

Division for Heart Disease and Stroke Prevention, CDC
Stroke Work Group
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Stroke Clinical Trials

Hacke W, K. M., Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR,, M. T. Medeghri Z, Schneider D, von Kummer R, Wahlgren N, Toni D; ECASS, et al. (2008). "Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke." N Engl J Med. **359**(13): 1317-29.

BACKGROUND: Intravenous thrombolysis with alteplase is the only approved treatment for acute ischemic stroke, but its efficacy and safety when administered more than 3 hours after the onset of symptoms have not been established. We tested the efficacy and safety of alteplase administered between 3 and 4.5 hours after the onset of a stroke. **METHODS:** After exclusion of patients with a brain hemorrhage or major infarction, as detected on a computed tomographic scan, we randomly assigned patients with acute ischemic stroke in a 1:1 double-blind fashion to receive treatment with intravenous alteplase (0.9 mg per kilogram of body weight) or placebo. The primary end point was disability at 90 days, dichotomized as a favorable outcome (a score of 0 or 1 on the modified Rankin scale, which has a range of 0 to 6, with 0 indicating no symptoms at all and 6 indicating death) or an unfavorable outcome (a score of 2 to 6 on the modified Rankin scale). The secondary end point was a global outcome analysis of four neurologic and disability scores combined. Safety end points included death, symptomatic intracranial hemorrhage, and other serious adverse events. **RESULTS:** We enrolled a total of 821 patients in the study and randomly assigned 418 to the alteplase group and 403 to the placebo group. The median time for the administration of alteplase was 3 hours 59 minutes. More patients had a favorable outcome with alteplase than with placebo (52.4% vs. 45.2%; odds ratio, 1.34; 95% confidence interval [CI], 1.02 to 1.76; P=0.04). In the global analysis, the outcome was also improved with alteplase as compared with placebo (odds ratio, 1.28; 95% CI, 1.00 to 1.65; P<0.05). The incidence of intracranial hemorrhage was higher with alteplase than with placebo (for any intracranial hemorrhage, 27.0% vs. 17.6%; P=0.001; for symptomatic intracranial hemorrhage, 2.4% vs. 0.2%; P=0.008). Mortality did not differ significantly between the alteplase and placebo groups (7.7% and 8.4%, respectively; P=0.68). There was no significant difference in the rate of other serious adverse events. **CONCLUSIONS:** As compared with placebo, intravenous alteplase administered between 3 and 4.5 hours after the onset of symptoms significantly improved clinical outcomes in patients with acute ischemic stroke; alteplase was more frequently associated with symptomatic intracranial hemorrhage.

Ridker, P. M. and J. D. Silvertown (2008). "Inflammation, C-reactive protein, and atherothrombosis." *Journal of Periodontology* 79(8 Suppl): 1544-51.

Atherothrombosis of the coronary and cerebral vessels is understood to be a disorder of inflammation and innate immunity, as well as a disorder of lipid accumulation. From a vascular biology perspective, the processes of cellular adhesion, monocyte and macrophage attachment, and transmigration of immune cells across the endothelium are crucial steps in early atherogenesis and in the later stages of mature plaque rupture, particularly the transition of unstable plaque at the time of acute thrombosis. There is abundant clinical evidence demonstrating that many biomarkers of inflammation are elevated years in advance of first ever myocardial infarction (MI) or thrombotic stroke and that these same biomarkers are highly predictive of recurrent MI, recurrent stroke, diabetes, and cardiovascular death. In daily practice, the inflammatory biomarker in widest use is high-sensitivity C-reactive protein (hsCRP); when interpreted within the context of usual risk factors, levels of hsCRP <1, 1 to 3, and >3 mg/l denote lower, average, and higher relative risk for future vascular events. Risk-prediction models that incorporate hsCRP, such as the Reynolds Risk Score, have been developed that improve risk classification and the accuracy for global risk prediction, particularly for those deemed at "intermediate risk" by usual algorithms, such as the Framingham Risk Score. With regard to cerebral vessels, increased biomarkers of inflammation, including hsCRP, have been associated with increased stroke risk as well as an increased rate of atherosclerosis progression in the carotid vessels. Although the proportion of variation in hsCRP explained by genetic factors may be as large as 20% to 40%, diet, exercise, and smoking cessation remain critical tools for risk reduction and CRP reduction. Statin therapy reduces hsCRP in a largely low-density lipoprotein (LDL)-independent manner, and the "anti-inflammatory" properties of these agents have been suggested as a potential mechanism beyond LDL reduction for the efficacy of these agents. The ongoing multinational Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial of 17,802 initially healthy men and women with low levels of LDL cholesterol but increased levels of hsCRP will help to define whether vascular protection can be achieved with statin therapy, even in the absence of hyperlipidemia. Targeted anti-inflammatory therapies are being developed that may provide a direct method of translating the biology of inflammation into new clinical treatments across multiple vascular beds. This article summarizes data supporting a role for inflammation in cardiovascular disease and offers the possibility that other disorders characterized by inflammation, such as periodontal disease, may have an indirect role by influencing the risk, manifestation, and progression of vascular events.

N Engl J Med. 2008 Nov 20;359(21):2195-207. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008 Nov 20;359(21):2195-207.

BACKGROUND: Increased levels of the inflammatory biomarker high-sensitivity C-reactive protein predict cardiovascular events. Since statins lower levels of high-sensitivity C-reactive protein as well as cholesterol, we hypothesized that people with elevated high-sensitivity C-reactive protein levels but without hyperlipidemia might benefit from statin treatment. **METHODS:** We randomly assigned 17,802 apparently healthy men and women with low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter (3.4 mmol per liter) and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher to rosuvastatin, 20 mg daily, or placebo and followed them for the occurrence of the combined primary end point of myocardial infarction, stroke, arterial revascularization, hospitalization for unstable angina, or death from cardiovascular causes. **RESULTS:** The trial was stopped after a median follow-up of 1.9 years (maximum, 5.0). Rosuvastatin reduced LDL cholesterol levels by 50% and high-sensitivity C-reactive protein levels by 37%. The rates of the primary end point were 0.77 and 1.36 per 100 person-years of follow-up in the rosuvastatin and placebo groups, respectively (hazard ratio for rosuvastatin, 0.56; 95% confidence interval [CI], 0.46 to

0.69; $P < 0.00001$), with corresponding rates of 0.17 and 0.37 for myocardial infarction (hazard ratio, 0.46; 95% CI, 0.30 to 0.70; $P = 0.0002$), 0.18 and 0.34 for stroke (hazard ratio, 0.52; 95% CI, 0.34 to 0.79; $P = 0.002$), 0.41 and 0.77 for revascularization or unstable angina (hazard ratio, 0.53; 95% CI, 0.40 to 0.70; $P < 0.00001$), 0.45 and 0.85 for the combined end point of myocardial infarction, stroke, or death from cardiovascular causes (hazard ratio, 0.53; 95% CI, 0.40 to 0.69; $P < 0.00001$), and 1.00 and 1.25 for death from any cause (hazard ratio, 0.80; 95% CI, 0.67 to 0.97; $P = 0.02$). Consistent effects were observed in all subgroups evaluated. The rosuvastatin group did not have a significant increase in myopathy or cancer but did have a higher incidence of physician-reported diabetes. CONCLUSIONS: In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.

Stroke Telemedicine

Ehlers, L., W. M. Muskens, et al. (2008). "National use of thrombolysis with alteplase for acute ischaemic stroke via telemedicine in Denmark: a model of budgetary impact and cost effectiveness." *CNS Drugs* **22**(1): 73-81.

AIM: The purpose of this analysis was to assess the budgetary impact and cost effectiveness of the national use of thrombolysis with alteplase (recombinant tissue plasminogen activator; rt-PA) for acute ischaemic stroke via telemedicine in Denmark. METHODS: Computations were based on a Danish health economic model of thrombolysis treatment of acute ischaemic stroke via telemedicine. Cost data for stroke units and satellite clinics were taken from the first practical experiences in Denmark with implementing thrombolysis via telemedical linkage to the Stroke Department at Aarhus University Hospital. Effectiveness data were taken from a published pooled analysis of results from randomized controlled trials of alteplase. RESULTS: The calculations showed that the additional total costs to the hospitals of implementing thrombolysis with alteplase for acute ischaemic stroke via telemedicine were approximately \$US3.0 (range 2.0-5.8) million per year in the case of five centres and five satellite clinics, or \$US3.6 (range 2.4-7.0) million per year based on seven centres and seven satellite clinics. The incremental cost-effectiveness ratio was calculated to be approximately \$US50,000 when taking a short time perspective (1 year), but thrombolysis was dominant (both cheaper and more effective) after as little as 2 years and cost effectiveness improved over longer time scales. CONCLUSION: The budgetary impact of using thrombolysis with alteplase for acute ischaemic stroke via telemedicine depends on the existing capacity and organizational conditions at the local hospitals. The health economic model computations suggest that the macroeconomic costs may balance with savings in care and rehabilitation after as little as 2 years, and that potentially large long-term savings are associated with thrombolysis with alteplase delivered by telemedicine, although the long-term calculations are uncertain.

Meyer, B. C., R. Raman, et al. (2008). "Efficacy of site-independent telemedicine in the STRoKE DOC trial: a randomised, blinded, prospective study.[see comment]." *Lancet Neurology* **7**(9): 787-95.

BACKGROUND: To increase the effective use of thrombolytics for acute stroke, the expertise of vascular neurologists must be disseminated more widely. We prospectively assessed whether telemedicine (real-time, two-way audio and video, and digital imaging and communications in medicine [DICOM] interpretation) or telephone was superior for decision making in acute telemedicine consultations. METHODS: From January, 2004, to August, 2007, patients older than 18 years who presented with acute stroke symptoms at

one of four remote spoke sites were randomly assigned, through a web-based, permuted blocks system, to telemedicine or telephone consultation to assess their suitability for treatment with thrombolytics, on the basis of standard criteria. The primary outcome measure was whether the decision to give thrombolytic treatment was correct, as determined by central adjudication. Secondary outcomes were the rate of thrombolytic use, 90-day functional outcomes (Barthel index [BI] and modified Rankin scale [mRS]), the incidence of intracerebral haemorrhages, and technical observations. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00283868. FINDINGS: 234 patients were assessed prospectively. 111 patients were randomised to telemedicine, and 111 patients were randomised to telephone consultation; 207 completed the study. Mean National Institutes of Health stroke scale score at presentation was 9.5 (SD 8.1) points (11.4 [8.7] points in the telemedicine group versus 7.7 [7.0] points in the telephone group; $p=0.002$). One telemedicine consultation was aborted for technical reasons, although it was included in the analyses. Correct treatment decisions were made more often in the telemedicine group than in the telephone group (108 [98%] vs 91 [82%], odds ratio [OR] 10.9, 95% CI 2.7-44.6; $p=0.0009$). Intravenous thrombolytics were used at an overall rate of 25% (31 [28%] telemedicine vs 25 [23%] telephone, 1.3, 0.7-2.5; $p=0.43$). 90-day functional outcomes were not different for BI (95-100) (0.6, 0.4-1.1; $p=0.13$) or for mRS score (0.6, 0.3-1.1; $p=0.09$). There was no difference in mortality (1.6, 0.8-3.4; $p=0.27$) or rates of intracerebral haemorrhage after treatment with thrombolytics (2 [7%] telemedicine vs 2 [8%] telephone, 0.8, 0.1-6.3; $p=1.0$). However, there were more incomplete data in the telephone group than in the telemedicine group (12% vs 3%, 0.2, 0.1-0.3; $p=0.0001$). INTERPRETATION: The authors of this trial report that stroke telemedicine consultations result in more accurate decision making compared with telephone consultations and can serve as a model for the effectiveness of telemedicine in other medical specialties. The more appropriate decisions, high rates of thrombolysis use, improved data collection, low rate of intracerebral haemorrhage, low technical complications, and favourable time requirements all support the efficacy of telemedicine for making treatment decisions, and might enable more practitioners to use this medium in daily stroke care.

Switzer, J. A. and D. C. Hess (2008). "Development of regional programs to speed treatment of stroke." *Current Neurology & Neuroscience Reports* **8**(1): 35-42.

The pathophysiology of ischemic stroke dictates that treatments be administered shortly after symptom onset to be beneficial. Intravenous tissue plasminogen activator is the only drug proven to be effective in stroke; it is approved for administration within a 3-hour window. To optimize the number of potential candidates for thrombolytic therapy, patients and families must understand the symptoms and signs of stroke and how to respond. Emergency medical services and emergency departments also must be prepared for rapid evaluation to determine if a patient is appropriate for reperfusion therapy. Due to a lack of stroke specialists in many communities, some hospitals may not be prepared to provide intravenous thrombolytic therapy around the clock, and time lost transporting patients to tertiary centers may mitigate the benefits of thrombolysis. Telestroke may be the best alternative in this scenario, extending acute stroke therapies to patients who would otherwise not receive treatment.

Vatankhah, B., J. Schenkel, et al. (2008). "Telemedically provided stroke expertise beyond normal working hours. The Telemedical Project for Integrative Stroke Care." *Cerebrovascular Diseases* **25**(4): 332-7.

BACKGROUND: State-of-the-art stroke management requires neurological expertise for the recognition of complex cerebrovascular syndromes or stroke-mimicking symptoms and initiation of proven acute therapies. Many community hospitals struggle to fulfill these premises particularly at evening/nighttimes or weekends. Telemedicine can improve that situation by offering rapid access to neurological expertise, but it has not been shown to

what extent it is used beyond working times. **METHODS:** The Telemedical Project for Integrated Stroke Care is a telemedical network of 2 stroke centers and 12 regional general hospitals with newly established stroke wards in Bavaria. This analysis comprises all teleconsultations from 1st February 2003 to 15th December 2006. The consultations were prospectively documented and categorized according to predefined indications and direct impact on clinical decisions. The teleconsultations were analyzed concerning whether they were requested during regular working time or during off-time (at evening/night times or weekends). **RESULTS:** A total of 10,239 teleconsultations were carried out in 8,326 patients. The 6,679 patients with cerebrovascular diagnosis comprised 51% of all admitted stroke cases between 2003 and 2006. During off-time 6,306 consultations (62%) were requested; 1,598 teleconsultations yielded nonstroke diagnoses, with 68% beyond working hours. Of all presented stroke patients 567 (8.5%) received systemic thrombolysis, with 58% off-time. Interhospital transports were initiated in 1,050 patients (10.5% of all), mainly for specific diagnostic workup or interventional treatments. Sixty percent of these transfers were launched off-time. **CONCLUSIONS:** The majority of teleconsultations were requested beyond normal working times and a significant proportion had an immediate impact on clinical decisions.

Zhang, S., H. Hu, et al. (2008). "An interactive Internet-based system for tracking upper limb motion in home-based rehabilitation." Medical & Biological Engineering & Computing **46**(3): 241-9.

In this paper, we introduce an interactive telecommunication system that supports video/audio signal acquisition, data processing, transmission, and 3D animation for post stroke rehabilitation. It is designed for stroke patients to use in their homes. It records motion exercise data, and immediately transfers this data to hospitals via the internet. A real-time videoconferencing interface is adopted for patients to observe therapy instructions from therapists. The system uses a peer-to-peer network architecture, without the need for a server. This is a potentially effective approach to reducing costs, allowing easy setup and permitting group-rehabilitation sessions. We evaluate this system using the following steps: (1) motion detection in different movement patterns, such as reach, drink, and reach-flexion; (2) online bidirectional visual telecommunication; and (3) 3D rendering using a proposed offline animation package. This evaluation has subjectively been proved to be optimal.

Stroke EMS

Brice, J. H., K. R. Evenson, et al. (2008). "Emergency medical services education, community outreach, and protocols for stroke and chest pain in North Carolina." Prehospital Emergency Care **12**(3): 366-71.

OBJECTIVE: Prehospital care of stroke and chest pain patients is dependent on adequate emergency medical services (EMS) education and evidence-based protocols. We sought to describe the amount of education offered, community outreach implemented, and protocols established for stroke and for chest pain among North Carolina EMS agencies and personnel. **METHODS:** A survey was developed to measure EMS system characteristics regarding the prehospital care of stroke and chest pain patients. Each of the 83 primary EMS agencies in North Carolina was asked to participate. **RESULTS:** Of the 83 agencies surveyed, 72 (87%) responded. Both advanced life support (ALS) and basic life support (BLS) services were provided by 54% of agencies; 44% offered ALS only and 1% offered BLS only. While 89% of the EMS agencies provided stroke education to EMS personnel and 96% chest pain education to EMS personnel in the previous two years, the median hours devoted to stroke was one-half that for chest pain (6.0 vs. 12.0 hours, respectively). In the previous six months, 14% of EMS agencies had conducted community outreach programs for stroke compared with

17% for chest pain. The majority of EMS agencies had protocols specifically for managing stroke (83%) and for managing chest pain (99%). Diagnostic scales to identify stroke patients were used by 54% of agencies (20% Los Angeles Prehospital Stroke Screen, 20% Cincinnati Prehospital Stroke Scale, and 14% a locally developed scale). Thrombolytic checklists were used to identify eligible stroke patients at 37% of the EMS agencies, compared with 28% for eligible chest pain patients. CONCLUSIONS: In North Carolina, primary EMS agencies appear to have stroke and chest pain protocols in approximately the same frequency, yet their personnel receive only one-half as much education about stroke as they do about chest pain. Many stroke protocols were lacking basic components and would benefit from standardization across the state. Community outreach programs for both stroke and chest pain are minimal.

Maestroni, A., C. Mandelli, et al. (2008). "Factors influencing delay in presentation for acute stroke in an emergency department in Milan, Italy." Emergency Medicine Journal 25(6): 340-5.

BACKGROUND AND AIMS: Early treatment is critical for successful intervention in acute stroke. The aim of this study was to describe delays in presentation to hospital and in the emergency department (ED) management of patients with acute stroke and to identify factors influencing these delays in an Italian urban hospital. METHODS: The present series includes all patients presenting with acute stroke, in whom arrival delay was ascertainable. To describe delays into the ED, the triage-visit delay, visit-computed tomography (CT) delay and visit-CT report delay were registered. Type of stroke, severity of stroke assessed using the modified National Institute of Health Stroke Scale (mNIHSS) scale, level of consciousness, history of previous stroke or previous hospital admission, use of the emergency medical service (EMS), onset of stroke during day or night and admission during working or non-working day were registered for every patient. Univariate and multivariate analysis were performed to evaluate factors influencing early arrival. RESULTS: Over a one-year period 537 patients with acute stroke were evaluated; 375 patients in whom arrival delay was ascertainable were included in the study. Median arrival delay was 5.4 h (interquartile range (IQR) 2.7-11.6); 104 patients (28%) arrived within 3 h and 198 (53%) within 6 h. Triage-visit delay was 0.3 h (IQR 0.2-0.7), visit-CT scan delay was 1.2 h (IQR 0.8-1.9), visit-CT report delay was 2.7 h (IQR 1.7-4.5). Triage-visit delay and visit-CT delay were shorter for patients presenting within 3 h. The type of stroke was ischaemic in 240 (64%), haemorrhagic in 61 (16%) and transient ischaemic attack in 74 (20%). The median basal mNIHSS score was 5 (IQR 3-10); 64 patients (17%) had an altered level of consciousness, 103 (27%) had had a previous stroke, 223 (59%) had had a previous hospital admittance. In this series 214 patients (57%) arrived with the EMS, 323 (86%) presented with symptoms during the day, 261 (70%) were admitted during working days. Univariate analysis showed a significantly shorter arrival delay in patients calling the EMS (median 4.2 vs 7.2 h; $p < 0.001$) and in patients with a higher basal mNIHSS score (Spearman rho = -0.204; $p < 0.001$) or altered level of consciousness (normal 5.8 h, not alert but arousable 3.8, not alert but arousable with strong stimulation 2.5, totally unresponsive 6.0; $p = 0.005$). Multivariate analysis showed that use of the EMS and higher basal mNIHSS score were independent variables associated with a shorter arrival delay. CONCLUSION: A substantial proportion of patients does not arrive at the ED in a suitable time for reperfusion therapy. Patients using the EMS have a shorter arrival delay. Approximately half of the patients with stroke are sufficiently aware of the urgency of this clinical condition to activate the emergency telephone system.

McNamara, M. J., C. Oser, et al. (2008). "Stroke knowledge among urban and frontier first responders and emergency medical technicians in Montana." Journal of Rural Health 24(2): 189-93.

PURPOSE: To assess stroke knowledge and practice among frontier and urban emergency medical services (EMS) providers and to evaluate the need for additional prehospital stroke training opportunities in Montana. **METHODS:** In 2006, a telephone survey of a representative sample of EMS providers was conducted in Montana. Respondents were stratified into 2 groups: those working in urban and frontier counties. **FINDINGS:** Compared to EMS providers from urban counties, those from frontier counties were significantly more likely to be older (mean age 44.7 vs 40.1 years), have fewer personnel working in their service (mean 17.7 vs 28.6), to be located farther away from a computed tomography scan (CT scan) (mean 41.3 vs 17.6 miles), and to be volunteers (84% vs 49%). They were also less likely to have a stroke protocol (58% vs 66%) and use a stroke screening tool (36% vs 47%) than their urban counterparts. There were no significant differences between frontier and urban EMS respondents' ability to correctly identify 4 or more stroke warning signs (58% vs 61%), 4 or more stroke risk factors (46% vs 43%), or the 3-hour recombinant tissue plasminogen activator (rt-PA) treatment window (56% vs 57%). Approximately two thirds of respondents from urban and frontier counties believed they had adequate stroke knowledge, but 90% indicated they were interested in additional stroke-related training. **CONCLUSIONS:** Although stroke knowledge did not differ between urban and frontier groups, stroke screens and stroke protocols were less likely to be used in the frontier areas. Training opportunities and the implementation of stroke protocols and screening tools are needed for EMS providers, particularly in frontier counties.

Ramanujam, P., K. Z. Guluma, et al. (2008). "Accuracy of stroke recognition by emergency medical dispatchers and paramedics--San Diego experience." Prehospital Emergency Care **12**(3): 307-13.

BACKGROUND: Prehospital personnel in Emergency Medical Service (EMS) systems have varying levels of accuracy in stroke recognition. Identifying the accuracy of emergency medical dispatcher using Medical Priority Dispatch Systems (MPDS) stroke protocol and paramedics may help understand the accuracy of stroke recognition in about 3000 emergency medical dispatch systems and prehospital systems world wide. **OBJECTIVE:** Our aim was to assess the accuracy of stroke identification in emergency medical dispatchers (EMD) with high compliance to MPDS protocol and paramedics using Cincinnati Prehospital Stroke Scale (CSS). **METHODS:** This was a retrospective observational study. Data was acquired from a computer assisted dispatch (CAD) system, a computerized paramedic record database and discharge diagnosis from billing records or stroke registry containing all stroke assessments of patients who presented to the participating study hospitals within 12 hours of symptom onset. We included patients 18 years or older, identified as having stroke by EMD and city agency paramedics. We excluded patients taken to hospitals not participating in the study, patients with a dispatch determinant of Stroke (card 28) not transported by City EMS agency (SDMSE) to participating hospitals, patients in the stroke registry not transported by SDMSE or patients with no final outcome data. A stroke neurologist or hospital discharge diagnosis of stroke (physician diagnosis) was used to determine the sensitivity and predictive values of EMD and paramedic recognition of stroke. **RESULTS:** Of 882 patients with a dispatch determinant of stroke using MPDS Stroke protocol, 367 had a final discharge diagnosis of stroke. This gives a sensitivity of 83% and a positive predictive value of 42% for EMD using MPDS Stroke protocol. Of 477 patients with a paramedic assessment of stroke using CSS, 193 had a final discharge diagnosis of stroke. This gives a sensitivity of 44% and a PPV of 40% for paramedics using CSS. **CONCLUSIONS:** In our EMS system, EMD using MPDS Stroke protocol with a high compliance has a higher sensitivity than paramedics using CSS.

Disparities

Avendano, M. and M. M. Glymour (2008). "Stroke disparities in older Americans: is wealth a more powerful indicator of risk than income and education?" *Stroke* **39**(5): 1533-40.

BACKGROUND AND PURPOSE: This study examines the independent effect of wealth, income, and education on stroke and how these disparities evolve throughout middle and old age in a representative cohort of older Americans. **METHODS:** Stroke-free participants in the Health and Retirement Study (n=19,565) were followed for an average of 8.5 years. Total wealth, income, and education assessed at baseline were used in Cox proportional hazards models to predict time to stroke. Separate models were estimated for 3 age-strata (50 to 64, 65 to 74, and >or=75), and incorporating risk factor measures (smoking, physical activity, body mass index, hypertension, diabetes, and heart disease). **RESULTS:** 1542 subjects developed incident stroke. Higher education predicted reduced stroke risk at ages 50 to 64, but not after adjustment for wealth and income. Wealth and income were independent risk factors for stroke at ages 50 to 64. Adjusted hazard ratios comparing the lowest decile with the 75th-90th percentiles were 2.3 (95% CI 1.6, 3.4) for wealth and 1.8 (95% CI 1.3, 2.6) for income. Risk factor adjustment attenuated these effects by 30% to 50%, but coefficients for both wealth (HR=1.7, 95% CI 1.2, 2.5) and income (HR=1.6, 95% CI 1.2, 2.3) remained significant. Wealth, income, and education did not consistently predict stroke beyond age 65. **CONCLUSIONS:** Wealth and income are independent predictors of stroke at ages 50 to 64 but do not predict stroke among the elderly. This age patterning might reflect buffering of the negative effect of low socioeconomic status by improved access to social and health care programs at old ages, but may also be an artifact of selective survival.

Ottenbacher, K. J., J. Campbell, et al. (2008). "Racial and ethnic differences in postacute rehabilitation outcomes after stroke in the United States." *Stroke* **39**(5): 1514-9.

BACKGROUND AND PURPOSE: Incidence, prevalence, and mortality for stroke vary by race and ethnicity with higher rates for blacks compared with non-Hispanic whites. Little information is available regarding differences in postacute care outcomes for racial and ethnic groups after a stroke. **METHODS:** A retrospective analysis was conducted of 161,692 patients from the Uniform Data System for Medical Rehabilitation who received inpatient medical rehabilitation after a first stroke in 2002 and 2003. Multivariable models examined the effects of race and ethnicity on length of stay, functional status, rehabilitation efficiency, and discharge setting. **RESULTS:** The mean age was 70.97 years (SD=12.87), 53% were female, and 76% were non-Hispanic white. Mean length of stay was similar for all groups ranging from 17.39 days (SD=10.86) to 17.93 (SD=10.59). Non-Hispanic white patients had higher admission and discharge functional status ratings compared with patients in the minority groups (P<0.01). Differences in functional status across racial/ethnic groups were related to age (F=20.49, P<0.001); the older the comparison group, the greater the difference in functional status. Non-Hispanic whites were discharged home less often than blacks (OR=0.64, 95% CI=0.62 to 0.66), Hispanics (OR=0.58, 95% CI=0.55 to 0.62), or other minority groups (OR=0.67, 95% CI=0.57 to 0.67). **CONCLUSIONS:** The findings suggest racial and ethnic disparities exist in postacute care outcomes for persons with stroke.

GIS & Geographic Disparities

Voeks JH, McClure LA, Go RC et al. Regional differences in diabetes as a possible contributor to the geographic disparity in stroke mortality: the REasons for Geographic And Racial Differences in Stroke Study. *Stroke* **39**(6):1675-80, 2008.

BACKGROUND AND PURPOSE: Diabetes and hypertension impart approximately the same increased relative risk for stroke, although hypertension has a larger population-attributable risk because of its higher population prevalence. With a growing epidemic of obesity and associated increasing prevalence of diabetes that disproportionately impacts the southeastern Stroke Belt states, any potential contribution of diabetes to the geographic disparity in stroke mortality will only increase. **METHODS:** Racial and geographic differences in diabetes prevalence and diabetes awareness, treatment, and control were assessed in the REasons for Geographic And Racial Differences in Stroke study, a national population-based cohort of black and white participants older than 45 years of age. At the time of this report, 21 959 had been enrolled. **RESULTS:** The odds of diabetes were significantly increased in both white and black residents of the stroke buckle (OR, 1.26; [1.10, 1.44]; OR, 1.45 [1.26, 1.66], respectively) and Stroke Belt (OR, 1.22; [1.09, 1.36]; OR, 1.13 [1.02, 1.26]) compared to the rest of the United States. In the buckle, regional differences were not fully mediated and remained significant when controlling for socioeconomic status and risk factors. Addition of hypertension to the models did not reduce the magnitude of the associations. There were no significant differences by region with regard to awareness, treatment, or control for either race. **CONCLUSIONS:** These analyses support a possible role of regional variation in the prevalence of diabetes as, in part, an explanation for the regional variation in stroke mortality but fail to support the potential for a contribution of regional differences in diabetes management

Glasser, S. P., M. Cushman, et al. (2008). "Does differential prophylactic aspirin use contribute to racial and geographic disparities in stroke and coronary heart disease (CHD)?" Preventive Medicine **47**(2): 161-6.

CONTEXT: Aspirin use may reduce the risk of stroke and coronary heart disease. Differential use for vascular prophylaxis may contribute to racial and geographic disparities in stroke and coronary heart disease morbidity or mortality. **OBJECTIVE:** To assess the prevalence and predictors of aspirin use for primary prophylaxis of stroke in the general population free of clinically diagnosed stroke or coronary heart disease. **DESIGN AND SETTING:** Cross-sectional analysis of 16,908 participants (age 45 or greater), from a population-based national cohort study (REasons for Geographic And Racial Differences in Stroke) enrolled from February 2003-August 2006 with oversampling from the southeastern Stroke Belt and African Americans. Individuals with a prior stroke or coronary heart disease, or regular use of aspirin for pain relief were excluded from analyses. **MAIN OUTCOME MEASURES:** Aspirin use and reasons for use were assessed using a computer-assisted telephone interview. **RESULTS:** Prophylactic aspirin use was substantially higher among whites (34.7%) than African Americans (27.2%; $p < 0.0001$). There was a higher prevalence of aspirin use for prophylaxis in the Stroke Belt (32.1%) than in the rest of the nation (30.8%; $p = 0.07$). After adjustment for measures of socio-economic status, the odds ratio of aspirin use in the rest of the nation compared to Stroke Belt was 0.90 (95% CI 0.84-0.97). There was a higher likelihood of prophylactic aspirin use among participants who were white, male, older, past cigarette smokers, or of higher socio-economic status (higher income or education). **CONCLUSIONS:** In this study, aspirin use to prevent stroke and coronary heart disease was higher among whites than African Americans, raising the possibility that differential aspirin use could contribute to the racial disparities in vascular disease mortality. Counter to our hypothesis, aspirin use was more common in the Stroke Belt than the rest of the country, so differential aspirin use in the Stroke Belt is unlikely to contribute to geographic disparities in stroke.

Leira, E. C., D. C. Hess, et al. (2008). "Rural-urban differences in acute stroke management practices: a modifiable disparity." *Archives of Neurology* **65**(7): 887-91.

Acute stroke management practices in rural areas of the United States are suboptimal, which creates an unacceptable health disparity between urban patients with stroke and their rural counterparts. The existing gap between urban and rural stroke care may widen in the future as more urban-tested interventions are incorporated into the treatment of acute stroke. We conducted a PubMed search to identify all the articles published from 1997 to 2007 that addressed acute stroke, paramedics, ambulances, emergency services, and interhospital transportation pertaining to the US rural, urban, or nonurban environment. We review herein the problems and potential solutions that exist in 3 aspects of the current rural stroke care system: prehospital care, rural local hospital emergency department care, and interhospital transfer of patients and subsequent reception at a larger tertiary care institution, which often involve long distances and considerable time. We conclude that the current gap in rural-urban stroke management practices could be overcome with a comprehensive strategy that addresses the existing issues, including further education of rural caregivers, remote support from tertiary care institutions, and implementation of future acute clinical trials that test the rural strategies to stroke care.

Stroke Quality Improvement

Gargano, J. W., S. Wehner, et al. (2008). "Sex differences in acute stroke care in a statewide stroke registry." *Stroke* **39**(1): 24-9.

BACKGROUND AND PURPOSE: Many studies have reported poorer stroke outcomes in women, and some studies have reported sex differences in care. We analyzed data from a hospital-based stroke registry to determine whether acute stroke care and discharge status differed by sex. **METHODS:** Detailed chart-level information was collected on 2566 subjects admitted for acute stroke or transient ischemic attack to 15 Michigan hospitals in 2002. Sex differences in stroke care and patient status at discharge (in-hospital mortality and modified Rankin Scale score) were assessed after adjusting for differences in demographics, clinical characteristics, and comorbidities by multivariable models. Modified Rankin Scale score data were analyzed by proportional-odds models. **RESULTS:** Women were older than men (70 vs 67 years) and were more likely to have congestive heart failure and hypertension. Men were more likely to smoke and have a history of heart disease and dyslipidemia. After multivariable adjustment, women were less likely to receive thrombolytic therapy (odds ratio [OR]=0.56; 95% CI, 0.37 to 0.86) or lipid testing (OR=0.76; 95% CI, 0.61 to 0.94) and were more likely to suffer urinary tract infections (OR=2.57; 95% CI, 1.87 to 3.54). In-hospital mortality was similar in women and men (9% vs 8%); however, women had poorer discharge modified Rankin Scale scores (OR=1.17; 95% CI, 1.01 to 1.35). **CONCLUSIONS:** Although considerable parity exists in many aspects of acute stroke care, women were less likely than men to receive thrombolytic treatment and lipid testing, even after adjustment. However, given the largely similar care observed, it is unlikely that differences in care explain the poorer functional outcomes in female stroke survivors.

Lingsma, H. F., D. W. J. Dippel, et al. (2008). "Variation between hospitals in patient outcome after stroke is only partly explained by differences in quality of care: results from the Netherlands Stroke Survey.[see comment]." *Journal of Neurology, Neurosurgery & Psychiatry* **79**(8): 888-94.

BACKGROUND AND PURPOSE: Patient outcome is often used as an indicator of quality of hospital care. The aim of this study is to investigate whether there is a straightforward relationship between quality of care and outcome, and whether outcome measures could

be used to assess quality of care after stroke. METHODS: In 10 centres in The Netherlands, 579 patients with acute stroke were prospectively and consecutively enrolled. Poor outcome was defined as a score on the modified Rankin scale ≥ 3 at 1 year. Quality of care was assessed by relating diagnostic, therapeutic and preventive procedures to indication. Multiple logistic regression models were used to compare observed proportions of patients with poor outcome with expected proportions, after adjustment for patient characteristics and quality of care parameters. RESULTS: A total of 271 (47%) patients were dead or disabled at 1 year. Poor outcome varied across the centres from 29% to 78%. Large differences between centres were also observed in clinical characteristics, prognostic factors and quality of care. For example, between hospital quartiles based on outcome, age ≥ 70 years varied from 50% to 65%, presence of vascular risk factors from 88% to 96%, intravenous fluids when indicated from 35% to 81%, and antihypertensive therapy when indicated from 60% to 85%. The largest part of variation in patient outcome between centres was explained by differences in patient characteristics (Akaike's Information Criterion (AIC) = 134.0). Quality of care parameters explained a small part of the variation in patient outcome (AIC = 5.5). CONCLUSIONS: Patient outcome after stroke varies largely between centres and is, for a substantial part, explained by differences in patient characteristics at time of hospital admission. Only a small part of the hospital variation in patient outcome is related to differences in quality of care. Unadjusted proportions of poor outcome after stroke are not valid as indicators of quality of care.

Rahiman, A., J. L. Saver, et al. (2008). "In-hospital initiation of secondary prevention is associated with improved vascular outcomes at 3 months." Journal of Stroke & Cerebrovascular Diseases **17**(1): 5-8.

BACKGROUND: Although various in-hospital stroke quality improvement programs have been associated with high treatment rates at hospital discharge, there are few data on the impact of these programs on clinical outcomes. We evaluated the impact of the PROTECT (Preventing Recurrence Of Thromboembolic Events through Coordinated Treatment) program on short-term vascular risk. METHODS: Prospective data collected after discharge for ischemic stroke or transient ischemic attack caused by presumed atherosclerotic mechanism from a PROTECT intervention hospital and a comparison community hospital, which used conventional care, were compared. The 3-month follow-up clinical outcome data were then evaluated and differences in outcome frequency data between the two hospital groups were analyzed using Fisher's exact test. Covariate adjusted comparisons of percent with a vascular event was computed via logistic regression methods. RESULTS: A total of 224 patients met study criteria: 126 patients at a PROTECT hospital and 98 patients at a comparator hospital. The 3-month postdischarge data were available for 78 patients at PROTECT hospital versus 65 control patients. Patients at a PROTECT hospital were more likely to be younger, be current smokers, and not have a history of atrial fibrillation. At 3 months, there was a covariate-adjusted difference in the intervention-hospital group versus the control-hospital group with regard to the incidence of a vascular event (transient ischemic attack, stroke, or myocardial infarction), 8.4% versus 22% ($P = .036$). CONCLUSIONS: Compared with conventional care, PROTECT was associated with better 3-month vascular outcomes after stroke hospitalization. Further study is needed to confirm the potential favorable impact of stroke quality improvement programs on clinical outcomes.

Rehabilitation

Ellis, C., H. L. Breland, et al. (2008). "Racial/ethnic differences in utilization of post-stroke rehabilitation services: a systematic review." Ethnicity & Disease **18**(3): 365-72.

OBJECTIVE: To examine racial/ethnic differences in utilization of stroke-related rehabilitation. METHODS: We searched Medline (from 1966-2007), CINAHL (from 1982-2007), PsycINFO (1966-2007), REHABDATA (1966-2007), the Cochrane Library, and reference lists of published articles. We identified 82 studies in our initial search, including randomized and quasirandomized controlled trials, working papers, technical reports, and conference presentations of stroke patients that reported utilization of rehabilitation services including physical therapy (PT), occupational therapy (OT), speech-language pathology (SLP), and at least two groups that differed by race/ethnicity. Because of limited information on outcomes and heterogeneity of the studies, a formal meta-analysis was not conducted. A qualitative aggregation of study findings was performed instead. RESULTS: Ten studies involving 214,229 patients met the final criteria for review. Racial/ethnic minorities were more likely to receive rehabilitation and have longer lengths of stays in studies that reported use of rehabilitation services. In contrast, when studies reported discipline-specific (PT, OT, SLP) utilization of services, the results were mixed. CONCLUSIONS: Racial/ethnic differences in the utilization of rehabilitation services primarily reflected the manner in which service utilization was reported. Future studies should be designed to ensure an accurate comparison of service utilization by race/ethnicity.

Korner-Bitensky, N., J. Desrosiers, et al. (2008). "A national survey of occupational therapists' practices related to participation post-stroke." Journal of Rehabilitation Medicine **40**(4): 291-7.

OBJECTIVES: First, to identify occupational therapists' stroke rehabilitation practices related to leisure and social aspects of participation and potential explanatory variables associated with these practices. Secondly, to identify occupational therapists' desired assessment and treatment practices related to participation. DESIGN: A Canada-wide telephone survey. SUBJECTS: A random sample of 480 occupational therapists providing stroke rehabilitation. METHODS: Two case studies were created: one representing a patient receiving inpatient stroke rehabilitation; the other receiving community-based rehabilitation. A standardized questionnaire was used to elicit information on: (i) clinician and environmental variables; (ii) management of the patient depicted; (iii) desired assessment and intervention use. RESULTS: 60.2% identified a problem relating to leisure or social aspects of participation, 23.1% would use an assessment and 36.5% would offer an intervention focusing on leisure or social participation. Desired assessment use was low (1%), as was desired intervention use (15.2%). Regression analyses using numerous potential explanatory variables explained little regarding clinician practices. CONCLUSION: Less than half of the occupational therapists focused interventions on leisure and social aspects of participation, suggesting a gap between what could be done to enhance successful community reintegration post-stroke and what is currently done.

Teasell, R. W., N. C. Foley, et al. (2008). "A blueprint for transforming stroke rehabilitation care in Canada: the case for change." Archives of Physical Medicine & Rehabilitation **89**(3): 575-8.

Stroke is a major source of disability in Canada and other developed countries, which carries with it a high toll in terms of personal suffering for the stroke survivor and their family in addition to the associated economic costs. Despite the impressive body of evidence describing effective and feasible stroke rehabilitation practices, stroke survivors, their families, and health professionals currently do not benefit from a rehabilitation system that is well organized and evidence based. Using the principles of best evidence, we make the case for needed changes to the current system based on 5 processes of care known to be important in the pursuit of optimal outcomes: (1) admission to specialized stroke rehabilitation units, (2) early admission to stroke rehabilitation units, (3) intensive stroke rehabilitation therapies, (4) task-specific rehabilitation therapies, and (5)

well-resourced outpatient programs. Implementation of these strategies will be expected to result in improved functional gain, fewer complications, decreased mortality, and reduced need for institutionalization. In addition to providing improved care for both the stroke survivor and their family, evidence-based stroke rehabilitation care is more efficient and may reduce costs. Our experience in Canada suggests that instituting these 5 measures alone will result in significant improvements to the health care system.

Stroke Costs

Pletcher MJ, Lazar L, et al. (2009). "Comparing impact and cost-effectiveness of primary prevention strategies for lipid-lowering." Ann Intern Med. **150**(4):243-54

BACKGROUND: Lipid-lowering therapy is costly but effective at reducing coronary heart disease (CHD) risk. OBJECTIVE: To assess the cost-effectiveness and public health impact of Adult Treatment Panel III (ATP III) guidelines and compare with a range of risk- and age-based alternative strategies. DESIGN: The CHD Policy Model, a Markov-type cost-effectiveness model. DATA SOURCES: National surveys (1999 to 2004), vital statistics (2000), the Framingham Heart Study (1948 to 2000), other published data, and a direct survey of statin costs (2008). TARGET POPULATION: U.S. population age 35 to 85 years. Time Horizon: 2010 to 2040. PERSPECTIVE: Health care system. INTERVENTION: Lowering of low-density lipoprotein cholesterol with HMG-CoA reductase inhibitors (statins). OUTCOME MEASURE: Incremental cost-effectiveness. RESULTS OF BASE-CASE ANALYSIS: Full adherence to ATP III primary prevention guidelines would require starting (9.7 million) or intensifying (1.4 million) statin therapy for 11.1 million adults and would prevent 20,000 myocardial infarctions and 10,000 CHD deaths per year at an annual net cost of \$3.6 billion (\$42,000/QALY) if low-intensity statins cost \$2.11 per pill. The ATP III guidelines would be preferred over alternative strategies if society is willing to pay \$50,000/QALY and statins cost \$1.54 to \$2.21 per pill. At higher statin costs, ATP III is not cost-effective; at lower costs, more liberal statin-prescribing strategies would be preferred; and at costs less than \$0.10 per pill, treating all persons with low-density lipoprotein cholesterol levels greater than 3.4 mmol/L (>130 mg/dL) would yield net cost savings. RESULTS OF SENSITIVITY ANALYSIS: Results are sensitive to the assumptions that LDL cholesterol becomes less important as a risk factor with increasing age and that little disutility results from taking a pill every day. LIMITATION: Randomized trial evidence for statin effectiveness is not available for all subgroups. CONCLUSION: The ATP III guidelines are relatively cost-effective and would have a large public health impact if implemented fully in the United States. Alternate strategies may be preferred, however, depending on the cost of statins and how much society is willing to pay for better health outcomes. FUNDING: Flight Attendants' Medical Research Institute and the Swanson Family Fund. The Framingham Heart Study and Framingham Offspring Study are conducted and supported by the National Heart, Lung, and Blood Institute.

Hoverman, C., L. R. Shugarman, et al. (2008). "Use of postacute care by nursing home residents hospitalized for stroke or hip fracture: how prevalent and to what end?" Journal of the American Geriatrics Society **56**(8): 1490-6.

OBJECTIVES: To examine nursing home (NH) residents' use of Medicare-paid skilled nursing facility (SNF) services and the outcomes of that care and to identify clinical and non-clinical factors associated with that care. DESIGN: Retrospective cohort. SETTING: United States. PARTICIPANTS: NH residents aged 65 and older with Medicare claims for a hospitalization for hip fracture or stroke during 2001 to 2003. MEASUREMENTS: Resident diagnoses and use of SNF postacute care were measured using Medicare hospital claims. Market and provider characteristics were drawn from the Provider of Services file. Baseline characteristics, institutionalization, and mortality outcomes were drawn from the Minimum Data Set and Medicare Denominator File. RESULTS: Of the NH population hospitalized for hip fracture (49,903) or stroke (23,084), 79.7% and 64.1%,

respectively, used the SNF benefit. Residents not using the SNF benefit had poorer baseline health status; their mortality rates and rates of resuming long-term care were similar to the rates of residents who used the SNF benefit. CONCLUSION: NH residents used postacute SNF benefits at high rates yet had similar mortality and institutionalization outcomes as those without SNF care.

Mauldin, P. D., K. N. Simpson, et al. (2008). "Design of the economic evaluation for the Interventional Management of Stroke (III) trial." International Journal of Stroke **3**(2): 138-44.

RATIONALE: Stroke is a common and costly condition where an effective early treatment may be expected to affect patients' future quality of life, the cost of acute medical treatment, and the cost of rehabilitation and any supportive care needed for their remaining lifetime. To assist in informing discussions on early adoption of potential treatments, economic analyses should accompany investigations that seek to improve outcomes for stroke patients. AIMS: The primary aim is to assess whether i.v./i.a. rt-PA therapy is cost-effective at 3 months compared with i.v. rt-PA, and provides cost-savings or is cost-neutral by 12 months. Design Cost-effectiveness of the two treatment arms will be measured at months 3, 6, 9, and 12. Cost-effectiveness will be calculated using 1. standard cost-effectiveness methodology (incremental cost-effectiveness ratios), and 2. an econometric model to assess multiple outcome measures while controlling for multiple subject and treatment-related factors that are known to affect both outcomes and costs. STUDY OUTCOMES: Total cost for the initial hospitalization of treating stroke subjects randomized to either i.v./i.a. or i.v. rt-PA treatment arms will be measured, as will differences in types of resource utilization over 12 months between the two arms of the trial. Quality-of-life data (EuroQol EQ-5D) will be collected over a 12-month period and quality-adjusted life years will be used as a morbidity-adjusted measure of effectiveness. Subgroup analyses will include dichotomized NIH Stroke Scale (<20, ≥20), country, time between onset and randomization, and i.a. devices.

Biomarkers

Bang, O. Y., J. L. Saver, et al. (2008). "Association of serum lipid indices with large artery atherosclerotic stroke." Neurology **70**(11): 841-7.

BACKGROUND: Low-density lipoprotein cholesterol (LDL) is the primary lipid target for vascular risk reduction in stroke patients, but emerging data suggest that other lipid indices may better predict vascular hazard. We evaluated the relationship between several measures of the classically obtained serum lipid panel and the occurrence of large artery atherosclerotic stroke. METHODS: Data prospectively collected over a 4-year period on subjects admitted with ischemic stroke or TIA to a university medical center were analyzed. Independent associations of fasting serum lipid indices with large artery atherosclerotic (LAA) stroke mechanism were evaluated. RESULTS: Of 1,049 patients, 247 (23.5%) were classified with LAA, 224 (21.4%) were classified with small vessel disease (SVD), and 578 (55%) were non-LAA, non-SVD subtype. Lipid levels were similar between LAA and SVD patients. Total cholesterol, triglycerides, LDL, non-high-density lipoprotein cholesterol (HDL), and triglyceride:HDL ratio were significantly higher in LAA vs non-LAA, non-SVD patients. After adjustment for age, hypertension, diabetes, smoking, body mass index, and pre-morbid statin use, significant odds ratios (ORs) for LAA compared with all other ischemic stroke subtypes for patients in the uppermost lipid quartiles (vs lowest) were triglycerides (OR 2.69, 95% CI 1.44 to 5.02) and non-HDL (OR 2.39, 95% CI 1.40 to 4.11). LDL was not associated with LAA. CONCLUSIONS: Compared with all other ischemic stroke subtypes, elevated levels of serum triglycerides and non-high-density lipoprotein, but not low-density lipoprotein (LDL), are associated with large artery atherosclerotic stroke. These non-LDL lipid measures may have utility in delineating atherosclerotic stroke risk.

Gorelick, P. B. (2008). "Lipoprotein-associated phospholipase A2 and risk of stroke." American Journal of Cardiology **101**(12A): 34F-40F.

Stroke is the second-leading cause of death worldwide and is a disabling disease of both older and younger adults. Stroke is also among the most highly preventable disorders because there are well-defined risk factors and preventatives. The establishment of new risk markers or factors for stroke risk assessment provides a new avenue for stroke prevention. Lipoprotein-associated phospholipase A(2) (Lp-PLA(2)) is an enzyme that hydrolyzes oxidized phospholipids, releasing lysophosphatidylcholine, which has proinflammatory properties thought to be involved in the development of atherosclerosis and plaque rupture. In 2005, the Lp-PLA(2) blood test was approved by the US Food and Drug Administration (FDA) for assessing the risk of ischemic stroke and coronary artery disease. In epidemiologic studies, low-density lipoprotein cholesterol and other lipid factors have not been shown to be consistent predictors of stroke risk. Lp-PLA(2) measures, on the other hand, have shown a consistent association with stroke risk, conferring about a 2-fold increase in stroke occurrence. This relation has been studied in both first and recurrent stroke and is reviewed in this article. Importantly, a recent study has now shown that Lp-PLA(2) may increase the area under the curve beyond that of traditional cardiovascular risk factors and C-reactive protein. Therefore, Lp-PLA(2) determination may provide a pivotal opportunity to appropriately classify previously misclassified persons who are actually at high risk of stroke and in need of aggressive stroke intervention.

Yong, M. and M. Kaste (2008). "Dynamic of hyperglycemia as a predictor of stroke outcome in the ECASS-II trial." Stroke **39**(10): 2749-55.

BACKGROUND AND PURPOSE: Baseline hyperglycemia has been considered an independent predictor of stroke outcome. The present study analyzes the dynamics of serum glucose levels within the first 24 hours and its impact on stroke outcome.

METHODS: We studied 748 patients with acute ischemic hemispheric stroke in the second European Cooperative Acute Stroke Study (ECASS-II). The patients had 2 serum glucose measurements, at baseline and at 24 hours. Four dynamic patterns were defined as baseline hyperglycemia present only at baseline, 24-hour hyperglycemia present only at 24 hours, persistent hyperglycemia, ie, hyperglycemia at baseline and at 24 hours, and persistent normoglycemia, ie, normoglycemia at baseline and at 24 hours. The end points were 7-day neurological improvement on National Institutes of Health Stroke Scale, 30-day favorable functional outcome (Barthel Index 95 or 100), 90-day negligible dependence (modified Rankin Scale 0 to 2), all-cause mortality within 90 days, and hemorrhagic transformation on CT within the first 7 days.

RESULTS: In nondiabetic patients, persistent hyperglycemia was inversely associated with neurological improvement (OR=0.31; 95% CI=0.16 to 0.60), 30-day favorable functional outcome (OR=0.27; 95% CI=0.12 to 0.62), and 90-day negligible dependence (OR=0.36; 95% CI=0.17 to 0.73); it was associated with an increased risk of mortality within 90 days (OR=7.61; 95% CI=3.23 to 17.90) and for parenchymal hemorrhage (OR=6.64; 95% CI=2.63 to 16.78), whereas it was inversely associated with hemorrhagic infarction (OR=0.30; 95% CI=0.13 to 0.71). Delayed hyperglycemia at 24 hours was associated with the risks of death (OR=5.99; 95% CI=2.51 to 14.2) and parenchymal hemorrhage (OR=5.69; 95% CI=2.05 to 15.8) and inversely associated with no and negligible dependency (OR=0.40; 95% CI=0.20 to 0.78). Hyperglycemia at baseline only was not associated with any parameter of worse outcome. In patients with diabetes, the dynamic patterns of hyperglycemia did not suggest an association with stroke outcome.

CONCLUSIONS: Persistent hyperglycemia was associated with all bad outcome end points studied. In addition to a single glucose measurement, the pattern of change should be considered in the prediction of stroke outcome.