

Get With The Guidelines-Stroke Performance Indicators: Surveillance of Stroke Care in the Taiwan Stroke Registry

Get With The Guidelines-Stroke in Taiwan

Fang-I Hsieh, PhD*; Li-Ming Lien, MD*; Sien-Tsong Chen, MD; Chyi-Huey Bai, PhD; Mu-Chien Sun, MD, MSc; Hung-Pin Tseng, MD; Yu-Wei Chen, MD; Chih-Hung Chen, MD; Jiann-Shing Jeng, MD, PhD; Song-Yen Tsai, MD, MSc; Huey-Juan Lin, MD, MPH; Chung-Hsiang Liu, MD, MSc; Yuk-Keung Lo, MD; Han-Jung Chen, MD, PhD; Hou-Chang Chiu, MD; Ming-Liang Lai, MD; Ruey-Tay Lin, MD; Ming-Hui Sun, MD; Bak-Sau Yip, MD, PhD; Hung-Yi Chiou, PhD; Chung Y. Hsu, MD, PhD; and the Taiwan Stroke Registry Investigators

Background—Stroke is a leading cause of death around the world. Improving the quality of stroke care is a global priority, despite the diverse healthcare economies across nations. The American Heart Association/American Stroke Association Get With the Guidelines-Stroke program (GWTG-Stroke) has improved the quality of stroke care in 790 US academic and community hospitals, with broad implications for the rest of the country. The generalizability of GWTG-Stroke across national and economic boundaries remains to be tested. The Taiwan Stroke Registry, with 30 599 stroke admissions between 2006 and 2008, was used to assess the applicability of GWTG-Stroke in Taiwan, which spends $\approx 1/10$ of what the United States does in medical costs per new or recurrent stroke.

Methods and Results—Taiwan Stroke Registry, sponsored by the Taiwan Department of Health, engages 39 academic and community hospitals and covers the entire country with 4 steps of quality control to ensure the reliability of entered data. Five GWTG-Stroke performance measures and 1 safety indicator are applicable to assess Taiwan Stroke Registry quality of stroke care. Demographic and outcome figures are comparable between GWTG-Stroke and Taiwan Stroke Registry. Two indicators (early and discharge antithrombotics) are close to GWTG-Stroke standards, while 3 other indicators (intravenous tissue plasminogen activator, anticoagulation for atrial fibrillation, lipid-lowering medication) and 1 safety indicator fall behind. Preliminary analysis shows that compliance with selected GWTG-Stroke guidelines is associated with better outcomes.

Conclusions—Results suggest that GWTG-Stroke performance measures, with modification for ethnic factors, can become global standards across national and economic boundaries for assessing and improving quality of stroke care and outcomes. GWTG-Stroke can be incorporated into ongoing stroke registries across nations. (*Circulation*. 2010;122:1116-1123.)

Key Words: anticoagulants ■ antiplatelets ■ thrombolysis

With the efficacy of thrombolytic therapy within a limited time window confirmed in clinical trials,¹ initiatives have been actively taken to improve the quality of stroke care in the United States.^{2,3} This was followed by the implementation of the American Heart Association/American

Stroke Association Get With the Guidelines-Stroke program (GWTG-Stroke).⁴ GWTG-Stroke was the first large-scale nationwide assessment of the quality of stroke care based on a set of predefined performance measures. The 790 participating hospitals showed substantial and sustained improve-

Received January 8, 2010; accepted July 15, 2010.

From the School of Public Health and Dr. Chi-Chin Huang Stroke Research Center, Taipei Medical University, Taiwan (F.I.H., H.Y.C., C.H.B.); Neurology, Shin Kong WHS Memorial Hospital, Taipei, Taiwan (L.M.L., H.C.C.); Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taiwan (L.M.L.); Neurology, Chang Gung University and Memorial Hospital, Linkou, Taiwan (S.T.C.); Central Laboratory, Shin Kong WHS Memorial Hospital, Taipei, Taiwan (C.H.B.); Neurology, Changhua Christian Hospital, Changhua, Taiwan (M.C.S.); Neurology, Lotung Poh Ai Hospital, Lotung, Taiwan (H.P.T.); Neurology, Landseed Hospital, Taoyuan, Taiwan (Y.W.C.); Neurology, National Taiwan University Hospital, Taipei (J.S.J., Y.W.C.); Neurology, National Cheng Kung University Hospital and National Cheng Kung University, Tainan, Taiwan (C.H.C., M.L.L.); Neurology, Changhua Christian Hospital Yunlin Branch, Yunlin, Taiwan (S.Y.T.); Neurology, Chi Mei Medical Center, Tainan, Taiwan (H.J.L.); Neurology, China Medical University Hospital, Taichung, Taiwan (C.H.L.); Neurology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan (Y.K.L.); Stroke Center, E Da Hospital, Kaohsiung, Taiwan (H.J.C.); Neurology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan (R.T.L.); Neurology, Kuang Tien General Hospital, Taichung, Taiwan (M.H.S.); Neurology, DOH Hsinchu General Hospital, Hsinchu, Taiwan (B.S.Y.); Graduate Institute of Clinical Medical Science, China Medical University, Taichung, Taiwan (C.Y.H.).

*Drs Hsieh and Lien contributed equally to this work.

The online-only Data Supplement is available with this article at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.110.936526/DC1>.

Correspondence to Hung-Yi Chiou, PhD, School of Public Health, Taipei Medical University, Taipei 11031, Taiwan (E-mail hychiou@tmu.edu.tw); or Chung Y. Hsu, MD, PhD, Graduate Institute of Clinical Medical Science, China Medical University, Taichung, 40447, Taiwan (E-mail: hsuc@mail.cmu.edu.tw).

© 2010 American Heart Association, Inc.

Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.110.936526

ment in the quality of stroke care over time. The significant impact of GWTG-Stroke on a large number of hospitals broadly covering both academic as well as community settings suggests the generalizability of this program across the nation.⁴

Clinical Perspective on p 1123

Stroke is the second leading cause of death globally,⁵ with nations with diverse health care systems facing a similar medical and economic burden.⁶ Whether the successful GWTG-Stroke is applicable beyond the United States remains to be tested. A key determinant that may hamper broad application of GWTG-Stroke around the world is the diversity of healthcare economies. It could be difficult for nations spending substantially less in healthcare dollars to apply GWTG-Stroke standards. To examine whether GWTG-Stroke is workable across nations with substantial disparities in health expenditures, we applied GWTG-Stroke to assess the quality of stroke care in Taiwan. Like the United States, stroke is the third leading cause of death in Taiwan. In 2008, the total cost of stroke in the United States, with 780 000 new or recurrent stroke cases, was estimated to be \$65.5 billion, with direct (medical) costs constituting two thirds or \$43.6 billion.⁵ Taiwan, with a population of 23 million (1/13 of that of the United States), with \approx 80 000 new or recurrent strokes a year, spent a total of US \$375 million in medical costs for stroke in 2007.⁷ The total medical costs per new or recurrent stroke patient were \approx 1/10 of those spent in the United States.⁵ The Taiwan Stroke Registry (TSR) is an appropriate program to assess the generalizability of GWTG-Stroke across national as well as economic boundaries. TSR, sponsored by the Department of Health (DOH), was launched in 2006. With the exception of anticoagulation for deep vein thrombosis (DVT) and measures for smoking cessation, all the parameters adapted by GWTG-Stroke for assessing quality of stroke care have been included in TSR.

Methods

TSR Design and the Criteria for Hospital Selection

TSR is the first nationwide effort in Taiwan to establish a reliable national stroke database for assessing the quality of stroke care and identifying areas that require improvement. TSR was designed and a TSR operation manual developed after a series of consensus conferences attended by an expert panel (16 stroke neurologists and 2 epidemiologists). The operation manual was revised after a 3-month pilot study to streamline the operation. Approval of TSR as a human study protocol and informed consent to be signed by the subjects giving permission for follow-up by TSR were obtained from the Institutional Review Board of each participating hospital. A total of 39 hospitals, caring for \approx 18% of all patients with stroke in the nation, which had conformed to the TSR criteria (see the online-only Data Supplement) were included. TSR was formally launched on August 1, 2006. Based on National Health Insurance (NHI) statistics of stroke admissions (International Classification of Diseases [ICD] codes, ICD430-437, excluding 432 [subdural hemorrhage] and 435 [transient ischemic attack (TIA)]) in 2005, 77.41% of stroke admissions were categorized as ischemic and 22.59% hemorrhagic in comparison with the TSR data with 79.72% ischemic and 20.28% hemorrhagic. These findings suggest that TSR is representative of the national stroke figure.

Case Ascertainment and Case Definition

TSR identified acute stroke admissions using a prospective design. All subjects meeting 1 of the 5 stroke type definitions, namely ischemic stroke, TIA, intracerebral hemorrhage (ICH), subarachnoid hemorrhage, and cerebral venous thrombosis (see the online-only Data Supplement) were entered if the following criteria were fulfilled: (1) the subject presented within 10 days of symptom onset to a TSR hospital and (2) received examination including computed tomography and/or magnetic resonance imaging for this index event. Ischemic strokes were classified into 5 major subtypes according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria⁸: large artery atherosclerosis, small vessel occlusion, cardioembolism, specific pathogenesis, and undetermined pathogenesis.

Data Collection

Data were compiled prospectively by TSR-trained neurologists and their study nurses. Investigators responsible for rating National Institutes of Health Stroke Scale (NIHSS) had to be certified by the Taiwan Stroke Society and trained for data entry through a web-based TSR database system. The key items in the TSR form include (1) preadmission data: demographic profiles, past medical history, preadmission medications, date and time of stroke onset and arrival at the emergency room, arrival mode, vital signs and coma scale, times of first examination by emergency room doctors and neurologists respectively, NIHSS at the emergency room, and time of intravenous tissue plasminogen activator (IV tPA) treatment; (2) inpatient elements: clinical care during hospitalization, NIHSS at admission, evolution of symptoms and signs, in-hospital complications, stroke risk factors (see the online-only Data Supplement), ECG, computed tomography, and magnetic resonance imaging findings, medications during admission; (3) discharge information: date, NIHSS, modified Rankin Scale (mRS), Barthel Index and medications; and (4) follow-up at 1, 3, and 6 months including disposition, mRS, Barthel Index and medications. The follow-up data were collected only from patients with written informed consents for follow-up evaluation. For the 1-month follow-up, 95.2% of the patients were available; for the 3-month, 90.6%, and for the 6-month, 87.8%. Laboratory results were categorized into two groups, with or without fasting, respectively (see the online-only Data Supplement).

Assurance of Data Quality

Four quality assurance processes were used to ensure the quality of TSR. The first was a logic check for consistency. Only data with the key items completed and that passed the logic check could be uploaded into the permanent databank. The second was a random auditing of 5% of all cases entered into TSR, first by web-based examination, followed by on-site auditing by a contract research organization independent of TSR to ensure the existence of the registered cases and the accuracy of the data entered. The third process was matching TSR data with NHI billings for stroke care. Finally, a data quality review meeting was held quarterly to review all the registry data and hospital enrollment record. Information security measures were also implemented after DOH certification with periodic follow-up review based on the DOH Information Security Check and Privacy Enforcement Act.

Quality Measures for Stroke Care and Prevention

Five GWTG-Stroke performance measures and one safety indicator were used to assess the quality of acute stroke care and prevention,⁴ in patients with ischemic stroke and TIA. One of the GWTG-Stroke quality indicators of anticoagulant prophylaxis for DVT was not included because symptomatic DVT is rare in immobilized patients, including those with stroke, in Asia.⁹ There were only 69 DVT cases (0.2%) in TSR during the period of 2006 to 2008. The GWTG-Stroke quality indicator on smoking cessation was also not included. Measures for smoking cessation are not paid for by NHI and cannot be validated in medical records or based on NHI billings. Administration of tPA for acute ischemic stroke in Taiwan followed a protocol established by the Taiwan Stroke Society.¹⁰ The composite

Table 1. Distribution of Stroke Types and Subtypes

Type	n	%
Ischemic stroke*	22 642	74.0
Large artery atherosclerosis	6270	27.7
Small vessel occlusion	8541	37.7
Cardioembolism	2465	10.9
Specific pathogenesis	332	1.5
Undetermined pathogenesis	5034	22.2
TIA	2053	6.7
ICH	4913	16.1
SAH	846	2.8
Cerebral venous thrombosis	46	0.2
Other	99	0.3
Total	30 599	100.0

*Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria⁸ were used to classify ischemic stroke subtypes.

SAH indicates subarachnoid hemorrhage; Other: stroke of more than one type.

measures, similar to those reported by GWTG-Stroke,⁴ were also derived, based on 5 individual performance indicators.

Statistical Analysis

To avoid the influence of outliers, a median with interquartile range was employed for variables including age, arrival time, length of stay, and NIHSS. The logistic regression model with generalized estimating equations (GEE)¹¹ accounting for within-hospital correlation was used to test the trends of performance and safety measures from 2006 to 2008. The linear regression model with GEE¹¹ was used to determine the extent of guideline adherence based on the composite measures. The unfavorable stroke functional outcome for the stroke performance indicator of IV tPA for 2 hours was defined as mRS ≥ 2 . For the other stroke performance indicators, the risks of cardiovascular events and death were analyzed based on any cardiovascular event, including stroke recurrence, ischemic cardiac event, or death from all causes within 1, 3, and 6 months post-stroke. Multivariable logistic regression models with GEE,¹¹ to account for within-hospital correlation, were used to determine the effects of guideline adherence based on 4 performance indicators on selected outcome measures. Only those variables significant in univariable logistic regressions with GEE were applied in the multivariable logistic regression models with GEE.¹¹ The variables used in the univariable logistic regressions with GEE were age, sex, hypertension, diabetes mellitus, ischemic heart disease, and NIHSS on admission. The statistical significance was set at a two-sided probability value less than 0.05. Analyses were performed using the SAS statistical software 9.1 (SAS Institute, Cary, NC).

Results

By the end of September 2009, a total of 46 049 stroke or TIA events were registered. Among these, 30 599 admissions between May 1, 2006 and July 31, 2008 with follow-up data available were presented in this report. A total of 29 195 patients with stroke contributed to these events, and 20 512 (70.3%) had first-ever strokes. Among the 30 599 stroke events, the majority were ischemic (74.0%). Other stroke types in order of frequency were ICH (16.1%), TIA (6.7%), subarachnoid hemorrhage (2.8%), and cerebral venous thrombosis (0.2%) (Table 1).

Patient Characteristics in Different Stroke Types

Patient characteristics including risk factors and in-hospital mortality and disposition profiles in TSR were comparable

with those in GWTG-Stroke,⁴ with few exceptions. In TSR, the average age was younger and body mass index smaller, with fewer patients carrying the diagnosis of TIA (Table 2). There was a reversal of sex dominance: female in GWTG-Stroke versus male in TSR. TSR hospital characteristics were comparable with the GWTG-Stroke report.⁴ In general, the hospital sizes (median: 966 beds) were larger with annual stroke discharges per hospital greater in TSR than in GWTG-Stroke. The proportion of hospitals participating in major teaching (43.6%) was comparable between TSR and GWTG-Stroke.

Guideline Adherence Based on GWTG-Stroke Measures

Quality of stroke care and prevention based on GWTG-Stroke measures showed variations between GWTG-Stroke and TSR (Table 3). IV tPA for those ischemic patients admitted within 2 hours was 7.67% with slight improvement to 10.42% in 2 years, as compared to an initial rate of 42.09% with improvement to 65% in 2 years in GWTG-Stroke.⁴ The great majority of patients with ischemic stroke or TIA were prescribed antithrombotic therapy during hospitalization (94.14%) comparable to the GWTG-Stroke figure. The prescription rate for antithrombotics at discharge (85.54%) was lower than the GWTG-stroke figure of greater than 95%. Among patients with atrial fibrillation, 28.28% were prescribed warfarin and another 37.87% were prescribed aspirin, which was also a treatment option for patients with atrial fibrillation. Even with the combination of these 2 regimens, only 61.98% of TSR patients with atrial fibrillation received anticoagulant or aspirin prophylaxis—far below the GWTG-Stroke figure of anticoagulant prophylaxis for atrial fibrillation (95.03% at baseline with improvement to 97.85% in 2 years). Only 38.69% of patients with dyslipidemia were prescribed lipid-lowering drugs at discharge, in comparison to the corresponding GWTG-Stroke figure of greater than 73%. The composite measures (73.12%) were also lower than the corresponding GWTG-Stroke figure (83.52% at baseline and 90.63% 2 years later). The rate of symptomatic ICH among patients receiving IV tPA therapy was 8.21%, which did not change significantly between 2006 and 2008 (range 6.78% to 9.41%, $P=0.9078$). The corresponding GWTG-Stroke figure ranges from 4.49% to 5.95%.⁴

Outcomes Based on Performance Indicators

As shown in Table 4, functional outcomes based on mRS at 1, 3, and 6 months post-stroke were better in those patients who were admitted within 2 hours of stroke onset and who received IV tPA, compared to those who were admitted within 2 hours of stroke onset but did not receive IV tPA, after adjustment for variables including age, sex, hypertension, diabetes mellitus, ischemic heart disease, and NIHSS at admission. Reduction in the risk of cardiovascular events and death within 1, 3, and 6 months post-stroke is noted in patients with stroke who received antithrombotics at discharge as compared to those without. The same favorable outcomes were noted in those patients with atrial fibrillation who received anticoagulation at discharge as compared to

Table 2. Key Variables in Different Stroke Types

Items	Ischemic Stroke/TIA n=24 695	ICH n=4913	SAH n=846
Age (median, IQR)	69.9 (59.6–77.9)	62.2 (51.9–73.7)	57.6 (47.4–70.4)
Sex			
Male (%)	59.8	65.7	40.7
Body mass index	24.3 (22.0–26.8)	23.9 (21.5–26.7)	23.5 (21.2–26.0)
Arrival time (hour)* (median, IQR)	5.5 (1.8–19.7)	2.1 (0.9–5.2)	2.7 (0.9–7)
Length of stay (day) (median, IQR)	8 (5–15)	13 (7–29)	17 (7–33)
MRI (%)	61.4	10.8	11.0
CT (%)	92.1	98.6	99.3
NIHSS (admission) (median, IQR)	5 (2–9)	10 (4–21)	4 (0–18)
Medical history (%)			
Atrial fibrillation	16.5	6.4	5.4
Previous stroke/TIA	34.1	24.1	8.4
CAD/prior MI	13.6	6.9	4.7
Carotid stenosis	10.6
Diabetes mellitus	45.4	37.0	37.2
Hypertension	79.2	84.9	65.3
Dyslipidemia	49.4	29.4	20.5
Obesity	23.7	22.7	17.8
Ever smoking	40.4	38.4	31.3
Men	63.4	55.8	61.9
Women	6.3	5.5	10.6
Discharge destination (%)			
Home	88.9	69.6	71.4
Nursing home	5.6	11.4	6.0
Respiratory care ward	0.4	1.9	1.5
Transfer to other hospital	5.2	17.1	21.1
Died	4.0	17.9	29.0
Functional status†			
1-Month mRS (%)			
0–1	6941 (38.8)	577 (21.4)	134 (35.1)
≥2	10 928 (61.2)	2126 (78.7)	248 (64.9)
3-Month mRS (%)			
0–1	7549 (45.5)	729 (29.6)	160 (45.3)
≥2	9048 (54.5)	1735 (70.4)	193 (54.7)
6-Month mRS (%)			
0–1	7915 (50.6)	824 (35.8)	184 (54.6)
≥2	7734 (49.4)	1481 (64.3)	153 (45.4)

MRI indicates magnetic resonance imaging; CT, computed tomography; CAD, coronary artery disease; MI, Myocardial Infarction. Data are expressed as % or median (IQR; interquartile range, 25th to 75th percentile).

*Only subjects with documented time of stroke onset were included.

†From patients with written informed consents.

those without. However, no apparent impact on outcomes was noted with lipid-lowering agents.

Discussion

Improving the quality of stroke prevention and care is a global priority. Evidence-based therapeutic and preventive measures are available for ischemic stroke but remain underutilized even in the United States. GWTG-Stroke, a landmark American Heart Association/American Stroke Associ-

ation initiative, showed substantial and sustained improvements, based on predefined performance measures, on quality of stroke care and prevention in 790 US hospitals. Whether GWTG-Stroke is applicable outside the United States to benefit nations with different healthcare infrastructures and economies remains to be determined. We used TSR, a national stroke registry with stringent quality control of data entry, to explore the applicability of GWTG-Stroke in a country that spends substantially less in healthcare dollars

Table 3. Performance Measures in Acute Stroke Care and Prevention From 2006 to 2008 in the Taiwan Stroke Registry

Performance/Safety Measures (%)	2006	2007	2008	Total	Trend Test β (SE), <i>P</i> Value
Performance measures					
IV tPA for 2 hours*	7.67	8.55	10.42	8.84	0.17 (0.09), 0.0581#
Antithrombotics during hospitalization†	92.39	94.54	94.76	94.14	0.21 (0.04), <0.001#
Antithrombotics at discharge‡	85.57	85.09	86.60	85.54	0.04 (0.03), 0.1012#
Anticoagulation for atrial fibrillation§	32.12	27.71	26.14	28.28	-0.15 (0.05), 0.0060#
Lipid-lowering drug at discharge	37.00	38.97	39.54	38.69	0.05 (0.03), 0.0629#
Safety measure					
Symptomatic ICH after IV tPA therapy	6.78	9.41	7.00	8.21	-0.03 (0.27), 0.9078#
Composite measure, mean \pm SD	74.00 \pm 4.59	74.20 \pm 5.82	73.19 \pm 6.32	73.12 \pm 5.33	0.02 (0.01), 0.0581**

*Patients with ischemic stroke presenting within 2 hours of symptom onset who received IV tPA within 3 hours of symptom onset.

†Antithrombotics (antiplatelet or anticoagulant) prescription for patients with ischemic stroke or TIA during hospitalization.

‡Antithrombotic (antiplatelet or anticoagulant) prescription for patients with ischemic stroke or TIA at discharge.

§Warfarin prescription for patients with ischemic stroke or TIA with atrial fibrillation at discharge.

||Lipid-lowering drug prescription for patients with ischemic stroke or TIA with low-density lipoprotein >100 mg/dl or patients taking lipid lowering agents on admission.

#Trends of performance/safety measures from 2006 to 2008 were tested by the logistic regression model.

**Composite measure by the linear regression model using generalized estimating equations accounting for within-hospital correlation.¹¹

SE indicates standard error.

under a public health insurance program. Patient characteristics, including stroke types/subtypes, risk factor profiles, and mortality, are largely comparable between TSR and GWTG-Stroke and stroke registries in Japan¹² the United States,¹³ and other countries.^{14,15} TSR contains all performance measures collected for assessing quality of stroke care defined by

GWTG-Stroke, with the exceptions of anticoagulant prophylaxis for DVT and interventions for smoking cessation. Five performance indicators, the composite measures, and a safety factor on the symptomatic ICH rate after IV tPA treatment in GWTG-Stroke could be derived from TSR by combing patients with ischemic stroke and TIA. Among the GWTG-

Table 4. Outcomes Based on Performance Indicators

	n	aOR‡	95% CI		<i>P</i> Value
Functional outcomes (mRS):* IV tPA for 2 hours					
At 1 month post stroke	1240	0.50	0.33	0.76	0.0012
At 3 months post stroke	1043	0.47	0.32	0.69	0.0002
At 6 months post stroke	960	0.52	0.35	0.76	0.0009
Risk of cardiovascular events and death:† antithrombotics at discharge					
Within 1 month post stroke	17952	0.19	0.16	0.23	<0.0001
Within 3 months post stroke	16908	0.33	0.28	0.39	<0.0001
Within 6 months post stroke	16163	0.41	0.35	0.47	<0.0001
Risk of cardiovascular events and death:‡ Anticoagulation for atrial fibrillation at discharge					
Within 1 month post stroke	2496	0.28	0.16	0.51	<0.0001
Within 3 months post stroke	2319	0.51	0.35	0.73	0.0003
Within 6 months post stroke	2190	0.59	0.44	0.80	0.0004
Risk of cardiovascular events and death:† lipid-lowering agents at discharge					
Within 1 month post stroke	8881	0.81	0.60	1.11	0.1930
Within 3 months post stroke	8406	0.92	0.73	1.15	0.4450
Within 6 months post stroke	8075	0.94	0.78	1.13	0.5115

aOR indicates adjusted odds ratio; CI, confidence interval.

*Functional outcomes were categorized as unfavorable with mRS \geq 2 at 1, 3, and 6 months post stroke.

†Risk of cardiovascular events including stroke recurrence, ischemic cardiac event, or death from all causes within 1, 3, and 6 months post stroke.

‡Odds ratios were adjusted for the variables that were significant in the univariable logistic regression model with GEE. The variables that had been evaluated in the univariable logistic regression models (with GEE) were age, sex, hypertension, diabetes mellitus, ischemic heart disease, and NIHSS at admission.

Stroke parameters, early prescription of antithrombotics was followed in a rigorous manner comparable with the GWTG-Stroke figure (94.14% in TSR versus 97.04% in GWTG-Stroke). Antithrombotics on discharge were prescribed at a lower rate (TSR: 85.54%, GWTG-Stroke: 98.88%). This could be attributed partly to the local practice, which does not favor aggressive stroke prevention in patients with poor functional outcomes (mRS <4: 92.37%; mRS ≥4: 77.45%). This gap suggests that more rigorous adherence to this GWTG-Stroke guideline is needed, including aggressive treatment for those with poor functional outcomes, especially when more favorable outcomes were noted among those receiving antithrombotics on discharge than those without. The other performance measures show substantial disparity between TSR and GWTG-Stroke. The most striking difference was IV tPA for those arriving within 2 hours of stroke onset: 8.84% in TSR versus 72.84% in GWTG-Stroke. TSR data also show that only 1.5% of patients with ischemic stroke received IV tPA treatment. This is lower than that which was reported by the Paul Coverdell National Acute Stroke Registry in the United States (3.0% ≈ 8.5%)¹³ and the German Stroke Registers Study Group (3.0%).¹⁴ IV tPA is an important measure of the quality of stroke care and reflects the readiness of a stroke center in treating patients with stroke in an emergency setting with adequate facilities, staffing, and training. The relatively late arrival of the patients with stroke is a likely cause of the low IV tPA rate. Only 26.2% of TSR patients with ischemic stroke arrived within 2 hours of stroke onset and in time for IV tPA treatment. More public education and more rigorous community outreach programs are needed. Together, these findings suggest that stroke centers in Taiwan are behind in fulfilling an important therapeutic measure in acute stroke care, especially when better functional outcomes were noted in patients with ischemic stroke who arrived within 2 hours and received tPA compared to those who also arrived within 2 hours but did not receive tPA. It should be noted that while IV tPA was approved by the Food and Drug Administration in the United States in 1996, it was not until 2004 that DOH approved NHI reimbursement for IV tPA treatment. A lag of 8 years could be a major reason that TSR hospitals are not up to the level of GWTG-Stroke hospitals in IV tPA performance. In Germany, with IV tPA approved in 2002, the figure (10.4%)¹⁴ was also relatively low, comparable to Taiwan (8.84%). The GWTG-Stroke IV tPA performance indicator can serve as a yardstick for countries outside the United States, such as Taiwan and Germany, to catch up.

Anticoagulant treatment for patients with atrial fibrillation was prescribed at a substantially lower rate in TSR than GWTG-Stroke. Even with anticoagulant and antiplatelet regimens combined, only 61.98% of TSR patients with atrial fibrillation received anticoagulant or aspirin prophylaxis, far below the comparable GWTG-Stroke figure on anticoagulant prophylaxis for atrial fibrillation (97.85%). This finding indicates that an important preventive measure is in great need of improvement in Taiwan, especially when the impact of anticoagulation on outcomes is favorable in TSR. It should be noted that only 30.5% of patients with atrial fibrillation received anticoagulant prophylaxis in a recent German

study.¹⁶ GWTG-Stroke performance on this stroke prevention measure offers another global standard to countries like Taiwan and Germany.

Only 38.69% of patients with dyslipidemia were taking lipid-lowering drugs at discharge. The corresponding GWTG-Stroke figure was greater than 73%. According to the NHI guideline in Taiwan, the lipid-lowering medication can be reimbursed only when the low-density lipoprotein level is greater than 130 mg/dL, which is higher than the GWTG-Stroke standard (low-density lipoprotein >100 mg/dL). Discrepancy between TSR and GWTG-Stroke on this parameter raises the need for NHI in Taiwan to review the lipid-lowering guidelines for changing reimbursement policies. Lack of impact of lipid-lowering medications on outcomes could be related to a relatively short follow-up period (6 months).

The composite measures (73.12%) were also lower than the corresponding GWTG-Stroke figure. In contrast to an improvement from 83.52% at baseline to 90.63% in 2 years, corresponding TSR numbers failed to show improvement with time. It should be noted that TSR had started before GWTG-Stroke results were published. Furthermore, DOH did not mandate improvement in quality in TSR over time. However, the impressive advances in the 790 GWTG-Stroke hospitals suggest that implementing GWTG-Stroke in TSR is likely to improve quality of stroke care.

The rate of symptomatic ICH among patients receiving IV tPA therapy was 8.21%, higher than the GWTG-Stroke figure (4.49% to 5.95%) or other US numbers (6.4% in the NINDS tPA trial¹ and 6.0% in the multicenter tPA acute stroke survey¹⁷). This safety indicator is another important objective for TSR hospitals to improve. The IV tPA guidelines established by the Taiwan Stroke Society follow the same tPA dosage used in the United States. The tPA dosage received by TSR patients, however, was lower than the recommended dosage of 0.9 mg/kg in more than half of the patients. The lower tPA dosage in a subset of TSR hospitals has been reported recently.¹⁸ Lower tPA dosage (0.6 mg/kg) has been shown to achieve comparable safety and efficacy in Japan.¹⁹ Further studies are needed to establish the efficacy of a smaller tPA dosage in Taiwan.

TSR does not contain a performance measure on compliance with anticoagulant prophylaxis for DVT, because DVT is rarely symptomatic among Asians.⁹ The low symptomatic rate of DVT in TSR patients (only 0.2%) is consistent with the earlier observation.⁹ Thus, this GWTG-Stroke performance measure may not be applicable in Taiwan. However, recent ultrasonographic studies found high incidence (16% to 45%) of DVT, mostly asymptomatic, among patients with stroke in Japan and Singapore.^{20,21} We will explore the merit of adding DVT prophylaxis as a performance indicator by searching for asymptomatic DVT among TSR patients in the future.

TSR data show that smoking, noted in 39.8% of patients, is also an important risk factor, especially in men (62.1%). Smoking could increase stroke risk by 2- to 4-fold.²² According to the 2007 annual DOH report in Taiwan,²³ smoking rates in men and women over the age of 18 years were 38.9% and 5.1%, respectively. Thus, smoking cessation should be an

important initiative for stroke prevention. Because measures for smoking cessation are not payable based on the current NHI reimbursement policies, validation of measures taken for smoking cessation by the participating hospitals was not possible in TSR. However, TSR findings substantiate smoking as a major stroke risk factor. GWTG-Stroke has insightfully made smoking cessation one of the 7 performance measures. Implementation of smoking cessation measures for stroke prevention should be a top priority in future revisions of NHI reimbursement policies in Taiwan.

Schwamm et al found that differences in quality of care defined by 7 performance measures had no measurable impact on short-term in-hospital outcomes. These GWTG-Stroke leaders suggest that the association between quality of care and outcomes will require analysis of post-discharge (eg, day 90) health status, stroke disability, and mortality.²⁴ Fonarow et al reported a reduced risk-adjusted in-hospital mortality rate in GWTG-Stroke hospitals. This same group of GWTG-Stroke leaders recommend further study to determine if these improvements in mortality are due to improvement in guideline adherence.²⁵ In TSR data, outcomes based on mRS at 1, 3, and 6 months post-stroke or risks of cardiovascular events and death at 1, 3, and 6 months post stroke are available. Patients receiving IV tPA within 2 hours of stroke onset, patients receiving antithrombotics at discharge, or patients with atrial fibrillation receiving anticoagulation at discharge had better outcomes than the corresponding groups without these therapies. The favorable outcomes associated with adherence to selected GWTG guidelines should be interpreted with caution because of possible inherent biases. However, these preliminary results are encouraging and provide a stronger drive for adherence to GWTG guidelines to overcome the inertia in improving stroke prevention and treatment performance in Taiwan.

Taiwan has an excellent public health insurance program that provides comprehensive medical services to its citizens. However, TSR data, presenting a national stroke profile, show that the quality of acute stroke care and prevention in Taiwan needs to be improved to reach the GWTG levels. More efforts and resources from the community, healthcare providers and the governments at different levels have to be devoted to improving the quality of stroke care and prevention in Taiwan. Based on the TSR findings and corresponding numbers noted in other countries (eg, Germany), GWTG-Stroke performance measures, with some exceptions (eg, anticoagulant for DVT prophylaxis), are applicable to countries outside the United States with different healthcare systems and economies. The GWTG-Stroke figures can serve as important global standards for improving quality of care and prevention around the world. An important feature of GWTG-Stroke is its effect on improving the quality of stroke care over time. Applying GWTG-Stroke in TSR and registries in other countries is likely to be an effective mechanism for quality improvement.

Acknowledgments

We thank Professor TC Li of China Medical University for her expert input on statistical analysis.

Sources of Funding

This work was supported in part by Department of Health grants (the Bureau of Health Promotion: DOH95-HP-1102, DOH96-HP-1105, DOH97-HP-2102, DOH98-HP-1102; Clinical Trial and Research Center of Excellence: DOH-TD-B-111-002; DOH99-TD-B-111-003, DOH99-TD-B-111-004), the Ministry of Education (Topnotch Stroke Research Center) and the Dr. Chi-Chin Huang Stroke Foundation. TSR is dedicated to Dr Chi-Chin Huang and family for their generous support to advance the quality of stroke care and prevention in Taiwan.

Disclosures

None.

References

1. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med*. 1995;333:1581–1587.
2. Adams R, Acker J, Alberts M, Andrews L, Atkinson R, Fenelon K, Furlan A, Giruso M, Horton K, Hughes R, Koroshetz W, Latchaw R, Magnis E, Mayberg M, Pancioli A, Robertson RM, Shephard T, Smith R, Smith SC Jr, Smith S, Stranne SK, Kenton EJ III, Bashe G, Chavez A, Goldstein L, Hodosh R, Keitel C, Kelly-Hayes M, Leonard A, Morgenstern L, Wood JO. Recommendations for improving the quality of care through stroke centers and systems: an examination of stroke center identification options: multidisciplinary consensus recommendations from the Advisory Working Group on Stroke Center Identification Options of the American Stroke Association. *Stroke*. 2002;33:e1–e7.
3. Schwamm LH, Pancioli A, Acker JE III, Goldstein LB, Zorowitz RD, Shephard TJ, Moyer P, Gorman M, Johnston SC, Duncan PW, Gorelick P, Frank J, Stranne SK, Smith R, Federspiel W, Horton KB, Magnis E, Adams RJ. Recommendations for the establishment of stroke systems of care: recommendations from the American Stroke Association's Task Force on the Development of Stroke Systems. *Circulation*. 2005;111:1078–1091.
4. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, Ellrodt G, Cannon CP, Liang L, Peterson E, Labresh KA. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. *Circulation*. 2009;119:107–115.
5. Di Carlo A. Human and economic burden of stroke. *Age Ageing*. 2009;38:4–5.
6. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol*. 2009;8:345–354.
7. Department of Health, Executive Yuan, Taiwan. Inpatient medical benefit claims of major illness/injury 2007. http://www.doh.gov.tw/CHT2006/DM/DM2_2.aspx?now_fod_list_no=10902&class_no=440&level_no=2. Accessed December 15, 2009.
8. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE III. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*. 1993;24:35–41.
9. Keenan CR, White RH. The effects of race/ethnicity and sex on the risk of venous thromboembolism. *Curr Opin Pulm Med*. 2007;13:377–383.
10. Guideline for IV tPA treatment. Taiwan Stroke Society. http://www.stroke.org.tw/guideline/guideline_3.asp. Accessed December 15, 2009.
11. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. 1986;42:121–130.
12. Kobayashi S. International experience in stroke registry: Japanese Stroke Databank. *Am J Prev Med*. 2006;31:S240–S242.
13. Reeves MJ, Arora S, Broderick JP, Frankel M, Heinrich JP, Hickenbottom S, Karp H, LaBresh KA, Malarcher A, Mensah G, Moomaw CJ, Schwamm L, Weiss P. Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry. *Stroke*. 2005;36:1232–1240.
14. Heuschmann PU, Berger K, Misselwitz B, Hermanek P, Leffmann C, Adelmann M, Buecker-Nott HJ, Rother J, Neundoerfer B, Kolominsky-Rabas PL. Frequency of thrombolytic therapy in patients with acute ischemic stroke and the risk of in-hospital mortality: the German Stroke Registers Study Group. *Stroke*. 2003;34:1106–1113.

15. Silver FL, Kapral MK, Lindsay MP, Tu JV, Richards JA. International experience in stroke registries: lessons learned in establishing the Registry of the Canadian Stroke Network. *Am J Prev Med.* 2006;31:S235–S237.
16. Weimar C, Benemann J, Katsarava Z, Weber R, Diener HC. Adherence and quality of oral anticoagulation in cerebrovascular disease patients with atrial fibrillation. *Eur Neurol.* 2008;60:142–148.
17. Tanne D, Kasner SE, Demchuk AM, Koren-Morag N, Hanson S, Grond M, Levine SR. Markers of increased risk of intracerebral hemorrhage after intravenous recombinant tissue plasminogen activator therapy for acute ischemic stroke in clinical practice: the Multicenter rt-PA Stroke Survey. *Circulation.* 2002;105:1679–1685.
18. Chao AC, Hsu HY, Chung CP, Liu CH, Chen CH, Teng MM, Peng GS, Sheng WY, Hu HH. Outcomes of thrombolytic therapy for acute ischemic stroke in Chinese patients: the Taiwan Thrombolytic Therapy for Acute Ischemic Stroke (TTT-AIS) Study. *Stroke.* 2010;41:885–890.
19. Yamaguchi T, Mori E, Minematsu K, Nakagawara J, Hashi K, Saito I, Shinohara Y. Alteplase at 0.6 mg/kg for acute ischemic stroke within 3 hours of onset: Japan Alteplase Clinical Trial (J-ACT). *Stroke.* 2006;37:1810–1815.
20. De Silva DA, Pey HB, Wong MC, Chang HM, Chen CP. Deep vein thrombosis following ischemic stroke among Asians. *Cerebrovasc Dis.* 2006;22:245–250.
21. Kawase K, Okazaki S, Toyoda K, Toratani N, Yoshimura S, Kawano H, Nagatsuka K, Matsuo H, Naritomi H, Minematsu K. Sex difference in the prevalence of deep-vein thrombosis in Japanese patients with acute intracerebral hemorrhage. *Cerebrovasc Dis.* 2009;27:313–319.
22. Shinton R, Beevers G. Meta-analysis of relation between cigarette smoking and stroke. *BMJ.* 1989;298:789–794.
23. Department of Health, Executive Yuan, Taiwan. 2007 Annual Report of the Bureau of Health Promotion. <http://health99.doh.gov.tw/media/public/pdf/21592.pdf>. Accessed December 15, 2009.
24. Schwamm LH, Reeves MJ, Pan W, Smith EE, Frankel MR, Olson D, Zhao X, Peterson E, Fonarow GC. Race/ethnicity, quality of care, and outcomes in ischemic stroke. *Circulation.* 2010;121:1492–1501.
25. Fonarow GC, Reeves MJ, Smith EE, Saver JL, Zhao X, Olson DW, Hernandez AF, Peterson ED, Schwamm LH. Characteristics, performance measures, and in-hospital outcomes of the first one million stroke and transient ischemic attack admissions in Get With The Guidelines-Stroke. *Circ Cardiovasc Qual Outcomes.* 2010;3:291–302.

CLINICAL PERSPECTIVE

Stroke is a leading cause of death around the world. Improving quality of stroke care is a global priority, despite diverse healthcare economies across nations. The American Heart Association and American Stroke Association have launched a nation-wide drive to improve quality of stroke care and prevention applying the Get With the Guidelines-Stroke (GWTG-Stroke) program. GWTG-Stroke has improved the quality of stroke care in 790 US academic and community hospitals over a period of 5 years (2003–2007). These favorable results have broad implications in the United States. Whether GWTG-Stroke is applicable across national and economic boundaries was tested in the Taiwan Stroke Registry with 30 599 stroke admissions. Taiwan spends $\approx 1/10$ of what the United States spends in medical costs per new or recurrent stroke. The Taiwan Stroke Registry, sponsored by Taiwan Department of Health and engaging 39 academic and community hospitals, covers the country with 4 steps of quality control to ensure reliability of entered data. Five GWTG-Stroke performance indicators and 1 safety indicator are applied to assess Taiwan Stroke Registry quality of stroke care. Demographic and outcomes figures are comparable between GWTG-Stroke and Taiwan Stroke Registry. Two indicators (early and discharge antithrombotics) are close to GWTG-Stroke standards while 3 others (intravenous tissue plasminogen activator, anticoagulation for atrial fibrillation, lipid-lowering medication) and 1 safety indicator fall behind. Results show that GWTG-Stroke can be the global standard for improving the quality of stroke care outside the United States. GWTG-Stroke can be incorporated into national stroke registries around the world. Preliminary analysis shows compliance with selected GWTG-Stroke guidelines is associated with better outcomes.

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Get With The Guidelines-Stroke Performance Indicators: Surveillance of Stroke Care in the Taiwan Stroke Registry. Get With The Guidelines-Stroke in Taiwan

Fang-I Hsieh, Li-Ming Lien, Sien-Tsong Chen, Chyi-Huey Bai, Mu-Chien Sun, Hung-Pin Tseng, Yu-Wei Chen, Chih-Hung Chen, Jiann-Shing Jeng, Song-Yen Tsai, Huey-Juan Lin, Chung-Hsiang Liu, Yuk-Keung Lo, Han-Jung Chen, Hou-Chang Chiu, Ming-Liang Lai, Ruey-Tay Lin, Ming-Hui Sun, Bak-Sau Yip, Hung-Yi Chiou and Chung Y. Hsu
the Taiwan Stroke Registry Investigators

Circulation. published online August 30, 2010;

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2010 American Heart Association, Inc. All rights reserved.

Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circ.ahajournals.org/content/early/2010/08/30/CIRCULATIONAHA.110.936526.citation>

Data Supplement (unedited) at:

<http://circ.ahajournals.org/content/suppl/2010/08/26/CIRCULATIONAHA.110.936526.DC1>

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

Reprints: Information about reprints can be found online at:
<http://www.lww.com/reprints>

Subscriptions: Information about subscribing to *Circulation* is online at:
<http://circ.ahajournals.org/subscriptions/>

SUPPLEMENTAL MATERIAL

Online Appendix I

The criteria for a hospital to qualify for TRS:

Criteria	Content
1	Fully staffed and equipped emergency care services including accessibility to head CT on a 24-hour a day basis.
2	Neurologist and neurosurgeon on call around-the-clock.
3	Full stroke inpatient services including intensive care units and neurosurgical facilities for acute surgical intervention.
4	Adequate stroke outpatient services for follow-up and stroke prevention.
5	Well staffed for conducting stroke registry.

Online Appendix II

The definitions of stroke type in the Registry form

Stroke types	Definitions
Transient ischemic attack	Transient focal neurologic deficit of ischemic causes that resolved within 24 hours
Ischemic stroke	Acute onset of neurological deficit with signs or symptoms persisting longer than 24 hours with or without acute ischemic lesion(s) on brain CT or with acute ischemic diffusion-weighted imaging lesion(s) on MRI that corresponded to the clinical presentations.
Intracerebral hemorrhage	Non-traumatic abrupt onset of symptoms with relevant focal neurological deficit with or without headache or altered level of consciousness with a focal collection of blood within the brain parenchyma on CT or MRI that was not a hemorrhagic conversion of a cerebral infarction.
Subarachnoid hemorrhage	Characteristic clinical manifestations of neurologic deficit, usually with sudden onset of severe headache and either subarachnoid blood on brain CT or/and non-traumatic bloody (or xanthochromic) cerebrospinal fluid with or without confirmation of the existence of aneurysm by magnetic resonance angiography (MRA) or conventional cerebral angiography.

Cerebral venous thrombosis Infarct or/and ICH on CT, and evidence of a cerebral sinus or venous occlusion on MRI and MRA or on conventional angiography.

Online Appendix III

The items and definitions of risk factors in the Registry form

Items	Definitions
Hypertension	On antihypertensive agents, or documented to have hypertension in prior clinic visits or hospital admissions
Diabetes	On oral hypoglycemic agents or insulin, or documented to have diabetes mellitus in prior clinic visits or hospital admissions
Previous stroke	Confirmed to have stroke in prior hospital admissions
Previous TIA	Confirmed to have TIA by a neurologist in prior clinic visits or hospital admissions
Heart disease	Confirmed to have heart disease by a cardiologist in prior clinic visits or hospital admissions
Renal disease	Confirmed to have chronic renal disease by a nephrologist in prior clinic visits or hospital admissions
Smoking	Past or current history of smoking, more than 1 cigarette per day for more than 6 months
Alcohol	Past or current history of alcohol consumption, more than once per day for more than 1 year
Vegetarian	Have had a vegetarian diet for more than 1 year prior to stroke or TIA onset
Dyslipidemia	On lipid-lowering agents or with one of the following:, fasting-serum cholesterol level ≥ 200 mg/dl:

	fasting-serum LDL level ≥ 130 mg/dl; fasting-serum HDL level <40 mg/dl; fasting-serum TG level ≥ 150 mg/dl
Polycythemia	Confirmed to have polycythemia by a hematologist in prior clinic visits or hospital admissions.
Physical inactivity	Failure to meet the physical activity criteria: exercise for at least 30 min, at least 3 times per week for more than 6 months
Family history of stroke	Diagnosis of stroke among parents or siblings
Birth control pill	On birth control pill for at least 1 year
Recent infection	To have the symptoms a week before onset: fever, urinary tract infection, pneumonia, helicobacter pylori positive peptic ulcer, periodontitis, or other confirmed infectious diseases
Snoring	Need to match one of the following criteria: (1) snoring during sleep and excessive day-time sleep; (2) carrying a diagnosis of sleep apnea
Depression	On anti-depression agents or documented to have depression by a psychiatrist in prior clinic visits or hospital admissions
Body mass index	Weight (kg)/Height ² (m ²)
Waist-to-hip ratio	Waist (cm)/Hip (cm)

Online Appendix IV

Laboratory results were categorized into two groups with or without fasting as follows.

Categories	Items
Fasting blood	Glucose, uric acid, total cholesterol, triglyceride, high-density lipoproteins, low-density lipoproteins, glutamate oxaloacetate transaminase (GOT), and glutamic pyruvic transaminase (GPT).
Non-fasting blood	Hemoglobin, hematocrit, platelet, white blood cell count, partial thromboplastin time, International Normalized Ratio, glucose (non-fasting), blood urea nitrogen, creatinine, albumin, C reactive protein, glycosylated hemoglobin, fibrinogen, and homocysteine.

Online Appendix V

List of TSR Investigators:

National Taiwan University Hospital: Jiann-Shing Jeng (Principal Investigator),

Shin-Joe Yeh, Li-Kai Tsai

Shin Kong WHS Memorial Hospital: Hou-Chang Chiu (Principal Investigator),

Li-Ming Lien, Wei-Hung Chen, Chyi-Huey Bai, Tzu-Hsuan Huang, Chi-Ieong Lau,

Ya-Ying Wu

Taipei Medical University Hospital: Rey-Yue Yuan (Principal Investigator),

Chaur-Jong Hu, Jau- Juan Sheu, Jia-Ming Yu, Chun-Sum Ho

Taipei Medical University - Wan Fang Hospital: Wen-Ting Chung (Principal

Investigator), Jia-Ying Sung, Chin-I Chen, Hsing-Yu Weng, Yu-Hsuan Han,

Chun-Ping Huang

Chi Mei Medical Center: Huey-Juan Lin (Principal Investigator), Der-Shin Ke,

Chia-Yu Chang, Poh-Shiow Yeh, Kao-Chang Lin, Tain-Junn Cheng, Chih-Ho Chou,

Chun-Ming Yang

Kaohsiung Veterans General Hospital: Yuk-Keung Lo (Principal Investigator),

Yu-Te Lin, Ching-Hwung Lin

Tri Service General Hospital: Jiann-Chyun Lin (Principal Investigator),

Yaw-Don Hsu, Jong-Chyou Denq, Giia-Sheun Peng, Jiunn-Tay Lee, Chang-Hung

Hsu, Chun-Chieh Lin, Che-Hung Yen, Chun-An Cheng, Yueh-Feng Sung,

Yuan-Liang Chen, Ming-Tung Lien, Chung-Hsing Chou, Chia-Chen Liu, Fu-Chi

Yang, Yi-Chung Wu, An-Chen Tso, Yu- Hua Lai, Chun-I Chiang, Chia-Kuang Tsai,

Meng-Ta Liu, Ying-Che Lin, Yu-Chuan Hsu

China Medical University Hospital: Chung-Hsiang Liu (Principal Investigator),

Chon-Haw Tsai, Wei-Shih Huang, Chung-Ta Lu, Tzung-Chang Tsai, Chun-Hung

Tseng, Kang-Hsu Lin, Woei-Cherng Shyn, Yu-Wan Yang, Yen-Liang Liu,
Der-Yang Cho, Chun-Chung Chen

Kuang Tien General Hospital: Ming-Hui Sun (Principal Investigator),
Shih-Chieh Yu, Li-Ying Ke

National Cheng Kung University Hospital: Ming-Liang Lai (Principal
Investigator), Chih-Hung Chen

Changhua Christian Hospital Yunlin Branch: Jiunn-Rong Chen (Principal
Investigator), Song-Yen Tsai

Cathay General Hospital: Tsuey-Ru Chiang (Principal Investigator),
Mei-Ching Lee

Buddhist Tzu Chi General Hospital Taipei Branch: Shinn-Kuang Lin (Principal
Investigator), Yuan-Fu Tseng, Jing-Er Lee, Cheng-Lun Hsiao, Jen-Feng Liang

Chung Shan Medical University Hospital: Chiu-Mei Chen (Principal Investigator),
Chao-Hsin Wu

Landseed Hospital: Yu-Wei Chen (Principal Investigator), Kuo-Ying Lee, Yun-Yu
Lin, Chen-Hua Li, Eric E. Smith, Hui-Fen Tsai, Chuan-Fa Hsieh, Chih-Dong Yang,
Shiumn-Jen Liaw, How-Chin Liao

Taipei Veterans General Hospital: Han-Hwa Hu (Principal Investigator),
Wen-Jang Wong, Yun-On Luk, Chang-Ming Chern, Li-Chi Hsu, Chih-Ping Chung

Changhua Christian Hospital: Mu-Chien Sun (Principal Investigator), Shey-Lin
Wu

Lotung Poh Ai Hospital: Hung-Pin Tseng (Principal Investigator),
Chin-Hsiung Liu, Chun-Liang Lin, Hung-Chih Lin

Cheng Hsin General Hospital: Ta-Chang Lai (Principal Investigator), Jiu-Haw Yin,
Chung-Jen Wang, Kai-Chen Wang, Li-Mei Chen, Jong-Chyou Denq

Far Eastern Memorial Hospital: Lung Chan (Principal Investigator), Siu-Pak Lee

En Chu Kong Hospital: Yu Sun (Principal Investigator), Chieh-Cheng Huang,

Chang-Hsiu Liu, Cheng-Huai Lin, Chien-Jung Lu

Cheng Ching General Hospital: Shouou-Jeng Yeh (Principal Investigator), Ling-Li

Wu, Liang-Po Hsieh, Yong-Hui Lee, Chung-Wen Chen

Taichung Veterans General Hospital: Po-Lin Chen (Principal Investigator),

Yu-Shan Lee, Shu-Yi Chen

E Da Hospital: Han-Jung Chen (Principal Investigator), Shih-Pin Hsu, Cheng-Sen

Chang, Hung-Chang Kuo, Shu-Lung Wu, Huan-Wen Tsui, Jung-Chi Tsou,

Feng-Hsiung Chou, Pei-Jung Lin, Chin-Sung Tung, Kan Lu, Po-Chou Liliang,

Yu-Duan Tsai, Cheng-Loong Liang, Kuo-Wei Wang, Hao-Kuang Wang, Te-Yuan

Chen

Buddhist Tzu Chi General Hospital: Yue-Loong Hsin (Principal Investigator),

Chih-Yuan Lin

Hsin Chu General Hospital: Bak-Sau Yip (Principal Investigator), Pei-Chun Tsai,

Ping-Chen Chou, Tsam-Ming Kuo, Yi-Chen Lee, Yi-Pin Chiu, Kun-Chang Tsai

Kaohsiung Medical University Chung-Ho Memorial Hospital: Ruey-Tay Lin

(Principal Investigator), Chun-Hung Chen, Gim-Thean Khor, A-Ching Chao,

Hsiu-Fen Lin

Min Sheng General Hospital: I-Sheng Lin (Principal Investigator)

Taipei City Hospital Ren Ai Branch: Sui-Hing Yan (Principal Investigator),

Yi-Chun Lin, Pei-Yun Chen, Sheng-Huang Hsiao

Mackay Memorial Hospital: Helen L. Po (Principal Investigator), Ya-Ju Lin

Miao Li General Hospital: Hao-Chieh Tu (Principal Investigator)

National Taiwan University Hospital Yunlin Branch: Sung-Chun Tang (Principal Investigator), Fu-Yu Lin

Lin Shin Hospital: Ping-Kun Chen (Principal Investigator), Pai-Yi Chiu

Cardinal Tien Hospital: Ping-Keung Yip (Principal Investigator), Vin-Chi Wang, Kaw-Chen Wang, Chung-Fen Tsai, Chao-Ching Chen, Chih-Hao Chen, Yi-Chien Liu

Show Chwan Memorial Hospital: Chung-Hsin Yeh (Principal Investigator), Chou-Hsiung Pan, Shin-Yi Jih, Po-Chi Chan, Min-Hsien Hsu, Hai-Ming Shoung, Yi-Chen Lo, Fu-Hwa Wang

Chang Bing Show Chwan Memorial Hospital: Cheng-Yu Wei (Principal Investigator), Jun-Yu Lee

Wei Gong Memorial Hospital: Ryh-Huei Lin (Principal Investigator), Ching-Hua Chu

Taipei Medical University - Shuang Ho Hospital: Chaur-Jong Hu (Principal Investigator)

Buddhist Dalin Tzu Chi General Hospital: Ming-Chin Hsu (Principal Investigator)