

Multi-disciplinary rehabilitation for acquired brain injury in adults of working age (Review)

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ABSTRACT

Background

Evidence from systematic reviews demonstrates that multi-disciplinary rehabilitation is effective in the stroke population, where older adults predominate. However, the evidence base for the effectiveness of rehabilitation following acquired brain injury (ABI) in younger adults is not yet established, perhaps because there are different methodological challenges.

Objectives

To assess the effects of multi-disciplinary rehabilitation following ABI in adults, 16 to 65 years. To explore approaches that are effective in different settings and the outcomes that are affected.

Search strategy

We used a wide range of sources including: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1966 to 2004), EMBASE (1988 to 2004), CINAHL (1983 to 2004), PsycLIT (1967 to 2004), AMED, the National Research Register 2004 and ISI Science Citation Index (1981 to 2004).

Selection criteria

Randomised controlled trials (RCTs) comparing multi-disciplinary rehabilitation with either routinely available local services or lower levels of intervention; or trials comparing intervention in different settings or at different levels of intensity. Quasi-randomised and quasi-experimental designs were also included, providing they met pre-defined methodological criteria.

Data collection and analysis

Two authors selected trials and rated their methodological quality independently. A third reviewer arbitrated when disagreements could not be resolved by discussion. We performed a 'best evidence' synthesis by attributing levels of evidence, based on methodological quality. We sub-divided trials in terms of severity of ABI and the setting and type of rehabilitation offered.

Main results

We identified ten trials of good methodological quality and four of lower quality. Within the subgroup of predominantly mild brain injury, 'strong evidence' suggested that most patients make a good recovery with provision of appropriate information, without additional specific intervention. For moderate to severe injury, there is 'strong evidence' of benefit from formal intervention. For patients with moderate to severe ABI already in rehabilitation, there is strong evidence that more intensive programmes are associated with earlier functional gains, and 'moderate evidence' that continued outpatient therapy can help to sustain gains made in early post-acute rehabilitation. There is 'limited evidence' that specialist in-patient rehabilitation and specialist multi-disciplinary community rehabilitation may provide additional functional gains, but the studies serve to highlight the particular practical and ethical restraints on randomisation of severely affected individuals for whom there are no realistic alternatives to specialist intervention.

Authors' conclusions

Problems following ABI vary; different services are required to suit the needs of patients with different problems. Patients presenting acutely to hospital with moderate to severe brain injury should be routinely followed up to assess their need for rehabilitation. Intensive

intervention appears to lead to earlier gains. The balance between intensity and cost-effectiveness has yet to be determined. Patients discharged from in-patient rehabilitation should have access to out-patient or community-based services appropriate to their needs. Those with milder brain injury benefit from follow-up, and appropriate information and advice. Not all questions in rehabilitation can be addressed by traditional research methodologies. There are important questions still to be answered and future research should employ the most appropriate methodology.

PLAIN LANGUAGE SUMMARY

Multi-disciplinary rehabilitation for brain injury in working-age adults

Studies show that multi-disciplinary (MD) rehabilitation is beneficial to patients with brain damage from stroke. Some MD programs are targeted to working-age adults who have brain injuries through trauma or other causes. These patients are younger than most stroke patients and may have different goals, such as returning to work or parenting. Brain injured patients can have a variety of issues, including problems with physical functions, communication, thought processes, behaviour, or emotions. Severity of problems can vary from mild to severe. MD rehabilitation addresses one or more of the above areas instead of focussing on an aspect such as physical function.

The authors of this Cochrane review looked for evidence for the effectiveness of MD rehabilitation in adults, aged 16 to 65 years, with acquired brain injury (ABI) from any cause. They looked for controlled trials in which one group of people received a treatment (such as MD rehabilitation) and was compared with a similar group which received a different treatment. They found 14 studies. As a whole, the studies suggested that patients with moderate to severe brain injury who received more intensive rehabilitation had earlier improvement. For mild brain injury, information and advice was usually more appropriate than intensive rehabilitation. There was not much evidence related to other aspects of MD rehabilitation, so the review authors recommend that more research be done. Rehabilitation for brain injury is such an individualised and long-term process that it can be difficult to draw general conclusions from research studies

BACKGROUND

Brain injury rehabilitation services are increasingly defined by the needs of patients, rather than by the underlying pathology (i.e. disease or diagnosis). Specialist multi-disciplinary rehabilitation services in the UK have been developed to serve the needs of 'younger' (16 to 65 years) or 'working age' adults. This separation from services for 'older adults' is not simply age-ist, but also arises because these individuals often have different goals for rehabilitation (such as returning to work or parenting) that may be less relevant in an older, predominantly retired, population. Moreover, younger adults may have greater potential for neuroplasticity and, in view of very long survival times over which to reap the gains of functional and financial independence, they may justify substantial initial investment in rehabilitation to optimise functional recovery (Jackson 1999). There is also some evidence that younger patients respond better in different environments from older populations (Gladman 1993; Kalra 1994). The Royal College of Physicians' National Clinical Guidelines for Stroke recommends that 'specialist rehabilitation services must recognise the medical, rehabilitation and social needs of younger patients, which must be provided in an environment suited to their personal needs' (RCP 2004).

The principal causes of acquired brain injury (ABI) in this younger adult group include:

- traumatic brain injury (TBI) – injury resulting from trauma to the head and its direct consequences including hypoxia, hypotension, intracranial haemorrhage and raised intracranial pressure;
- diffuse acquired brain injury – diffuse damage arising from trauma due to the above, or a range of other acute incidents including hypoxia (e.g. due to drowning, electrocution, anaesthetic accident), hypoglycaemia, viral encephalitis;
- cerebrovascular accident (stroke) which may be ischaemic or haemorrhagic, but includes a higher proportion of sub-arachnoid haemorrhage (from aneurysms or arterio-venous malformations) than the older population of strokes;
- other causes, such as neurosurgical operations (e.g. removal of a meningioma), radiotherapy, cerebral abscess, bacterial meningitis and gun shot wounds.

It is pertinent, therefore, to consider the evidence for the effectiveness of rehabilitation separately for the younger group of 'working age' adults, and to use a broad definition of 'acquired brain injury (ABI)' that encompasses all of the above conditions, and represents the group of patients which typically presents for rehabilitation following a single incident neurological insult. This approach is in keeping with the UK National Service Framework (NSF)

for Long-term Conditions, which focuses on common features of neurological conditions categorised by their pattern of progression (acute single insult, unpredictable variation, inevitable progression), rather than specific pathological diagnoses. This review has contributed to the evidence base to underpin the UK National Clinical Guidelines for Rehabilitation following Acquired Brain Injury (RCP/BSRM 2003) and to the UK NSF for Long-term Conditions (DoH 2005), which have also highlighted the particular needs of the working-aged adult.

Patients with ABI experience a wide range of different deficits, depending on the nature and location of their injury. They may present to rehabilitation with various combinations of physical, communicative, cognitive, behavioural, psychosocial and environmental problems. In terms of the vocabulary used in the expanded World Health Organization's International Classification of Functioning (WHO ICF) (Wade 2000; Wade 2003) they demonstrate heterogeneity at each of the different levels:

- they suffer a variety of different pathologies;
- they experience a great variety of different impairments, with each patient having a unique combination in terms of severity and nature of impairment;
- they also experience very varied limitations in or restrictions on activities (disabilities) and participation (handicap);
- they approach rehabilitation from a variety of different contexts – personal, social and physical.

This means that each individual has a unique set of needs. Different individuals need different programmes of rehabilitation and, moreover, the same individual will need different programmes of rehabilitation at different stages in their recovery. For example:

- following the initial stages of recovery from acute injury, some patients will need to undergo a period of intensive in-patient rehabilitation to return to functional independence and to make the transition from hospital back into the community; outcomes from these 'post-acute' programmes tend to focus on reduction of impairment and disability;
- once back in the community, attention turns more towards social integration, with return to work and financial independence if possible; community-based rehabilitation programmes supporting these activities correctly focus on outcome measures which reflect improved participation and psycho-social adjustment.

This heterogeneity of patients, rehabilitation services and outcomes poses a challenge to traditional research methodologies (Whyte 2002), and to systematic reviews and meta-analysis. The current review serves to:

- identify the existing trial-based evidence for multi-disciplinary rehabilitation in ABI in adults of working age;

- discuss explicitly the issues for future expansion of the evidence base by traditional research methods;
- identify gaps in knowledge and suggest appropriate methods by which these could be explored in future.

The methodology described below takes into account advice offered by Greener and Langhorne (Greener 2002) regarding the application of systematic reviews in the field of rehabilitation.

OBJECTIVES

Specific questions that are addressed by this review are:

- does organised multi-disciplinary rehabilitation achieve better outcomes than the absence of such services for this group of patients?
- does a greater intensity (time and/or expertise) of rehabilitation lead to greater gains?
- which type of programmes are effective and in which setting?
- which specific outcomes are influenced (dependency, social integration, mood, return to work etc.)?
- are there demonstrable cost-benefits for multi-disciplinary rehabilitation?

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We included all randomised controlled trials (RCTs) which compared multi-disciplinary rehabilitation with either routinely available local services or lower levels of intervention; or trials which compared intervention in different settings or at different levels of intensity (see types of intervention). We considered quasi-experimental designs, provided there was a large element of chance in the availability of a place within a given service versus the possibility of referral elsewhere (see Discussion).

Types of participants

We included trials if the study population was predominantly of working age (i.e. mean age between 16 and 65 years) and subjects had acquired brain injury (ABI) of any cause (including traumatic brain injury (TBI), diffuse brain injury, stroke, sub-arachnoid haemorrhage, intra-cranial haemorrhage, or mixed ABI populations). We also classified as eligible for inclusion, trials which encompassed all ages, but presented a separate sub-analysis of the population aged 16 to 65 so that outcomes for adults within this age group were separately identifiable. We have not yet identified any trials in this category.

Rehabilitation programmes designed principally to meet the needs of older people may include a minority of younger individuals, for lack of more appropriate services, but often fail in practice to address their more extended rehabilitation goals (Kersten 2002; Roding 2003). For this reason, we did not contact authors for extracted information on younger adults within predominantly elderly study groups, unless there was clear evidence that they were identified and treated as a separate group. Again we have identified no such trials.

The classification of patients who have experienced acquired brain injury is complex because, as noted above, individuals may have one or more of a wide range of impairments, each of differing severity. However, the nature and severity of neurological deficits tends to determine the type of rehabilitation programme offered, as well as the goals for treatment and the outcome measures used. For example, as a very crude generalisation, patients with mild ABI tend to have primarily cognitive losses and goals for rehabilitation tend to focus on enhanced participation, whereas patients in the moderate to severe category are more likely to have goals centred on improvement at the level of impairment and activity (disability). We did not include or exclude studies on the basis of severity, but were subgrouped them on this basis for the purpose of analysis and discussion.

Types of intervention

Rehabilitation is broadly defined as 'a problem-solving educational process aimed at reducing disability and handicap experienced by someone as a result of disease or injury' (Wade 1992). For the purposes of this review, we have defined multi-disciplinary rehabilitation as any intervention delivered by two or more disciplines which aims to meet these objectives.

There is no agreed classification of rehabilitation interventions and programmes and again, broadly speaking, programmes may be described in terms of setting and content.

Rehabilitation settings include:

- in-patient settings – where rehabilitation is delivered in the context of 24-hour care, which may be in a hospital ward or a specialist rehabilitation unit;
- out-patient or day treatment settings – which again may be in a hospital environment, a local community venue (such as a day centre) or a specialist rehabilitation environment;
- domiciliary or home-based – focused around the patients own home and local community.

Current terms found in the literature regarding programme content include:

- physical rehabilitation;
- cognitive and/or behavioural therapy;
- vocational/recreational therapy;

- psychosocial/counselling input.

However, it is probable that the actual content of any two programmes within the same category varied greatly, and also that similar programmes may have been given different labels.

Consequently, we included any study that stated or implied that it involved a multi-disciplinary or inter-disciplinary rehabilitation programme, or used any of the labels above, provided it compared the named intervention with some form of control condition.

For the same reasons, it is equally difficult to describe control conditions. For this review, we considered the following control conditions:

- a lower level or different type of intervention such as 'routinely available local services', or 'minimal intervention' (such as 'information only' or 'single session treatment');
- waiting list conditions;
- interventions given in different settings (such as in-patient versus community rehabilitation);
- lower intensity of the treatment programme.

We excluded studies assessing the effect of the following:

- therapy from a single discipline (e.g. physiotherapy), including studies intensity of treatment within that single discipline;
- a single uni-disciplinary intervention or modality (e.g. physical exercise);
- coma arousal programmes (already dealt with in a Cochrane review –Lombardi 2002), except where this formed part of a coordinated multidisciplinary approach.

Types of outcome measures

We were interested in those outcomes which reflect the burden of disabling illness on patients and their families, and in the services provided for them. We excluded studies which reported only outcomes at the level of impairment were not included.

The measurement of outcome after rehabilitation can be described on two principal axes:

- timing of measurement - from onset of disease or onset of rehabilitation;
- level of measurement within the WHO ICF.

Since many of these studies were undertaken when the previous WHO classification of Impairment, Disability and Handicap was current, we have included these terms in brackets alongside the current terms.

Time

For the purposes of this review:

- short-term refers to all those assessed at admission to discharge from the rehabilitation programme (regardless of its length) and up to six months after;
- long-term refers to any time over six months after the end of intervention – usually one year or longer.

Outcomes

Once again there is no agreed classification of outcome measures used in research into rehabilitation after ABI but, for this review, they have broadly been categorised as follows.

a) Outcome measures which focus on goals at the level of impairment and activities (disability) for example:

- residual symptoms (each post-traumatic amnesia (PTA), post-concussion symptoms);
- functional independence – including mobility, cognitive functioning and ability to perform basic activities of daily living (ADL) (e.g. the Barthel Index, the Functional Independence Measure (FIM) or Functional Assessment Measure (FIM+FAM), Glasgow Outcome Scale (GOS));
- carer burden and stress (e.g. Care Giver's Strain Index).

b) outcome measures that focus on goals at the level of participation ('handicap') and/or personal context (psychosocial adjustment, quality of life) (Langhorne 1995) for example:

- discharge destination (e.g. home / institution);
- return to work;
- social integration or activities (e.g. Rivermead Head Injury Follow-up Questionnaire (RHFUQ));
- extended activities of daily living (EADL) (e.g. the Community Integration Questionnaire(CIQ));
- health-related quality of life for patient and carer (e.g. the General Health Questionnaire (GHQ), Short-Form-36 (SF-36));
- patient and carer mood (e.g. Hospital Anxiety and Depression Scale (HADS)) and satisfaction with services.

Where given, we also included outcomes which reflected the use of resources. These included: length of stay or treatment, subsequent readmission to hospital, the need for care including level of care, and extent of support required after discharge.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The review drew on search strategies developed by the Cochrane Injuries Group and Cochrane Stroke Group. We identified relevant trials in:

- the Cochrane Central Register of Controlled Trials (CENTRAL);
- MEDLINE (1966- 2004);
- EMBASE (1988-2004);
- CINAHL (1983-2004);
- PsycLIT (1967-2004);
- AMED;
- National Research Register 2004;
- ISI Science Citation Index 1981-2004;
- ClinicalTrials.gov;
- Current Controlled Trials;
- RehabTrials.org.

Keyword-based searches in:

MEDLINE (Silverplatter) 1966 - 2004/03;
Cochrane Central Register of Controlled Trials (CD) 2004 issue 1;
National Research Register (CD) 2004 issue 1.

We searched MEDLINE using the following strategy, which was then modified to suit other databases:

```
#1 explode 'craniocerebral-trauma' / rehabilitation
#2 explode 'cerebrovascular-accident' / rehabilitation
#3 explode 'anoxia' / rehabilitation
#4 explode 'hypoxia-brain' / rehabilitation
#5 #1 or #2 or #3 or #4
#6 brain or head or intracran* or cerebr* or cerebellar or
brainstem or vertebrobasilar
#7 injur* or infarc* or isch?em* or thrombo* or apoplexy or
emboli* or h?emorrhag* or h?ematoma* or aneurysm* or anoxi*
or hypoxi*
#8 (#6 in ti) or (#6 in ab)
#9 (#7 in ti) or (#7 in ab)
#10 #8 and #9
#11 (encephaliti* or mening*) in ti or (encephaliti* or mening*)
in ab
#12 #10 or #11
#13 explode 'comprehensive-health-care' / all SUBHEADINGS
#14 explode 'critical-pathways' / all SUBHEADINGS
#15 explode 'delivery-of-health-care' / all SUBHEADINGS
#16 explode 'patient-care-team' / all SUBHEADINGS
#17 explode 'rehabilitation' / all SUBHEADINGS
#18 (multi?disciplinary or inter?disciplinary or integrated or
multi?modal or multi?professional) near5 care
#19 rehabilit* or therap* or restor*
#20 (activities near3 daily living) or adl* or eadl*
#21 (self or personal) near5 (care or manag*)
#22 dressing or feeding or eating or toilet* or bathing or mobil*
or driving or public transport*
```

#23 (daily or domestic or house or home) near5 (activit* or task* or skill* or chore*)
 #24 social near5 (activit* or function* or support* or skill* or adjust* or behavio?r or facilitat*)
 #25 community near5 (re?integrat* or rehabilit*)
 #26 (#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25) in ti
 #27 (#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25) in ab
 #28 #26 or #27 or #13 or #14 or #15 or #16 or #17
 #29 #12 and #28
 #30 (#29 or #5) and RCT filter

EMBASE 1980 - 2004/3:

#1 exp head injury/rh [rehabilitation]
 #2 exp cerebrovascular accident/rh [rehabilitation]
 #3 exp ANOXIA/rh [rehabilitation]
 #4 exp HYPOXIA/rh [rehabilitation]
 #5 (brain or head or intracran\$ or cerebr\$ or cerebellar or brainstem or vertebrobasilar).ti,ab
 #6 (injur\$ or infarc\$ or ischem\$ or ischaem\$ or thrombo\$ or apoplex\$ or emboli\$ or hemorrhag\$ or haemorrhag\$ or hematoma\$ or haematoma\$ or aneurysm\$ or anoxi\$ or hypoxi\$).ti,ab
 #7 #5 and #6
 #8 (encephaliti\$ or mening\$).ti,ab
 #9 #7 or #8
 #10 exp health care/
 #11 exp clinical pathway/
 #12 exp health care delivery/
 #13 exp rehabilitation/
 #14 ((activities adj3 daily living) or adl\$ or eadl\$).ti,ab
 #15 ((self or personal) adj5 (care or manag\$)).ti,ab
 #16 (dressing or feeding or eating or toilet\$ or bathing or mobil\$ or driving or public transport\$).ti,ab
 #17 ((daily or domestic or house or home) adj5 (activit\$ or task\$ or skill\$ or chore\$)).ti,ab
 #18 (social adj5 (activit\$ or function\$ or support\$ or skill\$ or adjust\$ or behavio?r or facilitat\$)).ti,ab
 #19 (community adj5 (reintegrat\$ or re-integrat\$ or rehabilit\$)).ti,ab. (943)
 #20 rehabilitat\$.sh.
 #21 ((multidisciplinary or multi-disciplinary or interdisciplinary or inter-disciplinary or integrated or multimodal or multi-modal or multiprofessional or multi-professional) adj5 care).ti,ab
 #22 #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
 #23 #9 and #22
 #24 #1 or #2 or #3 or #4
 #25 #23 or #24
 #26 (randomi\$ or (double adj blind\$) or (single adj blind\$) or (controlled adj trial\$)).ti,ab
 #27 exp randomized controlled trial/
 #28 #26 or #27

#29 #25 and #28

We also undertook searches using both MeSH headings and textural terms in the following databases:

- MEDLINE 1966 to March 2004;
- EMBASE 1988 to 2004 week 10;
- AMED 1985 to March 2004;
- CINAHL 1982 to March Week 1 2004.

We used the following strategy, subject to minor adaptations to suit each database:

- 1: brain injuries/ or brain injury.mp
- 2: cranio-cerebral trauma/ or head injuries/ or head injury.mp
- 3: stroke/ or cerebrovascular accident/ or subarachnoid haemorrhage/ or intracerebral haemorrhage/ or stroke.mp
- 4: 1 or 2 or 3
- 5: rehabilitation/ or rehabilitation, vocational/ or rehabilitation.mp
- 6: rehabilitation, cognitive/ or rehabilitation, psychosocial/ or home rehabilitation/
- 7: 5 or 6
- 8: randomized controlled trials/ or clinical trials/ or controlled trials/ or controlled study/ or randomised controlled trial.mp
- 9: 4 and 7 and 8.

We identified additional trials:

- from reference lists in review articles;
- by consultation with colleagues and trialists;
- by hand-searching the most relevant journals.

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

METHODS OF THE REVIEW

Because of the broad search strategy, we expected to find a large number of non-relevant articles. We assessed studies using a two-stage process

Stage 1

From an initial list of over 2,300 articles, we hand-sifted abstracts and titles to exclude totally irrelevant articles, leaving a shortlist of 248 articles. Two reviewers (LTS and AN) independently undertook a preliminary screen of titles and abstracts in these 248, considering 'type of study, participants and intervention'. This first selection stage resulted in categorisation to 'exclusion', 'selection' or 'indecisive'. The two reviewers discussed disagreements between the two reviewers were discussed in consensus meetings. If the first selection was indecisive or disagreement persisted, we obtained the full article for further assessment. We were prepared to seek further information about the method of randomisation or the

multi-disciplinary nature of rehabilitation interventions from the trialists where necessary. However, in practice, it was the earlier published studies (10 to 20 years old) where critical information was missing, and attempts to contact the authors were unsuccessful because they had usually retired or moved on. This process led to the exclusion of 227 articles, leaving 21 for probable inclusion.

Stage 2

For each trial selected for inclusion from stage 1, two reviewers (DTW and LTS and/or AN) assessed methodological quality independently. We resolved disagreements by discussion. Where we were not able to reach consensus, we designated the third reviewer to decide. All four authors contributed to the analysis and discussion.

Assessment of methodological quality

Three essential criteria were originally described by Jadad et al (Jadad 1996) for inclusion in Cochrane reviews. These are:

- randomisation (subsequently developed to include concealment of allocation);
- double blinding – i.e. both the participant and the outcome assessor are blinded to the intervention;
- descriptions of withdrawals (subsequently developed to include intention-to-treat analysis).

However, whilst these are important attributes of any RCT, they do not necessarily capture other important indicators of quality of trials in rehabilitation and other complex interventions. If consent procedures include a proper description of the trial alternatives (as they should), it is rarely then feasible to blind the patient properly to their allocated rehabilitation intervention. Even single blinding (through independent blinded assessment of outcomes) may be difficult in patients with cognitive impairment, who not uncommonly volunteer unsolicited information during the course of interview (Powell 2002). These problems with blinding may be overcome to some extent by use of standardised assessment instruments, but still represent a significant source of potential bias.

The Cochrane Musculoskeletal Group (van Tulder 1997) has proposed an alternative check list which includes the three Jadad criteria, but adds further criteria to reach a total of 19 (11 criteria for internal validity, six descriptive criteria and two statistical criteria). Although subsequent lists have tended to focus more on the internal validity criteria (van Tulder 2003), this original check list has been used for trials in low back pain and is increasingly being explored elsewhere in the context of complex intervention. It has been used in other reviews in rehabilitation, including a Cochrane review of occupational therapy for stroke (Stueltjens 2002; Stueltjens 2003b), and has recently been adapted (Stueltjens 2003a) to provide an abbreviated list for assessment of trials employing 'other designs' (including patient series and cohort studies).

We considered that this expanded list provided a more sensitive basis for discriminating between better and poorer quality trials in this context. In this review, therefore, we rated methodological quality using a standardised checklist based on that introduced by (van Tulder 1997) – see Table 01. We would like to draw particular attention to the definitions listed below.

Design

- We identified quasi-randomised *allocation* where procedures such as alternation, or reference to case record numbers, dates of birth, or day of the week were used.
- We identified quasi-experimental *designs* where there was no attempt at randomisation, but where there was: (a) a prospective allocation to study groups and (b) a large element of chance in the allocation. However, unacceptable designs include comparison of two entirely separate services and retrospective matching of controls from a separate unrelated database. We excluded studies using these designs.
- Fatal flaws in the study design or execution meant that we determined that the study was inadequate, and excluded it from the analysis. Examples of fatal flaws include: withdrawals by more than 40 percent of patients; total or nearly total non-adherence to the protocol; or very poor or non-adjusted comparability in the base-line criteria.

Blinding

The authors accepted that blinding of patients and their treating therapists was not feasible, and the best that could be achieved in this context was single blinding. We scored 'blinding of outcome assessors' positive if (a) the assessors were blinded regarding treatment allocation *and* (b) standardised assessment measures or procedures were used to structure the interviews. Otherwise we scored it negative.

Concealment of treatment allocation

We used the following guide to define 'adequate procedures' for treatment allocation concealment:

- where an independent person, not responsible for determining the eligibility of the patients, generated the assignment;
- any form of centralised randomisation scheme, e.g. a computer system providing allocations in a locked, unreadable file that could be assessed only after inputting the characteristics of an enrolled participant;
- numbered or coded containers, or sequentially numbered, sealed, opaque envelopes.

If the concealment of treatment allocation was described only as random or randomised, we classified it as unclear.

Adverse effects

Rehabilitation can certainly have 'adverse effects', but in clinical practice this has often been considered unlikely, and the absence

of adverse effects is, therefore, hardly ever specifically recorded. Because adverse effects can and do occur, they should be recorded. We looked for evidence on adverse effects, but found no study that explicitly investigated this.

Scoring

We considered RCTs to be of high methodological quality (using van Tulder's list) if the following were scored positively (Steultjens 2003a; Steultjens 2003b):

- at least 6 out of 11 internal validity items and...
- at least 3 out of 6 descriptive items and...
- at least 1 out of two statistical items.

Studies were rated as of low methodological quality if they achieved less than these scores.

Analysis and data synthesis

Meta-analysis can be undertaken only if the study populations, interventions, outcomes and study designs are agreed to be sufficiently consistent to allow pooling of data. While dichotomous data (e.g. return to work) might reasonably be pooled, most outcome instruments which are commonly used to assess activity and participation are in the form of 'long ordinal' scales. There are significant concerns about the validity of either treating these as continuous data, or reducing them to binary outcomes.

We expected that there would be too much clinical heterogeneity among the studies, particularly with regard to outcome measures (diversity of assessment tools/timing of measurements/presentation of results) to make quantitative analysis possible. Instead, we grouped the selected studies according broadly to the type of intervention and participants, and subjected them to a qualitative descriptive analysis. We performed a 'best evidence' synthesis by attributing levels of evidence based on the assessment of methodological quality described above and categorised into 'strong', 'moderate', 'limited' evidence as described by van Tulder 2003 (see Table 02). We highlighted the strength of trial findings discussed and gaps in current knowledge and identified future research directions.

DESCRIPTION OF STUDIES

From the 21 articles selected from Stage two, we identified 15 trials which met the eligibility criteria for consideration. We identified 13 of these through MEDLINE and EMBASE, and two through AMED. We excluded one trial on the basis of fatal flaws; Relander 1972 had more than 40% attrition at one year follow-up (see methodological assessment below).

Six of the articles were supplementary papers, either providing additional details of programme content (Braverman 1999 and Warden 2000 for the trial by Salazar 2000), subgroup or specific

analyses (King 1997 and Wenden 1998 for the trial by Wade 1997, and Kwakkel 2002 for Kwakkel 1999) or follow-up data (Paniak 2000 for Paniak 1998). Two trials (Wade 1997; Wade 1998) reported data from the same programme, but in different (sequential) cohorts of subjects, so we have treated these two papers as separate trials.

The 14 trials that we considered were:

- seven single-blinded RCTs (Kwakkel 1999; Paniak 1998; Powell 2002; Slade 2002; Wade 1997; Wade 1998; Zhu 2001);
- three unblinded RCTs (Salazar 2000; Shiel 2001; Smith 1981);
- three quasi-randomised controlled clinical trials (CCTs) (Bowen 2001; Ozdemir 2001; Werner 1996);
- one quasi-experimental study (Semlyen 1998).

Type of brain injury

Nine of the 14 trials studied subjects with traumatic brain injury; four studied stroke, and one (Slade 2002) studied a mixed population of ABI.

Subjects

The trials covered a range of different severities of acquired brain injury. Two studies (Wade 1997; Wade 1998) recruited brain injury of all severities, one (Paniak 1998) recruited only mild TBI, and the remainder recruited patients with moderate-severe ABI. Between them, the trials recruited 1814 subjects and 96 carers.

Interventions

The interventions were also varied. However, trials could broadly be divided into the following categories.

- Four trials (Paniak 1998; Salazar 2000; Wade 1997; Wade 1998) enrolled all patients presenting acutely to hospital with TBI, and therefore included populations predominantly in the milder ambulatory category. The emphasis of intervention was primarily targeted at increasing participation (social integration, return to work etc) and reducing post-concussional symptoms.
- Ten trials (Bowen 2001; Kwakkel 1999; Ozdemir 2001; Powell 2002; Semlyen 1998; Shiel 2001; Slade 2002; Smith 1981; Werner 1996; Zhu 2001) enrolled patients (following TBI or stroke) who were already presenting to rehabilitation services. This group therefore had greater levels of motor impairment and dependence in personal ADL, and interventions were targeted at improving function in activities of daily living (reduced 'disability'), although measures of participation (reduced 'handicap') were sometimes also included.

Within this second group trials covered a range of different interventions in different settings.

- Two trials assessed the impact of out-patient rehabilitation programmes: one testing programmes of different intensity (Smith 1981), the other testing therapy offered late after treatment (Werner 1996).

- Two trials assessed the benefits of a co-ordinated community-based MD team approach on patients (Powell 2002) and carers (Bowen 2001).
- Two trials assessed the benefits of a specialist in-patient rehabilitation programme as opposed to local services (Semlyen 1998) or home-based advice (Ozdemir 2001).
- Four trials compared higher intensity programmes with lower (standard) intensity of treatment: two with a view to assessing impact on length of stay (Shiel 2001; Slade 2002) and two (Kwakkel 1999; Zhu 2001) focussing on improving functional outcomes.

Outcomes

Within these groups, studies used differing outcomes, measured at different time intervals over a varying follow-up period. As anticipated, we found insufficient concordance between outcome measures, time points and type of intervention to allow pooling of data for meta-analysis.

METHODOLOGICAL QUALITY

Using the van Tulder scoring system, the maximum achievable score is 19. The results of scoring are shown in Table 03.

We identified ten RCTs which were of high methodological quality. Wade 1997 notes that only 478 of the originally randomised 1156 participants (41%) could be traced to attend for interview. However, this is not unexpected in the often itinerant group of people who suffer head injuries. A detailed analysis of baseline characteristics was offered and demonstrated no significant differences between the interviewed and non-interviewed groups.

We identified three quasi-randomised RCTs as being of low methodological quality (Bowen 2001; Ozdemir 2001; Werner 1996).

- The Werner 1996 started off as a randomised trial, with a weighted 2:1 chance of the patient being allocated to active intervention (by picking a number of 666 or less from a sample of 1 to 1000), but after nine of the initial 16 controls dropped out, trialists added a further five non-randomised control subjects. In addition, it did not include measures of variability as well as point estimates.
- Bowen 2001 and Ozdemir 2001 reported a quasi-randomised unblinded trials with only short term follow-up.

The remaining low-scoring trial had a quasi-experimental design. Semlyen 1998 reported a quasi-experimental study in which patients were either admitted to a specialist multi-disciplinary (MD) rehabilitation programme or passed back to their standard local services (LS), depending on geography and on the availability of a vacancy in the specialist programme. Although there was an element of chance in this allocation, those patients with the most

severe brain injuries, whose needs could not be met by their local services in fact remained on the acute ward for longer periods until a specialist bed became available, since they had no alternative option. The multidisciplinary rehabilitation group was therefore significantly more disabled to start with and was in hospital for longer than the group referred on to local services. The study reported in this paper illustrates some of the important practical, methodological issues which will be considered in the discussion.

RESULTS

Milder ambulatory patients

The four trials which predominantly addressed the milder ambulatory group (Paniak 1998; Salazar 2000; Wade 1997; Wade 1998) recruited a total of 927 patients (see Table 04).

Three of the trials (Paniak 1998; Wade 1997; Wade 1998) compared a programme of 'treatment as needed' (which was largely community-based) to a lesser condition (Paniak - 'information only'; Wade - 'standard follow-up arrangements', which usually meant no further input). Salazar 2000 compared an in-patient-based cognitive rehabilitation programme with weekly telephone counselling and advice at home. All four trials were rated as good quality RCTs on all assessment criteria, although the Salazar study was unblinded.

The general conclusion of all these studies was that intervention in a totally unselected group of all patients with mild TBI was not effective. Both the treatment group and control condition made substantial gains in terms of reduced post-concussional symptoms and enhanced participation, including return to work. No significant differences were recorded between the groups.

However, in the trial by Wade 1997, a post-hoc subgroup analysis demonstrated that those who were admitted to hospital or had post-traumatic amnesia (PTA) of >1 hr (n=121) did demonstrate significant gains with treatment. These gains were demonstrated in terms of fewer difficulties with everyday activities (increased participation), as measured by the Rivermead head injury follow-up questionnaire (RHFUQ) ($P<0.03$).

A subsequent trial (Wade 1998) (218 completing participants) was, therefore, undertaken that selected prospectively the group admitted to hospital, to confirm these findings. The second trial again demonstrated improved outcomes for the 'treatment as needed group' with significantly less post concussive symptoms (Rivermead post-concussion questionnaire (RPQ)) (Mann-Whitney U: $z = -2.27$; $P<0.02$) and improved participation (RHFUQ) ($z = -2.54$; $P<0.01$). The impact of proactive intervention appeared to be most marked for patients with PTA <7 days, who may be less likely than those more severely affected to present to services by themselves.

From the 'best evidence' synthesis of these studies, we concluded that there is 'strong evidence' to suggest that:

- the majority of patients with mild TBI make a good recovery;
- patients with post-traumatic amnesia of less than one hour, usually not admitted to hospital, do not need any specific intervention;
- patients with post-traumatic amnesia of one hour or more do benefit from routine follow-up contact giving information and advice;
- there is a subgroup of patients with moderate to severe injury who benefit from a higher level of intervention, and who may not present themselves unless routine follow-up is provided.

Patients with greater limitation on activities, generally more severe brain damage, and generally a greater multi-disciplinary rehabilitation input

The effectiveness of 'combined out-patient physiotherapy and occupational therapy' was investigated by two trials in stroke patients (see Table 05).

- Smith 1981 reported a good quality but unblinded RCT (n=133) that demonstrated improved functional ability (Northwick Park ADL index) for the groups attending outpatients, as compared with a no-treatment control group (P<0.01). A trend towards greater improvement with the more intense of two out-patient programmes was not tested for significance. However, the gains for both the treated groups were maintained at one year follow-up, while the control group deteriorated (P<0.05).
- Werner 1996 reported a single-blind CCT (n=49) that was of much lower quality (see Table 03). The study assessed the benefits of late out-patient intervention (offered at least one year after stroke). The treatment group demonstrated significant gains in function (FIM motor score increase of 6.6 compared with 1.5 (P<0.03)) and socialisation (sickness impact profile: -5.2 compared with an increase of 2.6 in the control group (P<0.04)) at three months, which were maintained at nine months. However, no significant change in mood (Beck depression inventory) was observed.

In summary, there is 'moderate evidence' that outpatient therapy improves the outcome of stroke rehabilitation, with 'limited evidence' that more intensive treatment regimens are associated with better outcomes. There is 'indicative evidence' that this type of intervention may be effective even late (at least one year) after stroke.

Effectiveness of 'community-based coordinated multi-disciplinary rehabilitation'

This was addressed by two trials (see Table 06).

- Slade 2002 reported a good quality single blind RCT (n=110) of an MD community outreach service providing a home-based goal-orientated programme of two to six hours intervention per week, compared with standard treatment. This was a more severely affected group than those studied by Wade 1998

(91% PTA seven days, as compared with only 7%). Follow-up was variable but averaged approximately two years. Gains for the intervention group were reported in reduced disability (35.4% showing improvement in Barthel index as compared with 19.6% in the control group (P<0.05)) and increased participation (significant changes in the self-organisation and psychological scales of the BICRO-39 (P<0.05)), but no gains were observed for the secondary outcomes, which included FIM+FAM and mood (hospital anxiety and depression scales (HADS)). Global disability scales such as the FIM and FIM+FAM were noted to be insensitive since the majority of items did not change. A 'maximal gain index' was therefore also calculated, which selected the subscale with maximal change. Rated in this way, change in both disability (FIM+FAM) and participation (Bicro-39) reached a greater level of significance (P<0.025).

- Bowen 2001 reported an unblinded CCT of lower quality in which carer outcomes were evaluated following input from a multi-disciplinary head-injury specialist rehabilitation team in addition to standard services. An 'early arm' (n=41) started the intervention before discharge, and a 'late' arm (n=28) started after discharge. However, despite best intentions, only 23/41 (56%) actually received early intervention and 19/28 (67%) late intervention, with some mixing between the groups and 14 patients receiving neither intervention. Nevertheless, an intention-to-treat analysis revealed that the early intervention group still received significantly earlier treatment (median five days (P<0.001)) than the late intervention group (median 40 days) post-injury. At six months, after adjusting for confounding factors, there was a clinically plausible superior outcome for both intervention groups in comparison to controls with regard to emotional status (Wimbledon self-report scale) and knowledge about brain injury. However, this did not reach Bonferroni-adjusted clinical significance (P<0.01). Logistic difficulties with recruitment and service provision led to significant under-powering of this study and may have interfered with the demonstration of a clinically significant effect.

In summary, for this group, there is 'limited evidence' that MD community-based rehabilitation team can improve functional outcome for patients at the level of 'activity' (disability) on the ICF (especially when targeted towards specific goals), but evidence of benefit for carers has yet to be demonstrated.

Specialist in-patient rehabilitation

Two studies have addressed the benefit of 'specialist in-patient rehabilitation' in comparison with local services (Semlyen 1998) (n=51) or a home-based advisory service (Ozdemir 2001) (n=60) (see Table 07). Both these studies were small and of low methodological quality.

- The methodological problems of Semlyen 1998 (n=51) have already been highlighted. The MD rehabilitation group was significantly more disabled at the outset. Thus the significantly greater gains which were evident at each measurement point

up to 24 months may have reflected this lower starting point and the fact that many of the 'other rehabilitation' group were already at ceiling levels on some scores. Carer distress was assessed the General Health Questionnaire. This identified higher proportion of 'cases' in the MD rehabilitation group at outset, which fell between six and 12 months. By contrast, the proportion of cases in the 'other rehabilitation' groups started from a lower point, but rose progressively throughout the follow-up period. By 12 months the carers in the 'other rehabilitation' group had significantly higher levels of distress than the MD rehabilitation group.

- Ozdemir 2001 reported an unblinded CCT in 60 stroke patients. The groups were well-matched to start with, but the treatment group made five-fold greater gains in FIM score (mean 59.6 +/-SD 14.1) versus (mean 12.3 +/-SD 13.4) ($P < 0.001$) and a two-fold change in minimal state examination (MMSE) (mean 4.8 +/-SD 5.0) versus (mean 2.0 +/-SD 2.1) ($P < 0.025$) in comparison with the control group.

In summary, there is 'limited evidence' at the current time that specialist in-patient rehabilitation services can improve functional outcome in terms of both activity (reduced disability) and carer distress in comparison with controls. However, this partly reflects the practical, and possibly ethical difficulties associated with allocating patients with severe brain injury no opportunity of coordinated multi-disciplinary rehabilitation (see Discussion).

Increased intensity of rehabilitation

Four trials have addressed the benefits of 'increased intensity' of rehabilitation (see Table 08).

- Kwakkel 1999 reported a good quality single-blinded RCT in 101 severely disabled stroke patients comparing a group with emphasis on arm training ($n=33$), a group with emphasis on leg-training ($n=31$) and a control group ($n=37$) whose arm and leg were immobilised in an inflatable splint. Each treatment was applied for 30 minutes, five days a week for the first 20 weeks after stroke, over and above basic level intervention which was consistent for all groups. Post-hoc analysis by Kruskal-Wallis test showed that leg training resulted in significantly greater independence (Barthel index) and mobility (functional ambulation categories) than the control group up to the first 20 weeks, and better dexterity (Action Research arm test) in the arm training group from week 12 onwards. The effects of treatment appear to be maintained at one year, but no significant differences between the groups were demonstrated beyond six months.
- Zhu 2001 reported preliminary results of a small but good-quality single-blind RCT in patients with traumatic brain injury ($n=36$) comparing different intensities of treatment (two versus four hours per day). Analysis of time utilisation showed that after the second week the majority of patients could tolerate over two hours therapy per day. FIM and Glasgow outcome scales were recorded monthly to six months in this report, although

the trial protocol continues follow-up bi-monthly to one year. Both showed a trend (but no significant difference) towards improvement in the intensive input group during the first two to three months, but thereafter the control group appeared to catch up. These early functional gains did not appear to impact significantly on length of stay in this series.

- Shiel 2001 reported a two-centre RCT ($n=51$ completing participants) in patients with moderate to severe traumatic brain injury. At each centre patients were randomised to receive routine treatment with or without additional input from an additional experienced member of staff acting in a trans-disciplinary capacity to supplement the rehabilitation programme. Those with added intensity of input made more rapid gains in independence (FIM+FAM) in both centres, with no evidence of any ceiling effect of therapeutic intensity beyond which no further response was observed. However, there were marked differences between the two centres in terms of staffing levels and intensity of the routine programme. This led to substantially shorter lengths of stay in one centre, so that no significant reduction in length of stay was observed for the trial as a whole, despite the more rapid gains in independence.
- Slade 2002 conducted a good-quality single-blind RCT ($n=131$) in a group of mixed ABI, comparing two rehabilitation programmes in the same setting, one more intensive than the other. Records of therapy input demonstrated that patients were able to tolerate the increased input with no adverse effects. Although it was intended for the 'intensive' group to receive 67% more therapy than the control group, they in fact only received 30% more. The intention to demonstrate a reduced length of stay as a result of more intensive therapy was confounded by external delays in discharge. Analysis by a regression model was, therefore, undertaken to account for confounding variables including impairment mix and factors that could not be controlled for in the study design (community delays and missed treatment). This demonstrated a significant reduction in length of stay (14 days, $P < 0.001$) for the intensive group. Similar Barthel scores between the groups at admission and discharge confirmed that this reduced length of stay was not at the expense of a poorer functional outcome.

In summary, there is 'strong evidence' that more intensive rehabilitation programmes are associated with earlier function gains, once patients are fit to engage. There was no evidence of a ceiling effect in therapeutic intensity in any of these studies. However, for intensive intervention to be cost-effective, it is necessary to demonstrate that it is associated with potential cost savings further down the line (for example, reduction in length of stay or long-term dependency) which might offset the additional costs of providing the initial programme. None of the studies undertook a direct analysis of cost-effectiveness, and at the current time, there is only moderate evidence that more intensive rehabilitation leads to reduced length of stay. On the other hand, 'length of stay' is

frequently affected by external confounders (such as the lack of a suitable place to discharge the patient to, or lack of community support for a patient otherwise ready for discharge) which may need to be controlled for before this benefit can be demonstrated.

DISCUSSION

Randomised controlled trials remain the primary means by which treatment efficacy is demonstrated, mainly because of their ability to control for unknown confounding factors - of which there are many in rehabilitation. However, whilst well suited to single easily identified interventions, such as specific drugs or procedures, their limitations in the area of complex intervention are well recognised; and so is the fact that they are often conducted on unrepresentative patients in the context of atypically meticulous care systems (Whyte 2002).

This review has served to highlight a number of challenges for RCT methodology in the context of ABI, which have been recognised elsewhere (RCP/BSRM 2003).

- Patient numbers are small, and there is marked heterogeneity with respect to the patient group, the intervention and setting, and to the outcomes that are relevant at each stage of recovery.
- The resources required to randomly assign whole systems of care to different patient groups are far greater than those required to deliver specific medications or procedures. Additionally, the length of time over which rehabilitation may have its effects (always many months and usually several years) is usually longer than any funded research project and hinders the use of 'wait-list' control groups.
- The expanding body of evidence for effectiveness of multi-disciplinary rehabilitation in other conditions (particularly stroke) makes it increasingly difficult, ethically and practically, to randomise patients to 'no treatment' or even 'standard' care - the more so since many patients with ABI may lack the mental capacity to give fully informed consent.

In addition, several of the studies identified in this review serve to illustrate further practical problems with sustaining RCTs in this area, as discussed below.

1. Recruitment and retention of participants

Where fully informed consent is obtained prior to engagement – as it should be – recruitment and retention can be problematic, especially for the control arm. Werner 1996 started out as a weighted randomised study. Once recruited, however, many of the control group demonstrated reluctance to attend for evaluations, expressing disappointment at not having been selected for treatment. After more than half the control group defaulted from follow-up, the trialists were forced to recruit an additional five controls in a non-randomised fashion.

2. Differences between centres

In view of the small number of patients available in any one centre, multi-centre studies may be required. However, the additional heterogeneity so introduced may outweigh the benefits of increased numbers in analysis. This problem was well-illustrated in the study by Shiel 2001 where the two centres, chosen initially for their similarity of service, turned out to have critical differences in staffing levels and, therefore, the intensity of rehabilitation offered as routine. This led to disparate lengths of stay sufficient to confound this critical outcome in statistical analysis.

3. Sensitivity versus homogeneity in outcome measurements pose a further problem for interpretation

Common (shared) measures are a necessary pre-requisite for assimilation of data. A number of global outcome assessments, such as the Barthel index and the FIM, have been developed with the aim of creating comparable datasets, and are increasingly widely used. Unfortunately, these pose a number of further problems.

- The measures themselves may be less homogeneous than previously supposed. Analysis indicates that even the most consistently applied instruments behave differently in different cultures and settings (Tennant 2002), and there are several different versions of the Barthel index in current usage (Turner-Stokes 1997).
- Rehabilitation is increasingly targeted towards specific goals set for the individual and their family. These global instruments address a range of different dimensions, many of which are not likely to change in response to such targeted efforts. The overall scores are therefore unlikely to reflect the true benefits of the intervention. The study by Powell 2002 attempted to overcome this problem by recording only the dimensions which demonstrated maximal gain (maximum gain index). This enhanced the statistical differences between the treatment and control arms but might be considered to represent excessive manipulation of the data, especially since these selected dimensions were not identified as the target areas prior to treatment.
- The study by Semlyen 1998 illustrates a dilemma for data interpretation. The participants who received MD rehabilitation were more disabled at the outset, but achieved the same level of function (Barthel index) as those in the 'Other rehabilitation' group by 12 months. This may be interpreted as an inverse bias for the treatment arm, who therefore demonstrated significantly greater gains during rehabilitation despite this lower starting point. Alternatively it may be argued that this lower starting point offers a statistical advantage by dint of greater opportunity for change in a scale with recognised ceiling effects.

As in other complex areas of medical practice, it may therefore be necessary to develop the evidence base for effective management through triangulation of a range of different research methodologies. In this review we have included quasi-randomised studies and quasi-experimental designs providing they met the pre-determined criteria. It is accepted that these research designs are open to

a certain level of bias. However, given the problems noted above, the authors accepted that in the real-life context of clinical practice, this level of 'randomness' may be the best that can be achieved in the context of severe brain injury.

Limitations of this review

This review has taken an inclusive approach to a broad area of clinical practice and a wide-ranging group of conditions under the collective banner of acquired brain injury, and this approach has posed significant challenges for the assessment and assimilation of the available evidence. It may be contended that we have adopted too low a threshold for inclusion of studies of low quality. On the other hand, we believe that the presented synthesis of 'best evidence' based on assessment of methodological quality, has facilitated a helpful comparison of the various studies available. It also allows open acknowledgement of the 'limited evidence' which comes from these poorer studies which is nevertheless the best available at the current time. Useful lessons have also been learned even from these lower quality studies which contribute to our understanding of the methodological challenges in this complex area of research.

Secondly, it may be argued that a more piecemeal approach – that is, individual reviews for the various different models of practice – would have been easier to interpret and analyse along more traditional lines. On the other hand, whilst some countries plan service provision around specific programmes of rehabilitation for specific diagnostic groups, the current dearth of multi-disciplinary rehabilitation services in the UK tends to favour a broader 'needs-led' approach to service provision for more mixed patient groups (RCP/BSRM 2003). Rehabilitation research may be likened to a 'Russian doll', with questions being posed at many different levels, ranging from the very specific testing of particular interventions, to the global assessment of effectiveness of services for whole populations and on a range of outcomes. The more global the question, the more global should be the study population, models of intervention and outcomes measured. In other words, it is scientifically appropriate for questions about the organisation and intensity of rehabilitation to be asked about large groups of patients, such as those with any neurological disease, as opposed to individual conditions. Meta-analysis for these global studies may be appropriate in the future, but would require the relaxation of clinical inclusion criteria and the development of new methods devised to accommodate very varied outcomes.

AUTHORS' CONCLUSIONS

Implications for practice

The various findings from this review serve to emphasise the varied nature of acquired brain injury and the need for different services to suit the needs of different populations. Implications for practice from this review are as follows.

- Whilst every patient presenting to hospital with ABI should be given information about the nature of brain injury and who to contact in case of problems, it appears that routine follow-up may be reserved for patients identified as having at least significant brain injury on the basis of their presentation or residual deficits. These are most easily defined as those admitted to hospital or, if not, with any documented period of coma or with post-traumatic amnesia extending for more than 30 minutes.
- For those patients engaged in rehabilitation, intervention should be offered as intensively as possible, although the balance between intensity and cost-effectiveness has yet to be determined.
- Patients discharged from in-patient rehabilitation settings, who have continued rehabilitation needs and goals, should have access to follow-up out-patient or community-based services as appropriate to their needs.

Implications for research

There are important questions still to be answered regarding the effectiveness of rehabilitation interventions in acquired brain injury. Where these cannot be answered by well-designed RCTs, they may still be appropriately addressed by alternative methodologies or by breaking down the research questions. In particular there is a need to explore:

- the effectiveness of specific interventions within the overall rehabilitation programme, and the characteristics which render patients most likely to gain benefit;
- development of a method to determine an individual's ability to engage in and benefit from intensive rehabilitation, and the most appropriate level of intensity;
- the cost-effectiveness of rehabilitation interventions and their impact on quality of life for both patients and carers;
- development of appropriate outcome measures, and better understanding of their behaviour in different cultural settings, as well as in statistical handling;
- improved measurement techniques for assessment of targeted interventions, such as goal attainment, or agreed methodologies for refining global instruments to focus on the areas of particular interest or relevance to the intervention;
- the long-term (over 12 months) effects of rehabilitation, both in terms of patient outcome and in terms of the social costs associated with ABI (care costs and loss of income for the patient and family);
- development of appropriate methods for incorporating 'other research designs' in formal reviews and meta-analyses.

POTENTIAL CONFLICT OF INTEREST

All authors are clinicians engaged in the field of brain injury rehabilitation, who naturally wish to provide an effective and efficient service for their patients. None have any personal or financial interests in the findings of this review.

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* Indicates the major publication for the study

T A B L E S**Characteristics of included studies**

Study	Bowen 2001
Methods	Unblinded quasi-RCT Moderate-severe TBI
Participants	Carers n=96 randomised Treatment n=69 Control n=27 (All completed)
Interventions	Head injury neurorehabilitation team (HINT) Early = started pre-discharge Late = started after discharge Control = Existing services
Outcomes	Carers' perception of how well-informed they are, Carers' mood/emotion
Notes	Follow-up 6 mths
Allocation concealment	D – Not used
Study	Kwakkel 1999
Methods	Single-blind RCT Middle cerebral artery stroke
Participants	Randomised (completed) Total n=101 (81)

Characteristics of included studies (Continued)

	Leg training n=31 (26) Arm training n=33 (29) Control n=37 (34)
Interventions	Intensive arm or leg training by physio/occupational therapists vs immobilisation with inflatable splint
Outcomes	Primary outcomes: ADL ability: Barthel Index Mobility: FAC Dexterity: AR Arm Test Secondary outcomes: Participation: SIP NHP Frenchay Activities Index
Notes	Follow-up 6 mths
Allocation concealment	B – Unclear

Study	Ozdemir 2001
Methods	Unblinded quasi-RCT Stroke
Participants	Subjects n=60 In-patient n=30 Home n=30 (All completed)
Interventions	In-patient rehabilitation vs home exercise programme
Outcomes	Impairment: Ashworth Scale Brunnstrom stages MMSE Activity: FIM
Notes	Variable measurement before and after rehabilitation (mean 64 days)
Allocation concealment	D – Not used

Study	Paniak 1998
Methods	Single-blind RCT Moderate-severe TBI
Participants	Randomised (completed) Total 119 (111) Treatment n=53 (59) Control n=58 (60)
Interventions	Treatment as needed with full MD programme vs single session - educational input
Outcomes	Impairment: Problem check-list Participation: CIQ Health status: SF-36 Work status
Notes	Follow-up 3-4 mths

Characteristics of included studies (Continued)

Allocation concealment B – Unclear

Study	Powell 2002
Methods	Single-blind RCT Moderate-severe TBI
Participants	Randomised (completed) n=110 (94) Treatment n= 54 (48) Control n= 56 (46)
Interventions	Community-based outreach MD Team Visits x 2 per week. Mean 6 months duration Control - written information only
Outcomes	Activity: Barthel Index FIM+FAM Participation: BICRO 39 scales Mood: HADS Maximum Gain Index (MGI)
Notes	Variable measurement (mean 2 yrs)
Allocation concealment	B – Unclear

Study	Salazar 2000
Methods	Unblinded RCT Defence veterans Moderate-severe TBI
Participants	Randomised (completed) n=120 (107) In-Pt n=67 (60) Home n=53 (47)
Interventions	In-pt intensive 8-week programme vs Home - weekly telephonic contact with counselling and advice from nurse
Outcomes	Work status: Return to work Fitness for military duty
Notes	Follow-up 1 yr
Allocation concealment	A – Adequate

Study	Semlyen 1998
Methods	Unblinded quasi-experimental design Mod-severe TBI
Participants	Subjects n=51 Treatment n=33 Control n=18 (All completed)
Interventions	Co-ordinated MD rehabilitation in a specialist brain injury rehabilitation unit (HM)

Characteristics of included studies (Continued)

	vs other rehabilitation (OR) in local district services
Outcomes	Activity and independence: Barthel index FIM+FAM NIAF Care-giver's health: GHQ-28
Notes	Follow-up to 2 yrs
Allocation concealment	D – Not used

Study	Shiel 2001
Methods	Unblinded RCT Moderate-severe TBI
Participants	Subjects n=51 Intensive n=24 Routine n=27 (All completed)
Interventions	Intensive rehabilitation (with additional health care professional experienced in BI vs standard treatment)
Outcomes	Disability: FIM+FAM Healthcare: Length of stay
Notes	Admission to Discharge
Allocation concealment	D – Not used

Study	Slade 2002
Methods	Single-blind RCT Mixed brain injury (Mod-severe) and stroke
Participants	Randomised (completed) n=161 (131) Intensive n= 80 (75) Standard n=81 (76)
Interventions	Intensive MD rehabilitation - intensive group received 67% more therapy
Outcomes	Healthcare: Length of stay - Controlled for ADL ability: Barthel Index
Notes	Admission to Discharge
Allocation concealment	A – Adequate

Study	Smith 1981
Methods	Unblinded RCT Stroke pts discharged from hospital
Participants	Subjects n=133 Intensive n=46

Characteristics of included studies (Continued)

	Conventional n=43 (All completed) Control n=44
Interventions	Out-patient physio / O/T for up to 6mths: Intensive = 4 days per week Conventional = 3 half days per week Control = health visitor encourages self exercise
Outcomes	ADL dependency: Northwick Park ADL index
Notes	Follow-up at 3 and 12 mths
Allocation concealment	B – Unclear

Study Wade 1997

Methods	Single-blind RCT TBI - All severities (presenting via A&E)
Participants	Randomised (completed) n=1156 (478) Treatment n=579 (252) Control n=577 (226)
Interventions	Oxford Head Injury service (OxHIS) Advice and referral as required Control: standard services only
Outcomes	Symptoms: Post concussion RPQ Social disability RHFUQ Post traumatic Amnesia
Notes	6 mths
Allocation concealment	C – Inadequate

Study Wade 1998

Methods	Single-blind RCT TBI - All severities (but only if admitted to hospital)
Participants	Randomised (completed) n=321 (218) Treatment n=184 (132) Control n= 130 (86)
Interventions	Oxford Head Injury Service (OxHIS) Advice and referral as required Control: standard services only
Outcomes	Symptoms: Post-concussion RPQ Social disability RHFUQ (RHFUQ) Post traumatic Amnesia
Notes	6 mths
Allocation concealment	A – Adequate

Study	Werner 1996
Methods	Single-blind quasi-RCT Stroke patients - At least 1 yr since stroke (mean 2.9 years)
Participants	Randomised (completed) n=49 (35) Treatment n=33 (28) Control n=16 (7) (5 additional non-randomised controls recruited)
Interventions	Late treatment: Out-patient physio / O/T for 3mths vs no treatment
Outcomes	Activity FIM -motor Limitation of Participation: SIP Mood Beck depression inventory
Notes	Follow-up at 3 and 9 mths
Allocation concealment	C – Inadequate

Study	Zhu 2001
Methods	Single-blind RCT Moderate-severe TBI
Participants	Subjects n=36 Intensive n=15 Standard n=21 (All complete to 6 months)
Interventions	4 hrs per day intensive MD treatment vs 2 hrs per day standard MD treatment
Outcomes	Global outcome: GOS Activity: FIM
Notes	Follow-up up to 6 mths in this report
Allocation concealment	D – Not used

Characteristics of excluded studies

Study	Reason for exclusion
Relander 1972	Fatally flawed: over 40% attrition to 1 year follow-up. Outcome measured by questionnaire only with no validity evidence presented.

ADDITIONAL TABLES

Table 01. Scoring criteria using the method of van Tulder 1997

Criterion	Score positive if:
a) Eligibility criteria specified	A list of inclusion/exclusion criteria was explicitly stated
bi) Method of randomisation	A random (unpredictable) assignment sequence was used.
bii) Treatment allocation concealment	Assignment was concealed from the investigators. Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.
c) Similarity of baseline characteristics	The study groups were comparable at baseline for the important prognostic parameters. In order to receive a “yes,” groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurologic symptoms, and value of main outcome measure(s).
d) Treatment and control interventions specifically described	Details are given of the programme, including disciplines involved and treatment duration.
e) Care provider blinded to the intervention	Treating team is blinded regarding the intervention (NB rarely possible in this context).
f) Co-interventions avoided or equal	Co-interventions should either be avoided in the trial design or similar between the index and control.
g) Compliance	Compliance was measured and satisfactory in all study groups.
h) Patient blinded to the intervention	Patient is blinded regarding the intervention. (NB: Rarely possible in this context if consent procedures are properly applied).
i) Outcome assessor blinded to the intervention	Outcome assessor blinded regarding treatment allocation and standardised assessment measures were used to structure the interviews. Scored negative if only self-reported (questionnaire) outcomes were used and no observer outcomes.
j) Outcome measures relevant	Outcome measures reflected disability (activity) or participation as relevant to the intervention.
k) Adverse effects described	Any adverse effects of the intervention are described.
l) Withdrawal rate described and acceptable	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for immediate and short-term follow-ups, 30% for intermediate and long-term follow-ups and does not lead to substantial bias a “yes” is scored.
mi) Short term outcome measurement	Outcomes were measured at the end of treatment (e.g. admission to discharge) or within 6 months of the end of treatment.
mii) Long term outcome measurement	Outcomes were measured at 1 year or more.
n) Timing of outcome assessment in both groups comparable	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.

Table 01. Scoring criteria using the method of van Tulder 1997 (Continued)

Criterion	Score positive if:
o) Sample size described for each group	Number of participants is stated for each group.
p) Intention-to-treat analysis	All randomised patients were included in the analysis (minus missing values), irrespective of non-compliance and co-interventions. If loss to follow-up was substantial (20% or more), an intention-to-treat analysis as well as an alternative analysis, which accounts for missing values (e.g., a worst-case analysis), should have been performed.
q) Point estimates and measures of variability	A mean or median figure was given for each important outcome parameter, together with a measure of variability such as standard deviation, standard error of the mean, or 95% confidence intervals.

Table 02. Method for synthesis of 'best evidence'

Category of evidence	Criteria
Strong evidence	Consistent statistically significant findings in outcome measures in at least 2 high quality RCTs.
Moderate evidence	Consistent statistically significant findings in outcome measures in at least 1 high quality RCT and at least one quasi-RCT or quasi-experimental design.
Limited evidence	Consistent statistically significant findings in outcome measures in at least 1 high quality RCT or Consistent statistically significant findings in outcome measures in at least 2 quasi-RCT or quasi-experimental design.
Indicative findings	Consistent statistically significant findings in process or outcome measures in at least 1 quasi-RCT or quasi-experimental design.
No evidence	Conflicting results between trials or in the case of insufficient data.

Table 03. Methodological Quality assessed by the van Tulder Method

Study ID	Internal Validity	Descriptive Criteria	Statistical Criteria	Total Score	Positive criteria
Kwakkel 1999	9	5	2	16	a,bi,bii,c,d,f,g,i,j,l,mi,mii,n,o,p,q.
Paniak 1998	8	5	2	15	a,bi,c,d,f,g,i,j,l,mi,mii,n,o,p,q.
Zhu 2001	9	4	2	15	a,bi,bii,c,d,f,g,i,j,l,mi,n,o,p,q.
Wade 1997	8	4	2	14	a,bi,bii,c,d,f,g,i,j,l,mi,n,o,q.
Wade 1998	8	4	2	14	a,bi,bii,c,d,f,g,i,j,l,mi,n,o,q.
Powell 2002	8	4	2	14	a,bi,bii,c,d,f,g,i,j,l,mii,n,o,q.
Smith 1982	7	5	2	14	a,bi,c,d,f,g,i,j,l,mi,mii,n,o.
Salazar 2000	7	5	2	14	a,bi,c,d,f,g,j,l,mi,mii,n,o,p,q.
Slade 2002	8	3	2	13	a,bi,bii,c,d,f,g,i,j,l,mi,o,p,q.
Shiel 2001	7	3	2	12	a,bi,d,g,h,i,j,l,mi,o,q.
Bowen 2001	5	4	2	11	a,bi,c,d,f,j,l,mi,n,o,p,q.

Table 03. Methodological Quality assessed by the van Tulder Method (Continued)

Study ID	Internal Validity	Descriptive Criteria	Statistical Criteria	Total Score	Positive criteria
Werner and Kessler	4	4	1	9	a,bi,d,i,j,mi,mii,n,o.
Semlyen 1998	4	4	1	9	a,d,f,g,j,l,mi,mii,n,o.
Ozdemir 2001	3	4	2	9	a,c,d,f,g,j,mi,o,q.
Relander 1972	1	4	0	5	a,c,d,l,mii.

GRAPHS AND OTHER TABLES

This review has no analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

Adolescent; Age Factors; Brain Injuries [*rehabilitation]; Cognitive Therapy; Counseling; Intensive Care [*methods; standards]; Randomized Controlled Trials; Rehabilitation, Vocational

MeSH check words

Adult; Aged; Humans; Middle Aged

COVER SHEET

Title	Multi-disciplinary rehabilitation for acquired brain injury in adults of working age
Authors	Turner-Stokes L, Disler PB, Nair A, Wade DT
Contribution of author(s)	LTS planned the review protocol and methodology, with input from DTW and PD. She also co-ordinated the search with support from the Cochrane Injuries group, and led the selection and evaluation of the trials. AN and LTS independently hand-screened the article abstracts and agreed the shortlist of trials for inclusion. Where opinion differed, DTW arbitrated. AN, LTS and DTW performed independent quality assessments and then agreed the final quality scores for articles included in the analysis. LTS played the role of lead author, but all the authors contributed to the final write-up and discussion.
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Date new studies found but not yet included/excluded	Information not supplied by author

Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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GRAPHS AND OTHER TABLES

Figure 01.

Table 4: Results from the four studies predominantly addressing the milder ambulatory group

Study	Subjects and Group comparison	Primary outcomes			
		Intervention Mean (SD)	Control Mean (SD)	Intervention minus control	P value (MANOVA)
Paniak 1996 and 2000	Subjects and Group comparison	Patients with TBI admitted to hospital (all severities). Mean age 33 yrs Intervention: 'Treatment as needed' (TAH) (n=56) Control: Single session (SS) of education and advice (n=53)			
	Primary outcomes	Impairment: Problem Checklist (PCL) Participation: Community Integration Questionnaire (CIQ) Health Status: Short-Form 36 (SF-36) Work Status: Socio-economic status (SES)			
	Assessment points	3-4 months (n=111) and 1 year (n=105)			
	Summary of Results	Participation (CIQ) did not change significantly for either group. Impairment (PCL) and health status (SF-36): Repeated measures MANOVA showed significant effects for time in both groups which were maintained at 1 year. There was no significant group interaction or time by group for any of the primary outcomes at either time point.			
	Health Status at 3-4 months	269 (30.7)	232 (19.9)	3.7	N/S
	Health Status at 1 year	243 (30.2)	228 (19.7)	-0.3	N/S
	Work Status at 3-4 months	348 (19.7)	367 (21.0)	-1.9	N/S
	Work Status at 1 year	348 (19.7)	367 (21.0)	-1.9	N/S
	Authors' conclusions	Both interventions appear to be equally effective			
	Salazar	Subjects and Group comparison	Active duty military personnel with moderate-severe TBI. Mean age 25 yrs Intervention: 8-week intensive in-patient cognitive behavioural programme (n=7) Control: limited home programme of weekly telephone support from psychiatric nurse (educational material, counselling and suggested home exercises) (n=53)		
Primary outcomes		Work status: Return to work Return to fitness for military duty			
Assessment points		1 year			
Summary of Results		No overall difference in outcome between the groups. Posthoc analysis demonstrated a significant group interaction (in favour of the intervention group) for 'fitness for military duty' at 1 year for the more severe subgroup who were unconscious for >1 hr.			
Health Status at 1 year		90%	94%	-4% (-5, 14)	N/S
Fit for military duty		73%	66%	7% (-10, 24)	N/S
Post hoc analysis of subgroup unconscious for > 1 hr (n=78)					
Fit for military duty		80% (n=35)	58% (n=40)	22%	0.05
Authors' conclusions		Overall benefit of in-patient cognitive rehabilitation programme similar to that of limited home rehabilitation, although institutional therapy may be beneficial for selected patients with severe TBI.			

Wade 1997	Subjects and Group comparison	All patients presenting to Accident and Emergency following TBI. Age 16-65 yrs Intervention: Telephone follow-up at 7-10 days with advice and referral as required (n=252) Control: no specific intervention (standard services only) (n=226) (NB: Despite major efforts to trace and contact patients, follow-up interview at 6 months could be achieved in only 478 of the 1156 (41%) of the patients randomised.)			
	Primary outcomes	Social disability: (Rivnessed) head injury Follow-Up Questionnaire (RFUQ) Symptoms: (Rivnessed) Post-concussion symptoms Questionnaire - (RPQ)			
	Assessment points	6 months			
	Summary of results	No overall difference between the intervention and control groups. Posthoc analysis revealed a significant group interaction (in favour of the active intervention group) with respect to social disability in a subgroup of patients with more severe injury (> 1 hr PTA).			
	Health Status at 6 months	Intervention Mean (SD)	Control Mean (SD)	P-value (Mann-Whitney)	
	RFUQ	3.6 (6.0)	3.3 (6.3)	N/S	
	RPQ	7.7 (10.9)	6.8 (10.0)	N/S	
	Post hoc analysis of subgroup with PTA > 1 hr (n=121)				
	RFUQ	0.85 (0.89) (n=71)	1.17 (1.07) (N=63)	0.003	
	RPQ	2.03 (0.85)	2.21 (0.89)	N/S	
Authors' conclusions	Routine follow-up does not appear to be necessary for all patients presenting with head injury, but a sub-group of patients with more severe TBI may benefit from such intervention.				
Wade 1998	Subjects and Group comparison	All patients admitted to hospital following TBI (i.e. a more severe group than the total group reported in Wade 1997). Age 16-65 yrs. Intervention: Telephone follow-up at 7-10 days with advice and referral as required (n=132) Control: no specific intervention (standard services only) (n=96) (NB: Follow-up data obtained in 218 (69%) of the 314 patients randomised.)			
	Primary outcomes	Social disability: (Rivnessed) head injury Follow-Up Questionnaire (RFUQ) Symptoms: (Rivnessed) Post-concussion symptoms Questionnaire - (RPQ)			
	Assessment points	6 months			
	Summary of results	Significant group interaction (in favour of the active intervention group) with respect to social disability and post-concussion symptoms. Subgroup analysis demonstrated that the main benefit appeared in the group with PTA < 7 days.			
	Health Status at 6 months	Intervention Mean (SD)	Control Mean (SD)	P-value (Mann-Whitney U test)	
	RFUQ	3.36 (7.81)	8.23 (8.75)	0.01	
	RPQ	9.3 (11.7)	13.9 (13.6)	0.02	
	Authors' conclusions	Early intervention by a specialist service significantly reduced social morbidity and severity of post-concussion symptoms 6 months after head injury, in the group of patients who required admission to hospital. Possibly most beneficial for the moderate to severe group some of whom may not present without pre-active intervention.			

TBI = traumatic brain injury, PTA = post-traumatic amnesia

Figure 02.

Table 5: Results from the two studies addressing out-patient rehabilitation

Smith 1981	Subjects and Group comparison	Patients suitable for out-patient rehabilitation following discharge from hospital after acute stroke (n=133). Mean age 63 years. Intervention: Out-patient physiotherapy and occupational therapy for 6 months at two levels of intensity: <ul style="list-style-type: none"> ▪ Intensive (4 whole days per week) (n=46) or ▪ Conventional (3 half days per week) (n=43) versus Control: (no routine rehabilitation, health visitor encourages home exercises as learned in hospital) (n=44)			
	Primary outcomes	Dependency for ADL: (Northwick Park ADL score)			
	Assessment points	3 and 12 months			
	Summary of Results	Significantly greater decrease in ADL scores in the intervention groups compared with control at 3 months. The difference is sustained at 1 year follow-up with a greater number of patients deteriorating in the control group. (Trend towards better result from intensive rehabilitation compared with conventional regimen not tested statistically)			
	Decrease in ADL score	Intensive rehabilitation	Conventional rehabilitation	Control	P value
	Mean change 0-3 m	3.54 (n=41)	2.87 (n=40)	1.50 (n=42)	1v3: p<0.01 1/2v3: p<0.01
	Mean change 0-12m	3.50 (n=36)	2.89 (n=36)	0.60 (n=35)	1v3: p<0.05
	Authors' conclusions	Out-patient rehabilitation following stroke appears to be effective <u>effective</u> . Decreasing intensity of rehabilitation was associated with both an increase in the proportion of patients who deteriorated and the extent to which they deteriorated			
Werner and Kessler	Subjects and Group comparison	Patients discharge from in-patient rehabilitation and at least 1 year (mean 2.9 years) after stroke (n=49). Mean age 63 years. Intervention: Out-patient Physiotherapy and Occupational therapy (2 hours, 4 times per week for 3 months) (n=33) Control: no specific intervention (n=16) (NB: 28% (5/33 intervention group and 9/16 controls) did not complete follow-up; 5 non-randomised controls were subsequently recruited to make control numbers up to 12)			
	Primary outcomes	Activity: Functional Independence Measure – Motor (FIM-MM) Limitation of Participation: Sickness Impact Profile (SIP) Depression: Beck Depression Inventory (BDI)			
	Assessment points	3 and 9 months			
	Summary of Results	Significant changes in FIM and SIP at 3 months maintained a 9 months. Trend towards improved mood did not reach significance.			
	Mean change in score	Intervention (n=28)	Control (n=12)	Intervention minus control	P value (T-tests)
	FIM-MM (0-3 mths)	6.6	1.5	5.1	0.03
	FIM-MM (3-9 mths)	0.7	-1.0	1.7	N/S
	SIP (0-3 mths)	-5.2	2.6	-7.8	0.04
	BDI (0-3 mths)	-2.6	0.2	-2.8	N/S
	BDI (3-9 mths)	0.7	0.5	0.2	N/S
	Authors' conclusions	Significant gains can still be attained in the post-acute stroke survivor, despite prior in-patient rehabilitation services			

ADL = activities of daily living

Figure 03.

⊕ **Table 6: Results from the two studies addressing community team-based rehabilitation**

Powell 2002	Subjects and Group comparison	Patients (16-65 yrs) with severe traumatic brain injury 3 mths-20 yrs previously (n=110 allocated: 94 (85%) completed follow-up) Intervention: Inter-disciplinary team interventions: 2 sessions per week for mean 27.3 (SD 19.1) weeks in community settings (home, work or day centres) (n=48) Control: Written information only (n=46)		
	Primary outcomes	Activity: Barthel Index (BI) Participation: Brain Injury Community Rehabilitation Outcome (BICRO-39)		
	Assessment points	Approximately 2 years (median 23 months (IQR 18-40))		
	Summary of Results	Intervention group made significant more gains on both the BI and BICRO scales. Median changes were small reflecting the diversity of the population, but 40% of intervention group and only 20% of controls made a clinically significant improvement of 2+ points on at least one BICRO subscale		
	Change scores from baseline	Intervention	Control	P value
	BI: % improving	35.4%	19.6%	
	Median (IQR) change	0 (-5, 5)	0 (-5, 4)	<0.05
	BICRO-39: %	80%	70%	
	Median (IQR) change	2.5 (-1.7, 6.2)	0.9 (-4.1, 6.8)	<0.05
	Authors' conclusions	Multi-disciplinary community rehabilitation, even years after injury, can make clinically significant gains which outlive the active treatment period.		
Bowen 2001	Subjects and Group comparison	Carers of young adult (16-65 yrs) TBI survivors with hospital stay of at least 3 days (n=96) Intervention: Active intervention from Head Injury Neurorehabilitation Team (HINT) <ul style="list-style-type: none"> ▪ Early intervention – whilst still in hospital (n=41) ▪ Late intervention – after discharge from hospital (n=28) Control: No specific intervention – existing services only (n=27) (NB: 20/96 (21%) received service other than that allocated – only 56% allocated to early intervention actually received it)		
	Primary outcomes	Information received: Carer perception of how well-informed they are – 7 questions Emotional state: Wimbledon Self-report Scale (WSS)		
	Assessment points	6 months post injury		
	Summary of Results	Analyses adjusting for potential confounding factors confirmed a clinically plausible superior outcome for both treatment groups compared to controls, but none of the results reached significance (set at p<0.01)		
	Mean change from baseline	Early (n=41)	Late (n=28)	Control (n=27)
	% poorly informed	46-64%	46-81%	63-89%
	WSS (median (IQR))	3 (0-9)	2 (0-6)	8 (1-15)
	Authors' conclusions	Hypothesis not confirmed, but absence of effect cannot be proven on these data, which may reflect a type II error in view of mixing of groups. Longer-term follow-up data also required.		

Figure 04.

Table 7: Results from the two studies addressing in-patient rehabilitation

⊕				
Semben 1998	Subjects and Group comparison	Consecutive patients in hospital with severe TBI and referred for in-patient rehabilitation within 4 weeks of injury. (Age 16-62 yrs) Intervention: Multi-disciplinary specialist rehabilitation service – Hunter’s Moor (HM) (n=33) Control: ‘Other rehabilitation’ (OR) in local non-specialist services in district hospitals (n=18)		
	Primary outcomes	Activity and independence: Barthel Index, FIM and Newcastle Independence Assessment form (NIAF) Care-givers’ Health: GHQ-28		
	Assessment points	1,2,3,6,12 and 24 months after injury		
	Summary of Results	Only Z values (BI) and t-values (FIM and NIAF) are given. HM intervention group were significantly more disabled at outset (as indicated by the FIM up to 3 months, the BI up to 6 months and the NIAF up to 12 months). By 12 months, therefore the HM group had caught up with the OR group in level of activity. The OR group made significant gains only up to 12 weeks on the NIAF and FIM Cognitive scale, but none on the FIM motor or BI (already at ceiling). By contrast the HM continued to make significant gains up to 24 months, as assessed by NIAF and BI. Significant improvements in carer distress for the HM group were also sustained at 2 yrs, whereas the OR group showed evidence of deterioration between 6 and 12 months. No difference in length of stay between the two groups.		
	Authors’ conclusions	The results support the efficiency of specialist rehabilitation services in achieving lasting gains for patients with more severe disability over similar lengths of stay.		
Oaedemic 2001	Subjects and Group comparison	Stroke patients referred for rehabilitation after medical stabilisation (n=60). Mean age 59.1 (SD 5.9). Group 1: in-patient rehabilitation (n=30) – at least 2 hours/day of formal therapy, 5 days per week Group 2: Home-based rehabilitation (n=30) – team visited home for 2 hrs/week and instructed family in home exercises – family provided therapy at least 2 hours/day, 7 days per week Mean duration of rehabilitation 64 days in both groups		
	Primary outcomes	Impairment: Brunstrom score, Ashworth (spasticity) Activity: FIM, Mini-mental state examination (MMSE)		
	Assessment points	Before and after rehabilitation		
	Summary of Results	Significant group differences in favour of the in-patient group for change in Brunstrom, FIM and MMSE scores, but no difference in spasticity		
	Change scores	Group 1	Group 2	P value
		Mean (SD)	Mean (SD)	(T-tests)
	Ashworth UE	0.5 (1.2)	0.2 (0.5)	N/S
	Ashworth LE	0.2 (1.2)	0.1 (0.3)	N/S
	Brunstrom (UE)	2.0 (1.2)	0.3 (0.6)	<0.001
	Brunstrom (LE)	2.4 (1.2)	0.8 (0.6)	<0.001
FIM	59.6 (14.2)	12.3 (13.4)	<0.001	
MMSE	4.8 (5.0)	2.0 (2.1)	<0.001	
Authors’ conclusions	Intensive in-patient rehabilitation provided significantly more favourable functional and cognitive outcomes than home based rehabilitation programme.			

Figure 05.

Table 8: Results from the four studies addressing enhanced intensity of rehabilitation

Study	Subjects and Group comparison	Primary outcomes	Assessment points	Summary of Results	Outcome at 6 months	Intensive	Conventional	P value (Fisher exact)	Authors' conclusions	
Kwakkel 1999 and 2002	Stroke patients within 2 weeks of onset (n=101) All groups received 15 mins arm training plus 15 mins leg training daily, plus 1.5 hours ADL training per week. In addition, for 30 mins 5 days/week, groups received: Group 1: intensive arm training (n=33) Group 2: intensive leg training (n=31) Group 3 (control): indolent patient (n=37)	ADL ability: Barthel Index (BI) Walking ability: Functional ambulation categories (FAC) Dexterity: Action Research Arm Test (AR Arm Test)	0, 6, 12, 20, 26, 38, 52 weeks	Analysis by Kwakkel/Walks demonstrated significant differences in walking ability, ADL and dexterity for the leg-training group compared with controls at week 20. The arm training group differed only in terms of dexterity. There were no significant differences between the arm and leg training groups at this time point. The effects of treatment were sustained at 1 year, but no significant differences between the treatment groups were demonstrated beyond 6 months.	Median (IQR) at 20 weeks	Arm training	Leg training	Control	P value (K-W test)	
					BI:	17 (14-20)	19 (16-20)	16 (10-19)	<0.05	
					FAC:	4 (3-5)	4 (3-5)	3 (1-4)	<0.05	
					AR Arm Test:	9 (0-39)	2 (0-56)	0 (0-2)	<0.01	
					Authors' conclusions	Greater intensity of leg training improves early functional recovery and whereas greater intensity of arm training improves only dexterity, providing further evidence that therapy primarily induces effects on the abilities at which training is specifically aimed. Functional gains were maintained up to one year.				
Zhu 2001	Patients aged 12-65 with moderate to severe TBI up to 6 months post injury (n=56) Interventions: Multi-disciplinary rehabilitation of two intensities: • Intensive: 4 hrs/day, 5 days/week (n=15) • Conventional: 2 hrs/day, 5 days/week (n=21)	Global outcome: Glasgow Outcome Scale (GOS) Activity (disability): FIM	0, 1, 2, 3, 4, 5 and 6 months presented; protocol continues up to 1 yr	Trend towards more patients in intensive group achieving good GOS scores or full FIM scores at 2-3 months, but conventional group catching up by 6 months	Outcome at 6 months	Intensive	Conventional	P value (Fisher exact)	Authors' conclusions	
					% good GOS: 3 mths	47%	14%	N/S	Preliminary results suggest that intensive therapy may possibly improve early functional outcome of TBI patients, but study should be expanded and continued	
					6 mths	53%	33%	N/S		
						% full FIM: 3 mths	47%	14%	N/S	
						6 mths	67%	48%	N/S	
Shiel 2001	Patients with moderate to severe TBI (age 16-70 yrs) admitted for rehabilitation (n=51). Stratified randomised on age and GCS									
Slade 2001	Patients with acquired brain injury (stroke, TBI or ME) aged 16-65 admitted for rehabilitation (n=131)									