Evidentiary Table: Use of a Stroke Scale

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Mosley 2007[1]	II	Prospective non-randomized trial	198 patients in 6 months with a stroke or TIA were assessed. Ambulance calls were evaluated for factors leading to faster evaluation in the hospital.	GCS <13, paramedic stroke recognition, and hospital prenotification led to shorter times from ambulance call to first medical assessment	Limited by paramedic's ability to identify strokes in the fields
Gropen 2014[2]	II	Retrospective Review	Review of ambulance and hospital records of patients with a discharge diagnosis of stroke to compare EMS impression with discharge diagnosis.	Stroke was confirmed in 18% of patients and missed by EMS half the time. Sensitivity improved with documented CPSS, motor signs and NIHSS quartile.	Retrospective
Oostema 2015[3]	II	Prospective cohort, non-randomized trial	441 EMS-transported patients were evaluated. Discharge diagnosis was compared with EMS diagnosis.	EMS sensitivity was 73% and PPV was 52%. Sensitivity improved when CPSS was documented. Half of EMS suspected strokes were false positives.	Does not assess dispatcher role of stroke assessment
Nor 2004[4]	II	Prospective Non-randomized trial	278 suspected stroke patients with 217 confirmed strokes were identified by paramedics and stroke physicians using the FAST scale.	Paramedics versus stroke physicians observed facial weakness 68% versus 70%, arm weakness 96% versus 95%, and speech disturbance 79% versus 77%	Did not assess strokes missed by the FAST scale in the field
Purrucker 2014[5]	II	Retrospective non-randomized cohort trial	Of 9154 emergency runs, 689 prehospital 'suspected central nervous system disorders' were evaluated. Retrospective assessment of CPSS, FAST, LAPSS, MASS, Med PACS, ROSIER, KPSS, LAMS, sNIHSS-5 were done	CPSS and FAST had a sensitivity of 83% and 85% and a specificity of 69% and 68%. LAPSS, MASS, and Med PACS had specificity 92-98% with sensitivity 44-71%. ROSIER sensitivity was 80%, specificity 79%. LAMS had low sensitivity	Retrospective

Harbison 2003[6]	II	Prospective non-randomized trial	Compared 487 patients with strokes or TIAs who were admitted via ambulance, PCDs and through the ER	Paramedics' stroke diagnosis was correct in 79% of stroke patients Paramedics referred more total anterior circulation strokes than PCDs (39% vs 14%) and fewer lacunar strokes (14% vs 31%) and admitted more patients within 3 hours of symptom onset	Only ¼ of stroke patients referred to the ER against protocol had the FAST completed
Kothari 1999[7]	II	Prospective non-randomized	Prehospital providers performed the CPSS and compared stroke analysis on 171 patients, 860 times	The scale demonstrated 88% sensitivity for patients with anterior circulation strokes, with 66% sensitivity for each one of three stroke scale items and 87% specificity. It was reproducible between physicians and prehospital personnel	Relatively small sample size, only 49 patients had a diagnosis of stroke or TIA. Only four prehospital providers were used.
Bray 2005[8]	II	Prospective non-randomized	18 paramedics assessed 73 stroke patients and 27 stroke mimics with the Melbourne ambulance stroke screen (MASS)	The MASS was 90% sensitive and 74% specific, and all patients misidentified by the MASS were ineligible for thrombolytic therapy	Small sample size. Only 100 patients were included in the study.
Asimos 2014[9]	II	Retrospective database search	Calculated sensitivity, specificity, and positive and negative likelihood ratios for EMS diagnosis of stroke for CPSS and LAPSS based on 1217 CPSS patients and 1225 LAPSS patients evaluated by 117 EMS agencies	CPSS had a sensitivity of 80% versus 74% for LAPSS. CPSS and LAPSS both had specificities of 48%.	Retrospective study. TIAs were included which could be a false diagnosis based on prehospital assessment with CPSS or LAPSS.
Mingfeng 2012[10]	II	Prospective non-randomized	540 patients were assessed by emergency physicians using either the ROSIER or the CPSS to determine the sensitivity, specificity, PPV, NPV, related coefficient and kappa value based on final discharge diagnosis.	CPSS sensitivity was 88.77%, specificity was 68.79%, PPV was 87.40%, NPV was 71.52%, and r was 0.503. ROSIER had a sensitivity of 89.97%, specificity of 83.23%, PPV of 92.66%, NPV of 77.91%, and r of 0.584. Kappa of ROSIER was 0.718. Kappa of CPSS was 0.582.	Done by emergency physicians, not in the prehospital setting.
Bray 2010[11]	II	Prospective Non-randomized, cross-sectional	Paramedics performed MASS on 850 of 5286 emergency transports including 199 of 207 confirmed stroke or TIA patients.	For patients with documented MASS, sensitivity was 93% and specificity was 87%	MASS was not performed on all neurologically compromised patients

Ramanu-jam 2008[12]	II	Retrospective observational study	Assessed the sensitivity and predictive values of EMD and paramedic recognition of stroke based on stroke neurologist or hospital discharge diagnosis.	882 patients were determined to have stroke by MPDS Stroke protocol. Sensitivity was 83%, PPV was 42%. Paramedics assessed 477 strokes using CPSS, giving a sensitivity of 44% and PPV of 40%.	No NPV or specificity were assessed.
Studnek 2013[13]	II	Retrospective observational study	Assessed the sensitivity and specificity of Med PACS and CPSS in a single EMS agency by analyzing EMR and Get With the Guidelines Stroke registries.	416 patients were enrolled, of which 186 had a stroke. Med PACS had a sensitivity of 0.742 and specificity of 0.32. CPSSS had a sensitivity of 0.79 and specificity of 0.239.	Retrospective chart review
You 2013[14]	II	Retrospective analysis of a prospective registry database of consecutive patients	EMTs performed CPSS on patients. Those results were compared to NIHSS scores and tPA usage.	There was a strong correlation between CPSS and NIHSS scores within 3 hours and 6 hours of symptom onset. A CPSS score of 2 or greater predicted tPA use.	Study was done in the ED. Inter-observer reliability was not studied. Changes could have occurred between assessment by CPSS and NIHSS.
Katz 2015[15]	II	Retrospective analysis	The Cincinnati Prehospital Stroke Severity Scale was derived to identify LVO strokes based on 2 NINDS tPA Stroke Study trials data set.	CPSSS had an area under the curve of 0.89, score greater than or equal than 2 was 89% sensitive, 51% specific with positive LR of 3.3 and negative LR of 0.15 in predicting severe stroke.	Test was not prospectively validated
Kidwell 2000[16]	II	Prospective, non randomized trial	Paramedics were trained in LAPSS and stroke identification was compared with emergency department and final hospital discharge diagnosis.	1298 runs were analyzed, of which 34% were for nontraumatic, noncomatose neurologic complaints. LAPSS was done on 206 patients with sensitivity of 91%, specificity of 97%, PPV of 86%, and NPV of 98%.	LAPSS forms often not completed on patients with neurological complaints thought not to be stroke
Kidwell 1998[17]	II	Retrospective validation	Designed and retrospectively tested the LAPSS. Also tested the amount of time that would have been saved had LAPSS been used.	38 of 41 patients with acute ischemic stroke would have been accurately identified by LAPSS. 1 hour and 50 minutes would have been saved if paramedics had identified stroke and administered neuroprotective drugs.	Retrospective without prospective validation. Small sample size.

Nazliel 2008[18]	II	Retrospective chart review	Data was drawn from consecutive patients enrolled in acute stroke clinical trials at the UCLA Stroke Center and patients entered into the UCLA Get with the Guidelines Stroke Registry. LAMS scores were derived from the NIHSS and physical exam entered.	119 patients were evaluated with 62% with PLVOs. LAMS scores were higher in patients with PLVOs, as were NIHSS stroke severity scores. At 4 or higher, LAMS score had a sensitivity of 0.81, specificity of 0.89 and accuracy of 0.85. Positive LR of LAMS greater than or equal than 4 was 7.36 and negative LR was 0.21.	No prospective and not done in the field by paramedics.
Llanes 2004[19]	II	Retrospective analysis	LAMS was constructed by assigning point values to LAPSS and it was analyzed to assess ability to predict long-term outcomes.	90 patients were studied. LAMS scores correlated closely with NIHSS scores and three-month functional outcomes.	Small sample size, retrospective analysis.
Fothergill 2013[20]	II	Prospective nonrandomized trial	Ambulance clinicians used ROSIER to assess patients with suspected stroke. That was compared with stroke neurologist diagnosis.	312 patients were assessed. 64% of strokes and 78% of nonstrokes identified by ambulance clinicians were confirmed by stroke neurologists. There was no difference in ROSIER and FAST.	Not all stroke patients were assessed with ROSIER.
Tirschwell 2002[21]	II	Retrospective Data Analysis	Derived and validated shortened versions of the NIHSS from data from two acute stroke clinical trials to identify a subset of clinical features that measures stroke severity and predicts outcome.	Right leg item, left leg, gaze, visual fields, language, level of consciousness, facial palsy, and dysarthria were most predictive of good outcome at three months after a stroke.	Tested the scale's ability to predict outcome, but not ability to identify a stroke.
Jang 2014[22]	II	Retrospective analysis of a prospective registry database	The Kurashiki prehospital stroke scale was assessed by EMTs in the emergency department to generate a cutoff KPSS score for candidates of thrombolysis	There was a strong correlation between KPSS and NIHSS within 6 hours and 3 hours of hospital admission. A KPSS score greater than or equal to 3 predicted tPA usage with OR 125.598; 95% CI 16.443-959.368 $p<0.0001$	Retrospective analysis. EMTs did their assessment in the ED. No inter-observer reliability was established.
Kimura 2008[23]	II	Prospective non randomized trial	Studied the Kurashiki prehospital stroke scale as assessed by EMTs on site and compared it to NIHSS score as determined by neurologists at the time of patient's arrival to the hospital.	90 consecutive patients were enrolled, 71 of whom had a stroke. KPSS score of 3-9 predicted tPA therapy with sensitivity of 84% and specificity of 93%.	Small sample size. Didn't include patients on whom the stroke scale was not done.

Yamashita 2011[24]	II	Retrospective Study	Univariate analysis followed by multivariate analysis to identify factors leading to ischemic stroke over hemorrhagic stroke.	227 patients were included with either ischemic or hemorrhagic strokes. Atrial fibrillation, diastolic blood pressure less than 100 mm Hg and lack of disturbance of consciousness were associated with ischemic stroke. KP3S greater than 1 had a sensitivity of 64% and specificity of 85% for ischemic stroke.	Retrospective analysis of consecutive patients
Iguchi 2011[25]	II	Prospective non randomized trial	KPSS score was evaluated by paramedics. NIHSS was evaluated by stroke neurologists on admission.	238 patients with ischemic stroke or TIA were analyzed. 147 were mRS 0-1 prior to stroke onset. Those demonstrated strong correlation between KPSS and NIHSS scores. KPSS predicted clinical outcome at 3 months with mRS score.	There may be interrater variability of mRS measurement.
Iguchi 2011[26]	II	Prospective non randomized trial	Analyzed paramedic assessment by KPSS versus in hospital assessment with NIHSS.	430 patients were included. There was excellent correlation between KPSS and NIHSS. KPSS score of 4 or more predicted IV tPA usage.	Not all patients were assessed with the KPSS
Hasegawa 2013[27]	II	Prospective nonrandomized trial	Developed the Maria Prehospital Stroke Scale (MPSS) including facial droop, arm drift, and speech disturbances, giving a grade from 0 to 5.	1057 patients were scored by EMTs. MPSS correlated with NIHSS. Onset-to-door time was longer with a low MPSS score. Rate of thrombolytic therapy correlated with increasing MPSS.	Delay from MPSS to NIHSS

Perez de la Ossa 2014[28]	II	Retrospective cohort development followed by prospective validation	Develop and validate the Rapid Arterial oCclusion Evaluation (RACE) scale based on the NIHSS items predictive of LVO.	654 patients with acute ischemic stroke were used to develop the scale. Then 357 patient transferred by EMS and assessed by neurologists were used to validate it. RACE includes facial palsy, arm motor function, leg motor function, gaze, and aphasia or agnosia. RACE showed strong correlation with NIHSS. RACE scale greater than or equal to 5 had sensitivity of 0.85, specificity of 0.68, PPV 0.42 and NPV 0.94 for detecting LVO.	Paramedics did not perform the RACE scale on 60% of patients transported by EMS.

Evidentiary Table: Blood Glucose Evaluation

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Jauch 2013[29]	I	Review	American Heart Association review of literature to make recommendations on care of acute stroke patients	Recommendations for care of stroke patients during identification, transport and hospital stay.	Review article, not a primary study.
Abarbanell 2005[30]	II	Retrospective review	All calls involving possible stroke for a 24 month period were included. Patient's blood glucose was measured and CPSS was assessed.	9495 paramedic run reports were reviewed including 185 possible strokes. 5 were hypoglycemic with BG less than 60 mg/dL. All were known diabetics.	Retrospective study. Didn't comment on hyperglycem-ia, which can also cause neurologic symptoms.
Shirayama 2004[31]	III	Case report	Case report of a 58 year old male with diabetes who presented with left hemiplegia when he injected 500 U of regular insulin subcutaneously in a suicide attempt.	Plasma glucose was 0.9 mmol/l and serum insulin was 1148 pmol/l. IV 10% glucose was given at 160 ml/h and returned the plasma glucose to 6.7 mmol/l in 15 minutes. Diffusion-weighted MRI showed increased signal intensity in the pons and patient was treated with IV argatroban. Patient's hemiplegia resolved within 48 hours.	Single case report. Increased signal intensity could have been due to ischemia from vasospasm or infarction, but angiography was not done.
Terakawa 2007[32]	III	Case report	63 year old male with a history of diabetes controlled by subcutaneous insulin 22 U daily awoke with right hemiparesis	Diffusion weighted MRI shoed hyperintense areas in the left internal capsule and the splenium of the corpus callosum. Plasma glucose was 24 mg/dL. Right hemiparesis resolved after administration of glucose. Repeat MRI 28 hours later showed normalization.	Single case report.
Wallis 1985[33]	III	Case Series	16 patients thought to have had a stroke had hypoglycemia.	Hypoglycemia caused hemiplegia that was reversible with correction of the hypoglycemia.	Small number of patients.
Yong 2012[34]	II	Review and two case reports	Systematic review of EMBASE and Medline for reports of adults with symptomatic hypoglycemia.	42 papers described CT or MRI in 65 patients plus two cases reported in the paper.	Small number of cases

Yoshino 2012[35]	II	Review and one case report	Case report and literature review including about 200 cases.	The most common neurologic deficit was right sided hemiparesis. Internal capsule or splenium of the corpus callosum most frequently had imaging abnormalities. Hemiparesis developed at an average of 1.8 mmol/L. 89 year old man with diabetes with hypoglycemic right hemiparesis and dysarthria with glucose of 1.8 mmol/L experienced resolution of his symptoms with 40 mL of 40% dextrose.	Review and case report, not a prospective study. No causation determined.
Malouf 1985[36]	II	Prospective nonrandomized trial	125 patients visited the Harlem Hospital Emergency Room for symptomatic hypoglycemia and symptoms were recorded.	65 had obtundation, stupor or coma, 38 had confusion or bizarre behavior, 10 were dizzy or tremulous, 9 had seizures, and 3 had hemiparesis.	Small sample size.
Adler 1986[37]	II	Prospective clinical trial	51 patients, 23 known diabetics and 28 not diabetic were given 1 ampule of dextrose 50% to quantify the rise in blood glucose from that treatment.	There was no statistically significant difference between the two groups. The mean rise in glucose was 166 mg/dL 3-5 minutes after glucose administration.	Some patients in the study were hyperglycemic and others were hypoglycemic. They were not analyzed separately. Etiology of baseline glucose level was not addressed.
Balentine 1998[38]	II	Prospective interventional study	25 healthy employee volunteers between the ages of 25 and 40 were given an IV bolus of 25 grams of 50% dextrose to determine the effect on blood glucose at 5 minutes, 15 minutes, 30 minutes, 1 hour, and 2 hours.	Mean baseline serum glucose was 82 mg/dL Mean post-infusion levels were 244 (4 min), 145 (15 min), 88 (30 min), 77 (60 min) and 83 (120 min). Thus, the D 50 had an effect for 30 min.	Study used healthy volunteers, not patients with altered mental status, neurological deficits or hypoglycemia
Ntaios 2011[39]	II	Retrospective Cohort Study	Analyzed patients in two groups – those with glucose less than or equal to 7.3 mmol/l or greater than 7.3 mmol/l at 24-48 hours after last known well time before a stroke.	Included 1984 patients with ischemic stroke. There was no statistically significant difference in favorable outcome between the two groups, as measured by mRS less than or equal to 2 at three months. Poor outcome was associated with age, NIHSS score on admission, prehospital mRS, antidiabetic drug usage, and glucose on admission.	Retrospective study using a database that had previously been established. Not interventional.

Gentile 2006[40]	II	Retrospective study	Retrospective study of patients who were hyperglycemic who suffered stroke to determine the effect of hyperglycemia and glycemic control on mortality.	Study of 960 patients with thromboembolic stroke, 373 of which were hyperglycemic. Admission hyperglycemia was associated with increased mortality. Persistent hyperglycemia during first 48 hours led to higher mortality, and glycemic control led to decrease in mortality.	Hyperglycemia was defined as BG greater than or equal to 130 mg/dL. Didn't investigate the difference between spontaneous normalization of glucose and intervention.
Baird 2003[41]	II	Prospective observational study	Studied blood glucose after acute ischemic stroke as it correlated with infarct volume changes using T2- and diffusion-weighted MRI. Continuous glucose monitoring was done on 25 patients after ischemic stroke. MRI and physical exams were done at 15 hours, 5 days and 85 days.	Mean continuous glucose monitoring correlated with infarct volume change between 15 hour and 5 day time points. Glucose also correlated with 85 day NIHSS and mRS.	Did not study intervention leading to improved glucose control.
Ribo 2007[42]	II	Prospective non-randomized trial	Studied 47 patients with transcranial Doppler documented artery occlusion treated with IV tPA to determine if hyperglycemia (>140 mg/dL) was associated with worse outcome.	48 hour NIHSS was higher in patients with hyperglycemia during occlusion time. Hyperglycemia was correlated with DWI growth on MRI.	10 patients were hyperglycemic on admission, 24 developed hyperglycemia. Small sample size. Low cutoff for hyperglycemia (>140 mg/dL).
Bruno 1999[43]	II	Observation of glucose in placebo controlled, randomized, double-blind trial treating acute ischemic stroke with low-molecular weight heparinoid	Analysis of the relationship between glucose and clinical outcome in 1259 patients enrolled in the Trial of ORG 10172 in Acute Stroke Treatment (TOAST).	Higher admission blood glucose was associated with worse outcome at three months in all strokes combined and nonlacunar strokes as assessed by Glasgow Outcome Scale, Barthel index, and NIH Stroke Scale.	Did not test intervention for hyperglycemic control

Bruno 2002[44]	II	Review of Stroke Trial data	Analysis of the effect of admission glucose on clinical outcome after acute ischemic stroke using the National Institute of Neurological Disorders and Stroke recombinant tissue plasminogen activator Stroke Trial data.	624 patients were included. Increasing admission glucose led to increased odds for symptomatic ICH. Increased glucose led to worsening odds of neurologic improvement as assessed by NIHSS improvement of 4 points or more, Glasgow Outcome score of 1, or Barthel Index 95 to 100 at 3 months.	Did not study intervention to control blood glucose
Els 2002[45]	II	Prospective observational trial	Observed hyperglycemia versus normoglycemia in patients admitted with stroke and treated with rtPA. Measured the NIHSS and MRI.	NIHSS was 4 in the normoglycemic group versus 7.4 in the hyperglycemic group at day 28. Infarction volume increased more as assessed by MRI in the hyperglycemic patients.	Small sample size. Only 14 hyperglycemic patients and 17 normoglycemic patients were evaluated.
Cucchiara 2008[46]	II	Review of data from Multicenter Recombinant Tissue Plasminogen Activator Stroke Survey Group	Developed a score to predict risk of post thrombolysis ICH. Score gave one point to each variable – age greater than 60 years, baseline NIHSS greater than 10, glucose greater than 8.325 mmol/L, and platelet count less than 150,000/ mm(3).	Rate of ICH increased with increasing scores on the scale. 0 points led to 2.6% rate of ICH, 1 point, 9.7%, 2 points 15.1%, greater than or equal to 3 points 37.9%.	Only a few factors were assessed. Continuous variables were dichotomized. Score has not been validated on an outside population.
Pundik 2008[47]	II	Database review – retrospective analysis of prospectively collected data	488 consecutive patients with ischemic stroke who received thrombolytic therapy to determine factors causing symptomatic ICH.	Hyperglycemia (>150 mg/dL) increased the odds of symptomatic ICH. There was no difference in rates of symptomatic ICH in patients older than 80 years old versus younger than 80 after controlling for route of administration, NIHSS, mean arterial pressure and glucose.	Only assessed a limited number of factors.

Evidentiary Table: Supplemental Oxygen

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Sulter 2000[48]	II	Prospective Non-randomized Trial	49 patients with acute hemiparetic strokes were monitored for 48 hours with pulse oximetry and treated with oxygen via nasal prongs or oxygen mask if their arterial oxygen saturation fell beneath 96% for more than 5 minutes.	31 patients desaturated. 28 were effectively treated with a flow rate of 5 L/min. 3 required 6-10 L/min. Oxygen desaturation occurred more frequently in patients with more severe strokes, patients with dysphagia and older patients.	Difficult to assess potential pathological effects of oxygen free radial formation.
Ronning 1999[49]	I	Quasi-randomized prospective trial	Patients who had suffered a stroke within 24 hours were randomized to treatment or control based on birth numbers. Treatment group received supplemental oxygen, 100% atmospheres, 3 L/min for 24 hours. Control group received no supplemental oxygen.	One year survival was 69% in the treatment group and 73% in the control group. Barthel Index scores were similar in the two groups at 7 months. For patients with Scandinavian Stroke Scale (SSS) scores of greater than or equal to 40, 82% in the treatment group and 91% in the control group survived. For those with less than 40, 53% in the treatment group and 48% in the control group survived.	Some patients in the treatment group did not receive oxygen for the full 24 hours and some patients in the control group received oxygen from the paramedics prior to arrival at the hospital.
Singhal 2005[50]	I	Prospective randomized trial	Patients with acute stroke were randomized to high-flow oxygen therapy via facemask for 8 hours or room air. 9 patients were in the treatment group. 7 patients were in the control group.	Stroke scales were similar at baseline and at 3 months. Stroke scales improved in the treatment group at 4 hours, 24 hours, and 1 week. Diffusion MRI lesion volumes were smaller in hyperoxia treated patients at 4 hours, but not subsequently.	Small sample size.
Branson 2013[51]	II	Review	Review of literature on the use of oxygen for various pathologies.	Routine use of oxygen after stroke shows no clear benefit.	Review article, not a primary study.

Evidentiary Table: Patient Positioning

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Feldman 1992[52]	II	Prospective interventional study	22 head-injured patients were placed in different positions – head elevated to 30 degrees or 0 degrees.	The higher the ICP with the patient positioned at horizontal, the greater the reduction in ICP when the patient was positioned at 30 degrees. CBF fell from a mean of 67 at 0 degrees to 50 at 30 degrees. MCP (83 versus 90) and ICP (18 versus 22) were lower with head elevated.	Small sample size. MCP was extrapolated by using MABP recorded with the transducer placed at the level of the foramen of Monro.
Ng 2004[53]	II	Prospective interventional trial	38 patients with severe closed head injury were studied by placing them in different bed positions and measuring physiological parameters.	ICP was lower at 30 degrees than 0 degrees. MAP was unchanged. CPP was slightly higher at 30 degrees. Global venous cerebral oxygenation and regional cerebral oxygenation were not significantly affected by head position.	Small sample size. Did not assess stroke patients.
Favilla 2014[54]	II	Prospective interventional trial	17 patients with unilateral acute ischemic strokes in the anterior circulation were put into different bed positions. CBF and arterial flow velocity were measured with diffuse correlation spectroscopy and transcranial Doppler ultrasound.	CBF decreased by 17% in the ipsilesional and 15% in the contralesional hemispheres when the head of bed was moved from flat to 30 degrees. There was no significant change in blood velocity.	Small sample size.
Schwarz 2002[55]	II	Prospective interventional trial	18 patients with MCA territory strokes were monitored in 43 sessions for MAP, ICP, MCA peak mean flow velocity (VmMCA) at 0 degrees, 15 degrees, and 30 degrees for 5 minutes each.	MAP went from 90 mm Hg to 82 to 76 at 30 degrees. ICP went from 13 at 0 degrees to 12 to 11 at 30 degrees. CPP decreased from 77 to 70 at 15 degrees to 64 at 30 degrees. VmMCA decreased from 72 to 67 to 61 at 30 degrees on the affected side.	Small sample size.
Hunter 2011[56]	II	Prospective interventional trial	8 patients 24 hours after ischemic stroke were studied with MCA transcranial Doppler monitoring as the head of bed was positioned at 0, 15, and 30 degrees.	MFV increased from 51 cm/s at 30 degrees to 55 cm/s at 15 degrees to 85 cm/s at 0 degrees.	Small sample size

Wojner-Alexander 2005[57]	II	Prospective interventional trial	20 patients with median NIHSS score of 14 were positioned with head of bed at different heights and physiological parameters were measured.	MAP and heart rate did not change. MCA MFV increased 20% as head of bed was lowered from 30 degrees to 0 degrees.	Small sample size.
Ouchi 2001[58]	II	Prospective interventional trial	Physiological parameters in 22 patients with minor unilateral internal carotid or middle cerebral artery occlusion were studied as position was changed.	rCBF was reduced in the cortical and subcortical regions distal to the artery occlusion when patients were sat upright. Magnitude of rCBF reduction correlated positively with local tissue oxygen extraction fraction and negatively with metabolic rates of oxygen.	Small sample size.
Hargroves 2008[59]	II	Prospective interventional trial	7 patients who had suffered a middle cerebral artery cortical ischemic stroke within 7 days were put in different positions for 15 minutes each and physiological parameters were measured with optodes. They were moved from supine lying to 45 degrees with legs straight to supine lying to sitting upright to supine lying.	There were no changes in heart rate or oxygen saturations. Cortical cerebral oxygenation was lowest when sitting upright using as measured by TOI using NIRS.	Small sample size.
Rowat 2001[60]	II	Prospective interventional trial	129 patients with acute strokes were put into 5 different positions to observe arterial oxygen saturation and heart rate. They were sat upright in a chair, sat up in bed, laid supine, laid on paretic and non-paretic sides.	Lying on the left side caused slightly lower SaO2 than lying on the right side. Patients able to sit in a chair had a higher mean SaO2 and heart rate when sitting upright. Hypoxia was most common on the left side.	Half of the patients were deemed to ill to be out of bed. Did not assess baseline comorbidities that could have caused desaturations.
Eliza-beth 1993[61]	II	Prospective interventional trial	10 patients with strokes and 10 patients with other acute medical conditions were put into different positions as arterial oxygen saturation was recorded with pulse oximeter. Patients spent one hour in each of four positions – supine, right side or left side dependent, and propped up to 45 degrees.	Mean SaO2 was 90% for stroke patients versus 94% for controls. Mean SaO2 values were lower in the lateral recumbent, 89.4%, and supine, 89.6%, positions for stroke patients. Propped up position had a mean of 90.9% in stroke patients. They repeated the study comparing 19 stroke patients lying versus propped up and found mean SaO2 of 91.9% versus 93.2%.	Small sample size. Mean SaO2 was low in the stroke group because of a couple of patients with low SaO2.

Chatterton 2000[62]	II	Prospective interventional trial	Patients within 72 hours of mild to moderately severe stroke were put into four positions, for one hour each. SaO2 was monitored by pulse oximetry. Positions were lying on the hemiplegic side at a 45 degree incline, lying on the nonhemiplegic side at a 45 degree incline, sitting up in bed with a 70 degree incline, and sitting up in an armchair.	24 patients were studied. No desaturation was observed. No significant difference in mean arterial oxygen saturation between the positions was observed.	Patients with respiratory infection, cardiovascular instability, preexisting respiratory deficits, those who were “medically unwell,” or those receiving medication that could cause respiratory depression were excluded. Small sample size.
Aviv 1996[63]	II	Prospective observational trial	15 stroke patients with dysphagia and 15 age matched controls were tested for sensory deficits by delivering an air pulse stimuli via flexible fiberoptic telescope to the mucosa innervated by the superior laryngeal nerve.	No sensory deficits were noted on the controls. 9 stroke patients had unilateral deficits. 6 stroke patients had bilateral deficits. 2 of 5 patients with moderate laryngopharynx sensory impairment and 5 of 8 with severe impairment went on to aspirate.	Small sample size. Difficult to reliably assess sensation with an air pulse from a fiberoptic telescope.

Evidentiary Table: 12 Lead EKG and Cardiac Monitoring

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Jauch 2013[29]	I	Review	American Heart Association review of literature to make recommendations on care of acute stroke patients	Recommendations for care of stroke patients during identification, transport and hospital stay.	Review article, not a primary study.
Christensen 2005[64]	II	Prospective observational trial	ECG and 12-24 hours of telemetry was assessed for 1192 patients with cerebrovascular disease admitted to an acute stroke unit within 6 hours. Data was collected prospectively then analyzed retrospectively by one observer.	There were ECG abnormalities in 60% of patients with cerebral infarction, 50% of those with ICH and 44% of those with TIA. Atrial fibrillation, AV block, ST elevation, ST depression, and inverted T waves all led to increased mortality in stroke patients.	Some patients were excluded because their ECGs could not be retrieved. Some of those had more severe strokes.
Sulter 2003[65]	II	Prospective randomized trial	54 patients with ischemic hemiparetic stroke were randomized to SCMU or SU. Blinded observer assessed mRS and Barthel Index at three months. SCMU patients were continuously monitored for at least 48 hours for cardiac rhythm, body temperature, oxygen saturation, and blood pressure. In the SU, Manual body temperature, blood pressure and heart rate were recorded four times a day. Oxygen saturation was determined as needed by the attending physician.	Poor outcomes were seen in 7 (25.9%) of the SCMU group and 13 (48.1%) of the SU group. That was defined as mRS greater than or equal to 4 or Barthel Index <60. Fewer patients in the SCMU group died – 1 (3.7%) versus 7 (25.9%). In the SCMU group, hypoxia was detected more frequently with resultant oxygen delivery, antipyretics were given more promptly, and more cardiac arrhythmias were detected.	Small study size. Poor outcome at 3 months was not significant, which is possibly due to small sample size.
Cavallini 2003[66]	I	Prospective randomized (according to availability of beds with SU filled first) trial	Analysis of 268 first time ischemic stroke patients admitted to either Stroke Unit (SU) or Cerebrovascular Unit (CU) to compare mortality, medical and neurological complications and length of hospitalization. SU has continuous monitoring of blood pressure, ECG, oxygen saturation, respiratory frequency, body temperature, and EEG.	A good outcome included mRS 0 to 3, patient able to live at home or suitable for an intensive rehabilitation program. 134 of 268 went to SU and 134 to CU. LOS was 9.2 days in SU patients and 17.1 in CU patients. 6 in the SU and 8 in the CU died. Good outcome at discharge was present in 114 SU patients and 78 CU patients.	Not truly a randomized study.

Lazzaro 2012[67]	II	Review of a prospective stroke registry	456 consecutive patients admitted for acute ischemic stroke or TIA were observed with holter and continuous cardiac telemetry. Those with atrial fibrillation on admission ECG were excluded.	An average of 29 hours of holter monitoring was done and 73 hours of CCT was done. Holter monitor detected atrial fibrillation in 6% of patients versus 0% in CCT.	Cardiologist interpreted Holter study. Nurses reviewed telemetry leads.
Myers 1982[68]	II	Prospective observational trial	100 stroke patients and 50 controls were observed in the ICU with Holter monitors for 24 hours.	More arrhythmias were observed in stroke patients, even after accounting for age and heart disease. Arrhythmias occurred more frequently in older patients and in those with infarction of the cerebral hemispheres rather than brainstem lesions.	It was unknown which of the stroke patients had preexisting cardiac disease.
Dimant 1977[69]	II	Prospective observational trial	100 consecutive patients with acute cerebrovascular accident were observed with ECG for three days after admission and compared with a control group of 100 patients admitted for carcinoma of the colon.	90% had ECG changes versus 50% in the control group. Patients with CVA had increased rates of ST segment depression, prolonged QTc interval, atrial fibrillation, T wave inversion, conduction defects, PVCs, and left ventricular hypertrophy.	Patients with carcinoma of the colon may be a biased control group.
McDermott 1994[70]	II	Prospective observational trial	51 patients admitted with ischemic stroke or TIA were monitored with continuous ECG for 48 hours.	29% had ST depression, 35% had ventricular arrhythmias. Increasing age and left-sided neurological event predicted ST segment depression.	Difficult to determine whether the underlying pathology was neurological or cardiac and which patients had baseline cardiac disease.

Evidentiary Table: Normal Saline Administration or Fluid Assessment

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Jauch 2013[29]	I	Review	American Heart Association review of literature to make recommendations on care of acute stroke patients	Recommendations for care of stroke patients during identification, transport and hospital stay.	Review article, not a primary study.
Leonardi-Bee 2002[71]	II	Analysis of data from the International Stroke Trial, a randomized, single-blind, controlled trial	19435 patients with acute presumed ischemic strokes were randomized to aspirin, subcutaneous heparin, the combination, or control. This study investigated the correlation between presenting BP and mortality.	For every 10 mm Hg increase in SBP above 150 mm Hg, risk of early death increased by 3.8%. For every 10 mm Hg fall in blood pressure below 150 mm Hg, there was an increased risk of early death of 17.9%.	There were few patients with SBP below 120 mm Hg. Patients with severely elevated or depressed BP may have been excluded from the study so as not to give them heparin or aspirin.
Stoll 1998[72]	II	Prospective interventional trial	10 stroke patients were given low molecular weight hydroxyethyl starch. Cardiac output, heart rate, blood pressure, and Scandinavian Stroke Scale (SSS) were assessed.	Cardiac output increased from 5.3 l/min to 6.5 l/m. SSS, heart rate and blood pressure did not demonstrate major changes.	Small sample size
Walzi 1998[73]	II	Prospective randomized controlled single blinded trial	200 patients with multi infarct dementia with fibrinogen of 500 mg/dl or above were randomized to treatment or control. Treatment was with the heparin-mediated extracorporeal LDL/fibrinogen precipitation (HELP) to reduce fibrinogen, cholesterol, LDL, and triglycerides.	After 11 days of treatments, there was a statistically significant difference between the HELP and control groups regarding Matthew Score for mental acuity.	Needs to be studied on acute ischemic stroke patients.
Mat-thews 1976[74]	I	Blind controlled trial	100 patients who had an ischemic stroke in the previous 48 hours were included in the study. Neurological exam was recorded. Treatment group received IV dextran 40 in 5% dextrose, 500 mL in 1 hour followed by 500 mL 12 hourly for the next 72 hours. Patients in the control group were given 5% dextrose, 500 mL in 1 hour followed by 500 mL 12 hourly for the next 72 hours.	7 of 13 control patients with severe strokes died in the first three weeks versus 4 of 21 in the treatment group. Many of the survivors went on to die in the next few months. Dextran did not prevent severe disability. In less severe strokes, no difference was found in the treatment group.	They did not successfully explain a mechanism of action for the proposed effects of mortality prevention.
The Hemodilution in Stroke Study Group 1989[75]	I	Randomized controlled trial	88 patients with acute ischemic stroke within 24 hours were randomized to either control with standard therapy or pentastarch.	Patients in the pentastarch group had a neurologic score that improved an average of 7 points from baseline to the end of treatment and 24 points by 3 months. Average Barthel disability scale index of the pentastarch group was 85 and control group was 70.	Treatment group had twice as may patients with severe strokes and less patients randomized within 12 hours.

Koller 1990[76]	I	Prospective randomized controlled trial	47 patients with acute ischemic stroke within 24 hours were randomized to either hypervolemic hemodilution or control. Hemodilution involved infusions of dextran 40, venesections and infusions of crystalloid to target hematocrit of 30-35%.	Mortality rates between treatment and control groups were the same. Neurologic outcome was better in the hypervolemic hemodilution group.	Different patients had different rates of hemodilution, which may have affected the results.
Strand 1992[77]	I	Prospective randomized controlled trial	36 hemodiluted patients and 30 control patients were monitored for a year after a stroke. The hemodiluted patients were treated with venesection and dextran 40.	2 patients in the treatment group and 9 in the control group were dependent in ADLs. 2 treated patients and 8 control patients were hospitalized. 92% of the treated patients were independent in walking versus 73% of the control group.	Small sample size. Gross neurological exam.
Italian Acute Stroke Study Group 1988[78]	I	Prospective multicenter randomized trial	1267 patients within 12 hours of hemispheric stroke were randomized to hemidilution or control. Hemidiultion group received venesection and replacement of that volume with dextran 40 in saline solution.	Treatment group hematocrit dropped from 43% to 37% at 48 hours and persisted for 7 days. At six months, severe disability and mortality was comparable in the control and treatment groups.	Used different neurological assessment from some of the other studies.
Scandinavian Stroke Study Group 1988[79]	I	Prospective multicenter randomized trial	183 patients within 48 hours of acute ischemic stroke were either treated with venesection and dextran 40 or and 190 were treated with a control. They were observed for 3 months.	There was no difference in mortality or neurological outcome at three months between treatment and control groups.	The amount of reduction in hematocrit caused by treatment therapy was variable.
Jost 2005[80]	II	Prospective interventional study	Used PET to measure quantitative rCBF in 6 patients with aneurysmal SAH with vasospasm who were euvolemic. rCBF was measured before and after normal saline bolus of 15 mL/kg delivered over 1 hour.	Mean rCBF increased from 19.1 to 29.9 with the normal saline bolus and persisted for 2 to 3 hours. There were no significant changes in pulmonary capillary wedge pressure, MAP, cardiac output, or CVP.	Small sample size. Analyzing SAH, not stroke.
Dhar 2012[81]	II	Analysis of data from three separate but similar prospective clinical trials	PET scans imaged patients to assess CBF before and after different interventions in patients with aneurysmal SAH at risk for delayed cerebral ischemia. Interventions included a fluid bolus of 15 mL/kg normal saline (9 patients), raising MAP 25% with phenylephrine (12 patients), and transfusing 1 U pRBC (17 patients).	Global CBF or oxygen delivery did not improve in any group. With low baseline oxygen delivery, transfusion led to an improvement of 23%, hypertension 14%, and normal saline 10%. CBF rose with each treatment.	Small sample size. Not studied in stroke.

Evidentiary Table: Stroke Regionalization

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Marler 2000[82]	I	Randomized controlled trial	Patients were randomized to receive alteplase or placebo either 0 to 90 minutes or 91 to 180 minutes after stroke onset. 624 patients were randomized.	Those treated at 0 to 90 minutes with rtPA had more improvement at 24 hours and 3 months than those treated between 91 and 180 minutes.	rtPA treated patients in the 91 to 180 minute group had less severe strokes.
Powers 2015[83]	I	Review	Review of 8 randomized clinical trials of endovascular treatment published since 2013 to update AHA/ASA recommendations for the treatment of stroke.	Some endovascular therapies are effective for the treatment of acute ischemic stroke.	Review. Not comprehensive review, just an update since 2013 of selected studies.
Jauch 2013[29]	I	Review	American Heart Association review of literature to make recommendations on care of acute stroke patients	Recommendations for care of stroke patients during identification, transport and hospital stay.	Review article, not a primary study.
Berglund 2012[84]	I	Randomized controlled trial	Patients with stroke symptoms were randomized to priority level 1 with immediate ambulance call or priority level 2 with ambulance call within 30 minutes.	942 patients were randomized. Level 1 priority patients reached the stroke unit 26 minutes faster and received thrombolysis 24% of the time, versus 10% of the time.	Difficult to assess the effects on other high priority patients.
Mosley 2007[1]	II	Prospective non-randomized trial	198 patients in 6 months with a stroke or TIA were assessed. Ambulance calls were evaluated for factors leading to faster evaluation in the hospital.	GCS <13, paramedic stroke recognition, and hospital prenotification led to shorter times from ambulance call to first medical assessment.	Limited by paramedic's ability to identify strokes in the fields
Bae 2010[85]	II	Retrospective database review	102 patients with suspected acute stoke were transported by EMS. 33 patients were given IV tPA without prehospital notification.	Mean transfer time after EMS call was 56 min. Door to imaging time (17.8 min versus 26.9 min) and door to needle time (29.7 min versus 42.1 min) were shorter in the patients with prehospital notification.	Observational, retrospective study. Difficult to assess the effect of false positive prehospital notification.
Salottolo 2011[86]	II	Retrospective cohort study	123 patients admitted to the ED with a stroke alert were analyzed to determine if multimodal CT delayed tPA administration.	Median time from arrival in the ED to tPA was 56 minutes – 55 with multimodal CT versus 78 with unenhanced CT. tPA within 60 minutes was associated with prehospital stroke alert, time to CT and onset-to-arrival time.	Time to perform the unenhanced CT is longer (15 minutes versus 5 minutes) suggesting that more time could be reduced from their baseline protocol.

Kim 2009[87]	II	Interventional study with a hotline system	A prehospital notification system was implemented with a 24 hour hotline system and the rate of IV tPA was observed.	tPA rate increased from 6.5% to 14.3%. Door to needle time was reduced from 47.7 minutes to 28.9 minutes. Time from symptom onset to IV tPA was longer with prehospital notification (144.2 minutes versus 118.5 minutes). There was no difference in 90 day clinical outcomes.	The lack of difference in clinical outcomes could be attributed in longer symptom onset to IV tPA time.
Fonarow 2014[88]	II	Intervention of a quality improvement initiative	Study assessed 27,319 patients in the preintervention period and 43,850 patients in the postintervention period after Get with the Guidelines interventions were implemented. Those included prenotification of hospital by EMS, stroke team page, rapid acquisition and interpretation of imaging, protocols, premixing tPA, use of a stroke team and continuous feedback.	Median door to needle time dropped from 77 minutes to 67 minutes. 36.5% of the patients in the preintervention period received tPA within 60 minutes versus 41.3% in the postintervention period. All-cause mortality in-hospital improved from 9.93% to 8.25%. Patients were discharged home more frequently after the intervention, 42.7%, than before the intervention, 37.6%.	There were no control hospitals, and hospitals included in the study were likely motivated participants. Clinical outcomes could have improved due to factors outside this study.
Llanes 2004[19]	II	Retrospective analysis	LAMS was constructed by assigning point values to LAPSS and it was analyzed to assess ability to predict long-term outcomes.	90 patients were studied. LAMS scores correlated closely with NIHSS scores and three-month functional outcomes.	Small sample size, retrospective analysis.
Oostema 2014[89]	II	Prospective cohort study	Compliance with 8 prehospital quality indicators was assessed for patients transported to stroke centers and subsequently discharged with a diagnosis of acute ischemic stroke.	186 patients were included. 86 patients had glucose level documented and 78.5% stroke screen done. 46.8% had an on-scene time less than or equal to 15 minutes. Hospital prenotification occurred 56.5% of the time and transportation at highest priority occurred 55.4% of the time. Transportation at highest priority and hospital prenotification were associated with faster door to CT time.	Did not assess neurological outcome. Study was underpowered. 23 of the 186 patients received tPA.

Sheppard 2015[90]	II	Cohort study of linked patient medical records	Medical records were analyzed to study the association between time to CT request and onset time, stroke recognition with FAST and sending of prealert message.	151 patients were included. Time of onset was recorded in 61 patients with FAST positive in 75%. Prealert was sent in 44% of cases. Those patients who had time of onset recorded, were positive for FAST, or for whom the hospital was prealerted were more likely to receive a CT quickly.	Many factors were not assessed including time to tPA and neurological outcome.
Patel 2011[91]	II	Retrospective data analysis of prospectively collected data	Database was reviewed to determine if mode of transport led to faster evaluation of stroke patients.	13894 patients included. EMS transport led to brain imaging completed within 25 minutes of ED arrival and imaging interpretation within 45 minutes. EMS prehospital notification led to faster evaluation and more tPA administration.	Did not assess neurological or mortality outcomes.
Abdullah 2008[92]	II	Observational data analysis	Analyzed patients with acute stroke who were transported by EMS to determine factors leading to faster treatment.	118 patients were included. Thrombolysis occurred in 41% of the patients with prenotification versus 21% of those without. Door to CT time was 40 minutes in those with prenotification and 47 minutes in those without.	Small sample size. Did not address neurological outcome.
Kothari 1999[7]	II	Prospective non-randomized	Prehospital providers performed the CPSS and compared stroke analysis on 171 patients, 860 times	The scale demonstrated 88% sensitivity for patients with anterior circulation strokes, with 66% sensitivity for each one of three stroke scale items and 87% specificity. It was reproducible between physicians and prehospital personnel	Relatively small sample size, only 49 patients had a diagnosis of stroke or TIA. Only four prehospital providers were used.

McKinney 2013[93]	II	Retrospective analysis of data from the Robert Wood Johnson University Hospital Brain Attack Database	Analysis of database to determine if hospital prenotification leads to increased frequency of tPA.	229 patients were included – 114 with prenotification and 115 without. When the hospital was prenotified, patients received tPA 27% of the time, versus 15% of the time without prenotification, but after adjusting for stroke severity the difference was insignificant. Older patients and those with more severe strokes were more likely to cause prenotification.	Retrospective study. Limited by identification of stroke by the EMS system.
Patel 2014[94]	II	Retrospective analysis of EMS protocols and scene time	EMS stroke protocols were assessed for language and their resulting scene times.	There was no difference in scene times between those protocols directing general instructions to limit scene time and those with no instructions to limit scene time. Those directing a specific limitation of 15 minutes scene time had a median and 90% percentile scene times about 2-3 minutes shorter as compared to the others.	No clinical significance of 2-3 minutes less on scene.
Albright 2010[95]	II	Review of data from the US Census Bureau and addresses from the US Postal Service	Authors used Census Bureau and Postal Service data to calculate the distance to the closest PSC for all US residents then calculated ground ambulance transport times.	They calculated that 22.3% of US citizens have access to a PSC within 30 minutes, 43.2% have access within 45 minutes and 55.4% have access within 60 minutes.	Does not take into account telemedicine, and upcoming drip and ship models. Travel time was derived from analysis of trauma patients.
Prabhakaran 2013[96]	II	Retrospective multicenter cohort study	Outcomes were evaluated throughout Chicago before and after an intervention leading to transport of certain patients to PSC. Those patients included those with symptom onset within 6 hours and abnormal CPSS score, and could also include those with sudden altered consciousness, sudden onset severe headache, or sudden onset loss of balance.	1075 stroke and TIA patients were included in the study before the intervention and 1172 after the intervention. EMS use increased from 30.2% to 38.1%. Prenotification increased from 65.5% to 76.5% tPA use increased from 3.8% to 10.1%. Symptom onset to treatment time decreased from 171.7 minutes to 145.7 minutes.	Data from non-PSC was not included. Not all PSC in Chicago were included in the analysis. Did not analyze patients with who were false positives on the prehospital stroke analysis.

Xian 2011[97]	II	Observational study of data from the New York Statewide Planning and Research Cooperative System	Analyzed data at the New York Statewide Planning and Research Cooperative System to determine mortality for patients admitted with acute ischemic stroke at designated stroke centers and nondesignated stroke centers. Controls were those with gastrointestinal hemorrhage and acute myocardial infarction.	30947 patients with acute ischemic stroke were included, of which 15297 went to designated stroke centers. Those at stroke centers had 10.1% 30 day all-cause mortality versus 12.5% at those in nondesignated stroke centers. Thrombolytic therapy was used in 4.8% of patients at stroke centers versus 1.7% of patients in nondesignated stroke centers. Control patients had similar 30 day all-cause mortality at stroke center and nondesignated stroke centers.	Did not analyze stroke severity or neurological function at discharge.
Lahr 2012[98]	II	Prospective multicenter observational trial	Two models of stroke care were used. In the centralized model, tPA was administered in 1 stroke center. In the decentralized model, 9 community hospitals are used.	283 patients were treated in the centralized model, of which 21.9% were treated with tPA. 801 were treated in the decentralized model, of which 14.1% were treated with tPA.	There were many fewer patients in the centralized model.
Lahr 2014[99]	II	Consecutive case observational study	Analyzed factors in the centralized versus decentralized stroke care models.	172 patients were treated in the centralized model and 299 were treated in the decentralized model. EMS was used more frequently, stroke was misdiagnosed more frequently, and odds of arrival within the tPA window were greater in the centralized model.	Many patient demographic factors were not analyzed.
Schuberg 2013[100]	II	Database review	Analyzed the Joint Commissions Website and determined EMS PSC routing policies to determine whether EMS routing to PSC motivated hospitals to achieve PSC certification.	PSC designation occurred more frequently after EMS routing policies. 51 PSCs were designated within 1 year, 85 PSCs within 2 years. Rate of adoption of PSC designation increased from 3.8% to 16.2%.	Many potentially confounding factors were not analyzed. The change in PSC could have been due to factors other than EMS policy change.

Parker 2015[101]	II	Interventional trial	The group developed a Mobile Stroke Unit in the United States.	The group found a project manager, developed a budget for 3 years, bought an ambulance and supplies, wrote protocols, got a license and insurance, established a base station, and networked with EMS communications.	Only one stroke unit was established and success of the unit was not tested in this paper.
Wendt 2015[102]	II	Interventional trial	Comparison of STEMO care with conventional care for 6182 patients.	29% were treated in a STEMO and 71% were treated conventionally. 11.6% of those with cerebrovascular events treated with conventional care were sent to hospitals without Stroke Units versus 5.5% of those treated with STEMOs. 43% of patients with ICH treated with conventional care were delivered to hospitals without neurosurgery departments versus 11.3% in STEMOs.	Expensive, new intervention that has not been well tried.
Ebinger 2015[103]	II	Interventional trial	STEMO or standard care was dispatched for suspected strokes and results were analyzed. STEMO was deployed during randomized weeks	6182 patients were included. 32.6% of 614 patients for whom STEMO was deployed received tPA and 22% of 1497 patients for whom conventional care was delivered received tPA. Rate of golden hour thrombolysis increased from 4.9% to 31% with STEMOs.	There were many more patients in the conventional care group.
Ebinger 2013[104]	II	Interventional trial	STEMO is deployed to suspected stroke where a neurologist does the neuro exam. A CT scan is done and telemetrically transmitted to a neuroradiologist. tPA can be started in the field and patient can then be transported to a stroke center.	152 patients were treated in the STEMO. 58% had an acute ischemic stroke and 51% received rtPA. Mean alarm-to-needle time was 62 minutes versus 98 minutes in a control cohort of 50 patients.	Difficult to assess the cost effectiveness.
Weber 2013[105]	II	Interventional trial	STEMO staffed with neurologist, paramedic, and radiographer was sent to the scene of suspected strokes. STEMO had on board CT scanner, point-of-care laboratory, and teleradiology system.	152 patients were treated in the STEMO. The STEMO was determined to be feasible. 9% had symptomatic intracranial hemorrhage and 4% (1 patient) died in the hospital. There was one CT dysfunction and 2 delayed CT image transmissions.	Not a prospective controlled study.

Kostopoulos 2012[106]	II	Interventional trial	Mobile Stroke Unit with CT angiography and CT perfusion, point-of-care testing, and neurologists was deployed to suspected stroke patients.	4 cases were analyzed. The STEMO was determined to be feasible.	Small sample size.
Ebinger 2012[107]	II	Interventional prospective trial	The group developed an ambulance with a CT scanner, point-of-care laboratory, teleradiological support, and an emergency-trained neurologist.	The group established a trial with primary outcome of alarm-to-needle time. Secondary outcomes are tPA, mRS at three months, alarm-to-imaging, imaging-to-needle, alarm-to-POC, alarm-to-INR normalization, proportion of patients referred to specialized centers, and cost effectiveness.	The trial is established, but needs to be completed.
Bergrath 2012[108]	II	Interventional prospective trial	Audio communication, real-time video streaming, vital data and still picture transmission was transmitted between the ambulance and teleconsultation center to assess stroke patients.	939 patients were treated, 289 with telemedicine, 650 with regular ALS units. There was no difference between telemedicine and conventional care door to brain imaging times or stroke diagnosis confirmation. They determined that teleconsultation was feasible, but not completely reliable.	Stroke history checklist was completed in only 78% of patients. Many more patients were transported via ALS than via telemedicine ambulances.
Liman 2012[109]	II	Interventional trial	Real-time audio-video streaming telemedicine devices were added to ALS ambulances. Two actors simulated middle cerebral artery strokes. NIHSS scores were done by hospital-based stroke physicians via telemedicine, by emergency physician via telemedicine and on video.	In 18 of 30 scenarios, loss of audio-video signal meant that NIHSS scale could not be completed. In the other scenarios interrater agreement was moderate to good.	Other studies have shown better results, so potentially better technology would have more efficacy. Patients were actors simulating strokes.
Walter 2012[110]	I	Randomized single-center controlled trial	Compared alarm to therapy decision between MSU and hospital. MSU were equipped with CT scanner, point-of-care laboratory, and telemedicine.	53 patients in the MSU group and 47 in the conventional treatment group. Use of the MSU reduced median time from alarm to therapy decision from 76 minutes to 35 minutes.	Did not assess neurological outcomes.
Gonzalez 2011[111]	II	Prospective Interventional trial	40 physicians performed the sNIHSS on standardized patients via telemedicine (cellular VP). That exam was compared with a bedside exam by an EMT.	480 standardized patients were assessed. There was strong interrater reliability. Using telemedicine took 38 seconds longer.	sNIHSS may not be the most comprehensive assessment. Only right middle cerebral artery stroke was assessed.

You 2010[112]	III	Correspondence	Description of a telemedicine modality.	EMS providers can use video telephony to help in the recognition of stroke.	Correspondence article needing prospective trial validation.
LaMonte 2000[113]	II	Interventional trial	Assessed the feasibility of using a mobile telecommunications system (MTS) to connect patient to stroke neurologist.	31 MTS tests were analyzed – 18 laboratory tests, 7 ambulance tests, and 6 patient transport tests. The MTS is feasible technology.	Small sample size with few stroke patients and no neurological outcomes assessed.
Audebert 2006[114]	II	Prospective interventional trial	Analysis of patients receiving tPA via a telemedicine system. 12 hospitals without stroke units had telemedicine access to stroke teams remotely.	115 of 4727 stroke or TIA patients in the 12 regional hospitals received tPA, versus 110 of 1889 in the 2 stroke centers. There was a symptomatic hemorrhage rate of 7.8%.	Did not assess the burden of having the telemedicine team available.
Wu 2014[115]	II	Interventional trial	Feasibility study of using telemedicine to assess acute strokes and treat with tPA. Actors played out 10 scripts, 4 times each. Vascular neurologists assessed the NIHSS via telemedicine. A second blinded vascular neurologist evaluated the same script to determine interrater reliability.	In 34 of 40 scenarios, there were no major technical difficulties. 10 of 15 items on the NIHSS had excellent interrater agreement and 5 of 15 had moderate agreement.	Feasibility study used actors, not real patients. Outcomes could not be assessed.
Hess 2006[116]	III	Commentary	Discussed REACH (Remote Evaluation of Acute IsCHemic Stroke), a telemedicine system based out of Augusta, Georgia to assess stroke and deliver tPA.	REACH includes video conferencing and CT imaging to connect to 8 community rural hospitals.	Not a prospective, controlled trial.
Ickenstein 2005[117]	II	Interventional trial	2 stroke centers created telemedicine networks to connect with 12 community hospitals in order to assess patients via videoconference.	In the 12 months before the network system, 10 patient received thrombolysis. In 6 months after the network system was created, 45 patients received tPA.	Small feasibility study.
Switzer 2009[118]	II	Interventional trial	Discussed REACH (Remote Evaluation of Acute IsCHemic Stroke), a telemedicine system based out of Augusta, Georgia to assess stroke and deliver tPA.	50 patients were assessed with REACH and given tPA. One patient had symptomatic hemorrhage.	Small sample size without long term neurological assessment. Not a randomized trial.

Schwab 2007[119]	II	Interventional Trial	TEMPiS (Telemedical Pilot Project for Integrative Stroke Care) linked 12 community hospitals to 2 stroke centers via telemedicine.	170 patients in the telemedicine hospitals received tPA versus 132 in the stroke centers. Mortality was 11.2% in the community hospitals versus 11.5% in the stroke centers at 3 months and 14.2% in the community hospitals versus 13% in the stroke centers at 6 months. Good mRS was present in 39.5% of the community hospitals versus 30.9% of the stroke centers at 6 months.	Early feasibility trial.
Meyer 2008[120]	I	Randomized, blinded, prospective trial	Assessment of the efficacy of telemedicine versus telephone for stroke assessment. Patients at four community hospitals were randomized to either telemedicine or telephone consultation for assessment for treatment with thrombolytics.	234 patients were included. NIHSS score was 9.5 in the telemedicine group versus 7.7 in the telephone group. Correct treatment decisions were made 98% of the time in the telemedicine group versus 82% of the time in the telephone group. That was assessed by subsequent blinded review. 90 day functional outcomes were similar for mRS and BI.	Telemedicine is clearly more efficacious than telephone, but other metrics might give a better gauge of absolute efficacy.
Demaerschalk 2010[121]	I	Prospective, randomized, blinded, controlled trial	Study to assess the feasibility of establishing a telestroke research network across Arizona. Assessed patients remotely with either telephone or audiovisual telemedicine.	54 patients were assessed remotely. There were many technical problems in the telemedicine arm. Correct treatment decisions were made in 89% of the telephone calls and 85% of the telemedicine calls. Thrombolytics were used in 30% of the calls overall. There was no difference in functional outcome at 90 days, mortality, or intracerebral hemorrhage.	The trial was not powered to show a difference between the two modes of communication.
Waite 2006[122]	II	Interventional study	Videoconferencing units were put into hospitals and neurologists' homes and CT scans were transmitted electronically.	88 patients were assessed, 26 of whom received tPA. Telemedicine was determined to be feasible.	Economics are still unassessed.
Van Hooff 2013[123]	II	Interventional feasibility study	Assessment of the feasibility and reliability of stroke severity quantification using the Unassisted TeleStroke Scale (UTSS). Healthy volunteers simulated strokes in 41 scenarios.	Mean exam time was 3.1 minutes. There was excellent interrater agreement.	Simulation without actual patients and neurological outcome assessments.

Evidentiary Table: Interfacility tPA

Study	LOE	Study Design	Methods and Outcomes	Results	Limitations
Powers 2015[83]	I	Review	Review of 8 randomized clinical trials of endovascular treatment published since 2013 to update AHA/ASA recommendations for the treatment of stroke.	Some endovascular therapies are effective for the treatment of acute ischemic stroke.	Review. Not comprehensive review, just an update since 2013 of selected studies.
Asaithambi 2013[124]	II	Retrospective review	Review of adherence by EMS to quality parameters during transport of patients while infusing IV rtPA. Patients were assessed with mRS at discharge.	40 patients were included. Vital signs were monitored at 10 to 20 minute intervals for 38 patients. Mean transit time was 37.7 minutes. 7 patients had BP above 180/105 and only 1 was treated with an antihypertensive. 5 had worsening neurological exam between outside ED and CSC ED without IV rtPA discontinuation. mRS less than or equal to 1 at discharge occurred in 41.7% of those with neurological deterioration and continued IV rtPA or hypertension and 35.7% of those with neither adverse event.	Not clear how the neurological exam before and after transport was done, or by whom. The differences noted could have been due to different examiners.

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