

ORIGINAL REPORT

EVIDENCE-BASED STROKE REHABILITATION: AN EXPANDED GUIDANCE DOCUMENT FROM THE EUROPEAN STROKE ORGANISATION (ESO) GUIDELINES FOR MANAGEMENT OF ISCHAEMIC STROKE AND TRANSIENT ISCHAEMIC ATTACK 2008\*

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**Objective:** Despite recent high-profile advances in our understanding of rehabilitation post-stroke, the evidence base remains weaker than in other areas of stroke management. Under the aegis of the European Stroke Organisation a select committee was assembled to collate and appraise the evidence base for rehabilitation interventions.

**Methods:** Following systematic literature searching, relevant abstracts were screened for data quality and relevance. These data were summarized and presented to the members of the expert panel, who, both individually and across group discussions, modified the content. The process was repeated until a final document was produced that all members of the panel and the European Stroke Organisation editorial group were happy with.

**Results:** The final guidelines offer a comprehensive review of post-stroke rehabilitation, incorporating discussion of optimal timing, setting and duration of therapy as well as individual sections on the role of professions allied to medicine; use of assistive technologies and dealing with the common complications encountered during the rehabilitation period.

**Conclusion:** There is a lack of robust evidence for many of the prevalent post-stroke rehabilitation interventions. Available data are discussed and presented as key points; more importantly, specific areas that require further study are also highlighted.

**Key words:** cerebrovascular accident, cognitive therapy, complications, occupational therapy, physical therapy, recovery of function, rehabilitation.

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INTRODUCTION

Stroke is the single greatest cause of disability (2) in most Western countries. Globally the burden of stroke is greater still (3). The resultant costs are substantial, with stroke care estimated to cost more than 5% of many countries' healthcare budgets (4).

Prevention of stroke would be the ideal, but remains incompletely effective. Despite increasing focus on evidence-based primary and secondary prevention, strokes still occur. Even with optimal acute care, fewer than one in 3 patients recover fully from stroke (5). Rehabilitation is necessary to optimize functional recovery in the remainder.

The European Stroke Organisation (ESO) (formerly the European Stroke Initiative (EUSI)) publishes guidelines on best practice in all aspects of stroke care, including rehabilitation. For the latest iteration, rather than update the previous rehabilitation guidelines, the writing group performed a new and independent systematic review and critical appraisal of the available literature. With input from specialists in the field, a comprehensive overview of evidence-based rehabilitation was created. For brevity, it was not possible to publish this complete document as part of the ESO guidelines: certain content including background and discussion had to be removed. We present here the complete stroke rehabilitation guidance, including key points and areas requiring further research. For the ESO grading of evidence and strength of recommendation the reader is referred to the source guideline (1).

METHODOLOGY

*Search strategy*

Abstracts of original research and reviews were selected using the following electronic databases: Medline (1966–

December 2007); EMBASE (1980–December 2007); CINAHL (1982–2007) and the Cochrane Central Register of Controlled Trials. Particular emphasis was given to systematic review/meta-analysis and larger scale randomized controlled trials. The initial selection of abstracts for review was deliberately inclusive with no chronological, ethnic, age or functional related exclusion criteria. Animal studies were not included; non-English language studies were included only if a good quality translation was available.

#### *Data extraction and synthesis*

Initial assessment of selected abstracts was by 2 independent reviewers. The ESO expert panel provided further assessment of data quality and validity. Disagreements were resolved by discussion. Heterogeneity in the selected studies precluded formal meta-analysis. Thus, the results presented are qualitative and represent the views of the ESO expert panel. Decisions as to the content of the final guidelines were reached by group consensus.

## EVALUATION OF REHABILITATION TRIALS

Rehabilitation aims to enable people with impairments and activity limitations to reach and maintain optimal functioning in physical, intellectual, psychological and/or social domains (6). This definition emphasizes the holistic nature of the approach and the need to focus on both environmental and personal factors (7). Rehabilitation goals can shift from initial input intended to minimize impairment, to more complex interventions that are designed to encourage active participation.

Rehabilitation encompasses a wide range of activities in addition to standard medical care. These include physical, cognitive and occupational therapy. The ultimate goal of rehabilitation is to guide the individual towards a life situation in which they are participating in society as much as they wish. Thus, rehabilitation encompasses a heterogeneous group of interventions, applied using disparate methodologies, at various stages in the patient's stroke journey. This holistic nature of rehabilitation complicates comprehensive assessment and synthesis of evidence (8). The inherent difficulties of conducting robust stroke rehabilitation research are well documented (9, 10). There are practical barriers to blinding trials, to controlling for individualized therapy and to defining valid yet clinically meaningful end-points (11, 12). To date, most rehabilitation research has been conducted in single centres with small numbers of patients, and the resulting statistical power is insufficient to detect modest but meaningful improvements in function (13). Meta-analysis can summarize such data, but the value of meta-analysis is compromised by heterogeneity of the interventions (14).

Where available, this review has focussed on the larger prospective trials, systematic reviews or meta-analyses, as these represent the most robust datasets available. Lack of evidence does not equate to lack of efficacy; but, unfortunately for many of the interventions commonly employed in stroke rehabilitation, there are currently insufficient data on which to base treatment recommendations.

When examining a complex, multifaceted therapy such as rehabilitation there is the danger of making a “type III” error, i.e. finding non-efficacy of individual components of a system and concluding that the whole system has a neutral effect (15). Rehabilitation may be greater than the sum of its parts. Although robust data for many rehabilitation interventions are lacking, the overall evidence base is in favour of post-stroke rehabilitation.

#### *Key point*

- Although there is expert consensus, there is little robust evidence for several of the common interventions employed in post-stroke rehabilitation Level A.

#### *Priority areas for further research*

- Adequately powered (multi-centre) trials of stroke rehabilitation interventions.
- Consensus on optimal outcome measures for rehabilitation trials.

## SETTING FOR REHABILITATION

The success of organized stroke unit care, thrombolysis and the ongoing development of other acute therapies necessitates that most patients after stroke should be admitted to hospital promptly. Rehabilitation should begin on a hospital ward. There is no evidence to support use of “hospital at home” services (16); in fact admission avoidance interventions for stroke may be harmful. A prospective trial ( $n=457$ ) comparing early domiciliary care with hospital admission highlighted the difficulties of providing early care at home, with one-third of the “therapy at home” group eventually requiring admission (17).

The Stroke Unit Trialists' Collaboration has demonstrated improved survival and functional outcomes for patients treated in a dedicated stroke ward, (with numbers needed to treat of 33 and 20, respectively) (18). There are long-term functional benefits of dedicated stroke unit input: follow-up at 5 and 10 years reveals persisting efficacy compared with control (19).

The components that contribute to the success of a stroke unit are debated. However, since a focus on rehabilitation was one of the key characteristic features of stroke units included in the meta-analysis (18), post-stroke rehabilitation should begin in a stroke unit.

“Stroke unit” rehabilitation has been delivered in a variety of settings within a dedicated stroke ward, as part of a general rehabilitation service or through a peripatetic stroke team (16). Of these models, the dedicated stroke ward produces the best outcomes, although differences in morbidity and functional outcomes were found to be small compared with general rehabilitation wards (18). “Mobile” stroke units that provide services to general medical wards have been declared inferior to geographically distinct rehabilitation settings (20).

The financial and social implications of prolonged hospitalization have prompted increasing interest in services to facilitate early return to the community. Meta-analysis of studies comparing early supported discharge (ESD) services

to conventional ward base rehabilitation concludes that a multidisciplinary ESD team with stroke expertise, comprising (at least) nursing, physiotherapy and occupational therapy input can significantly reduce bed days for selected patients after stroke with no corresponding increase in readmission or morbidity (21). Patients appreciated this service, with sustained improvement in quality of life measures (21). Greatest clinical benefits were seen for those patients with mild or moderate impairments at baseline (22). Specialist ESD services are required for successful implementation. In a study where patients were discharged early with generic community support, mortality was substantially increased (23).

On completion of initial rehabilitation, there is some evidence for continuing input in the community. Meta-analysis has shown that community stroke rehabilitation of any sort reduces incidence of functional deterioration and maintains or improves activities of daily living (ADL) (24). The included patients had completed a pre-defined period of inpatient rehabilitation and the community intervention was delivered at time of discharge, or within a year of event. However, the quoted studies represented a heterogeneous range of interventions (occupational therapy, physiotherapy, multidisciplinary teams) and no definitive statement can be made on the optimal mode of service delivery.

The optimal setting for ongoing community therapy has not been adequately studied. A systematic review of 13 trials assessing day hospital care in a mixed group of patients, including, but not restricted, to stroke survivors, reported improved outcomes compared with no intervention, but found no clear advantage in comparison with other forms of comprehensive community care (25). Patients seem to prefer specialist community stroke team input to generic community rehabilitation services (20).

#### *Key points*

- Hospital admission to a stroke unit is required for patients after acute stroke to receive evidence-based initial therapy and co-ordinated multidisciplinary rehabilitation.
- Rehabilitation outcomes are best if treatment begins in a dedicated stroke unit.
- Medically stable patients with mild or moderate impairment can complete initial rehabilitation in the community if a multidisciplinary team with stroke expertise is employed.
- Community rehabilitation therapy delivered within one year of hospital discharge can prevent functional deterioration and at least maintain ADL.

#### *Priority areas for further research*

- Effect of the "enriched environment" of the stroke unit, i.e. the effect of non-formal rehabilitation time.
- Study of the optimal setting for delivery of community-based rehabilitation.

## TIMING OF REHABILITATION

Optimal timing of rehabilitation remains poorly defined. Proponents of early therapy cite evidence from functional

neuroimaging and animal studies that define the peri-infarct period as the crucial time to begin rehabilitation (26). The statement "time is brain *recovery*" has been used to emphasize that maximal neurological recovery is dependent on early initiation of therapy. Proponents of delayed rehabilitation cite potential medical instability and complications associated with the first days post-stroke.

A key difference between stroke unit care and general ward care seems to be earlier initiation of rehabilitation (18). Observational studies have consistently shown early therapy to predict better outcome, however there is lack of consensus as to definition of "early therapy". Specific trials comparing "early" and "late" initiation or rehabilitation have reported improved prognosis if therapy is started before 30 days (27) and 20 days (28). The heterogeneity within trials precludes any definitive statement on when therapy should start.

Fears that early therapy is harmful may be unfounded. Initial results from the ongoing AVERT study of A Very Early Rehabilitation (within 24 h of ictus) suggest that immediate therapy is well tolerated with no increase in adverse events (29). The therapy given within the AVERT study consists principally of mobilization. The activation pattern employed as routine in many of the European stroke units seems already to be more active than the Australian centres first enrolled in AVERT (30).

The Trondheim stroke unit have reported excellent outcomes using a system of commencing rehabilitation as early as possible (19), and many other centres have successfully implemented similar models.

Titration of therapy with adjustment of goals according to patient progress is necessary. An Italian group demonstrated that early intensive treatment yielded excellent therapeutic response, but the risk of dropout was 5 times greater than for patients with delayed treatment schedules (28). Infrastructures for rehabilitation vary across Europe, and the optimal time for transfer from the acute setting to a dedicated rehabilitation service is unknown. If rehabilitation is offered at a location remote from acute services, a period of medical stabilization appears necessary before transfer.

A fundamental component of early rehabilitation is mobilization. Many of the immediate complications of stroke are related to immobility (deep vein thrombosis, skin breakdown, contracture formation, constipation, and hypostatic pneumonia) and thus early mobilization makes intuitive sense. Emerging data from ongoing trials of early mobilization provide some support (29). Meta-analysis was unable to determine the optimal timing of first mobilization, but did suggest that mobilization within the first few days is well tolerated (31).

There are few studies of rehabilitation offered in the "chronic" phase of stroke, i.e. more than one year after the acute event. A recent systematic review found only 5 trials ( $n = 487$ ) of therapy in the community involving a majority of patients who had reached more than one year post-stroke. Overall, there were inconclusive data to recommend any therapy in the chronic phase (32).

*Key points*

- Rehabilitative therapies appear to be well tolerated in medically stable patients.
- Early treatment appears reasonable, but there are outstanding questions over timing and efficacy.

*Priority areas for further research*

- Optimal timing of "early" rehabilitation
- Efficacy of early ADL-based rehabilitative strategies.
- Further trials of rehabilitation delivery in the "chronic" phase

#### DURATION AND INTENSITY OF REHABILITATION THERAPY

Greater intensity of rehabilitation, especially time spent working on ADL, is associated with improved functional outcomes (33). However, available data do not allow for a fixed "prescription" of optimal rehabilitation time.

Meta-analysis including 2686 stroke patients, underscores that augmented exercise therapy can improve performance on functional measures, resulting in a median one point change (5%) on the Barthel Index (34). Although clinically modest, at a population level this degree of improvement should have a significant impact on community resource needs. This meta-analysis included a heterogeneous collection of trials with exercise time ranging from 132 min to 113 h (median 16 h) over 6 months. The trend was for a dose-response relationship with increasing improvement accompanying increasing therapy time and no observed "ceiling effect". Greatest benefits were observed in studies of lower limb exercises and general ADL work. A further systematic review ( $n=939$ ) describing therapies for improving arm function again suggests a dose-response relationship, although heterogeneity of included studies precluded a formal measure of effect size (35).

Current evidence precludes any definitive recommendation on minimal or maximal therapy times. Observational data suggest that weekly time spent in active rehabilitation is modest in many centres (36) although these studies have not measured informal nurse-led rehabilitation that is part of daily routine in many stroke units. Even large increases in provision of rehabilitation are unlikely to reach a (theoretical) therapeutic plateau. Concern over patients' ability to tolerate intensive therapy has been expressed; however adverse events were infrequently reported in the available studies.

Organization and "quality" of care may be more important than absolute hours of therapy. In a comparison of a dedicated stroke multidisciplinary team with usual ward-based rehabilitation, the dedicated team achieved better outcomes with significantly fewer hours of therapy (37). The use of a formal care pathway to standardize stroke care and rehabilitation is of equivocal benefit, apparently decreasing incidence of certain post-stroke complications but increasing levels of dependency at discharge (38). Limited availability of therapists may hinder effective rehabilitation; a study comparing additional weekend therapy with usual care reported improved outcomes and

reduced length of stay, although this did not reach statistical significance (39).

There is some evidence for continuing rehabilitation upon discharge (24). However, no good quality data exist to describe duration or intensity of such therapy.

*Key points*

- Greater duration and intensity of rehabilitation predicts functional improvement, with a likely dose-response relationship.
- Available data do not allow for recommendations on minimal or maximal therapy times.
- Process and quality of care are likely to be as important as total hours of therapy.

*Priority area for further research*

- Limits for minimal and maximal therapy input, at various stages in stroke recovery

#### CONTENT OF THERAPY

The stroke unit trialists favour co-ordinated multidisciplinary teams of staff with expertise in stroke care (18). The composition of these teams is not formally prescribed, although core staff members in the included studies were: stroke physician; physiotherapists; occupational therapist (OT); and speech and language (SL) therapist. These professions allied to medicine, and the evidence base for their contribution to rehabilitation will be considered in turn.

*Physiotherapy*

Physiotherapy covers all "interventions that develop, maintain and restore maximum movement and functional ability throughout the lifespan" (40). Available evidence supports the efficacy (41) and popularity (42) of providing stroke-based physiotherapy.

The optimal delivery of physiotherapy is poorly described. Specific models of physical therapy include Bobath and motor relearning. Each has its proponents, and favoured techniques differ internationally. Systematic review found that provision of physiotherapy by a mix of the accepted models was superior to placebo/no therapy (41, 43). On comparing differing treatment approaches, no specific modality was favoured (43). Specific studies of short- (44) and long-term (45) efficacy of Bobath and motor relearning, described poorer initial outcomes in the Bobath group but no differences at long-term follow-up.

Some evidence exists for specific physiotherapy interventions. The EXCITE (Extremity Constraint Induced Therapy Evaluation) ( $n=222$ ) study (46) of constraint-induced movement therapy (CIMT) (i.e. intensive task-orientated practice involving the paretic limb, with restraint of the non-paretic limb) reported positive results for CIMT therapy 3–9 months post-stroke, in a group of medically stable stroke survivors with some persisting arm movement (46). Functional gains persisted at 1-year follow-up (47).



Previous reports that strengthening exercises should be avoided in the upper limb to avoid spasticity are not supported by trial evidence. Several groups have shown that strength can be improved, with meta-analysis reporting a dose-response relationship (35). Review of therapeutic functional electrical stimulation (24 trials) suggests that strength can be increased using this method, although there have been few studies looking at clinically relevant outcome measures (48).

Technological interventions have not been shown to improve functional end-points. A systematic review of 15 trials ( $n=622$ ) did not prove efficacy of treadmill training to improve walking (47). On subgroup analysis there was a trend towards better outcomes in groups who used treadmill training in combination with body weight support. There is limited evidence that electromechanical gait training may be more effective than conventional physiotherapy (49). Use of orthoses and adaptive personal and environmental equipment to enhance rehabilitative therapies is commonplace, although limited specific trial data exist (50).

Many other physiotherapy interventions exist and are frequently used in clinical practice. To date, there is insufficient evidence to comment on their efficacy. Novel therapies that have shown promise in reviews of small-scale trials include virtual reality (51), mental imagery (52) and bilateral movement training (53). It is recognized that patients' cardiovascular fitness can deteriorate during the recovery phase of a stroke. This physical deconditioning impairs active rehabilitation and is a risk marker for further events (54). Meta-analysis ( $n=480$ ) has shown that aerobic training can improve exercise capacity in individuals with mild to moderate motor deficit post-stroke (55).

#### Key points

- Physiotherapy is popular with patients and improves outcomes post-stroke.
- No specific model for delivery of therapy can be recommended.
- CIMT is effective 3–9 months post-stroke.
- Aerobic exercise training can improve exercise capacity post-stroke.
- Technological interventions have not yet been shown to improve functional end-points.

#### Priority areas for further research

- Optimal methods for physiotherapy-based stroke rehabilitation.
- Effect of patient therapist interaction.
- Effect of group work vs individual therapy.
- Better defining the role of CIMT and other interventions in the acute and chronic phase.

#### Occupational Therapy

OT aims to “enable people to achieve health, well-being and life satisfaction through participation in daily activities that provide structure to living and meaning to individuals, meeting human needs for self-care, enjoyment and participation

in society” (56). A systematic review of 9 trials comparing OT-based ADL therapy with usual care reported improved functional outcomes in the active intervention group (57). This result was echoed in an independent analysis of 32 trials comparing any OT intervention with control: OT input resulted in modest but statistically significant improvements in basic and extended ADL (58). The data do not justify conclusions on the optimal mode of OT delivery.

As OT aims to promote optimal functioning within the patient's chosen environment, several studies have been performed in the community. Meta-analysis of these trials, using individual data patient on 1143 patients, concluded that community-based OT can improve performance on ADL measures. The greatest effects are seen in an older cohort and when targeted interventions are used (59). Specific leisure-based OT therapies did not translate into improved ADL. A trial of providing OT intervention to care home residents ( $n=118$ ) post-stroke found less functional deterioration in the active intervention group, with a median difference of 1.9 (9.5%) in the Barthel Index at 6 months (60). No controlled trial data describe effectiveness of OT beyond one year after stroke.

Whilst there is evidence to support OT intervention after stroke, less is known about the optimal components of the therapeutic packages. Some specific interventions may be effective. A randomized controlled cross-over study found that a problem-solving approach to dressing practice administered by an occupational therapist improved functional outcome and had lasting benefits after treatment was withdrawn (61). Similarly, a randomized controlled trial found that targeted OT interventions were more successful than passive information provision in improving outdoor mobility (62).

#### Key points

- Hospital- and community-based OT can improve functional outcomes after stroke but there is little evidence to favour any specific approach.
- There is some evidence to suggest that targeted task specific interventions are effective in improving functional outcome, e.g. dressing and outdoor mobility.

#### Priority area for further research

- Optimal methods for OT for stroke, in hospital and community settings.

#### Speech and Language Therapy

SL therapists have 2 potential roles in stroke: to assess and optimize safe swallowing and to assist communication.

A variety of methods exist to screen for swallowing problems post-stroke. A simple intervention that requires minimal training is the water swallow test (63). This tool has been shown to have only modest sensitivity (>70%) and specificity (22–66%), but can be used as a bedside screening tool. As return of functional swallow is common in the first days post-event (64), patients should be frequently reassessed. For those patients found to have persistent dysphagia, it is common practice to obtain a formal SL therapy assessment. At present there is in-

sufficient evidence to recommend a particular methodology for this assessment (65). Treatment of dysphagia includes advice on posture and feeding, however, there is a limited evidence base to support benefits from this. Two trials of formal SL therapy input (total  $n=99$ ) found no statistically significant difference to usual care (66, 67). A study ( $n=115$ ) comparing simple written instruction with graded levels of SL intervention found no difference in outcomes across the groups (68).

Aphasia and/or dysarthria are common symptoms post-stroke and impact on quality of life (69). A systematic review of SL therapy for dysarthria in non-progressive brain damage (stroke and head injury) found no good quality evidence for benefit from intervention (70). Similarly, a systematic review of SL therapy input for aphasia reported insufficient good quality evidence to recommend formal or informal interventions over placebo (71). The studies included in this review were community-based and had an average time to therapy of 3 months: they offer little to inform acute ward-based rehabilitation. A related meta-analysis with less rigorous inclusion criteria concluded that improvement in speech is greater if SL therapy is initiated early (72). However, the quasi-experimental design of many of the included studies weakens the strength of this conclusion. Similarly, a review of treatment for post-brain injury aphasia that was mainly based on patients after stroke supported use of SL therapy strategies over control (73). The ACTNoW (Assessing Communication Therapy in the North West (of England)) prospective multicentre randomized controlled trial of SL therapy in aphasia and dysarthria is currently recruiting.

#### Key points

- There are insufficient data to recommend a specific approach to post-stroke swallow and speech problems.
- Small-scale studies have suggested that efficacy of therapy for aphasia is dependent on timing and intensity.

#### Priority area for further research

- Efficacy of SL therapy for dysphagia, aphasia and dysarthria with emphasis on timing and intensity of therapy.

#### Stroke Liaison

A recent systematic review comparing dedicated stroke liaison to usual care found no evidence of improvement in ADL, subjective health status or carers' health (74). On subgroup analysis, success of a stroke liaison service was predicted by younger age, less severe deficit, and when the content of the service had an emphasis on education.

Inadequate provision of information predicts poor quality of life in patients after stroke and their families (75). A meta-analysis comparing a single session of information provision with a more intense intervention, and comparing both with placebo/usual care, reported improved outcomes in the "information plus" group (76). The choice of therapist and mode of delivery of this information have not been assessed.

Sexuality can suffer after a stroke. Underlying physical limitations and co-morbid vascular disease may be compounded by

side-effects of medications (77). It may be desirable to discuss issues of sexuality and intimacy with patients (78). Provision of support and information is important: many patients fear that resuming an active sex life may result in further stroke (79).

#### Key point

- Improved information sharing with patient and carers is important but evidence does not support use of a dedicated stroke liaison service for all patients.

#### Priority areas for further research

- Effect of good quality information sharing on quality of life measures.
- Optimal method for information sharing.

#### Cognitive Intervention

Cognitive deficits are common following stroke and impact on quality of life. A recent Cochrane review, evaluating 2 small-scale studies (total  $n=18$ ) employing differing approaches, reported no evidence of efficacy for specific memory rehabilitation (80). A further systematic review of cognitive training for post-stroke attention deficit described 2 trials of suitable methodological quality ( $n=56$ ) (81). Although both studies reported improvements on markers of attention this did not translate into meaningful clinical improvement on ADL measures. A larger evidence base exists for cognitive rehabilitation in patients with spatial neglect. Meta-analysis of 12 studies reports that formal training can improve performance in standardized bedside tests of neglect, but had no effect on ADL or eventual placement post-rehabilitation (82). Delivery of these cognitive interventions was mainly by a formal neuropsychological service or an OT.

A more inclusive systematic review of cognitive rehabilitation following acquired brain injury found 5 randomized trials reporting efficacy of rehabilitation training strategies in visual inattention and apraxia. These included too few patients to recommend a particular approach. An effect on meaningful disability outcome measures was not reported (73).

#### Key point

- There are insufficient data to recommend a specific approach to cognitive problems post-stroke.

#### Priority area for further research

- Further research on cognitive interventions with emphasis on functional benefits.

### OTHER GROUPS

The above list is not comprehensive. Depending on patient-specific goals, input from various other allied health professions could be appropriate. Such groups include dietitians, orthoptists, and social workers, as appropriate for the patient. The importance of ward-based nurses to the optimal function-

ing of the stroke unit is also appreciated. Although there has been limited formal research in this area, some have argued that dedicated staffing creates an “enriched environment” that encourages practice in rehabilitation activities outwith periods of formal therapy (83).

As the patient progresses from hospital-based rehabilitation to the community, involvement of carers in rehabilitation becomes increasingly important. Formal training of caregivers in delivery of care may reduce personal costs and improve quality of life (84). The multi-centre “Training of Caregivers After Stroke” (TRACS) study is currently recruiting in an attempt to definitively answer the question.

#### *Key point*

- Training of carers may improve outcomes.

#### *Adjuvant Interventions*

Although less common in the West, in some parts of the world acupuncture is used as an aid to functional stroke recovery. Efficacy data are limited in extent and quality. Available evidence suggests that acupuncture has little clinically significant effect (85).

Animal models have suggested that use of amphetamine-based products may improve recovery rates following brain injury. Systematic review of human trials using amphetamine post-stroke suggests increased motor benefits, but a corresponding increase in serious adverse events (86). Amphetamine use is not recommended as an adjunct to rehabilitation.

#### *Key point*

- Acupuncture and amphetamines are not recommended as an aid to post-stroke rehabilitation.

#### *Priority area for further research*

- Development of effective adjuncts to rehabilitation.

### COST-EFFECTIVENESS

Initial investment in rehabilitation is expensive, but societal costs of failure to attain functional potential also pose a substantial drain on resources. Data on cost-effectiveness of services are limited. Available evidence is based mainly on results of UK and Swedish studies. The conclusions may not be generalizable to other countries with differing healthcare systems. The overall costs of admission to a dedicated stroke unit rather than a general ward are similar (87, 88) and hospital costs account for only a small percentage of total costs over the first year after stroke (88). Since outcomes for the stroke unit cohort are superior, this implies cost-effectiveness.

Cost-benefit analysis of an early supported discharge system is also favourable compared with usual stroke unit care (89). There are insufficient good quality data to allow comparison of ongoing co-ordinated community rehabilitation to usual care. Training carers of stroke patients is cost-effective (90). No good quality studies have performed cost-benefit analysis for

specific aspects of rehabilitation services, such as community OT or stroke liaison services, reflecting the lack of robust evidence to support many single interventions.

#### *Key point*

- Cost-effectiveness data are limited, but support the use of dedicated stroke units and early supported discharge services.

#### *Priority area for further research*

- Health economic data for all interventions

### PROGNOSIS

The stroke unit trials have shown that admission to a dedicated stroke unit can improve outcomes for all strokes. From their selection criteria we can recommend no specific age or functional exclusions to stroke unit care. Elderly patients derive the greatest benefit (18). Rehabilitation is goal-orientated and clearly ultimate goals will differ depending on co-morbidity, prognosis and previous functional status.

An important predictor of rehabilitation outcome is initial stroke severity; in this regard we hope that increasing use of established and emergent acute therapies may help decrease incidence of “severe” strokes. As would be expected pre-morbid disability is also a strong determinant of eventual outcome (91). Other factors, such as stroke aetiology (92) and topography of lesion (93), have been studied as potential predictors of rehabilitation, however results are conflicting (94) and at present there is no evidence that any of these non-modifiable factors should influence decisions on rehabilitation. Potentially modifiable factors, such as depression, nutrition and continence, can all influence rehabilitation prognosis. These will be discussed in turn in the “complications” section.

There is a limited evidence base to recommend treatment strategies for the most severely disabled, especially those patients who already required nursing/care home management. Previous guidelines have recommended the use of passive movements to prevent painful contracture or pressure sores in patients so disabled that they are unable to partake in any active rehabilitation (1). Similarly, the evidence base for treatment of patients with severe cognitive impairment is limited. As those patients with the most severe cognitive or physical impairments have been excluded from rehabilitation trials, we should be cautious in extrapolating results to this group. It appears from trials that specifically examined outcomes in the most disabled that active rehabilitation allowed more patients to return home after intervention (95). Selection for rehabilitation on the basis of prior independence remains a contentious issue and the ethical and clinical implications have been debated elsewhere (96).

Younger patients after stroke have inherently greater potential for survival and functional outcomes than elderly patients. They may also have rehabilitation goals that differ from those of an older, retired cohort. There is a lack of good quality trial evidence on rehabilitation of the younger stroke patient, especially in age-relevant areas such as return to work post-event. A systematic

review of therapy for acquired brain injury in patients of working age included 4 trials of interventions in stroke (97). These covered a range of treatments but concluded that outpatient stroke rehabilitation was beneficial, although some evidence suggests that benefit may be restricted to the subgroup with mild/moderate deficits. For patients with severe impairment, there is insufficient stroke-specific evidence, and conclusions that inpatient rehabilitation is beneficial can be drawn only by extrapolation from acquired brain injury trials.

#### *Key points*

- Provision of dedicated stroke unit rehabilitation is recommended for all patients at admission.
- Severity of stroke and pre-morbid state are strong predictors of rehabilitation prognosis.
- There is limited evidence on the most appropriate treatment for the most severely disabled patients; active intervention may decrease rates of care home admission.
- Rehabilitation after stroke is effective for patients of all ages. Therapy for younger stroke survivors can be delivered in an out-patient setting for patients with mild disability.

#### *Priority areas for further research*

- Efficacy of using prognostic variables to tailor rehabilitation.
- Possible use of brain imaging to better define rehabilitation strategy and prognosis.
- Interventions for severe stroke.
- Interventions for younger stroke patients.

## COMMON COMPLICATIONS DURING REHABILITATION

Successful stroke rehabilitation can be compromised by medical complications. Such complications impact negatively on rehabilitation progress and are strong predictors of poor functional outcome and mortality. Observational work suggests that the commonest complications during inpatient rehabilitation are: depression, shoulder pain, falls, urinary disturbance and aspiration pneumonia (98).

### ***Post-Stroke Depression***

Post-stroke depression (PSD) is associated with poor rehabilitation results and ultimately poor outcome (99). In clinical practice, only a minority of patients are diagnosed and even fewer are treated (100). Prevalence of up to 33% of stroke survivors compared with 13% of age- and sex-matched controls has been described (101), but reliable estimates of incidence and prevalence of PSD in a stroke cohort are limited by a lack of standardized definitions and scoring systems (99). Predictors of PSD in the rehabilitation setting include increasing physical disability, cognitive impairment and stroke severity (99). There is no consensus on the optimal method for screening or diagnosis of PSD. Standard depression screening tools are inappropriate for certain groups at high risk of PSD, such as patients with aphasia or cognitive impairment (102).

A number of therapies have been used in the treatment and prevention of affective disorder in stroke. Meta-analysis of pharmacotherapy consistently shows that selective serotonin reuptake inhibitors (SSRI) and heterocyclics can improve mood post-stroke (103). There is less evidence that these agents can effect a full remission of a major depressive episode, or prevent PSD. Of the available drugs, SSRIs appear to cause fewer withdrawals from treatment due to side-effects than do heterocyclics (104). There is no good evidence to recommend psychotherapy for treatment or prevention of PSD, although these therapies elevate mood (105). There have been no trials of electro-convulsive therapy in PSD. There is a dearth of robust evidence regarding the effect of treating PSD on rehabilitation or functional outcomes.

Emotionalism is a distressing symptom for patients and carers. Antidepressant pharmacotherapy may reduce emotional outbursts, but effects on quality of life are not clear (106).

#### *Key points*

- Post-stroke depression is under-diagnosed.
- Drug therapy and non-drug interventions may improve mood following stroke.
- There is limited evidence regarding screening and intervention to treat depression in stroke patients.
- Drug therapy can improve manifestations of post-stroke emotionalism.

#### *Priority area for further research*

- Optimal therapy for treatment of PSD, especially in patients with aphasia.

### ***Pain and Spasticity***

Post-stroke shoulder pain (PSSP) is increasingly recognized, with an incidence of up to 80% in the first year post-event (107). Risk is highest in patients with impaired arm function and poor functional status (108). The aetiology is poorly defined, but appears multifactorial related to both central and mechanical factors (109). The presence of PSSP has a negative association with good rehabilitation outcomes (108).

Review of interventions for PSSP suggests that passive movement of a paretic limb may be preventive (109). Electrical stimulation is commonly used for treatment, but efficacy is unproven by a systematic review of the small trials (110). Treatments for shoulder subluxation, a common precipitant of PSSP, have been reviewed. The review group concluded insufficient data to recommend use of slings or orthoses, but reported a trend towards efficacy for arm strapping of the affected limb (111).

Central or neuropathic pain is a common post-stroke sequelae, especially affecting patients with thalamic pathologies. Literature review for all chronic pain subtypes suggests that amitriptyline, lamotrigine and gabapentin are suitable therapeutic agents that are tolerated and can reduce pain compared with placebo (112).

Spasticity is a common problem in the chronic phase and can have adverse effects on ADL and quality of life (113). Posture



and movement therapy, relaxing therapy, splints and supports are all commonly employed, but a sound evidence base is lacking (114). There is some evidence for use of pharmacotherapy with botulinum toxin, with proven effects on muscle tone in arms and legs. Functional benefits are less well studied. Other agents, such as tinzadine, are limited in their use due to side-effects, principally sedation (115).

#### *Key points*

- Post-stroke shoulder pain is common.
- Passive movements may help prevent this complication, but there is no good evidence on treatment.
- Tricyclic and anticonvulsant therapy may ease post-stroke neuropathic pain.
- Botulinum toxin may be useful for post-stroke spasticity.

#### *Priority area for further research*

- Recognition and treatment of post-stroke shoulder pain, neuropathic pain and spasticity.

#### **Falls**

A considerable amount of literature is available on incidence, prediction and interventions to reduce falls amongst older patients (116). Data on falls in stroke survivors are more limited, but consistently confirm that falls are common, both in the acute setting (up to 25% during in-patient rehabilitation (117)) and in the long-term (118). Conflicting data are available on predictors of falls in stroke survivors (119). Likely risk factors include cognitive impairment, depression, polypharmacy and sensory impairment (120). Falls are common during patient transfers and so special moving and handling training is recommended for stroke unit staff (121). At present there is insufficient evidence to recommend an intervention to prevent falls in stroke survivors, although a multidisciplinary prevention package that focuses on personal and environmental factors has been found to be successful in general rehabilitation settings (122).

Amongst post-stroke fallers, the 5% incidence of serious injury is small, but still clinically important: hip fracture rates are 4-fold higher than in age-matched controls (123). Outcomes following fractured neck of femur are especially poor in stroke survivors (124). As a result of immobility, hypovitaminosis-D and possible other factors, bone mineralization is suboptimal following stroke (125). Exercise (126), calcium supplements (127) and bisphosphonates (128) improve bone strength and decrease rate of fracture in stroke patients. There is insufficient evidence to recommend a particular approach, although problems with dysphagia can complicate oral bisphosphonate use and intravenous preparations have been advocated by some. Hip protectors can reduce incidence of fracture for high risk groups in institutional care, but evidence is less impressive for their use in a community setting (129).

#### *Key points*

- Falls are common post-stroke. Subsequent fractures are associated with considerable morbidity and mortality.

- Bone mineralization is impaired post-stroke: exercise, calcium/vitamin-D supplements or bisphosphonates may improve bone strength.

#### *Priority areas for further research*

- Interventions to reduce falls risk in a stroke population.
- Interventions to minimize harm from falls in a stroke population.

#### **Continence**

Post-stroke urinary incontinence (UI) is common, with increasing incidence in older, more disabled and cognitively impaired stroke survivors (130). Recent estimates are of 40–60% prevalence in an acute stroke population, with 25% still incontinent at discharge and 15% incontinent after one year (131). These figures may be confounded by a high prevalence of pre-morbid UI, but remain concerning as UI is a strong predictor of poor functional outcome, even after correcting for age and functional status. Aetiology is generally multifactorial including abnormalities of normal voiding mechanism, lower urinary tract infection, and “functional incontinence” (77).

There is limited evidence to support physical interventions such as bladder retraining and pelvic floor exercises for UI (131). Structured assessment and physical management improved continence rates in both inpatients and outpatients (132). Trials of other mechanical or physical therapy are of insufficient number and quality to make any recommendation (132).

Literature on faecal incontinence (FI) is limited. Estimates of prevalence suggest that FI is common in the acute stages and remains a problem for many patients, with 30% prevalence in the first week and 11% after one year (133). Prevalence in the chronic phase is less well defined, with estimates of 4–15% (134): considerably higher than age-matched controls (1% prevalence). Use of constipating drugs and difficulty with toilet access predict ongoing FI (133). One trial of structured assessment and advice found a positive effect on bowel habit that was sustained to one year (135).

#### *Key points*

- Urinary and faecal incontinence are common in the acute stages of stroke and persist in a significant percentage of patients.
- A co-ordinated programme of assessment and intervention may help restore normal toileting.

#### *Priority area for further research*

- Interventions to improve continence post-stroke.

#### **Dysphagia and Feeding**

Oropharyngeal dysphagia occurs in up to one-third of patients presenting with a unilateral hemiplegic stroke (136). Frequency may be higher in patients with brain stem stroke. Prevalence of dysphagia is highest in the acute stages of a stroke and declines to around 15% at 3 months (67). Dysphagia is associated with a higher incidence of medical complications and overall mortality (137).

Withholding or limiting oral intake for a patient with dysphagia can worsen the catabolic state that may be associated with an acute insult such as stroke. Estimates of malnutrition on admission vary from 7 (138), increasing to 22–35% at 2 weeks (139). For disabled patients requiring prolonged rehabilitation, a 50% prevalence of malnutrition is reported (140). Malnutrition predicts poor functional outcome and mortality (140, 141). However, routine supplementation for all acute stroke patients did not improve outcomes or reduce complications ( $n=859$  Absolute Risk Reduction (ARR) death/poor outcome 0.7%; 1.4–2.7) (142). This may relate, in part, to the low observed incidence of malnutrition at baseline (7.8%). There are no adequately powered trials of targeting supplementation to stroke patients with evidence or at risk of malnutrition.

For patients with ongoing dysphagia, options to provide enteral nutrition include nasogastric feeding or creation of a percutaneous endoscopic gastrostomy (PEG). A trial of early vs delayed (one week) nasogastric feeding found no compelling benefit of early feeding, although there was a trend to fewer deaths in the early nasogastric group ( $n=859$  ARR death 5.8%; 0.8–12.5) (142). A related trial examining PEG and nasogastric feeding within 30 days revealed that PEG feeding was no better than nasogastric feeding and may in fact be harmful ( $n=321$  ARR death/poor outcome 7.8%; 0–15.5) (142). For patients with longer term dysphagia, PEG feeding may be considered. Two trials (combined  $n=49$ ) comparing PEG with nasogastric feeding found a trend towards improved nutrition with PEG feeding that did not reach statistical significance (66). In discussions with patient and family it should be remembered that overall mortality following PEG placement is 50% after one year (143). This reflects the severity of the underlying disease. Quality of life measures following PEG are poorly researched. In those studies that have addressed this issue, quality of life was not improved by PEG (143). The use of calcium channel blockers to aid swallow has no convincing evidence base (144).

#### Key points

- Malnutrition rates are high in patients requiring longer term inpatient rehabilitation.
- Current evidence does not support routine use of dietary supplements for all strokes.
- Early insertion of a PEG feeding tube is not recommended.

#### Priority area for further research

- Use of targeted nutritional supplementation.
- Longer term outcomes, including patient and relative views post-PEG.

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