



## How do stroke units affect patient outcomes

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### Abstract

**Background and Purpose:** We tried to explain the manner by which organized inpatient (within stroke unit) care can deliver decreases in case fatality and in the requirement for institutional care after stroke.

**Methods:** We tried to perform an analysis of a cooperative systematic review randomized trials that compared inpatient in stroke unit care with alternative forms of care. Twenty-eight trials (5855 patients) provided outcome information on death, spot of living location, and last functional outcome. also an analysis of a variety of subgroups examined the impact of stroke unit on patient death, institutional care or dependency. When dealing with missing data for the outcomes of death, dependency or institutionalization, we assumed the participant to be alive, independent and living at home. We aimed to explore the implications of these assumptions in sensitivity analyses.

**Results:** The decreases in case fatality of patients treated in a stroke unit setting were more progressed after the index stroke. The decreases in the chances of death were apparent in particular for those deaths considered to be secondary to immobility. The relative increment in the number of patients sent home from stroke units compared to alternative general medical care was owing to an increase in the number of patients returning home physically independent. Over the scope of stroke severity, stroke unit care was related with non-significant increments in the increases in the number of patients regaining independence.

**Conclusions:** Inside the constraints of the accessible data, we conclude that organized inpatient stroke unit care most likely benefits a wide scope of stroke patients in many different ways, i.e., reducing death from secondary complications of stroke and reducing the urge for institutional care via reduction in disability.

**Keywords:** subgroups, fatality, patients, significant, scope

### Introduction

A performed systematic review which was investigating randomized trials have compared organized inpatient managed in a stroke unit care with alternative general care has demonstrated that stroke patients managed in an organized stroke unit setting are less likely to die, remain physically reliant, or need long-term institutional care [1]. These findings were astounding because the stroke units investigated did not routinely utilize any medical or surgical interventions that could be expected to influence the pathological process or immediate neurological complications of stroke disease. Besides, no routine surgical or medical therapies have yet appeared to be effective in acute stroke [2].

Earlier, a suggestion stated that stroke unit care might be effective through various mechanisms [3]. The provision of standardized assessment and early management protocols may allow a more precise diagnosis to be reached, more appropriate investigations, and more appropriate individual-patient care. Secondary complications of stroke (eg, chest infection, venous thromboembolism) could possibly be prevented through improved assessment procedures and early active rehabilitation. Also more intensive care and better coordinated rehabilitation procedures may help patients to achieve the best outcome. However, to date there has been no direct evidence to any of these proposals.

An improved comprehension of the manner by which stroke units apply their valuable impact on stroke outcomes is of significant clinical importance since it could clarify the mechanisms of improved recovery and therefore, important practical aspects of stroke care.

Furthermore, Stroke units differ in various places around the world [4]. Each builds according to local standards, needs, customs and public awareness. This is due to differences in acute stroke teams; telemetry monitoring; brain imaging; cerebral vasculature and cardiac imaging; early initiation of rehabilitation therapies; and certification by an independent body, including a site visit and disease performance measures [5]. A German stroke registers study group performed a

Voluntary network of 9 regional registers for monitoring quality of acute stroke care in Germany stated that differences in demographical and clinical characteristics regarding the probability of Stroke Units admission were observed [6].

Stroke Unit in Meilahti Tower Hospital, Helsinki, serves acutely cerebrovascular disorder patients who require special monitoring and treatment. Seven beds are monitored. Approximately 800 patients are treated in the unit [7]. Patients are admitted mainly via an emergency clinic. Patients can also be transferred from other wards if their treatment requires monitoring and treatment of patients with

cerebrovascular disorders. Catalan Stroke Program is an example of innovation. In Catalonia, reperfusion treatment rates have increased recently and currently are among the highest in Europe (17.3% overall, 14.3% for IVT, and 6% for EVT in 2016)<sup>[8]</sup>. Catalonia has 3 HASUs in Barcelona (approximately 1500 cases/year). Nearly half of the patients remain 2-3 days before they return to the hospital that transferred them.

London stroke unit has 8 HASU where all stroke cases get admitted for about 48 hrs.

Transfer from HASU to ASU when required<sup>[9]</sup>. A study of trends in stroke care and outcomes in- stroke unit in south of London found that patients who are managed in stroke units have potential advantages of ready access to high quality stroke care<sup>[10]</sup>. Another one that studied the impact and sustainability of acute stroke services in English stroke units concluded that Centralised models of acute stroke care (stroke units), where all stroke patients receive hyperacute care, can reduce mortality and length of acute hospital stay<sup>[11]</sup>.

A study that was performed in Australia examining 20,786 stroke events, 1182 (5.1%) occurred in-hospital (median age 77 years, 49% male) stated that patients with in-hospital stroke treated in Stroke Units died less often within 30 days<sup>[12]</sup>.

In this review we use data accessible from a collaborative systematic review of the available randomized trials of stroke unit care to identify the aspects of recovery for which stroke unit care showed to make the greatest effect.

### Specifically, we wanted to identify the following

1. Did stroke unit care decrease patient case fatality?
2. Did stroke unit care contributed in more patients surviving in a physically dependent state?

## Methods

### Systematic Review

The methods used for the collaborative systematic review of the randomized trials of stroke unit care have been portrayed previously. In summary, we identified randomized trials of organized inpatient (stroke unit) care for the period up to January 2014 using a number of search strategies. We intended to include all trials that compared management in an organized (stroke unit) setting with that of alternative care (usually given within general medical wards). The trial coordinators provided data in a standardized format regarding the trial attributes, patient selection characteristics, and the numbers of patients in every outcome group.

### Outcomes

The fundamental outcomes of interest in this analysis were (1) death, (2) the cause of death (i.e., certified diagnosis), (3) the last functional state (Rankin score or equivalent measure of dependency, and (4) the need for long-term institutional care (i.e., within the home of residence, nursing house, or hospital setting).

The primary cause of death that has been reported was included in the following seven categories: (1) Neurological: cause of death due to the index stroke or recurrent stroke, i.e., stroke, cerebral infarction, cerebral edema, recurrent stroke; (2) Cardiovascular: MI, CHF, cardiac arrhythmia, cardiac arrest; (3) Complications of

Immobility: any death that might be due to complication of immobility, i.e., sepsis (e.g. chest or urinary tract), venous thromboembolism, decubitus ulceration; and (4) other causes: other illnesses (e.g., malignancy).

### Statistical Methods

Patterns of fatality in cases, for which data was available, were analyzed over time as the proportion of patients, those who died at specific census times after the index stroke. This simple technique, offered a series of “snapshots” of outcomes at different census times, was beneficial because there was not enough individual patient data available for more sophisticated survival curve analysis.

Relative differences in outcomes were analyzed by calculating the odds ratio (OR) (plus the 95% confidence interval [CI]) of an adverse outcome occurring in the stroke unit group relative to the control (alternative medical care) group.<sup>13</sup> Risk difference was used to calculate the absolute outcome rates (i.e., the proportion of patients with a particular outcome) because this can give more clinical information to relative outcomes. However, when the results of the stroke unit and control groups were compared, all calculations of statistical significance were based on the statistic of the OR of that comparison<sup>[14]</sup>.

When information from multiple trials was used to calculate a summary outcome, the heterogeneity was calculated between the individual trial data contributing to that summary outcome using standard techniques. Non-significant heterogeneity tests ( $P > .05$ ) indicate that the results from the individual trials were all compatible with the summary result. Fixed effects statistical models were used unless heterogeneity tests were significant when a “random effects” model was used.

## Results

### Description of Trials

The search of a total of 48 trials of which 13 were excluded (Abissi 1995; Asplund 2000; Davis 2000; Di Lauro 2003; Durastanti 2005; Koton 2005; Langhorne 2001; Moloney 1999; Ricauda 2004; Ronning 1998a; Ronning 1998b; Silva 2004; Walter 2005), two were ongoing (Stone 1998; Wang 2004) and two were awaiting for further assessment (HAMLET 2009; Pearson 1988). The assessors agreed on including four trials (Guangdong 2008; Guangdong 2009; Huaihua 2004; Hunan 2007) and excluding four trials (Diagana 2008; Middleton 2006; Pappa 2009; Shiraiishi 2004). The assessors also agreed to exclude seven of the 31 trial in an attempt to avoid the risk of bias assessment. These seven trials performed informal randomization procedures (quasi-randomised) based on bed availability (Cavallini 2003; Strand 1985; von Arbin 1980; Yagura 2005), a strict admission Rota (Hamrin 1982; Patel 2000) or patient date of birth (Ronning 1998). Of the four trials that were awaiting further assessment or were ongoing at the time of the search, the assessors agreed on the exclusion of three trials as no outcome information was accessible (Pearson 1988; Stone 1998; Wang 2004) and one trial as no information about the comparison of intensive monitoring versus standard ward-based (HAMLET 2009). Therefore, this review incorporates an individual patient data analysis for 28 randomized controlled trials with 5855 participants<sup>[15]</sup>.

Typically all patients allocated to organized inpatient (stroke

unit) care received inpatient rehabilitation characterized by a period of (12 months) coordinated multidisciplinary rehabilitation by a professional team with a specialist interest in stroke disease and/or rehabilitation that had programs of education and training in stroke.

Most of the control patients (4807 of control patients) were exposed to some multidisciplinary rehabilitation in a mixed rehabilitation setting. A small number (1048) received conventional care in a general medical ward that did not incorporate the above characteristics. (Fig3) illustrates the results of the updated searches

### Case Fatality

Outcome data was available for all 28 trials (5855 participants) in which a novel organized inpatient (stroke unit) intervention was compared with an alternative (less-organized) care service. Case fatality recorded at the end of scheduled follow-up (median follow-up 12 months; range six weeks to 12 months) was less than the organized (stroke unit) care group in 21 of 28 trials <sup>[16]</sup>.

The total summary estimate was an OR of 0.76 (95% CI 0.66 to 0.88;  $P = 0.0001$ ). There was a subgroup interaction of a borderline significance ( $P = 0.04$ ) with more positive impacts seen in subgroups based on trials of stroke wards. When analysis was restricted to those trials in which scheduled follow-up was continued for a fixed period of six or twelve months (that is excluding Beijing 2004; Goteborg-Ostra 1988; Groningen 2003; Guangdong 2008; Guangdong 2009;

Illinois 1966; Montreal 1985; New York 1962; Orpington 1993; Orpington 1995), the overall OR was essentially unchanged (OR 0.80, 95% CI 0.69 to 0.93;  $P = 0.0001$ ) (Fig 1) illustrates the proportion of patients who were known to be dead at intervals after the index stroke. (Fig4) shows the analysis of patient characteristics on effectiveness of organized stroke unit care versus alternative service for the outcome of death by the end of scheduled follow-up.

To estimate the impact of stroke unit on patient death, institutional-care or dependency, a variety of predefined subgroup analyses were carried out based on service characteristics. Two different models of care (comprehensive stroke ward, mixed assessment or rehabilitation ward) tended to be more effective than the alternative (general medical) ward care. However, for the comparison of rehabilitation stroke wards or mobile team care (peripatetic service) versus general medical wards, there were no statistically significant differences <sup>[17]</sup>. Overall, stroke unit care showed reductions in the odds of death recorded at final (median one year) follow-up (OR 0.81, 95% CI 0.69 to 0.94;  $P = 0.005$ ) the odds of death or institutionalized care (OR 0.78, 95% CI 0.68 to 0.89;  $P = 0.0003$ ) and the odds of death or reliance (OR 0.79, 95% CI 0.68 to 0.90;  $P = 0.0007$ ). Interpretation of length of stay data was complicated by substantial heterogeneity. (Fig 2) shows the proportion of subjects living at home and the cumulative difference between stroke unit patients and the control group.

### Discussion

This article review is an updated version of a previous analysis of the randomized stroke unit trials <sup>[18]</sup>.

The first (hypothesis testing) component of this project used an a priori hypothesis that organized inpatient (stroke unit)

care is more effective than alternative care and obtained primary outcome data (death, institutionalization, dependency) from all relevant trials. All the primary outcomes were significantly less frequent among patients managed in an organized stroke unit setting compared with alternative care (usually in general medical wards). The current updated analysis aimed to identify the way in which these apparent benefits were achieved. This analysis is therefore considered to be more exploratory.

Many suggestions stated that organized stroke unit care might improve outcomes after a stroke in a more significant way compared to alternative care <sup>[19]</sup>. It has been considered that the initial stroke pathology and the immediate neurological on sequences of the stroke may be affected by a nonspecific intervention such as stroke unit care. However, some authors suggested that the repeated patterns of several common complications after stroke (in particular, cardiovascular complications, venous thromboembolism, and infections) may be affected <sup>[20]</sup>. although the current analysis appears to support this view, there is no sufficient statistical authority to give an unequivocal conclusion, even within this pooled analysis.

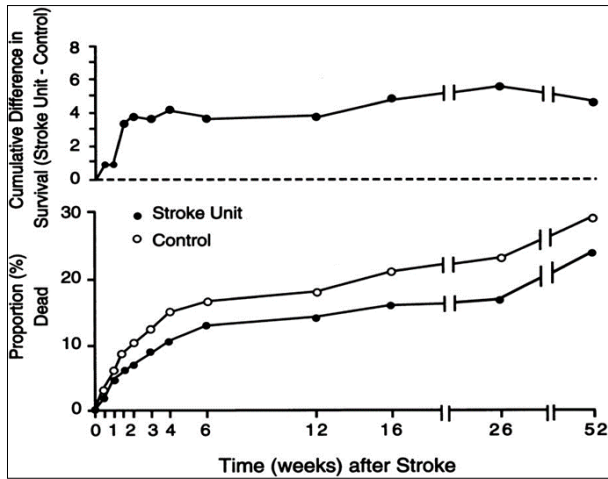
We had previously observed that organized stroke unit care resulted in a reduction in the requirement for long-term hospital or institutional care. This reduction could in theory have resulted from either a more aggressive discharge policy or from a reduction in the number of patients who remained disabled or immobilized (and therefore required institutional care).

Clearly the former is of doubtful clinical value, while the latter is of great therapeutic interest. The current analysis indicates that the reduction in the need for institutional care is largely attributed to a reduction in patient dependency. Across the range of levels of stroke severity observed, stroke unit care appeared to result in an increase in the numbers of survivors who were judged to be physically independent.

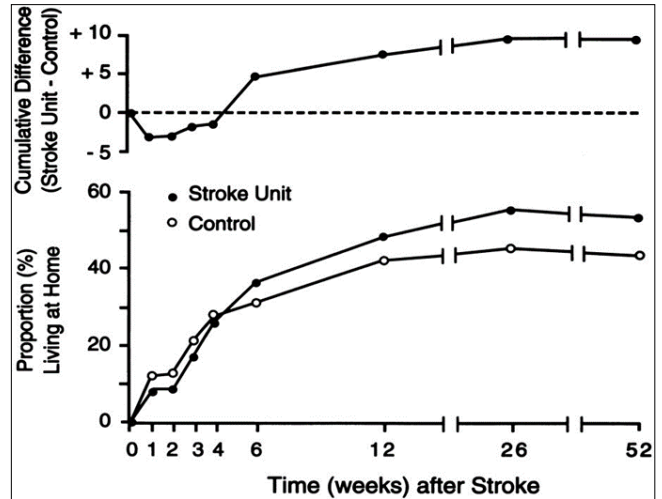
We can argue on how stroke unit care would reduce disability (dependency) after stroke. A more coordinated and focused program of rehabilitation involving patients and caregivers may well allow caregivers to better assist with the rehabilitation process to continue therapeutic strategies beyond formal therapy sessions and thereby allow more patients to achieve independence. Some but not all of the stroke units used a more intensive physiotherapy and occupational therapy input than alternative care. In addition, less tangible factors, such as the level of patient motivation and morale, may have been improved in the stroke unit setting. Observational

studies comparing patient activity within stroke unit and the general ward settings have indicated that stroke unit patients spend more of their time in more appropriate and purposeful activity.

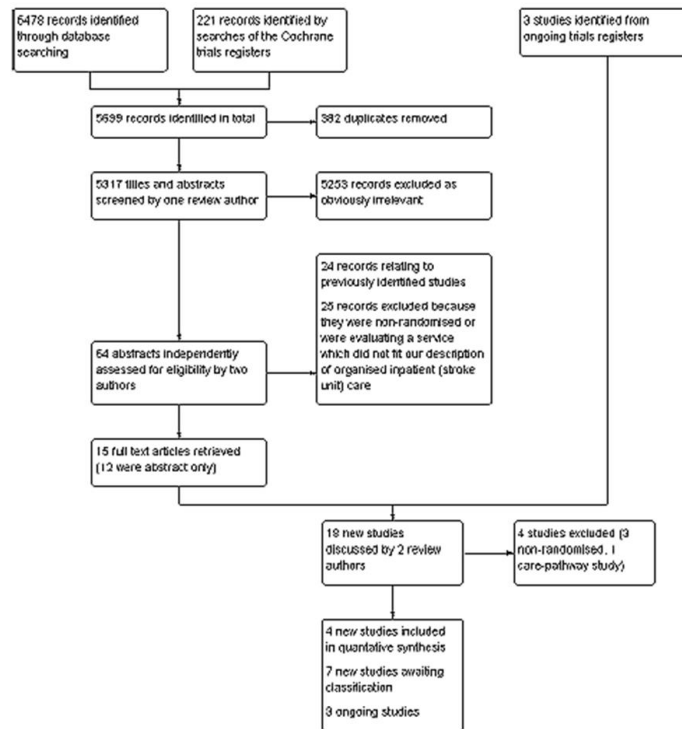
Finally, to summarize this updated analysis of a systematic review of the randomized stroke unit trials, the indicated apparent benefits of stroke unit care was probably attributable to the reduction in deaths caused by secondary complications of stroke (predominantly complications of immobility) and a reduced need for institutional care by reducing patient dependency <sup>[21]</sup>. The impact of stroke unit care appears to shift the distribution of all observed outcomes in a favorable direction <sup>[22]</sup>.



**Fig 1:** Proportion of patients known to be dead after the index stroke and cumulative difference between stroke unit and control subjects.



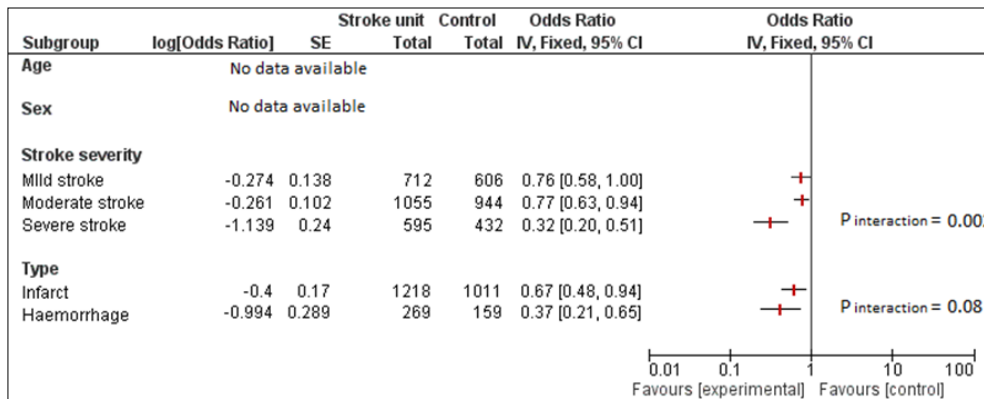
**Fig 2:** Proportion of patients living at home after the index stroke and cumulative difference between stroke unit and control subjects



**Fig 3:** Flow diagram illustrating the results of the updated searches

Subgroup	log[Odds Ratio]	SE	Stroke unit		Control		Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI	P interaction
			Total	Total	Total	Total			
<b>Age</b>									
Age up to 75 yrs	-0.151	0.175	482	417	0.86	[0.61, 1.21]	+	P interaction = 0.94	
Age over 75 yrs	-0.139	0.181	277	321	0.87	[0.61, 1.24]	+		
<b>Sex</b>									
Male	-0.315	0.203	312	313	0.73	[0.49, 1.09]	+	P interaction = 0.98	
Female	-0.329	0.186	350	315	0.72	[0.50, 1.04]	+		
<b>Stroke severity</b>									
Mild stroke	0.03	0.219	741	634	1.03	[0.67, 1.58]	+	P interaction = 0.03	
Moderate stroke	-0.261	0.111	1347	1233	0.77	[0.62, 0.96]	+		
Severe stroke	-0.616	0.141	640	471	0.54	[0.41, 0.71]	+		
<b>Type</b>									
Infarct	-0.386	0.199	985	760	0.68	[0.46, 1.00]	+	P interaction = 0.51	
Haemorrhage	-0.635	0.308	231	131	0.53	[0.29, 0.97]	+		

**Fig 4:** Analysis of patient characteristics on effectiveness of organized stroke unit care versus alternative Service for the outcome of death by the end of scheduled follow-up.



**Fig 5:** Analysis of patient characteristics on effectiveness of organized stroke unit care versus alternative Service for the outcome of death or dependency by the end of scheduled follow-up

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