that met the inclusion criteria for the review were identified.

Effects of interventions
We identified no RCTs or CCTs that met the inclusion criteria for the review.

DISCUSSION

Summary of main results
No RCTs or CCTs were identified that addressed the effectiveness of multidisciplinary rehabilitation in people with brain tumours. Brain tumour is a complex and rare but devastating condition, which places many demands on patients, carers and health professionals. Patients with brain tumour can present with diverse presentations and varied level of disability for rehabilitation requiring an individualized approach. Rehabilitation itself is defined as a ‘complex’ intervention (when the active ingredient in the intervention is not easily identifiable) (MRC 2000). Although RCTs are considered ‘gold standard’ to study effect of an intervention and provide high-level evidence, they may be less appropriate for studying ‘complex’ interventions such as rehabilitation. Previously, challenges associated with conducting RCTs in neuro-rehabilitation settings have been identified (Khan 2010; Khan 2011). These include difficulties such as: heterogeneous patient populations, interdependent components and contexts, multifaceted and multilayered treatments involving organizational restructure; individual interventions and ethical considerations (Khan 2011). For the overall completeness of this review, data from other designs or observational studies are presented 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
No RCTs or CCTs were identified in this review. However, the literature search identified 12 observational studies (Bartolo 2012; Fu 2010; Geler-Kulcu 2009; Greenberg 2006; Huang 2000; Huag 2001; Huang 1998; Marciniak 2001; O’Dell 1998; Pace 2007; Sherer 1997; Tang 2008) reporting various outcomes following multidisciplinary rehabilitation in patients with brain tumours and are described in Table 3. In the absence of formal trial based evidence, the limited evidence from these studies is summarised below:

• Seven studies were conducted in USA, two in Italy and one each in Turkey, Israel and Canada.
• Each study was conducted within a single institute/facility, with all studies totaling 805 participants with various types of brain tumours.
• Ten studies involved inpatient rehabilitation settings, two involved ambulatory settings (one outpatient setting (Sherer 1997); one home-based (Pace 2007)).
• Seven studies were retrospective audits of hospital medical records (Fu 2010; Greenberg 2006; Huang 2000; Huang 1998; Marciniak 2001; O’Dell 1998; Tang 2008).
• Seven were case-control studies, of which six compared the rehabilitation outcomes of the brain tumour subjects with other non-oncological neurological conditions 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); and one (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.
• All studies were rated as ‘very low’ quality due to lack of methodological robustness, and unsystematic clinical observations (Table 3).

The effects of intervention and results of these studies are summarised in Table 4.

Findings based on observational studies:
Ten studies addressed the efficacy of inpatient multidisciplinary rehabilitation (N = 671 participants) (Bartolo 2012; Fu 2010; Geler-Kulcu 2009; Greenberg 2006; Huang 2000; Huang 2001; Huang 1998; Marciniak 2001; O’Dell 1998; Tang 2008) and reported significant reduction in disability (improvement in function) after a period of multidisciplinary rehabilitation as measured by various functional measurement tools (FIM, BI, Karnofsky Performance Status Scale (KPS) (Table 4). One study (Huang 2001) reported continued functional improvements 3 months after discharge in a post-hoc analysis. Six studies compared multidisciplinary rehabilitation outcomes of patients with brain tumours with individuals 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 2000; Huang 1998; O’Dell 1998). One study (Fu 2010) compared functional outcomes between different types of brain tumour and found no significant differences. Four studies (Greenberg 2006; Huang 1998; Huang 2000; Huang 2001) noted shorter LOS in
brain tumour patients compared with either stroke or traumatic brain injury, in contrast with findings of one study (O’Dell 1998) which reported no difference in LOS between brain tumour and traumatic brain injury groups. The percentage of patients discharged to home/community environments, was comparable or greater in the brain tumour group, compared with patients with stroke or traumatic brain injury (Greenberg 2006; Huang 1998; Huang 2000; O’Dell 1998).

Two studies (N = 134 participants) (Pace 2007; Sherer 1997) evaluated the effectiveness of ambulatory multidisciplinary rehabilitation. One study (Sherer 1997) reported favourable participation outcomes (community independence and employment) after outpatient multidisciplinary rehabilitation in patients with brain tumours. These gains generally were maintained at 8 months after discharge. Another study (Pace 2007) showed significant functional gain (BI, KPS) and improved QoL after multidisciplinary home-based rehabilitation (Table 4).

Limitations of findings

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

- Lack 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
- No studies provided direct evidence for organised multidisciplinary rehabilitation in achieving better outcomes when compared with control conditions
- No studies addressed the longer-term outcomes in brain tumour population (participation, QoL), or cost benefits of multidisciplinary rehabilitation, nor information about caregiver burden or needs

The observational studies included in this section also included the above mentioned limitations. They addressed a broad spectrum of outcomes with limited follow-up. The study participant were heterogeneous (disease severity, diagnostic criteria used) with varying rehabilitation practices across countries (USA, Turkey, Italy, Israel), limiting generalizability of findings.

Issues for consideration in brain tumour multidisciplinary rehabilitation

Despite 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). There are many issues that need to be considered in improved care for brain tumour survivors, these include:

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 very poor prognosis, particularly in malignant tumours with 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 optimizing QoL of the patient (Kirshblum 2001; Huang 2011).

Compared to other similar neurological impairments (such as traumatic brain injury, stroke), the time frames for intervention in brain tumour patients are shorter (due to high mortality rate), thus requiring well-defined functional goals. Further, detrimental effects of treatment in this population are significantly higher (Kirshblum 2001).

Despite advances in treatment of brain tumours, rehabilitation has not gained similar momentum amongst 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 patients with brain tumours annually (Boake 1993). This may be due to either poor awareness of extent of rehabilitation services available amongst the 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 patients with cancer diagnoses (Franklin 2007; Dietz 1969). These serve as a tool for identification of issues, symptoms, and functional deficits that occur most frequently at each stage of the cancer journey (i.e., Staging/Pretreatment, 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 cancer patients (Franklin 2007). Generic measures used in brain tumour (and other cancer populations) in general rehabilitation settings (e.g. the FIM or BI) are not sensitive enough to capture the relevant gains following intervention, and have ceiling effects (Khan 2009; Franklin 2007). The FIM constitutes an ordinal rating scale and therefore should not be summed to a single total score nor sub-
The KPS is frequently used in the brain tumour research but it does not provide sufficient specific information to guide the selection of appropriate and timely rehabilitation interventions (Franklin 2007). Thus, more information is required to determine whether the functional efficiency reported in the identified observational studies have 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 ICF (WHO 2001). The ICF provides a comprehensive framework and classification system for a universal language for health professionals, researchers, patients (and carers), and consumer organizations to facilitate communication and agreement amongst treating clinicians with respect to clinical approach (Khan 2010; Khan 2011; Turner Stokes 2011). An ICF 'core set' for head and neck cancers (lists of ICF categories selected by experts for targeted management) has been developed (Tschiesner 2010), and validated (Leib 2011; Tschiesner 2010a); and in the future can assist with scale development using ICF item banking techniques (Cieza 2008).

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 is not routinely available (including rehabilitation and palliative care input), especially over a longer time period. In Australia, the national rehabilitation dataset - the Australasian Rehabilitation Outcomes Centre (AROC) collates inpatient and ambulatory data from 182 accredited public and private rehabilitation facilities across the country (AROC 2011). The AROC dataset 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 the 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, hospital length of 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 dataset more clinically relevant in the future.

Quality of the evidence

There were no well-designed clinical trials (RCTs, CCTs) for multidisciplinary rehabilitation in brain tumour population. This does not suggest ineffectiveness of rehabilitation but the need for better designed studies. Existing 'very low level' evidence from 12 observational studies (with methodological limitations) was included to provide a more complete picture of the available literature. The best evidence synthesis from these twelve observational studies at high risk of bias (Bartolo 2012; Fu 2010; Geler-Kulcu 2009; Greenberg 2006; Huang 2000; Huang 2001; Huang 1998; Marciniak 2001; O’Dell 1998; Pace 2007; Tang 2008) suggests that multidisciplinary rehabilitation (inpatient, home-based) may improve function; and ambulatory programmes (outpatient and home-based) may improve vocational outcomes and QoL in persons after brain tumour treatment 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 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, an extended range of terms were used to capture the widest possible selection of the relevant literature.

2. Publication bias cannot be ruled out as we cannot exclude the possibility that there have been negative trials that have not reached the published literature (Egger 1998).

3. Similarly, reference bias (Goetzsche 1987) is a further possible confounder, 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.

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.

Agreements and disagreements with other studies or reviews

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

AUTHORS’ CONCLUSIONS

Implications for practice

There are no robust clinical trials (RCTs and/or CCTs) of multidisciplinary rehabilitation in patients with primary brain tumours.
This does not indicate ineffectiveness of multidisciplinary rehabilitation, but rather highlights the need for appropriately designed studies incorporating neuro-oncology, rehabilitation and palliative care models to guide treating clinicians. This review identified 12 observational studies providing very limited evidence for multidisciplinary rehabilitation in these patients. In clinical settings multidisciplinary rehabilitation can address the various functional, behavioral and cognitive difficulties in brain tumour survivors which compromise their ability to perform everyday living activities and participation. Rehabilitation should be integrated with neuro-oncology and palliative care services to provide appropriate treatment for each phase of the cancer survivor journey. More evidence is needed to support specific multidisciplinary rehabilitative interventions in this patient population.

Implications for research

The lack of methodologically robust studies in multidisciplinary rehabilitation in brain tumour population needs to be addressed urgently.

- Well-designed research methodology using both randomised 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.
- Longitudinal and longer-term data are required to ascertain long-term care needs.
- More research about patient and caregiver perspective, caregivers’ burden and involvement in rehabilitation programmes are required.
- Research about specific rehabilitation modalities and interventions to improve evidence-based practices are needed.
- Cost effectiveness of multidisciplinary rehabilitation needs further exploration.
- Development of more sensitive and appropriate outcome measurement is required, especially participatory domains.
- More research and emphasis on psychological care over the longer term is needed.
- Research into return to work programmes for appropriate support to these patients is required.

Acknowledgements

We thank Ms Jessica Thomas and the Editorial Board of the Cochrane Pain, Palliative and Supportive Care Review Group for their support and assistance. We particularly like to thank Professor Lynne Turner-Stokes for her advice in the preparation of the protocol of this review.

References

References to studies excluded from this review

Bartolo 2012 [published data only]

Cohen 2002 [published data only]

Fu 2010 [published data only]

Gehring 2009 [published data only]

Geler-Kulcu 2009 [published data only]

Greenberg 2006 [published data only]

Huang 1998 [published data only]

Huang 2000 [published data only]
Multidisciplinary rehabilitation after primary brain tumour treatment (Review)

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Huang 2001 [published data only]

Kawahira 2004 [published data only]

Marciniak 1996 [published data only]

Marciniak 2001 [published data only]

O’Dell 1998 [published data only]

Pace 2007 [published data only]

Rummans 2006 [published data only]

Sherer 1997 [published data only]

Tang 2008 [published data only]

Vereeck 2008 [published data only]

Additional references

Andrews 2004

Arber 2010

AROC 2011

Aziz 2003

Boake 1993

Brain Foundation 2011

Campbell 1999

Cancer Reform Strategy 2007

Cieza 2008

Corner 2007

Dietz 1969

Egger 1998

Fisk 1994
Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WE. Measuring the functional impact of fatigue: initial

Flowers 2000

Franklin 2007

Gabanelli 2005

Ganz 1992

Gilworth 2003

Goetzschke 1987

Granger 1998

Higgins 2011

Hodgkinson 2007

Huang 2001a

Huang 2011

Jemal 2009

Khan 2009

Khan 2010

Khan 2011

Kirshblum 2001

Leib 2011

Louis 2007

Lovibond 1995

MacVicar 1986

MacVicar 1989

Mahoney 1965

Markes 2006

McNeely 2010
Multidisciplinary rehabilitation after primary brain tumour treatment (Review)

Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
WHO 2001

World Health Organization (WHO). *International Classification of Functioning Disability and Health (ICF).*

* Indicates the major publication for the study
## Characteristics of excluded studies

[ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartolo 2012</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Cohen 2002</td>
<td>Uni-disciplinary - physical therapy</td>
</tr>
<tr>
<td>Fu 2010</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Gehring 2009</td>
<td>Uni-disciplinary - psychological intervention</td>
</tr>
<tr>
<td>Geler-Kulcu 2009</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Greenberg 2006</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Huang 1998</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Huang 2000</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Huang 2001</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Kawahira 2004</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Marciniak 1996</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Marciniak 2001</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>O’Dell 1998</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Pace 2007</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Rummans 2006</td>
<td>Details of brain tumour subgroup not provided</td>
</tr>
<tr>
<td>Sherer 1997</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Tang 2008</td>
<td>Not RCT or CCT</td>
</tr>
<tr>
<td>Vereeck 2008</td>
<td>Uni-disciplinary - physical therapy</td>
</tr>
</tbody>
</table>
DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Levels of quality of individual studies

<table>
<thead>
<tr>
<th>Judgement of risk of bias</th>
<th>Quality rating of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of bias of all domains low</td>
<td>High methodological quality = 'high-quality study'</td>
</tr>
<tr>
<td>Unclear or high risk of bias for one or more domains</td>
<td>Low methodological quality = 'low-quality study'</td>
</tr>
<tr>
<td>High risk of bias for most domains</td>
<td>Very low methodological quality = 'very low-quality study'</td>
</tr>
</tbody>
</table>

Table 2. Levels of evidence quality using the GRADE approach

<table>
<thead>
<tr>
<th>Underlying methodology</th>
<th>Quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised trials or double-upgraded observational studies</td>
<td>High</td>
</tr>
<tr>
<td>Downgraded randomised trials or upgraded observational studies</td>
<td>Moderate</td>
</tr>
<tr>
<td>Double-downgraded randomised trials or observational studies</td>
<td>Low</td>
</tr>
<tr>
<td>Triple-downgraded randomised trials or downgraded observational studies or case series/case reports</td>
<td>Very low</td>
</tr>
</tbody>
</table>

Table 3. Characteristics of observational studies

<table>
<thead>
<tr>
<th>Bartolo 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
</tr>
<tr>
<td>Case-control study, Italy</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
</tr>
<tr>
<td>N = 150; Intervention: N = 75 with brain tumours (meningioma and glioblastoma), control: N = 75 with stroke</td>
</tr>
<tr>
<td>Inclusion: all admitted patients to an inpatient neurorehabilitation unit after surgery for brain tumours (meningiomas or glioblastomas) over a 2-year period (2007-2009)</td>
</tr>
<tr>
<td>Control participants were stroke patients (Ischaemic or hemorrhagic), matched one-to-one for age, sex and side of lesion</td>
</tr>
<tr>
<td>Exclusion: patients with oligoastrocytoma, oligodendroglialoma, and ependymomas to obtain homogeneous group</td>
</tr>
</tbody>
</table>
### Table 3. Characteristics of observational studies  
(Continued)

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Inpatient multidisciplinary rehabilitation - administered by experienced physical therapists 60-min session, 6-days/week for four consecutive weeks; which included: passive/assisted stretching exercises, strengthening exercises, balance exercises, ground-floor walking (including step control) and four weeks of speech therapy (individual 60-min sessions, once daily, six days per week) when aphasia was diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Sitting balance, standing balance, Hauser Index - gait disorders, MGHFAC - severity of gait disorders, FIM</td>
</tr>
<tr>
<td>Assessment time points</td>
<td>Before and after the intervention</td>
</tr>
</tbody>
</table>
| Risk of Bias  | Adequate sequence generation: No  
 Adequate allocation concealment: No  
 Blinding: No  
 Incomplete outcome data addressed: Unclear  
 Free of selective reporting: Yes  
 Other bias:  
 • Study design: case-control study  
 • Intervention did not include multidisciplinary input from other disciplines, apart from speech pathologists. Also unclear if all the subjects within 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  | N = 42; Intervention: N = 21 patients with low-grade gliomas, control: N = 21 patients with high-grade gliomas  
 Inclusion: 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 |
| Intervention  | Inpatient multidisciplinary rehabilitation (details not provided) |
| Outcomes      | FIM; LOS; discharge to home rate |
| Assessment time points | Admission and discharge  
 Risk of Bias  | Adequate sequence generation: No  
 Adequate allocation concealment: No  
 Blinding: No  
 Incomplete outcome data addressed: N/A  
 Free of selective reporting: Yes  
 Other bias:  
 • Study design: retrospective (medical records) case-control |
Table 3. Characteristics of observational studies (Continued)

<table>
<thead>
<tr>
<th>Quality rating of the study</th>
<th>Very low</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Geler-Kulcu 2009</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Case-control study, Turkey</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>N = 42; Intervention: N = 21 with brain tumours (benign and malignant), control: N = 21 with stroke</td>
</tr>
<tr>
<td><em>Inclusion</em>: all admitted patients to an inpatient neurorehabilitation unit, control participants were stroke patients (Ischaemic or hemorrhagic), matched by side of lesion</td>
<td></td>
</tr>
<tr>
<td><em>Exclusion</em>: patients with oligoastrocytoma, oligodendroglioma, and ependymomas to obtain homogeneous group</td>
<td></td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Inpatient “conventional” rehabilitation programme single 60-min sessions, 5 days/week for four 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</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>PAS for Stroke, BBS, MAS, FIM (mobility)</td>
</tr>
<tr>
<td><strong>Assessment time points</strong></td>
<td>Admission and discharge</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Adequate sequence generation: No</td>
</tr>
<tr>
<td></td>
<td>Adequate allocation concealment: No</td>
</tr>
<tr>
<td></td>
<td>Blinding: No.</td>
</tr>
<tr>
<td></td>
<td>Incomplete outcome data addressed: Unclear</td>
</tr>
<tr>
<td></td>
<td>Free of selective reporting: Yes</td>
</tr>
<tr>
<td><strong>Other bias</strong>:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Study design: case-control study.</td>
</tr>
<tr>
<td></td>
<td>- Intervention not adequately described and did not include multidisciplinary input from other disciplines apart from PT and OT</td>
</tr>
<tr>
<td></td>
<td>- No sample size calculation performed</td>
</tr>
<tr>
<td><strong>Quality rating of the study</strong></td>
<td>Very low</td>
</tr>
<tr>
<td><strong>Greenberg 2006</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Retrospective case-control study, Israel</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>N = 1828; Intervention N = 168 with brain tumours (128 meningiomas, 40 gliomas), control: N = 1660 with stroke (Ischaemic or hemorrhagic)</td>
</tr>
</tbody>
</table>
| *Inclusion*: all admitted patients to an inpatient neurorehabilitation unit over an 11 year period (1993-
<table>
<thead>
<tr>
<th>Interventions</th>
<th>Inpatient multidisciplinary rehabilitation provided by PT, medical staff, OT and speech pathologist. Details of the multidisciplinary rehabilitation not provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>FIM, FIM efficiency, LOS days, discharge destination (rate discharge to home)</td>
</tr>
<tr>
<td>Assessment time points</td>
<td>Admission and discharge</td>
</tr>
</tbody>
</table>
| Risk of Bias  | Adequate sequence generation: No  
Adequate allocation concealment: No  
Blinding: No.  
Incomplete outcome data addressed: No  
Free of selective reporting: Yes  
**Other bias:**  
• 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 2001    |                                                                                                                                                                                            |
| Methods       | Prospective case series, USA                                                                                                                                                                 |
| Participants  | N = 10 (brain tumour)  
*Inclusion:* 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 |
| Outcomes      | FIM, DRS, KPS, FACT-BR                                                                                                                                                                       |
| Assessment time points | Admission and discharge, post hoc analysis at 3-month post discharge                                                                                                                       |
| Risk of Bias  | Adequate sequence generation: No  
Adequate allocation concealment: No  
Blinding: No.  
Incomplete outcome data addressed: Unclear  
Free of selective reporting: Yes  
**Other bias:**  
• Study design: case-series study, no control group  
• Contents, duration and nature of multidisciplinary rehabilitation not clearly defined  
• Small sample size
<table>
<thead>
<tr>
<th>Quality rating of the study</th>
<th>Very low</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Huang 2000</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Retrospective case-control, USA</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Inclusion</strong></td>
<td>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 hrs. of therapy, willingness and motivation to participate in a rehabilitation programme</td>
</tr>
<tr>
<td><strong>Exclusion</strong></td>
<td>patients who did not complete rehabilitation due to medical complications or death</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Inpatient multidisciplinary rehabilitation (details not provided)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>FIM; FIM efficiency; LOS; discharge destination to community rate</td>
</tr>
<tr>
<td><strong>Assessment time points</strong></td>
<td>Admission and discharge</td>
</tr>
<tr>
<td><strong>Risk of Bias</strong></td>
<td>Adequate sequence generation: No</td>
</tr>
<tr>
<td></td>
<td>Adequate allocation concealment: No</td>
</tr>
<tr>
<td></td>
<td>Blinding: No.</td>
</tr>
<tr>
<td></td>
<td>Incomplete outcome data addressed: Unclear</td>
</tr>
<tr>
<td></td>
<td>Free of selective reporting: Yes</td>
</tr>
<tr>
<td><strong>Other bias:</strong></td>
<td>Study design: retrospective case-control</td>
</tr>
<tr>
<td></td>
<td>Contents, duration and nature of multidisciplinary rehabilitation not clearly defined</td>
</tr>
<tr>
<td></td>
<td>Unclear selection criteria: medically stable, motivated and interested candidates only were selected by a single psychiatrist for multidisciplinary rehabilitation with support arrangements for discharge to the community</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality rating of the study</th>
<th>Very low</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Huang 1998</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Retrospective case-control study, USA</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Inclusion</strong></td>
<td>all patient admitted to an inpatient rehabilitation centre</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Inpatient multidisciplinary rehabilitation (details not provided)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>FIM; FIM efficiency; LOS; discharge destination to community rate</td>
</tr>
</tbody>
</table>
Table 3. Characteristics of observational studies  (Continued)

<table>
<thead>
<tr>
<th>Assessment time points</th>
<th>Admission and discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk of Bias</strong></td>
<td></td>
</tr>
<tr>
<td>Adequate sequence generation: No</td>
<td></td>
</tr>
<tr>
<td>Adequate allocation concealment: No</td>
<td></td>
</tr>
<tr>
<td>Blinding: No</td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data addressed: unclear</td>
<td></td>
</tr>
<tr>
<td>Free of selective reporting: Yes</td>
<td></td>
</tr>
<tr>
<td><strong>Other bias:</strong></td>
<td></td>
</tr>
<tr>
<td>• Study design: retrospective case-control study</td>
<td></td>
</tr>
<tr>
<td>• Contents, duration and nature of multidisciplinary rehabilitation not clearly define</td>
<td></td>
</tr>
<tr>
<td><strong>Quality rating of the study</strong></td>
<td>Very low</td>
</tr>
</tbody>
</table>

**Marciniak 2001**

**Methods**
Retrospective case series, USA

**Participants**
N = 132 subjects divided into 4 groups: astrocytomas 26%; meningiomas 33%, metastatic tumours 16%; other tumours 25%. Subjects also grouped into those with tumour recurrence and those with initial tumour presentation

*Inclusion:* all patient > 18 years, inpatient rehabilitation within a 3-year period (1993-1996)

**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**
Adequate sequence generation: No
Adequate allocation concealment: No
Blinding: No
Incomplete outcome data addressed: unclear
Free of selective reporting: Yes

**Other bias:**
• Study design: retrospective case-control study
• Contents, duration and nature of multidisciplinary rehabilitation not clearly define

**Quality rating of the study**
Very low

**O’Dell 1998**

**Methods**
Retrospective case-control, USA

**Participants**
N = 80; Intervention: N = 40 subjects with brain tumours (benign and malignant), control: N = 40, case matched by admission FIM score, age, and gender to 40 subjects with traumatic brain injury

*Inclusion:* all patient admitted to an inpatient acute rehabilitation programme over a 2-year period
### Table 3. Characteristics of observational studies (Continued)

<table>
<thead>
<tr>
<th>(1994-1996)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
</tr>
<tr>
<td><strong>Assessment time points</strong></td>
</tr>
</tbody>
</table>
| **Risk of Bias** | Adequate sequence generation: No  
Adequate allocation concealment: No  
Blinding: No  
Incomplete outcome data addressed: unclear  
Free of selective reporting: Yes  
**Other bias:**  
- 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 & after) study, Italy |
|---|
| **Participants** | N = 121 with malignant brain tumours  
_Inclusion:_ all patients discharged from hospital over 3 year period (2000-2003) with neurological deficits |
| **Intervention** | Home neurorehabilitation programme including physiotherapy one hour/3 times a week for 3 months, neurologist evaluation, psychological assistance, nursing and palliative care team if needed (further details not provided) |
| **Outcomes** | Barthel Index (BI), Karnofsky Performance status (KPS), EORCT QLQ-C30-BM 20 |
| **Assessment time points** | Before and 3-months after rehabilitation |
| **Risk of Bias** | Adequate sequence generation: No  
Adequate allocation concealment: No  
Blinding: No  
Incomplete outcome data addressed: Patients who completed only basal questionnaire were excluded  
Free of selective reporting: Yes  
**Other bias:**  
- Study design: prospective before-after study without control  
- Contents, duration and nature of multidisciplinary rehabilitation (intervention) not clearly define |
| **Quality rating of the study** | Very low |

**Sherer 1997**

<p>| <strong>Methods</strong> | Multidisciplinary rehabilitation after primary brain tumour treatment (Review) |
|---|
| <strong>Participants</strong> | |
| <strong>Intervention</strong> | |
| <strong>Outcomes</strong> | |
| <strong>Assessment time points</strong> | |
| <strong>Risk of Bias</strong> | |
| <strong>Quality rating of the study</strong> | Very low |</p>
<table>
<thead>
<tr>
<th>Methods</th>
<th>Retrospective case series, USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>N = 13 (primary malignant brain tumours with a history of surgical resection, radiation and chemotherapy)</td>
</tr>
<tr>
<td>Inclusion</td>
<td>all patients receiving outpatient rehabilitation who had a diagnosis of malignant brain tumour and adequate medical records to characterize their tumour and courses of therapy</td>
</tr>
<tr>
<td>Intervention</td>
<td>Outpatient rehabilitation with input from psychologists, speech/language pathologists, OT, and vocational specialists. Patients received an average of 2.6 ± 1.9 months of therapy (duration of 5 hours/day) (further details not provided)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Level of independence, vocational (productivity) outcomes</td>
</tr>
<tr>
<td>Assessment time points</td>
<td>Admission, discharge and 8 month follow up</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td>Adequate sequence generation: No</td>
</tr>
<tr>
<td></td>
<td>Adequate allocation concealment: No</td>
</tr>
<tr>
<td></td>
<td>Blinding: No</td>
</tr>
<tr>
<td></td>
<td>Incomplete outcome data addressed: Yes</td>
</tr>
<tr>
<td></td>
<td>Free of selective reporting: Yes</td>
</tr>
<tr>
<td></td>
<td>Other bias:</td>
</tr>
<tr>
<td></td>
<td>• Study design: retrospective case series without control.</td>
</tr>
<tr>
<td></td>
<td>• Contents, duration and nature of multidisciplinary rehabilitation not clearly defined</td>
</tr>
<tr>
<td></td>
<td>• Small sample size</td>
</tr>
<tr>
<td></td>
<td>• No validated measures use</td>
</tr>
<tr>
<td>Quality rating of the study</td>
<td>Very low</td>
</tr>
<tr>
<td>Tang 2008</td>
<td></td>
</tr>
<tr>
<td>Methods</td>
<td>Retrospective case series, Canada</td>
</tr>
<tr>
<td>Participants</td>
<td>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%</td>
</tr>
<tr>
<td>Inclusion</td>
<td>all patients admitted to an inpatient rehabilitation ward over a 3 year period (2003-2006)</td>
</tr>
<tr>
<td>Exclusion</td>
<td>Patients with meningiomas</td>
</tr>
<tr>
<td>Intervention</td>
<td>Inpatient multidisciplinary rehabilitation (details not provided)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>FIM, FIM efficiency, LOS; discharge destination to home rate, survival</td>
</tr>
<tr>
<td>Assessment time points</td>
<td>Admission and discharge</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td>Adequate sequence generation: No</td>
</tr>
<tr>
<td></td>
<td>Adequate allocation concealment: No</td>
</tr>
<tr>
<td></td>
<td>Blinding: No</td>
</tr>
</tbody>
</table>
Table 3. Characteristics of observational studies (Continued)

| Incomplete outcome data addressed: | Unclear |
| Free of selective reporting: | Yes |
| Other bias: | |
| • Study design: retrospective case series without control. |
| • Contents, duration and nature of multidisciplinary rehabilitation not clearly defined |

Quality rating of the study: Very low

ADL = activities of daily living; BBS = Berg Balance Scale; BI = Barthel Index; DRS = Disability Rating Scale; EORCT QLQ-C30-BM 20 = European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FIM = Functional Independence Measure (FIM); FACT-BR = Functional Assessment of Cancer Therapy-Brain; KPS = Karnofsky Performance Status Scale; LOS = length of stay; MAS = Motor Assessment Scale; MGHFAC = Massachusetts General Hospital Functional Ambulation Classification; N = total number; OT = Occupational Therapists; PAS = Postural Assessment Scale; PT = Physio Therapist; USA = United States of America

Table 4. Results of observational studies

Bartolo 2012

### Statistical analysis
- Student’s t test, Chi² test, Wilcoxon matched-pairs signed-rank test, Mann-Whitney U test, Kruskal-Wallis ANOVA

### Results
- All the measures of outcome (FIM: mobility, ADL, cognition; Balance tests, MGHFAC) were indicative of substantial improvements for brain tumour and for stroke patients \((P = 0.000\) for all).
- The values of functional gain in all scores were comparable between brain tumour and stroke groups.
- Analysis of subgroups showed that patients affected by meningioma achieved better results (in efficiency terms) as regards independence in ADL \((P = 0.02)\) and mobility \((P = 0.04)\) compared with patients 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, Chi² test, Kruskal-Wallis test, Mann-Whitney U test

### Results
- 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 patients with high-grade astrocytoma was significantly \((13\) vs. \(9\) days, \(P = 0.04)\) longer than low grade.
- Discharge to home rate was also comparable between groups; 90% in both groups.
### Table 4. Results of observational studies (Continued)

<table>
<thead>
<tr>
<th>Author's conclusion</th>
<th>Geler-Kulcu 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants made significant functional gains from admission to discharge. Compared with patients with low-grade astrocytoma, patients with high-grade astrocytoma had higher total functional independence measure gain but also longer lengths of stay. Functional independence measure efficiencies were comparable between the two groups.</td>
<td></td>
</tr>
</tbody>
</table>

| Statistical analysis | Friedman test, Chi² test, Mann-Whitney U test, ANOVA |

| Results | Patients with brain tumour progressed as well as patients with stroke in a post-acute inpatient rehabilitation programme |

<table>
<thead>
<tr>
<th>Greenberg 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistical analysis</td>
</tr>
</tbody>
</table>

| Results | Functional variables during inpatient multidisciplinary rehabilitation were found to be similar in the all 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 patients with meningiomas, 80.7 for patients with gliomas, and 87.8 for stroke patients (P = 0.76). |

| | There was no significant difference in functional gain amongst groups: functional gain was 17.9 for meningioma patients, 17.2 for glioma patients, and 21.8 for stroke patients (P = 0.4). |

| | FIM efficiency analysis showed that both brain tumour groups had similar efficacy and that stroke patients had the lowest efficiency (P = 0.001). |

| | Average length of stay was 24 days for the meningioma group, 23 days for the glioma group, and 75.4 days for stroke patients. |

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

| Author's conclusions | Brain tumour patients with both gliomas and 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 |

<table>
<thead>
<tr>
<th>Huang 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistical analysis</td>
</tr>
</tbody>
</table>

| Results | 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-month follow-up scores. |
Table 4. Results of observational studies (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Results</th>
<th>Author's conclusion</th>
</tr>
</thead>
</table>
|       | • 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 post discharge relative to admission.  
  • FIM, KPS, and DRS did not show significant correlation with FACT-BR.  
  • 90% of patients were initially discharged to a home environment. | Although patients make functional gains during and after inpatient multidisciplinary rehabilitation, gains in QoL are not significant until 1 month post discharge. QoL does not appear to correlate well with functional outcomes. Further, the KPS is less sensitive than the FIM and DRS in detecting change in functional status. |
| Huang 2000 | **Statistical analysis** | ANOVA, Chi² test |
| **Results** | • 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: significantly shorter in tumour group (22 days vs. 32 days, P < 0.01).  
  • Discharge community rate: significantly greater in tumour group (87%) vs. traumatic brain injury (74%) (P < 0.05). | Individuals with brain tumour can achieve comparable functional outcome and have a shorter rehabilitation length of stay and greater discharge to community rate than individuals with traumatic brain injury. |
| Huang 1998 | **Statistical analysis** | ANOVA, Chi² test |
| **Results** | • 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  
  • FIM efficiency was comparable between groups (FIM change/week: 8.4 brain tumour vs. 7.2 stroke, P = 0.29)  
  • LOS: 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). | Individuals with brain tumour can achieve comparable functional outcome and discharge to community rate, and have a shorter rehabilitation length of stay than individuals with stroke. |
| Marciniak 2001 | **Statistical analysis** | Descriptive analysis, Analysis of variance |

Multidisciplinary rehabilitation after primary brain tumour treatment (Review)  
Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### Table 4. Results of observational studies  (Continued)

| Results |  
|---|---|
| • 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.  
• FIM motor subscores change was significantly smaller for those with metastasis (8.6) and astrocytomas (16.2) when compared with meningiomas (20) and other tumours (21).  
• 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.  
• Patients who received radiation during rehabilitation had significantly greater motor efficiency score (1 ± 0.79) than those who did not (P < 0.05).  
• Patient in metastatic disease group had significantly shorter LOS than other tumour groups (P = 0.03).  
• Overall 65% of the 132 admissions were discharged home. Patients with meningiomas were less likely to be discharged home (47%) than those with metastatic tumours (71%), astrocytic tumours (71%), or 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. Patients receiving concurrent radiation therapy make greater functional improvement per day than those not receiving radiation. Patients with recurrent tumours make significantly smaller functional motor gains than those completing inpatient multidisciplinary rehabilitation after the tumour’s initial diagnosis |

| O’Dell 1998 |  
|---|---|
| Statistical analysis | Descriptive analysis, Chi² test, Kruskal-Wallis test, Mann-Whitney U test |
| Results |  
|• Both group made significant functional gains in their FIM scores: total FIM, ADL and mobility subscores scores from admission to discharge.  
• Total FIM change was significantly greater in traumatic brain injury group compared to 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 persons with brain tumour undergoing multidisciplinary rehabilitation were similar to those made by a group of persons with traumatic brain injury matched by age, gender, and admission functional status |

| Pace 2007 |  
|---|---|
| Statistical analysis | Chi² test, Student t test (paired or not, as appropriate) |
| Results | At 3-month follow up:  
• Barthel Index (BI) improved in 47 (39%) patients, 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% patients by median 10 points (P < 0.001).  
• No significant difference was observed between various subgroups of brain tumour and in between those with initial diagnosed and those treated for recurrences. |
Table 4. Results of observational studies (Continued)

<table>
<thead>
<tr>
<th>Author’s conclusion</th>
<th>Multidisciplinary rehabilitation at home in brain tumour patients 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</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sherer 1997</td>
<td>Descriptive analyses only</td>
</tr>
</tbody>
</table>
| Results             | At the time of discharge from the programme 6 patients had increased independence 6 were unchanged, and 1 patient had decreased independence.  
                    | At discharge 8 patients 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 of patients had increased independence, 4 were unchanged, 1 had decreased independence, 1 patient had died. |
| Author’s conclusion | Patients with primary malignant brain tumours achieved increased community independence and vocational outcomes (such as employment, education) after individualized multidisciplinary outpatient rehabilitation. Such treatment programme appears to be an attractive, relatively low cost option for these patients, however, additional investigation is needed. |
| Tang 2008           | ANOVA, Chi² 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             | 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 patients with brain tumours.  
                    | Discharge to home rate was comparable between groups (76% - GBM, 72% - metastatic and 70% - other).  
                    | Estimated median survival was 141 days for brain metastases, 214 days for GBM and 439 days for other tumours. |
| Author’s conclusion | Patients 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; BI = Barthel Index; DRS = Disability Rating Scale; EORCT QLQ-C30-BM 20 = European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FIM = Functional Independence Measure; FACT-BR = Functional Assessment of Cancer Therapy-Brain;
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 neuroepitheli* or neuroepitheli* or neuronal* or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening* or sellar) near/5 (neoplasm* or tumour* or tumor* or malignant* or carcinoma* or cancer*))
#5 (#1 OR #2 OR #3 OR #4)
#6 Any MeSH descriptor with qualifier: RH
#7 MeSH descriptor Rehabilitation explode all trees
#8 MeSH descriptor Ambulatory Care explode all trees
#9 MeSH descriptor Physical Therapy Modalities explode all trees
#10 MeSH descriptor Home Care Services explode all trees
#11 MeSH descriptor Inpatients, this term only
#12 MeSH descriptor Outpatients, this term only
#13 MeSH descriptor Behavior Therapy explode all trees
#14 MeSH descriptor Social Work explode all trees
#15 MeSH descriptor Dietetics, this term only
#16 MeSH descriptor Dietary Services explode all trees
#17 MeSH descriptor Counseling explode all trees
#18 MeSH descriptor Patient Care Team explode all trees
#19 (multidisciplinary or multi-disciplinary or integrated or interdisciplinary or inter-disciplinary)
#20 rehabilitation* or physicaltherap* or physical therap* or speech or occupation* or social work"
#21 (cogniti* or behavior or behaviour or counsel* or nutrition* or diet* or food)
#22 (outpatient* or inpatient* or hospital* or home)
#23 (#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 OR #21 OR #22)
#24 (#5 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 neuroepitheli* 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 malignant* or carcinoma* or cancer*)).mp.
5. 1 or 2 or 3 or 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/
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 behavior* or counsel* or nutrition* or diet* or food).mp.
22. ((outpatient* or inpatient* or hospital* or home).mp.
23. 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 or 21 or 22
24. 5 and 23
25. randomized controlled trial.pt.
26. controlled clinical trial.pt.
27. randomized.ab.
28. placebo.ab.
29. clinical trials as topic.sh.
30. randomly.ab.
31. trial.ti.
32. (control* and comparative).mp.
33. (before and after).mp.
34. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35. 24 and 34
36. exp animals/ not humans.sh.
37. 35 not 36

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 neuroepitheli* or neuroepitheli* or neuronal* or pineal or embryonal or haemopoietic or hemopoietic or germ cell or mening* or sellar) and (neoplasm* or tumour* or tumor* or malignan* or carcinoma* or cancer*).mp.
5. 1 or 2 or 3 or 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 behavior therap* or counseling or nutrition* or diet* or food).mp.
23. (outpatient* or inpatient* or hospital* or home).mp.
24. 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 or 21 or 22 or 23
25. 5 and 24
26. exp controlled clinical trial/
27. crossover procedure/
28. double-blind procedure/
29. randomized controlled trial/
30. single-blind procedure/
31. random*.mp.
32. factorial*.mp.
33. (crossover* or cross over* or cross-over*).mp.
34. placebo*.mp.
35. (double* adj blind*).mp.
36. (singl* adj blind*).mp.
37. assign*.mp.
38. allocat*.mp.
39. volunteer*.mp.
40. (control* and comparative).mp.
41. (before and after).mp.
42. 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41
43. 25 and 42
44. (exp Animal/ or Nonhuman/ or exp Animal Experiment/) not Human/
45. 43 not 44
key:
mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword

WHAT’S NEW

Last assessed as up-to-date: 28 June 2012.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 September 2012</td>
<td>Amended</td>
<td>Change of title</td>
</tr>
</tbody>
</table>
Contributions of Authors

Fary Khan (FK) and Bhasker Amatya (BA) were involved in all aspects of the review. FK, BA and LN screened, identified and analysed all relevant studies. BA and LN drafted the results whilst FK drafted the discussion. Comments from all authors including John Olver (JO) and Kate Drummond (KD) were included in the 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.

None have personal or financial conflicts of interest in the findings of this review.

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

Title has been amended.

Index Terms

Medical Subject Headings (MeSH)

Brain Neoplasms [∗rehabilitation; therapy]; Combined Modality Therapy [methods]; Quality of Life

MeSH check words

Adult; Humans