

## Late-Breaking Science Oral Abstracts

Thursday, February 23, 2017, 1:30pm – 3:00pm

*LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2017:*

*For late-breaking science being presented at ISC 2017, the embargo lifts when the first presentation begins in the scientific session in which the abstract is being presented: either 11:20 am CST on Wednesday, Feb. 22; 6:15 pm CST on Wednesday, Feb. 22; 11:00 am CST on Thursday, Feb. 23; 1:30 pm CST on Thursday, Feb. 23; or 11:53 am CST on Friday, Feb. 24. News media activities promoting late-breaking science are under embargo until the times noted above.*

**Presentation Number:** LB9

**Presentation Title:** Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack of Atherosclerotic Origin

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**Abstract Body:** BACKGROUND: Ticagrelor is an effective antiplatelet therapy among patients with coronary atherosclerotic disease and therefore could be more effective than aspirin in preventing recurrent stroke and cardiovascular events among patients with acute cerebral ischemia of atherosclerotic origin. METHODS: We randomized 13,199 patients with a non-cardioembolic, non-severe ischemic stroke or high-risk transient ischemic attack to ticagrelor (180 mg loading dose on day 1 followed by 90 mg twice daily for days 2-90) or aspirin (300 mg on day 1 followed by 100 mg daily for days 2-90) within 24 hours of symptom onset. Investigators classified all patients into atherosclerotic and non-atherosclerotic groups to perform this pre-specified, exploratory analysis. The primary endpoint was the time to the occurrence of stroke, myocardial infarction, or death within 90 days. RESULTS: Potentially symptomatic ipsilateral atherosclerotic stenosis was reported in 3081 (23%) patients. There was evidence of a treatment-by-atherosclerotic stenosis interaction ( $P=0.017$ ). A primary end-point occurred in 103/1542 (6.7%) patients randomized to ticagrelor and in 147/1539 (9.4%) patients randomized to aspirin (HR 0.68; 95% CI, 0.5 to 0.9,  $P=0.0030$ ). Among 10,118 patients with no ipsilateral stenosis, a primary end-point occurred in 6.8% and 6.9% on ticagrelor and aspirin, respectively, HR 0.97 (95% CI, 0.8 to 1.1,  $P=0.72$ ). CONCLUSION: In this pre-specified exploratory analysis

ticagrelor was superior to aspirin in preventing stroke, myocardial infarction and death at 90 days among patients with acute ischemic stroke or TIA when associated with ipsilateral atherosclerotic stenosis (Funded by AstraZeneca; ClinicalTrials.gov number, NCT01994720).

**Author Disclosure Block:** **P. Amarenco:** Research Grant; Significant; Pfizer. Speakers' Bureau; Modest; Amgen, Daiichi Sankyo. Speakers' Bureau; Significant; Pfizer, Bayer. Honoraria; Modest; Amgen, Daiichi Sankyo. Honoraria; Significant; AstraZeneca, Pfizer, Bayer, GSK, Fibrogen. Consultant/Advisory Board; Modest; Amgen. Consultant/Advisory Board; Significant; Pfizer. **G.W. Albers:** Other; Modest; AstraZeneca. **H. Denison:** Employment; Significant; AstraZeneca. **J.D. Easton:** Research Grant; Significant; AstraZeneca. Consultant/Advisory Board; Modest; Boehringer Ingelheim, Bristol-Myers Squibb. Other; Significant; NIH/NINDS/Sanofi. **S.R. Evans:** Consultant/Advisory Board; Modest; AstraZeneca. **P. Held:** Employment; Significant; AstraZeneca. **M.D. Hill:** Honoraria; Modest; Boehringer Ingelheim, BMS-Pfizer, Bayer Canada. Ownership Interest; Modest; Calgary Scientific Inc.. Consultant/Advisory Board; Modest; Merck LLC. Research Grant; Significant; Medtronic LLC, Stryker, Bayer Canada, Boehringer Ingelheim. Other Research Support; Significant; Alberta Innovates Health Solutions. **J. Jonasson:** Employment; Significant; AstraZeneca. **S.E. Kasner:** Research Grant; Significant; AstraZeneca, Bayer, Bristol Myers Squibb, WL Gore, Acorda. Consultant/Advisory Board; Modest; Merck, Abbvie, Johnson&Johnson, Boehringer Ingelheim, Daiichi Sankyo. **P. Ladenvall:** Employment; Significant; AstraZeneca. **K. Minematsu:** Honoraria; Modest; Bayer Healthcare, Otsuka Pharmaceuticals, AstraZeneca, Boehringer Ingelheim, Pfizer Inc, Mitsubishi Tanabe Pharma Inc, Japan Stryker, Kowa, Nihon Medi-Physics Co Ltd, BMS, Sawai Pharmaceutical Co Ltd, Sumitomo Dainippon Pharma Co Ltd, Medico's Hirata Inc, Daiichi Sankyo, Astellas Pharma Inc, Kyowa Hakkō Kirin Pharma, Sanofi S.A., MSD, Eisai Co Ltd, Towa Pharmaceutical Co Ltd. **C.A. Molina:** None. **Y. Wang:** None. **K.L. Wong:** Consultant/Advisory Board; Modest; AstraZeneca, Boehringer Ingelheim, Bayer, Pfizer, Sanofi. **S.C. Johnston:** Consultant/Advisory Board; Modest; AstraZeneca.

**Presentation Number:** LB10

**Presentation Title:** E-cigarette Exposure Alters Brain Glucose Utilization and Stroke Outcome

**Author Block:** Ali E. Sifat, Buvaneshwar Vaidya, Heidi Villalba, Mohammad A. Kaisar, Luca Cucullo, Thomas Abbruscato, TTUHSC Sch of Pharmacy, Amarillo, TX

**Abstract Body: Background:** Use of electronic cigarettes (e-Cig) is a growing health concern in both smoking and nonsmoking populations and rigorous studies are needed to investigate the effects of the nicotine exposure via e-Cig on the neurovascular unit (NVU) and stroke outcome. Previous studies by our group have shown that nicotine and tobacco smoke (TS) exposure exerts specific effects on paracellular blood-brain barrier (BBB) permeability in response to stroke conditions. **Methods:** In the present study, we specifically tested the effects of chronic e-Cig vaping on ischemic stroke outcome and brain glucose utilization. Nicotine was administered to mice by either osmotic pump at a dose of 4.5 mg/kg/day for 1, 7, 14 days or by e-Cig vapor (2.4% nicotine) delivered by an electronic nicotine delivery system for 7, 10, 14, & 30 days. Ischemia-reperfusion injury was induced by transient middle cerebral artery occlusion (tMCAO) followed by 24 hour reperfusion. Glucose transport was estimated with an in situ brain perfusion technique using radiolabeled glucose as a substrate. Brain deoxy-D-glucose uptake was also determined in brain slices exposed to 30 minute oxygen glucose deprivation (OGD) utilizing an acute brain slices (ABS) technique. **Results:** Nicotine exposure for 7 and 14 days resulted in a significant reduction in D-glucose influx rate (Kin) across the BBB, with a 49% reduction in 14 days nicotine infused animals. E-cig exposure for 7 and 14 days also decreased deoxy-D-glucose uptake in ABS experiments exposed to OGD. Interestingly, both 10 days and 30 days e-Cig exposed animals developed worsened stroke outcome, as measured by TTC staining and measurement of neurological deficits, which outpaced the stroke damage promoted by TS exposure. Both e-cig and TS exposure for 30 days significantly downregulated circulating levels of thrombomodulin, suggesting a pro-coagulant predisposition and potential risk for stroke and worsened secondary brain injury. **Conclusions:** These data suggest, from a cerebrovascular perspective, that e-Cig vaping is not safer than tobacco smoking, and may pose a similar, if not higher risk for stroke severity. We believe this exacerbation of stroke outcome could be due to an enhanced glucose deprived and/or thrombotic state at the NVU.

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**Presentation Number:** LB11

**Presentation Title:** Shake, Rattle & Roll Trial - Improving Blood Pressure Control Among African Americans

**Author Block:** Mai N Nguyen-Huynh, Joseph D Young, Stacey Alexeeff, Meghan Hatfield, Terrence Chinn, Mike Sorel, Stephen Sidney, Kaiser Permanente, Oakland, CA

**Abstract Body:** Background: In Kaiser Permanente Northern California (KPNC), an integrated healthcare system with a high overall rate of hypertension (HTN) control, blacks still had poorer blood pressure (BP) control than whites. It has been suggested that greater difficulty in controlling BP and lifestyle differences may account for this difference. The “Shake, Rattle and Roll” (SRR) trial is named for: 1) “shake” the salt habit; 2) “rattle” the intensity of current BP management; and 3) adapt and “roll” out the interventions to other communities. Methods: SRR is a pragmatic cluster-randomized controlled trial conducted at Kaiser Oakland from April 2013 to June 2016. All PCPs and their panels of black patients were randomized, stratified by panel size, to one of 3 arms: 1) usual care (UC); or 2) enhanced monitoring (EM) of KPNC BP management protocol; or 3) culturally tailored lifestyle (LS) coaching focused on the DASH eating plan. Black patients from KPNC HTN Registry with an identifying high BP reading  $\geq 140/90$  qualified to be recruited into SRR. The intervention period lasted 12 months. We assessed rates of BP control using the latest follow-up BP measurements between enrollment and 15 months post-enrollment. Data on demographics and medications were collected from participants’ EMRs. Results: We randomized 98 PCPs. There were 1,129 enrolled in UC, and 346 in EM and 286 in LS. Median age was 61 years. Among those enrolled, BP control rates were higher in LS than in UC (69% vs. 62%,  $p=0.03$ ; Table). After intervention completion, there was no difference across arms for adherence to BP medications, change in weight, or outpatient primary care utilization. Conclusions: For black patients with persistent HTN in SRR, LS arm had better BP control than UC at the end of 12 months of intervention. Further research is needed to assess the most cost-effective way to implement this successful intervention into clinical practice.

Blood pressure control rates at the end of intervention period in Shake Rattle & Roll

	Usual Care	Enhanced	p-value
Participants enrolled, N	1,129	386	
Participants with BP control at 12 months, N	700	222	
BP control, % (95% CI)	62.1 (59.0-65.0)	64.1 (58.8-69.1)	0.50
	Usual Care	Lifestyle	
Participants enrolled, N	1,129	286	
Participants with BP control at 12 months, N	700	198	
BP control, % (95% CI)	62.1 (59.0-65.0)	69.3 (63.6-74.4)	0.03

**Author Disclosure Block:** M.N. Nguyen-Huynh: None. J.D. Young: None. S. Alexeeff: None. M. Hatfield: None. T. Chinn: None. M. Sorel: None. S. Sidney: None.

**Presentation Number:** LB12

**Presentation Title:** Safety and Feasibility of Combination of Ticagrelor and Aspirin in Patients With Minor Stroke or TIA :Interim Analyses of the Platelet Reactivity in Acute Stroke or Transient Ischemic Attack (PRINCE) Trial

**Author Block:** **Yilong Wang**, Weiqi Chen, Capital Medcal Univ, Beijing tiantan hospital, Beijing, China; Yi Lin, Dept of Neurology and Inst of Neurology, First Affiliated Hosp, Fujian Medical Univ, Fuzhou, China; Yuesong Pan, Dept of Epidemiology and Health Statistics, Sch of Public Health, Capital Medical Univ, Beijing, China; Xia Meng, Yongjun Wang, Capital Medcal Univ, Beijing tiantan hospital, Beijing, China

**Abstract Body: Introduction:** PRINCE is a pilot, prospective, multicenter, open label, randomized controlled clinical trial, assessing the anti-platelet effects of ticagrelor plus aspirin versus clopidogrel plus aspirin on reducing the proportion of patients with high on-treatment platelet reactivity (HOPR) at 90 days in high-risk patients with minor stroke or TIA. The safety and feasibility of ticagrelor combined with aspirin in patients with minor stroke or TIA is still unknown.

**Methods:** Patients with minor stroke or TIA were randomly assigned in a 1:1 ratio to receive aspirin plus ticagrelor or aspirin plus clopidogrel. The primary outcome is the proportion of patients with HOPR at 90 days which has not been analyzed yet. The main outcome measure for the interim analysis was the 90-day rate of severe adverse events, bleed events (PLATO definition), stroke and death. This trial is registered with the US National Institutes of Health clinical trial registry, number NCT02506140.

**Results:** The trial enrolled 580 patients(ticagrelor group, n=290; clopidogrel group, n=290) till November, 2016. Between randomization and 90 days, there were 17 (5.9%) events of all stroke in the ticagrelor group compared with 20 (6.7%) events in the clopidogrel group (P=0.61). There were fewer bleeding events of any severity ( PLATO definition) in the clopidogrel group than in the ticagrelor group (17 vs 41 events; p=0.001). However, the major bleeding(fatal or life-threatening) events in both groups were similar(ticagrelor group: 2/290; clopidogrel group: 3/290). It should be noted that the incidence of dyspnea and other respiratory disorders was much higher in ticagrelor group (23/290, 7.9%) than that in clopidogrel group (1/290, 0.3%). In the ticagrelor and clopidogrel group, there were 25(8.6%) and 9 (3.1%) patients discontinued study drugs due to adverse events respectively(P=0.005).

**Conclusion:** The interim analysis results of the trial offer important data on safety and feasibility of ticagrelor combined with aspirin treating patients with minor stroke or TIA. Notably, adverse events especially respiratory disorders and minimal bleed in ticagrelor group caused higher incidence of discontinuation of study drug than that in clopidogrel group.

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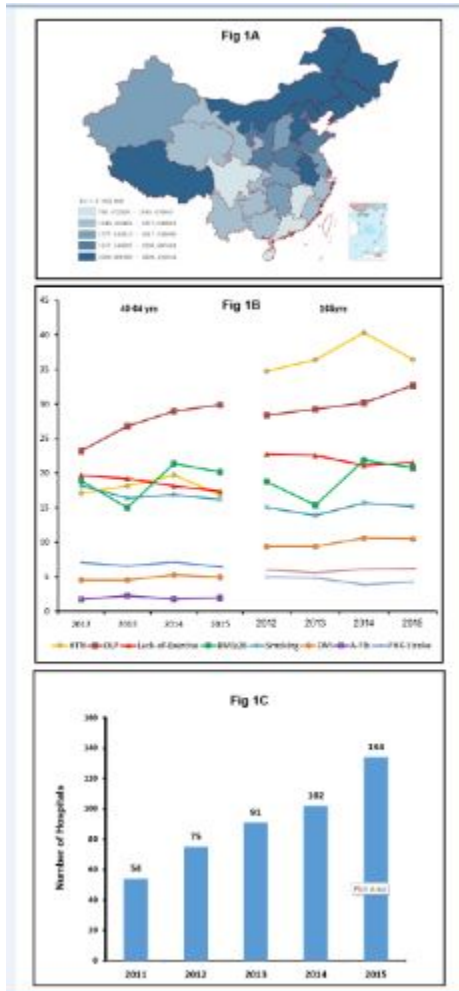
**Presentation Number:** LB13

**Presentation Title:** Effect of a Nationwide Hospital-based Stroke Network on Key Processes of Evidence-based Stroke Care: The China National Stroke Prevention Project

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**Abstract Body: Background:** Unlike western countries, Stroke is the No.1 cause of death and disability in China. The personal and societal burdens of stroke are immense. To address this worrisome public health and economic issue, the China National Stroke Prevention Project (CNSPP) was initiated in 2010 by the Chinese Government (Ministries of Health and Finance) as a high priority nationwide initiative to improve the prevention and treatment of stroke. **Objective:** To establish whether participation in CNSPP was associated with improvements in key processes of evidence-based stroke care. **Methods:** CNSPP has 3 components: 1) Stroke Epidemiology Project; 2) Stroke Education Project (patients and providers); and 3) Stroke Management Project (acute treatment and prevention). The Stroke Management Project, a prospective quality improvement program involved a goal of certifying 1000 primary stroke centers and 100 comprehensive stroke centers within 5 years. We assessed stroke care processes at 306 major hospitals, 1200+ regional hospitals and 2700+ community hospitals/clinics in 31 provinces over a 5 year period (2011 to 2015). **Results:** Among 2,647,552 subjects in the database, we observed that the occurrence of stroke was higher in the northern and western provinces (**Fig1A**) and stroke risk factor trajectories varied over time and by age (**Fig1B**). The number of hospitals capable of conducting carotid endarterectomy rose from 54 in 2011 to 136 in 2015 ( $p<0.001$ , **Fig1C**). The number of patients who received r-tPA tripled (from 5,236 in 2011 to 17,625 in 2015,  $p<0.001$ ), and the median door-to-needle time among the comprehensive stroke centers was 58.2 minutes in 2015. **Conclusion:** These data show that a government-driven nationwide program to improve hospital-based stroke care is associated with temporal enhancements in key care processes and capabilities. CNSPP may serve as a model for

developing countries with especially heavy stroke burdens to systematically address gaps in stroke care.



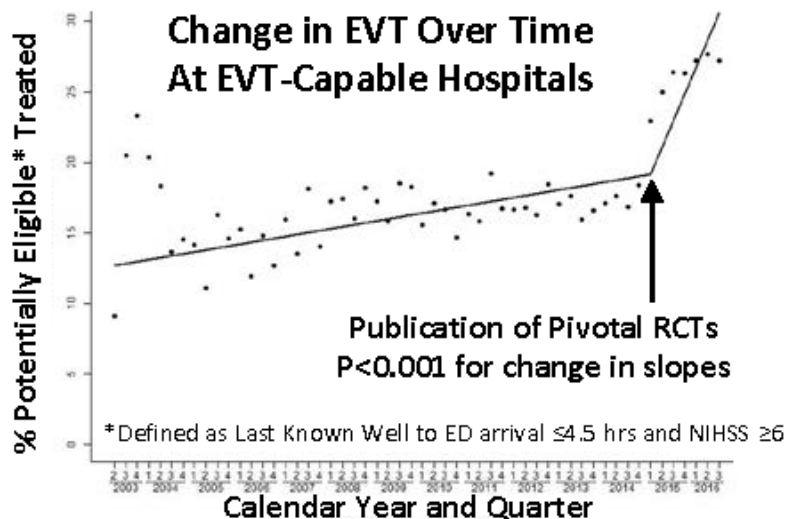
**Author Disclosure Block:** X. Ji: None. F. Yan: None. Y. Hua: None. L. Jiao: None. H. Zhang: None. Y. Shen: None. X. Wang: None. J. Hao: None. W. Feng: None. B. Ovbiagele: None. L. Wang: None.

**Presentation Number:** LB14

**Presentation Title:** Rapid Increase in Endovascular Thrombectomy for Acute Ischemic Stroke in the United States: Data From Get With the Guidelines-Stroke

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**Abstract Body: Purpose:** We report recent temporal trends in endovascular thrombectomy (EVT) use for acute ischemic stroke, hypothesizing EVT use would accelerate after December 2014 following publication of pivotal randomized controlled trials (RCTs). **Methods:** Data were from 2,403,635 patients seen at 2,203 hospitals participating in Get With The Guidelines-Stroke hospitals from 4/1/2003 to 9/30/2016. Analyses of the number of hospitals providing EVT were restricted to hospitals submitting  $\geq 4$  quarters of data with  $\geq 100$  ischemic stroke admissions (1,347,714 patients, 964 sites). EVT use was analyzed among all ischemic stroke patients and among the subset who were potentially eligible per ASA guidelines, defined as patients with NIHSS  $\geq 6$  arriving to the ED within 4.5 hours, allowing a door to puncture interval of up to 90 minutes. **Results:** Prior to online publication of the pivotal RCTs beginning quarter 1 (Q1) of 2015, the number of hospitals providing EVT/intra-arterial therapy increased slowly from 7.1% to 28.0% from 2003-2014 ( $p < 0.001$  for linear trend), and then more rapidly from 28.0% to 30.8% in Q3 2016 ( $p < 0.001$  for difference). Mean annualized average case volume increased from 25.0 patients in Q4 2014 to 52.7 patients in Q2 2016 ( $p < 0.001$ ). Among EVT-providing hospitals there was a sharp increase in the number of potentially eligible patients treated after Q4 2015 (Figure), such that by Q3 2016 27.2% were treated representing 7.1% of all ischemic stroke patients admitted to those hospitals. Among all patients at all hospitals (those providing and not providing EVT) the proportion of potentially eligible patients treated was 14.4% in Q3 2016, representing 3.0% of all ischemic strokes. **Conclusions:** Use of EVT accelerated markedly in the two years following RCT publication and guidelines updates, with more hospitals providing EVT and substantially increased volume at each hospital.





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**Presentation Number:** LB15

**Presentation Title:** Interhospital Transfer Prior to Thrombectomy is Associated With Delayed Treatment and Worse Outcome in the STRATIS Registry

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**Abstract Body:** *Introduction:* Endovascular treatment is beneficial for most acute stroke patients suffering a large vessel occlusion (LVO), though the efficacy of treatment is highly time-dependent. We hypothesized that interhospital transfer from a non-endovascular-capable hospital to an endovascular-capable center would result in treatment delays and worse clinical outcomes compared to direct presentation. *Methods:* STRATIS is a prospective, multicenter, observational, single-arm registry of LVO stroke patients treated with Solitaire/Mindframe. Subjects were separated by direct presentation (direct group) vs. interhospital transfer to the enrolling hospital (transfer group). The primary clinical outcome was mRS at 90 days. A hypothetical 'bypass' scenario was calculated by comparing door-to-tPA times and adding the transfer time to the direct group for an extremely conservative estimate of additional travel time. *Results:* A total of 984 subjects from 55 sites were analyzed. Median time from stroke onset to revascularization was 204 minutes for direct vs. 312 minutes for transfer patients ( $p < 0.0001$ ). Clinical outcomes at 90 days were better in the direct group with 60.0% (299/498) achieving mRS 0-2, compared to 52.5% (214/408) in the transfer group ( $p = 0.02$ ; odds ratio 1.38, 95%CI 1.06-1.79). Likewise, excellent outcome of mRS 0 or 1 was achieved in 47.4% (236/498) of direct patients vs. 38.0% (155/408) of transfer patients ( $p = 0.005$ ; odds ratio 1.47, 95%CI 1.13-1.92). Comparing overall outcome by mRS shift analysis also favored direct presentation ( $p = 0.012$  by Cochran-Mantel-Haenszel test). Mortality did not differ between the two groups (15.1% for direct, 13.7% for transfer;  $p = 0.55$ ). Hypothetical bypass calculations suggested that IV tPA could be delayed by as much as 22.4 minutes but thrombectomy would be performed 90.2 minutes sooner. *Conclusions:* In this large, real-world study, interhospital transfer was associated with significant delays to treatment and significantly lower chance of good outcome. Strategies to facilitate more rapid identification of LVO and direct routing to endovascular centers for severe stroke patients may help to improve outcomes.

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trials. Honoraria; Modest; Medtronic. Consultant/Advisory Board; Modest; Medtronic, Neuralanalytics, Inc.. Other; Modest; ESCAPE trial DSMB member. **T.L. Yao:** Consultant/Advisory Board; Modest; Medtronic (proctor). **D.S. Liebeskind:** Research Grant; Significant; NIH. Consultant/Advisory Board; Significant; Stryker, Medtronic. **N.H. Mueller-Kronast:** Consultant/Advisory Board; Modest; Medtronic.