

# Stroke Care and Application of Thrombolysis in Ibero-America

## Report From the SITS-SIECV Ibero-American Stroke Register

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**Background and Purpose**—Standardized registries may provide valuable data to further improve stroke care. Our aim was to obtain updated information about characteristics of stroke patients and management of stroke across the Ibero-American countries, using a common in-hospital registry (Safe Implementation of Treatments in Stroke–Sociedad Iberoamericana de Enfermedades Cerebrovasculares) as a basis for further quality improvement.

**Methods**—Data for this study were entered into the Safe Implementation of Treatments in Stroke registry from September 2009 to December 2013 by 58 centers in 14 countries. Data included demographics, risk factors, onset-to-door time, National Institutes of Health Stroke Scale score, stroke subtype, ischemic stroke etiology, treatments, 3-month mortality, and modified Rankin Scale score. Time to treatment was also recorded for patients treated with thrombolysis.

**Results**—Five thousand four hundred one patients were registered; median age, 65 years; 46% women; 3915 (72.5%) ischemic strokes; 686 (13.7%) hemorrhagic strokes; 213 (4.3%) subarachnoid hemorrhages; 414 (8.3%) transient ischemic attacks; and 31 (0.6%) cerebral vein thrombosis. The most prevalent risk factors were hypertension (71.3%), dyslipidemia (35.2%), and diabetes mellitus (23.6%). Atrial fibrillation was present in 15.1%. Three hundred one ischemic strokes were treated with intravenous thrombolysis (IVT; 7.7%). Patients undergoing IVT were more severely affected (median baseline National Institutes of Health Stroke Scale score, 11 versus 6). The rate of symptomatic intracerebral hemorrhages after IVT was 5.7%. At 3 months, 60.3% of IVT-treated patients and 59.1% of untreated patients were independent (modified Rankin Scale score, 0–2). Mortality was 11.4% in treated and 12.8% in untreated patients.

**Conclusions**—Safe Implementation of Treatments in Stroke–Sociedad Iberoamericana de Enfermedades Cerebrovasculares is the largest registry of a general stroke population and the first study to evaluate the level of IVT use in Ibero-America. It provides valuable information that may help to improve the quality of stroke care in the Ibero-American region. (*Stroke*. 2019;50:2507-2512. DOI: 10.1161/STROKEAHA.119.025668.)

**Key Words:** Latin America ■ risk factors ■ stroke ■ thrombolytic therapy

Efficient implementation of current recommendations for stroke treatment rely on 3 main pillars: education and commitment of health providers, public awareness about the disease so that people may comply with treatment

recommendations, and, finally, advanced health policies that ensure the availability of necessary resources within the health systems. The latter requires an adequate knowledge of the real burden of the disease to help match needs and resources.

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Currently, there are scarce data regarding stroke epidemiology in Ibero-America. Only a few epidemiological studies exist and only from certain countries. Some of them are community-based studies,<sup>1–10</sup> and others are published data from in-hospital registries.<sup>11–13</sup> There is also uncertainty on how well new treatments such as intravenous thrombolysis (IVT) or thrombectomy have been implemented in clinical practice. Therefore, a global picture that reflects the characteristics of patients, stroke subtypes, prevalence of risk factors, as well as trends in stroke management that permit comparisons between countries is necessary.

The development and completion of well-designed registries and databanks may help to achieve this knowledge. Moreover, involvement in clinical registries has been shown to increase adherence to clinical guidelines among participating physicians.<sup>14</sup>

In this view, the Ibero-American Stroke Organization Sociedad Iberoamericana de Enfermedades Cerebrovasculares (SIECV) started a joint regional project within Safe Implementation of Treatments in Stroke (SITS) with the objective of obtaining updated information about the characteristics of stroke patients and management of stroke across the Ibero-American countries to systematically evaluate the status of stroke care as a basis for quality improvement, using a common in-hospital stroke registry (SITS-SIECV). The aim was to conduct a prospective observational study of stroke subtypes, risk factors, severity grades, level of care, use of IVT, time to treatments, and functional outcomes in the Ibero-American Stroke Organization (SIECV) countries within the SITS-SIECV network during the period of 2009 to 2013.

## Methods

Data for this study were entered into the SITS international registry (<http://www.sitsinternational.org>). The data that support the findings of this study can be made available on reasonable request from qualified researchers, following approval from the SITS Scientific Committee. SITS is an independent, nonprofit, research-driven, international collaboration, the mission of which is to collect clinical data from stroke patients and to monitor treatments with the intention of increasing knowledge and providing the safe implementation of stroke treatment in routine clinical practice. SITS provides an internet-based interactive stroke registry for structured data entry. Local users can enter data in the database using a personal password to ensure confidentiality. Identifiable personal data are not registered in the database, and subjects included are identified by a confidential code. Ethics approval and patient consent for participation in the SITS International Stroke Treatment Registry were obtained in countries that so required it; other countries approved the register for anonymized audit. The SITS International Coordination Office monitored the SITS International Stroke Treatment Registry data online and checked individual patient data monthly to identify errors or inconsistencies.

Regional networks are built within SITS to strengthen collaborative research through provision of a common database for documentation and statistical evaluation.

In 2009, a joint collaboration between SITS International and the Ibero-American Stroke Organization (SIECV) was initiated with the aim to set up a hospital-based Ibero-American stroke registry (SITS-SIECV). SITS-SIECV has a regional status within SITS, meaning that scientific projects of regional character can be proposed. SITS-SIECV is coordinated by a regional steering committee.

The SITS-SIECV database included demographics, risk factors, onset-to-door time, National Institutes of Health Stroke Scale score, stroke subtype, ischemic stroke etiology coded according

to the *International Classification of Diseases, Tenth Revision*, treatments applied, symptomatic cerebral hemorrhage, as well as 3-month mortality and modified Rankin Scale (mRS) score. For patients treated with IVT, onset-to-needle and door-to-needle time was also recorded.

The initial SITS-SIECV project planned a prospective registry, with the possibility to also register patients retrospectively. Prospectively entered data from the initial phase of the registry (September 2009 to December 2013) are presented here. Descriptive data from the whole sample are expressed as medians with interquartile ranges for continuous variables or as absolute and relative frequencies for categorical variables. For patients with acute ischemic stroke, characteristics of those treated and untreated with IVT are shown separately.

## Results

SITS-SIECV started in 90 centers from 18 countries that stated their willingness to participate. In the end, only 14 countries with 58 centers actively recorded valid and confirmed data. A total of 5401 patients were prospectively recruited (Table 1). Of these, 3915 (72.5%) were ischemic strokes, 686 (13.7%) hemorrhagic strokes, 213 (4.3%) subarachnoid hemorrhages, 414 (8.3%) transient ischemic attacks, and 31 (0.6%) cerebral vein thrombosis. In addition, 32 (0.6%) patients had a final diagnosis of stroke mimics. The type of stroke was not registered in 110 patients (2%). Demographics, risk factors, and outcomes of patients in the registry are shown in Table 2. The most likely etiology of ischemic strokes is shown in Table 3. At 3 months, 43.3% of patients had excellent outcome (mRS, 0–1) and 59.8% were independent (mRS, 0–2), while 11.5% were dead.

Regarding acute management, 55.4% of all patients were treated in a stroke unit. Among ischemic stroke patients, 301 (7.7%) received IVT, 12 (0.3%) intraarterial thrombolysis, 21 (0.5%) primary mechanical thrombectomy, 9 (0.2%) IVT+intraarterial thrombolysis, and 7 (0.2%) IVT+mechanical thrombectomy. Sixty patients (1.5%) underwent hemicraniectomy. Outcome data are available in 82% of the total sample. Early mortality (at 7 days) was 7%. At 3 months, mortality was 11.5%, while 59.9% were independent (mRS score, 0–2).

Baseline characteristics, logistics, risk factors, stroke etiology, and outcomes in acute ischemic stroke patients treated with or without IVT are shown in Table 4.

## Discussion

SITS-SIECV has managed to establish an in-hospital registry for the Ibero-American region that has led to obtain the largest study of a general stroke population in Ibero-America. It is also the first study to show the rate of thrombolysis in the region. The burden of stroke in Ibero-America is considered to be similar to that reported in high-income countries from other continents, but considerable between-country variations exist according to the Global Burden of Disease report.<sup>15</sup> Reliable and comparable data about stroke characteristics, management, and outcomes in this area are lacking because of paucity of studies in certain countries, as well as methodological differences in case ascertainment, classification, and reference populations between previous studies. Differences in delivery and quality of stroke care between countries in Latin America have been recently described.<sup>16</sup> Most countries

**Table 1. Participating Countries and Recruitment per Country (September 2009 to December 2013)**

Country	No. of Sites	No. of Patients	Treated With IVT, n (%)
Argentina	8	645	18 (3)
Bolivia	1	0	0
Brazil	1	1198	204 (17)
Chile	6	716	51 (7)
Colombia	7	28	4 (14)
Costa Rica	1	0	0
Dominican Rep	1	5	0 (0)
Ecuador	4	173	1 (0.6)
El Salvador	3	0	0
Guatemala	3	24	1 (4)
Honduras	3	1	0 (0)
Mexico	8	390	13 (3)
Nicaragua	1	0	0
Panama	4	6	5 (83)
Paraguay	1	125	1 (0.8)
Peru	10	784	3 (0.4)
Uruguay	0	0	0
Venezuela	1	1275	0 (0)

IVT indicates intravenous thrombolysis.

have few stroke-ready hospitals, and in some of them, there are no stroke units. In the majority of countries, there is not a program for quality monitoring. Only Brazil and Chile, which have the greatest number of stroke units, have a National Stroke Policy.<sup>16</sup>

Considering the large sample size, relevant data can be obtained from this registry, despite differences in participation between countries. This updated information may contribute to the development of prevention programs and improvement of systems for stroke care aimed to reduce the burden of this disease in the region.

It has been suggested that the incidence and prevalence of stroke in Ibero-America might be lower than in higher income countries.<sup>1-3,17</sup> However, this has been attributed to poorer quality of assessment, derived from limited resources, and to a higher mortality during the acute phase of stroke. More recent studies indicate that stroke is a major health problem in the Ibero-American region, with high incidence and mortality rates.<sup>4-8,10</sup> Although there may be a declining trend in mortality, stroke remains as a major cause of death and is also an important cause of disability-adjusted life-years lost.<sup>4-8,15</sup>

The most common etiology of ischemic stroke in the SITS-SIECV registry was large vessel atherosclerosis, which accounted for 29.3% of all cases, followed by cardiac embolism. Previous studies suggested a higher frequency of lacunar strokes or small vessel disease in Ibero-America.<sup>4,12-14,17,18</sup> Variation in admission patterns, degree of completeness of diagnostic workups and in clinical definition of stroke subtypes, might be the reason for this difference. It should also be considered that, because of its in-hospital nature, there is

**Table 2. Demographics, Risk Factors, and Outcomes**

	n/Valid	Median (IQR) or %
Patient characteristics		
Age, y	5399	65 (54-76)
Male sex	2921	54.1
NIHSS baseline	4379	6 (2-13)
Risk factors		
Diabetes mellitus	1223/5181	23.6
Hypertension	3734/5236	71.3
Hyperlipidemia	1760/4993	35.2
Atrial fibrillation	778/5148	15.1
Heart failure	404/5121	7.9
Smoker, current	1026/5159	19.9
Smoker, previous	1034/4654	22.2
Previous stroke >3 mo	910/5170	17.6
Previous stroke ≤3 mo	147/5155	2.9
Previous TIA	338/5139	6.6
Mortality at 7 d	316/4423	7.1
Outcome at 3 mo (mRS)		
0	1031	23.2
1	896	20.1
2	734	16.5
3	652	14.7
4	475	10.7
5	140	3.2
6	510	11.5

Valid patients indicate the number of patients with data recorded in each category. IQR indicates interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and TIA, transient ischemic attack.

a possibility for selection bias toward more severe strokes in the registry, which might lead to an underestimation of lacunar strokes.

Regarding the distribution of stroke risk factors in the registry, the most frequent was hypertension, followed by hyperlipidemia and smoking. Relative frequencies of vascular risk factors may vary among countries depending on geographic, environmental, sociocultural, and economic factors. The recognition of their relative contribution to the burden of stroke is important to establish prevention strategies. Of particular interest is the proportional frequency of atrial fibrillation (AF) among included patients. There are few local studies available on the prevalence of AF, mainly small series from single centers. Most published numbers on AF in Ibero-America are extrapolations from reviews of the literature.<sup>19,20</sup> It is well known that AF is associated with a 5-fold increase in risk of stroke and that 15% to 20% of all ischemic strokes are attributed to this arrhythmia, the risk being substantially reduced with proper oral anticoagulation. However, the prevalence of AF may vary among ethnic groups or geographic areas; thus local data are needed to reliably estimate the local burden of

**Table 3. Pathogenesis of Ischemic Strokes in the Registry**

Type of Ischemic Stroke	n (%)
Large vessel atherosclerosis with stenosis >50%	422 (11.3)
Large vessel atherosclerosis, without stenosis	665 (18)
Cardiac emboli	1063 (28.5)
Small vessel, lacunar	719 (19.3)
Unusual	198 (5.3)
Multiple/unknown	695 (18.6)

Complete data in 3731 of 3915 patients (95.3%).

AF. For example, data from the Atahualpa Project showed a low prevalence of AF in Amerindians.<sup>21</sup> The estimated average prevalence of AF in Ibero-American countries is 1.6%, increasing with age up to 8%.<sup>22</sup> In these estimates, stroke appears to be associated with AF in 3% to 12.7% of cases. The SITS-SIECV registry shows that AF was present in 15% of all stroke patients included and in 17% of ischemic stroke patients, thus confirming AF as a major risk factor for stroke in the region. Yet, reports indicate an underuse of anticoagulation for stroke prevention in patients with AF and a poor adherence to the recommendations of current guidelines.<sup>20,22</sup> Available data emphasize the need to adequately implement these recommendations and to monitor compliance within local policies for stroke prevention.

Clinical characteristics, distribution of risk factors, and etiology of stroke in this cohort were similar to those reported from a cohort of general stroke patients included in the SITS registry. The SITS-SIECV cohort showed higher mortality at 7 days (7.1% versus 4.7%) but higher proportion of patients achieving good outcome (mRS, 0–2) at 3 months

(59.8% versus 52.1%).<sup>23</sup> Outcomes of IVT-treated patients in SITS-SIECV were similar to those in the SITS-MOST (Safe Implementation of Thrombolysis in Stroke-Monitoring Study) and subsequent SITS International Stroke Treatment Registry studies.<sup>24,25</sup> IVT-treated patients had more severe neurological deficit than the general stroke population, which probably indicates a selection bias for treatment in favor of more severely affected patients, as well as the propensity of more severe cases to arrive more rapidly to the hospital.

The study indicates that the use of IVT in Ibero-America varies between countries and between centers. In certain countries, such as Venezuela, access to thrombolysis is inexistent, whereas in others (Brazil, Colombia, Chile), it is more widely used. Several initiatives have emerged in recent years that are leading to an increase of IVT use in some countries (eg, Mexico, Paraguay, Perú, Panamá, Costa Rica).<sup>16</sup> Reasons for low use of IVT may be its cost, which is probably considered high in low-income countries with reduced investment in health care. Another explanation may be that patients arrive too late at the hospital. Almost 8% of ischemic stroke patients included in this registry underwent thrombolysis. However, the registry probably overestimates the use of IVT because of a selection bias. It is likely that participating countries and centers are precisely those with better organized systems for stroke care and the broader use of this treatment. Also, it is possible that IVT-treated patients were more likely to be enrolled in the registry. The percentage of thrombolysis use gives some measure of activity and efficiency of prehospital and hospital systems of stroke care. Published data from Brazil indicate that the rate of thrombolysis use is around 6% of all ischemic strokes,<sup>26</sup> this percentage growing over time, and in better structured services for stroke care.

**Table 4. Characteristics of Ischemic Stroke Patients Treated With or Without IVT**

	No IVT, n/Valid	Median (IQR) or %	IVT, n/Valid	Median (IQR) or %
Baseline characteristics				
Age, y	4058	67 (55–76)	300	66 (56–75)
Male sex	2233/4059	55	164/301	54.5
Baseline NIHSS	3576	6 (2–12)	299	11 (6–17)
OTD (hh:mm)	3809	11:00 (3:40–32:00)	298	1:41 (1:01–2:30)
DTN (hh:mm)			281	1:06 (0:46–1:32)
OTN (hh:mm)			284	3:00 (2:15–3:45)
Stroke Unit care	2146/4059	52.9	217/301	73.3
Outcomes				
SICH per SITS-MOST			2/285	0.7
SICH per ECASS II			16/283	5.7
SICH per NINDS			21/284	7.4
mRS 0–1 at 3 mo	1504/3457	43.5	103/253	42.8
mRS 0–2 at 3 mo	2084/3457	60.3	139/253	59.1
Death at 3 mo	400/3469	11.4	30/235	12.8

Valid indicate the number of patients with data recorded in each category. DTN indicates door-to-needle; ECASS II, European Cooperative Acute Stroke Study-II; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NINDS, National Institute of Neurological Disorders and Stroke; OTD, onset-to-door; OTN, onset-to-needle; SICH, symptomatic intracranial hemorrhage; and SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study.

It is also possible that the good results observed in stroke outcomes may be biased for the reasons given above. However, these potentially biased results bring to light an area for improvement: local systems should be organized and investment in health care should be increased so that patients may arrive early enough at the hospital to receive the acute treatment that increases their probability to have a good outcome.

## Conclusions

SITS-SIECV is a free-of-charge tool available to every hospital admitting acute stroke patients, which allows recording and comparing standardized data regarding demographics, risk factors profile, patterns of stroke subtypes, and information on stroke care in the region pertaining to, for example, stroke unit care and recanalization therapies. It remains active, thus further analysis of data from individual countries may help to better understand differences in epidemiology and management of stroke due of socioeconomic and ethnic variations. This valuable information may help modify local policies of health systems to improve the quality of stroke care in the Ibero-American countries.

## Appendix

SITS-SIECV Steering Committee: Exuperio Diez-Tejedor (Chairman), Spain; Nils Wahlgren (Chairman of SITS International), Sweden; Nicolaus Kostulas (Secretariat), Sweden; María Alonso de Leciñana (Regional Coordinator), Spain; Carlos Abanto, Peru; Oscar H. Del Brutto, Ecuador; Mario de Bastos, Venezuela; Fernando Góngora-Rivera, Mexico; Sheila Martins, Brazil; Ayrton R. Massaro, Brazil; Claudio Sacks, Chile. SITS-SIECV National Coordinators: Patricio Abad (Ecuador), Carlos Abanto (Perú), Sebastián Ameriso (Argentina), Antonio Arauz-Góngora (Mexico), William Arias Sifontes (El Salvador), Mario de Bastos (Venezuela), Óscar H. Del Brutto (Ecuador), Margarita Cerda (Dominican Republic), Franz Chávez-Sell (Costa Rica), Juan Carlos Duran (Bolivia), Gabriel de Freitas (Brazil), Fernando Góngora-Rivera (Mexico), Arnold Hoppe (Chile), Jorge Martínez Cerrato (Nicaragua), Sheila Martins (Brazil), Ayrton R. Massaro (Brazil), Marco Tulio Medina (Honduras), Gloria Meza (Paraguay), Nelson Navarro (Panamá), Jamary Oliveira-Filho (Brazil), Octavio Pontes Neto (Brazil), German Enrique Perez (Colombia), Claudio Sacks (Chile), Luis Salguero (Guatemala). SITS-SIECV Collaborators: Argentina: Marina Romano, Claudia Gandolfo, Gustavo Herrera, Lorena Jure, María Elena Masih, Raul Rey, Facundo Enrique Tomas. Brazil: Magda Carla Martins. Chile: Carlos Aguilera, Pablo Araya, Ludwig Codjambasis, Juan Gigoux, Rodrigo Rivas. Colombia: Mario Muñoz, Juan Camilo Vargas. Ecuador: Tomás Alarcón, Braulio Martínez, Jorge Moncayo. Mexico: José Luis Ruiz-Sandoval, Jorge Villarreal, Rosalía Vázquez, Juan Nader, Luis Murillo-Bonilla, Carolina León. Panama: Arón Benzádon, Ernesto Triana. Paraguay: Aurora Olmedo, Donoband Melgarejo, Margarita Paredes. Peru: Rosa Ecos, Frank Solis, Víctor Gómez, Greasse Muñoz, Juliana Aparcana, Luis Miguel Uchuya, Taly Paredes, Antero Peralta, Enrique Salcedo, Luis Huaroto Luis Vera, Martín Gavidia, Alejandro Calvo, Evelyn Mariños, Luis Sandoval, Marcos Vilca, René Valderrama, Isolina Villanueva, Daniel Diez-Canseco, Juan Barreto, Guillermo Castillo, Juan Carlos Lazo, José Cruz. Venezuela: Aglaé Duplat, Juan Carlos Guedes.

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## Disclosures

Dr Mazya holds the position of International Network and Research Executive at Safe Implementation of Treatments in Stroke (SITS) International. Dr Wahlgren is Senior Advisor of SITS International. Dr Martins received honoraria as a speaker in symposia from Boehringer-Ingelheim. The other authors report no conflicts.

## References

- Jaillard AS, Hommel M, Mazetti P. Prevalence of stroke at high altitude (3380 m) in Cuzco, a town of Peru. A population-based study. *Stroke*. 1995;26:562–568.
- Uribe CS, Jiménez I, Mora MO, Arana A, Sánchez JL, Zuluaga L, et al. [Epidemiology of cerebrovascular diseases in Sabaneta, Colombia (1992–1993)]. *Rev Neurol*. 1997;25:1008–1012.
- Nicoletti A, Sofia V, Giuffrida S, Bartoloni A, Bartalesi F, Bartolo ML, et al. Prevalence of stroke: a door-to-door survey in rural Bolivia. *Stroke*. 2000;31:882–885.
- Lavados PM, Sacks C, Prina L, Escobar A, Tossi C, Araya F, et al. Incidence, 30-day case-fatality rate, and prognosis of stroke in Iquique, Chile: a 2-year community-based prospective study (PISCIS project). *Lancet*. 2005;365:2206–2215. doi: 10.1016/S0140-6736(05)66779-7
- Hochmann B, Coelho J, Segura J, Galli M, Ketzoian C, Pebet M. [The incidence of cerebrovascular accidents in the town of Rivera, Uruguay]. *Rev Neurol*. 2006;43:78–83.
- Cabral NL, Gonçalves AR, Longo AL, Moro CH, Costa G, Amaral CH, et al. Incidence of stroke subtypes, prognosis and prevalence of risk factors in Joinville, Brazil: a 2 year community based study. *J Neurol Neurosurg Psychiatry*. 2009;80:755–761. doi: 10.1136/jnnp.2009.172098
- Cantu-Brito C, Majersik JJ, Sánchez BN, Ruano A, Becerra-Mendoza D, Wing JJ, et al. Door-to-door capture of incident and prevalent stroke cases in Durango, Mexico: the Brain Attack Surveillance in Durango Study. *Stroke*. 2011;42:601–606. doi: 10.1161/STROKEAHA.110.592592
- Lange MC, Cabral NL, Moro CH, Longo AL, Gonçalves AR, Zétola VF, et al. Incidence and mortality of ischemic stroke subtypes in Joinville, Brazil: a population-based study. *Arq Neuropsiquiatr*. 2015;73:648–654. doi: 10.1590/0004-282X20150081
- Del Brutto OH, Santamaría M, Zambrano M, Peñaherrera E, Pow-Chon-Long F, Del Brutto VJ, et al. Stroke in rural coastal Ecuador: a community-based survey. *Int J Stroke*. 2014;9:365–366. doi: 10.1111/ijs.12102
- Del Brutto OH, Mera RM, Zambrano M, Del Brutto VJ. Severe edentulism is a major risk factor influencing stroke incidence in rural Ecuador (The Atahualpa Project). *Int J Stroke*. 2017;12:201–204. doi: 10.1177/1747493016676621
- Cantu-Brito C, Majersik JJ, Sánchez BN, Ruano A, Quiñones G, Arzola J, et al. Hospitalized stroke surveillance in the community of Durango, Mexico: the brain attack surveillance in Durango study. *Stroke*. 2010;41:878–884. doi: 10.1161/STROKEAHA.109.577726
- Del Brutto OH, Mosquera A, Sánchez X, Santos J, Noboa CA. Stroke subtypes among Hispanics living in Guayaquil, Ecuador. Results from the Luis Vernaza hospital stroke registry. *Stroke*. 1993;24:1833–1836.
- Sapostnik G, Gonzalez L, Lepera S, Luraschi A, Sica RE, Caplan LR, et al. Southern Buenos Aires stroke project. *Acta Neurol Scand*. 2001;104:130–135.
- Herrera AL, Góngora-Rivera F, Muruet W, Villarreal HJ, Gutiérrez-Herrera M, Huerta L, et al; GECEN Investigators. Implementation of a stroke registry is associated with an improvement in stroke performance measures in a tertiary hospital in Mexico. *J Stroke Cerebrovasc Dis*. 2015;24:725–730. doi: 10.1016/j.jstrokecerebrovasdis.2014.09.008

15. Owens Johnson C, Nguyen M, Roth GA, Nichols E, Alam T, Abate D, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18:439–458.
16. Ouriques Martins SC, Sacks C, Hacke W, Brainin M, de Assis Figueiredo F, Marques Pontes-Neto O, et al. Priorities to reduce the burden of stroke in Latin American countries. *Lancet Neurol.* 2019;18:674–683. doi: 10.1016/S1474-4422(19)30068-7
17. Saposnik G, Del Brutto OH; Iberoamerican Society of Cerebrovascular Diseases. Stroke in South America: a systematic review of incidence, prevalence, and stroke subtypes. *Stroke.* 2003;34:2103–2107. doi: 10.1161/01.STR.0000088063.74250.DB
18. Lavados PM, Hennis AJ, Fernandes JG, Medina MT, Legetic B, Hoppe A, et al. Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean. *Lancet Neurol.* 2007;6:362–372. doi: 10.1016/S1474-4422(07)70003-0
19. Lip GYH, Brechin CM, Lane DA. The global burden of atrial fibrillation and stroke: a systematic review of the epidemiology of atrial fibrillation in regions outside North America and Europe. *Chest.* 2012;142:1489–1498. doi: 10.1378/chest.11-2888
20. Cubillos L, Haddad A, Kuznik A, Mould-Quevedo J. Burden of disease from atrial fibrillation in adults from seven countries in Latin America. *Int J Gen Med.* 2014;7:441–448. doi: 10.2147/IJGM.S62819
21. Del Brutto OH, Costa AF, Cano JA, Peñaherrera E, Plaza KJ, Ledesma EA, et al. Low prevalence of atrial fibrillation in Amerindians: a population-based study in frequent fish consumers living in rural coastal Ecuador (The Atahualpa Project). *Aging Clin Exp Res.* 2018;30:539–542. doi: 10.1007/s40520-017-0810-z
22. Gamra H, Murin J, Chiang CE, Naditch-Brûlé L, Brette S, Steg PG; RealiseAF Investigators. Use of antithrombotics in atrial fibrillation in Africa, Europe, Asia and South America: insights from the international realiseAF survey. *Arch Cardiovasc Dis.* 2014;107:77–87. doi: 10.1016/j.acvd.2014.01.001
23. Rukn SA, Mazya MV, Hentati F, Sassi SB, Nabli F, Said Z, et al. Stroke in the Middle-East and North Africa: A 2-year prospective observational study of stroke characteristics in the region. Results from the safe implementation of treatments in Stroke (SITS)–Middle-East and North African (MENA) [published online March 12, 2019]. *Int J Stroke.* doi: 10.1177/1747493019830331
24. Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, et al; SITS-MOST Investigators. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet.* 2007;369:275–282. doi: 10.1016/S0140-6736(07)60149-4
25. Wahlgren N, Ahmed N, Dávalos A, Hacke W, Millán M, Muir K, et al; SITS Investigators. Thrombolysis with alteplase 3–4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. *Lancet.* 2008;372:1303–1309. doi: 10.1016/S0140-6736(08)61339-2
26. Moro CH, Gonçalves AR, Longo AL, Fonseca PG, Harger R, Gomes DB, et al. Trends of the incidence of ischemic stroke thrombolysis over seven years and one-year outcome: a population-based study in Joinville, Brazil. *Cerebrovasc Dis Extra.* 2013;3:156–166. doi: 10.1159/000356984