Canadian Stroke Best Practices

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables

Stroke Unit Care

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ACUTE STROKE MANAGEMENT Writing Group

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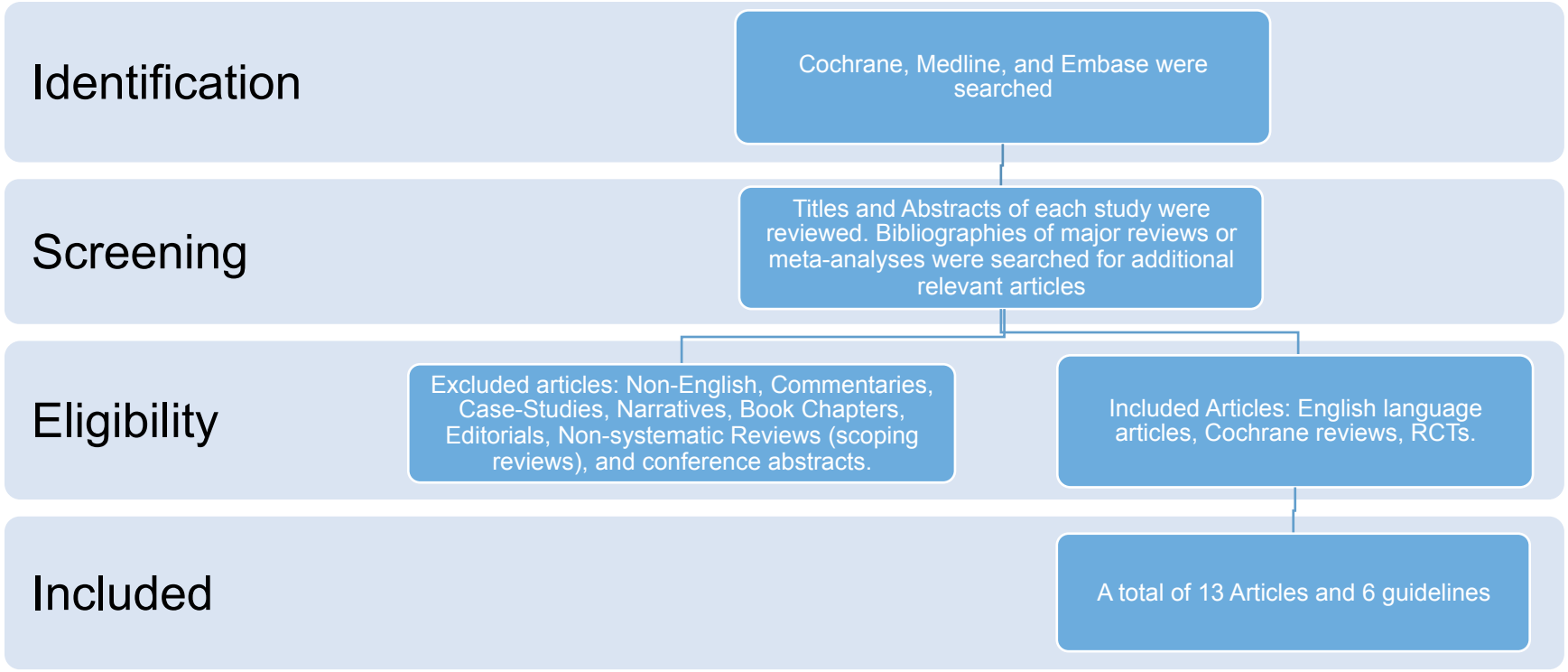
Search Strategy



Cochrane, Medline, and Embase were searched using the terms “stroke” and “stroke unit” OR “organized stroke care”. The title and abstract of each article was reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 13 articles and 6 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; on behalf of the American Heart Association Stroke Council. **2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke.* 2018; Mar;49(3):e46-e110**	Stroke Units 1. The use of comprehensive specialized stroke care (stroke units) that incorporates rehabilitation is recommended. Class I; LOE A. 2. The use of standardized stroke care order sets is recommended to improve general management. Class I; LOE B-N.
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation.	Strong recommendation All stroke patients should be admitted to hospital and be treated in a stroke unit with an interdisciplinary team. Strong recommendation New All acute stroke services should implement standardised protocols to manage fever, glucose and swallowing difficulties in stroke patients. Practice points • All stroke patients should be admitted directly to a stroke unit (preferably within three hours of stroke onset). • For patients with suspected stroke presenting to non-stroke unit hospitals, transfer protocols should be developed and used to guide urgent transfers to the nearest stroke unit hospital. • Where transfer is not feasible, smaller isolated hospitals should manage stroke services in a manner that adheres as closely as possible to the criteria for stroke unit care. Where possible, stroke patients should receive care in geographically discrete units.
Intercollegiate Stroke Working Party. National clinical guideline for stroke, 5th edition. London: Royal College of Physicians, 2016.	People with suspected acute stroke (including when occurring in people already in hospital) should be admitted directly to a hyperacute stroke unit and be assessed for emergency stroke treatments by a specialist physician without delay.

Guideline	Recommendations
Bernhardt et al. 2015 **Australian Commission on Safety and Quality in Health Care. Acute Stroke Clinical Care Standard. Sydney: ACSQHC, 2015.**	A patient with stroke is offered treatment in a stroke unit as defined in the Acute stroke services framework.
National Collaborating Centre for Chronic Conditions. Stroke. Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jul. 37 p. (Clinical guideline; no. 68).	Specialist Stroke Units All people with suspected stroke should be admitted directly to a specialist acute stroke unit following initial assessment, either from the community or from the A&E department. (An acute stroke unit is a discrete area in the hospital that is staffed by a specialist stroke multidisciplinary team. It has access to equipment for monitoring and rehabilitating patients. Regular multidisciplinary team meetings occur for goal setting).
Management of patients with stroke or TIA: assessment, investigation, immediate management and secondary prevention. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2008. 103 p. (SIGN publication; no. 108).	In-Hospital Care A - Stroke patients requiring admission to hospital should be admitted to a stroke unit staffed by a coordinated multidisciplinary team with a special interest in stroke care.

Evidence Tables

Organization of Care

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Stroke Unit Trialists' Collaboration 2013 **UK** **Cochrane Review**	NA	28 RCTs (n= 5,855), including participants admitted to hospital following acute stroke.	Comparisons between organized stroke unit care with alternative, less organized service, usually general medical wards. Acute stroke units included those that accept patients acutely but discharge early (usually within seven days) and were classified according to intensity of care: i) intensive care with intensive monitoring, ii) semi-intensive care, but with no life support facilities and iii) non-intensive care. Other forms of more organized care included combined acute and rehabilitation stroke units, mixed rehabilitation ward and mobile stroke teams.	**Primary Outcomes:** Death, dependency (e.g. mRI>3 or BI <18), and institutionalization at the end of scheduled follow-up. **Secondary Outcomes**: Quality of life, patient and carer satisfaction, and length of hospital stay.	**Stroke Unit vs. General Medical Ward** Stroke units were associated with a reduction in the risk of death 6-52 wk follow-up: OR= 0.81, 95% CI 0.69 to 0.94, p = 0.005. Results from 23 trials included. 5-yr follow-up: OR=0.74, 95% CI 0.59 to 0.94, p=0.01. Results from 3 trials included. 10-yr follow-up: OR=0.67, 95% CI 0.43 to 1.03, p=0.066. Results from 3 trials included. Stroke units were associated with a reduction in the risk of death/need for institutional care: 6-52 wk follow-up: OR= 0.78, 95% CI 0.68 to 0.89, p = 0.0003. Results from 20 trials included. 5-yr follow-up: OR= 0.5, 95% CI 0.33 to 1.05, p= 0.073. Results from 2 trials included. 10-yr follow-up: OR=0.57, 95% CI 0.37 to 0.88, p=0.012. Results from 2 trials included. Stroke units were associated with a reduction in the risk of death/dependency: 6-52 wk follow-up: OR= 0.79, 95% CI 0.68 to 0.90, p = 0.0007. Results from 19 trials included. 5-yr follow-up: OR=0.54, 95% CI 0.22 to 1.34, p=0.18. Results from 2 trials included. 10-yr follow-up: OR=0.70, 95% CI 0.27 to 1.80, p=.45. Results from 2 trials included. Stroke units were not associated with reductions in the length of stay in hospital and/or institutionalization: SMD= -0.08, 95% CI -0.23 to 0.06, p=0.26. Results from 13 trials included.
Ronning & Guldvog, 1998	CA: ☒ Blinding:	550 stroke patients, ≥60 years admitted to	Participants were randomized (on the basis	**Primary Outcome:** **Primary Outcomes:**	7-month outcomes: SU patients were hospitalized a median of 7.7 days

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Stavem and Ronning 2011 (follow-up to 1998) **Norway** **Quazi-Randomized Trial**	Patient ☒ Therapist ☒ Assessor ☒ ITT: ☑	hospital within 24hrs of stroke onset. Patients with subarachnoid hemorrhage or subdural hematoma were excluded.	of birth date) to receive care on a stroke unit (SU; n=271) or general medical ward (GMW; n=279).	Death, institutionalization, and number improved, deteriorated, or dead at 7-month follow-up. **Secondary outcome:** Long-term survival	vs. 9.5 days for GMW patients. Stroke units were not associated with a reduction in the risk of death (OR=0.87, 95% CI 0.59 to 1.28, p>0.05), the need for institutionalization (OR=0.95, 95% CI 0.60 to 1.52, p>0.05), deterioration (OR=0.63, 95% CI 0.30 to 1.33, or death/deterioration (OR=0.79, 95% CI 0.55 to 1.14) at 7-months. Patients treated on the stroke unit had significantly higher Scandinavian Stroke Scale scores and a lower incidence of recurrent stroke compared to patients treated on the general medical ward (p<0.05). Long-term outcome: Median follow-up period was 3.7 (range=0 to 13.3) yrs. There was no significant difference in long-term survival between groups (SU=90%, GMW=83%, p=0.15).
Di Carlo et al. 2011 **Italy** **Observational Study (EROS Project)**	NA	355 consecutive patients with a first-ever stroke. Patients with subarachnoid hemorrhage were excluded.	Patients were admitted to a stroke unit, which was provided in an 8-bed, semi-intensive, multidisciplinary care unit (n=140) or to a general medical ward (n=215).	**Primary Outcomes:** Death, death/dependency (Barthel Index = 0-9), and death/institutionalization.	Mean length of hospital stay was 12.5 (SU) and 13.1 (GMW), respectively Stroke unit care was associated with a reduction in the risk of 3-month mortality (RR=0.57, 95% CI 0.33 to 0.97) and 1-year mortality (RR=0.54, 95% CI 0.34 to 0.84). Stroke unit care was associated with a reduction in the risk of death/dependency at 3 months (RR=0.58, 95% CI 0.40 to 0.83) and 1 year (RR=0.65, 95% CI 0.48 to 0.89). Stroke unit care was associated with a reduction in the risk of death/institutionalization at 3 months (RR=0.53, 95% CI 0.33 to 0.86) and 1 year (RR=0.51, 95% CI 0.33 to 0.79).
Saposnik et al. 2011 **Canada**	NA	6,223 patients with a first-ever ischemic stroke admitted to one of 12 stroke centers	Consecutively admitted patients were admitted to either a stroke unit (n=4157) or a non-stroke	**Primary Outcome:** 30-day mortality **Secondary Outcomes:**	For all patients combined, 30-day mortality was 12.2%. Across all stroke types, patients treated in stroke

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Prospective Cohort Study		participating in a national stroke registry.	unit (n=2066): admissions decisions were based primary on bed availability. Patients were categorized according to the following stroke subtypes: cardioembolic, large artery disease, small vessel disease, or other.	7-day mortality, and death/institutionalization at discharge.	units had significantly reduced 30-day mortality, controlling for age, gender, comorbidity and stroke severity: cardioembolic (OR=0.46, 95% CI 0.36 to 0.59), large artery disease (OR=0.39, 95% CI 0.27 to 0.56), small vessel disease (OR=0.48, 95% CI 0.27 to 0.88), and other (OR=0.45, 95% CI 0.29 to 0.70), all at p<0.01. 7-day mortality and death/ institutionalization were also significantly reduced among patients treated on a stroke unit.
Seenan et al. 2007 **Systematic Review and Meta-analysis**	NA	25 observational studies comparing stroke unit care to non-stroke unit care (42,236 participants).	Comparisons of outcomes of patients treated in stroke units to those treated in non-stroke units.	**Primary Outcome:** 12-month mortality. **Secondary Outcome:** Poor outcome (death, discharge location other than home, dependence in daily activities).	Stroke units were associated with a reduction in the risk of death (OR=0.79, 95% CI 0.73 to 0.86, p<0.001). Results from 17 trials included. Using the results from 8 multi-centred trials only, stroke units were associated with a reduced risk of death (OR=0.82, 95% CI 0.77 to 0.87, p<0.001). Stroke units were associated with a reduction in the risk of a poor outcome (OR=0.87, 95% CI 0.80 to 0.95, p<0.01). Results from 15 trials included.
Silva et al. 2005 **Spain** **RCT**	CA: ☒ Blinding: Patient: ☒ Therapist: ☒ Assessor: ☒ ITT: ☒	530 patients with ischemic stroke or ICH consecutively admitted to a stroke unit within 24 hours of symptoms. Mean age: 70 years, 40% female.	Based on bed availability, patients were allocated to either) a conventional stroke unit (C-SU, n = 209) or a semi-intensive stroke unit (SI-SU, n = 321), which provided continuous monitoring of cardiac, respiratory, metabolic and neurological functions during the first 72 h. Both groups were treated following the same medical and nursing protocols.	**Primary Outcome:** Mortality, and combined mortality and dependency (mRS>2) at one year. **Secondary outcomes:** Mortality or mortality/dependency at hospital discharge and in-hospital complications	At 1 year, mortality and combined mortality and dependency were not significantly different between the two groups (SI-SU 48.7% vs. C-SU 45.8%, p>0.05). At 1 year, admission to SI-SU was associated with a lower risk of mortality in comparison with C-SU allocation (OR= 0.19, 95% CI, 0.07–0.54), among patients with more severe stroke. At hospital discharge, mortality or combined mortality and dependency were not significantly different between the two groups SI-SU 64.1% vs. C-SU 65.8%, p>0.05). More patients admitted to the SI-SU were diagnosed/treated for previously unknown atrial fibrillation, hypotension hyperthermia and hypoxemia.

CA Concealed allocation; ITT intention-to-treat

In-Hospital Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Cumbler et al. 2014 **Controlled study** **USA**	NA	21,349 patients who experienced an in-hospital ischemic stroke who were admitted to 1,280 hospitals participating in the Get with the Guideline Stroke registry from 2006-2012 and 928,885 patients admitted to hospitals from the community during the same time frame. The median age of patients in both groups was 73 years. Women experienced in-hospital stroke more frequently (54.3% vs. 51.9%, p<0.0001)	Comparison of risk factor profile, processes of care and outcomes between groups using univariate and multivariable methods.	**Primary outcome:** In-hospital mortality, discharge home, independent ambulation at discharge. For patients who received t-PA, symptomatic ICH, other serious complications	Patients who experienced in-hospital stroke were significantly more likely to have atrial fibrillation, prosthetic heart valve, heart failure, CHD/MI, diabetes, dyslipidemia and peripheral vascular disease and to be taking antihypertensive agents and cholesterol-lowering and diabetic medication. They were also more likely to have suffered a more severe stroke. Patients who experienced stroke onset in the community were significantly more likely to have experienced a previous stroke, HTN and to be a smoker. In-hospital stroke patients were significantly less likely to meet 7 achievement standards (t-PA within 3 hours, early antithrombotics, DVT prophylaxis, antithrombotics/anticoagulants on discharge, statin meds), and were less likely to receive a dysphagia screen or receive t-PA within 3.5-4.5 hours but were more likely to receive a rehab referral and receive intensive statin therapy. When quality/achievement measures were combined, in-hospital stroke patients were less likely to receive investigations/care for which they were eligible (82.6% vs. 92.8%, p<0.0001). In-hospital stroke patients were less likely to be independent in ambulation at discharge (adj OR=0.42, 95% CI 0.39-0.45, p<0.001), and to be discharged home (adj OR=0.37, 95% CI 0.35-0.39, p<0.001). The odds of mortality were higher (adj OR=2.72, 95% CI 2.57-2.88, p<0.001). More in-hospital stroke patients were treated with t-PA (11% vs. 6.6%). Among patients who received t-PA, the odds of symptomatic ICH were not increased significantly compared with community-onset patients (adj OR=0.84, 95% CI 0.66-1.08).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					The odds of being an independent ambulator at discharge, or being discharged home were significantly lower, while the odds of in-hospital mortality remained significantly higher.
Manawadu et al. 2014 **Controlled study** **UK**	NA	1,836 patients admitted to a single academic hospital from 2009-2010. 95% of patients experienced onset of stroke symptoms while living in the (n=1,752). 5% (n=84) of cases were in-hospital strokes of which 63% were early referrals (n-53) to a stroke specialist (within 3 hours of symptom onset) and 37% (n=31) were late referrals. The mean age of in-hospital stroke patients was 74 years, 51% were male. The median NIHSS score was 10.	Comparisons of outcomes of in-hospital stroke patients who were referred early vs. later to a stroke specialist.	**Primary outcome:** Excellent (mRS score 0-1) or favourable (mRS score 0-2) outcome at 90 days. **Secondary outcomes:** Symptomatic ICH in thrombolyzed patients, all-cause and stroke-related mortality at 90 days and medical complications.	Of the 84 in-hospital strokes, 78 were ischemic and 6 were hemorrhagic. Of these, 29 patients (34.5%) were treated with t-PA. Of the eligible in-hospital stroke patients, 49% early-referral were thrombolyzed compared with 10% of late referrals. A greater proportion of early-referral patients treated with t-PA experienced a favourable outcome (40% vs. 7%, p=0.001), but not an excellent outcome (17% vs. 3%, p=0.60). There were no differences in the proportion of early vs. late referral patients who were dead at 90 days. Independent predictors of an excellent or favourable outcome at 90 days among 78 patients with ischemic stroke included younger age, index diagnosis (admission for TIA or cardiac procedures vs. surgical procedures), higher baseline NIHSS score, and early specialist management (adj OR=1.04, 95%CI 1.01-1.46, p=0.007). Thrombolysis was not an independent predictor of a favourable outcome. Early referral to a stroke specialist was also an independent predictor of a favourable outcome among the whole cohort of in-hospital strokes (i.e. including ICH admissions) adj OR=1.13, 95% CI 1.10-1.27, p=0.002).
Cumbler et al. 2011 **Controlled study** **USA**	NA	116 patients who experienced an in-hospital ischemic stroke and 4,946 out of hospital stroke patients admitted to 16 hospitals in a single state participating in the Get with the Guideline	Comparisons of GWTG quality of care indicators of in-hospital vs. community-onset stroke patients (excluding thrombolysis)	**Primary outcome:** Adherence to 9/10 GWTG measures of quality of care measures **Secondary outcomes:** Adherence to individual GWTG measures	Mean NIHSS score was significantly higher among in-hospital stroke patients (9.5 vs. 7.0, p=0.01). A significantly greater proportion of in-hospital stroke patients received stroke education and stroke rehabilitation services. There were no differences between groups in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		(GWTG) Stroke registry, from 2005-2009. Mean age did not differ between groups (70.8 vs. 71.5) years.			percentage of patients who received smoking cessation counseling, antithrombotic treatment by day 2, anticoagulation therapy, DVT prophylaxis, cholesterol-lowering therapy or a dysphagia screen. A higher percentage of in-hospital patients received deficit-free care (a composite measure of all GTWT measures) 52.8% vs. 23.3%, p<0.0001.
Vera et al. 2011 **Prospective cohort** **Spain**	NA	273 patients admitted to 13 hospitals over a 1-year period (2008) who had experienced an in-hospital stroke. Mean age was 72 years, 57.1% were male.	Clinical characteristics, processes of care and outcomes were recorded	Time to neurological assessment/CT, thrombolysis with t-PA and in-hospital mortality	There were 210 cases of ischemic stroke, 37 TIAs and 26 hemorrhages. 45.8% of strokes were related to admissions for surgery or invasive vascular procedures. Median baseline NIHSS score was 7. Patients with ICH had higher median scores compared with ischemic stroke (14 vs. 9, p<0.001). Stroke risk factors: arterial HTN 65.2%, diabetes 34.1%, cardiac sources of embolism 50.5%, dyslipidemia 33%, current smoker 13.6%, 52% of patients received a neurological examination within 3 hours of symptom onset, 57.9% received a CT scan within 3 hours. 83 patients (30.3%) were assessed by a neurologist beyond 6 hours. 64 patients (30.5%) were eligible to received t-PA. Of these, 31 were treated and 31 were not, due to delays in calling the neurologist. The remaining 2 patients were treated with endovascular procedures. In-hospital mortality was 18.4% and was higher in patients admitted with ICH. In-hospital mortality associated with stroke was 82%.
Park et al. 2009 **Controlled study** **Korea**	NA	111 patients who developed an ischemic stroke during their admission to a single institution from 2002-2006 and 1,907 patients	Comparisons of clinical characteristics, stroke type and outcome of in-hospital vs. community onset stroke patients	In-hospital mortality, cause of death	The majority of in-hospital strokes occurred within 7 days of admission and were associated with cardiovascular surgeries. In-hospital patients tended to be younger (60.8 vs. 63.9 years, p=0.052), and were more likely to have

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		admitted to the same institution with ischemic stroke			a history of HTN and acute MI. In-hospital stroke patients were more likely to have suffered a cardioembolic stroke (41% vs. 21%), or stroke of undetermined etiology (7% vs. 3%). Fewer in-hospitals stroke patients were treated with t-PA (2.7% vs. 6.0%). A significantly higher number of patients died during hospital admission (19% vs. 2%, p<0.001). Sepsis was the most frequent cause of death among in-hospital stroke patients while brain herniation was the most common cause among community stroke onset patients.
Farooq et al. 2008 **Controlled study** **USA**	NA	2,743 patients included in an acute, state-wide stroke registry over a 6-month period in 2002 admitted to 15 hospitals. Of these, 177 patients experienced an in-hospital stroke and 2,566 were admitted with community onset.	Comparison of interventions, complications and outcomes between in-hospital stroke and community-onset stroke patients	In-hospital case fatality, mRS scores at discharge	There were no differences between groups in the distribution of ages, sex, race, stroke subtypes (ischemic vs. ICH), or initial imaging results, or in the number of stroke risk factors (previous stroke, atrial fibrillation, diabetes, HTN, dyslipidemia and current smokers). Significantly more in-hospital stroke patients had a history of MI/CHD and CHF. There were no differences between groups in the number of patients who received initial imaging within 25 minutes of stroke recognition or arrival to hospital (3.1% vs. 3.5%, p=0.27), treatment with t-PA (8.6% vs. 2.6%, p=0.28), cardiac monitoring, cerebral angiography, echocardiography, dysphagia screen or DVT prophylaxis. Fewer in-hospital stroke patients were discharged home (22.9% vs. 52.2%, p<0.01). Significantly fewer in-hospital stroke patients received cerebral vasculature investigations (55.2% vs. 75.6%, p<0.01), or lipid profile (23.6% vs. 38.0%, p=0.01). Significantly more in-hospital patients had a documented DVT/PE (6.4% vs. 1.0%, p=0.01) and pneumonia (15.9% vs. 5.2%, p<0.01).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					There were no differences in the number of patients receiving discharge treatment (anticoagulants/antithrombotics, lipid-lowering, diabetes or antihypertensive medications) or smoking cessation counseling. In-hospital case fatality was significantly higher among in-hospital patients (14.6% vs. 6.9%, p=0.04). The distribution of mRS scores was shifter towards poorer outcomes for the in-hospital group (p<0.001).
Kimura et al. 2006 **Controlled study** **Japan**	NA	15,815 consecutive patients included in the J-MUSIC registry. 694 (4.4%) experienced an in-hospital ischemic stroke and 15,121 (95.6%) were admitted with an acute ischemic stroke. All participants were admitted to 156 hospitals from 1999-2000.	Comparison of characteristics, risk factors and outcomes between in-hospital stroke and community-onset stroke patients	Case fatality rate, mRS score at discharge	In-hospital stroke patients were significantly older (73.4 vs. 70.4 years, p<0.0001) and there as a greater proportion of females (49.1% vs. 38.1%, p<0.0001). A higher percentage of in-hospital stroke patients had a history of stroke (42.6% vs. 30.1%, p<0.0001) and atrial fibrillation (34.6% vs. 20.4%, p<0.0001). There were no differences between groups in the percentage of patients with HTN or diabetes. The mean admission NIHSS score was significantly higher for patients with in-hospital stroke (14.6 vs. 8.1, p<0.0001). In-hospital stroke was an independent predictor of severe stroke defined as NIHSS score ≥11 (OR=3.27, 95% CI 2.7-3.88, p<0.0001). Significantly more in-hospital stroke patients died in hospital (19.2% vs. 6.8%, p<0.0001) and within 28 days (12.1% vs. 4.8%, p<0.0001). The distribution of mRS scores was shifted towards poorer outcomes for the in-hospital group (p<0.0001). In-hospital stroke was an independent predictor of death at discharge (OR=1.44, 95% CI 1.11-1.84, p=0.003).

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