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Title pages

Relationship between Hospital Performance Measures and Stroke Outcomes in Patients with Acute Ischemic Stroke

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ABSTRACT

Objectives: Guideline-recommended performance measures were increasingly used to evaluate hospital quality of stroke care, but their impact on stroke outcome has not been verified. We aimed to evaluate the correlation between hospital performance measures and outcomes among acute ischemic stroke patients.

Methods: Data was derived from 120 hospitals participating in the China National Stroke Registry between September 2007 and August 2008. Adherence to 9 guideline-recommended performance measures was examed, and the composite score of hospital performance measures was calculated. Primary stroke outcomes were hospital-level, 30-day and 1-year risk-standardized mortality (RSM). Association of hospital individual performance measures and composite score with stroke outcomes was assessed by using Pearson correlation coefficients.

Results: The overall composite score of performance measures was 63.3%. The correlations coefficients between individual performance measures ranged widely from 0 to 0.87. The composite score was modestly associated with 30-day and 1-year RSM (Pearson correlation coefficients, 0.23 and 0.34, respectively; $P<0.05$ for both), and explained only 5.24% and 11.80% of hospital-level variation in 30-day and 1-year RSM for acute stroke patients.

Conclusions: The adherence to guideline-recommended performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance measures. The association of hospital performance measures with hospital-level short- and long-term mortality rates was modest.

Article summary

Strengths and limitations of this study:

1. This study found that the adherence to guideline-recommended performance measures for acute ischemic stroke was suboptimal in China.

2. The association of hospital performance measures with hospital-level short- and long-term mortality rates was modest.

3. The study was limited that results reported herein came from the Chinese healthcare system and therefore may not necessarily be generalisable to other countries.

INTRODUCTION

Guideline-recommended hospital performance measures are increasingly used for quality improvement,[1] certification for stroke centres,[2] public reporting[3] and remuneration for performance.[4] Performance measures evaluate the structure, process and outcome of care, and provide a metric that can be tracked, reported and improved.[5] Although performance measures have been associated with higher scores on measured metrics,[6] there has been limited evidence demonstrating an association between adherence to performance measures and better patient outcomes.[7]

Using data from the China National Stroke Registry (CNSR), we sought to determine whether evidence-based hospital performance measures were associated with short- and long-term outcomes in acute ischemic stroke patients in China. Specifically, we (1) reported the hospital variation in adherence to evidence-based performance measures, (2) assessed the correlation between each individual performance measures, and (3) quantified the association between performance measures and hospital-level, risk-standardised, 30-day and 1-year mortality among acute ischemic stroke patients in China.

METHODS

CNSR overview

The CNSR was the first nationwide, hospital-based, prospective stroke registry of quality assessment in China. It was sponsored by the Ministry of Health of the People's Republic of China to establish a national stroke database for evaluating stroke care quality and outcomes, and conducted between September 2007 and August 2008. The study design of CNSR has been described previously.[8] Briefly, the criteria used for hospital selection included: (1) having at least one stroke neurologist, (2) at least two sites were included from each of the 31 provinces and municipalities in mainland China, (3) commitment to participate voluntarily and (4) ability to conduct research.[8 9] The CNSR recruited

consecutive patients older than 18 years and diagnosed with ischemic stroke, transient ischemic attack (TIA), intracerebral haemorrhage, or subarachnoid haemorrhage within 14 days of the index event. We collected patients' demographics, adherence to performance measures in hospitals, and status at discharge, 90-day, 6-month and 1-year follow-up after symptom onset. The study was approved by the Central Institutional Review Board of CNSR. Written informed consent was acquired from the patient or legally authorised representative.

Data collection

Hospitals' characteristics were surveyed. According to annual report on health statistics of China,[10] hospitals were divided into three regions: eastern, central and western. Academic status was defined as a hospital affiliated with a specific university. Hospital bed size was the number of total inpatient beds per site. Annual stroke discharge was the number of discharged patients diagnosed with stroke per year per hospital.

Trained research coordinators at each hospital reviewed medical records daily to identify, obtain informed consent, and enrol consecutive patients in accordance with the procedures indicated in a standard data collection manual. The key variables in the CNSR were assessed, including: (1) demographic characteristics and medical history; (2) pre-stroke modified Rankin scale (mRS), and National Institutes of Health Stroke Scale (NIHSS) at admission, vascular risk factors, and clinical care during hospitalization and (3) 30-day and 1-year all-cause mortality after stroke. Patients who survived to discharge, or their authorised caregivers, were contacted via telephone by trained research personnel who used standardised scripts for follow-up at 90 days, 6 months and 1 year after stroke symptom onset[8]. Specific death events and dates were recorded in detail, and 30-day and 1-year all-cause mortality after stroke were confirmed.

Performance Measures

We evaluated nine hospital performance measures, including six "core" measures for acute ischemic stroke as recommended by American Heart Association/American Stroke Association (AHA/ASA) Get With The Guidelines-Stroke (GWTG-Stroke)[11] and three additional guideline-recommended secondary prevention metrics.[12] These nine performance measures included three acute performance measures: (1) intravenous tissue-type plasminogen activator (tPA) in patients who arrive within 2 hours after symptom onset and treated within 3 hours (IV rt-PA for 2 Hour), (2) antithrombotic medication within 48 hours of admission (early antithrombotics), (3) deep vein thrombosis (DVT) prophylaxis within 48 hours of admission for nonambulatory patients (DVT prophylaxis); and 6 discharge performance measures: (1) antithrombotic medication, (2) anticoagulation for atrial fibrillation (AF), (3) antihypertensive medication for patients with hypertension, (4) medications for lowering low-density lipoprotein (LDL) ≥100 mg/dL, (5) hypoglycemia medication for diabetes mellitus, (6) smoking cessation. Details of the performance measures were described in the Table 1.

Adherence to hospital-level individual performance measures was calculated as the proportion of patients who received the indicated care from among all the patients who were eligible for the indicated care. The overall hospital performance measures was measured as the composite score, which was calculated by the total number of interventions actually performed among all eligible patients at a hospital, divided by the total number of recommended interventions in all eligible patients.[13] Although the composite score was analysed as a continuous variable, hospitals were also divided, for descriptive purposes, into quartiles based on this continuous variable. To ensure the stability of the measure, hospitals with fewer than 20 patients in the denominator of a measure were excluded.

Table 1. Specifications of guideline-recommended performance measures

Performance measure of ischemic stroke care	Performance measure definition for eligible patients*
Acute performance measures	
IV rt-PA <2 Hour	Intravenous recombinant tissue plasminogen activator (IV rtPA) in patients who arrive within 2 hours after initial symptom onset and treated within 3 hours
Early Antithrombotics	Antithrombotic therapy prescribed within 48 hours of hospitalization, including antiplatelet or anticoagulant therapy
DVT Prophylaxis	Patients at risk for deep vein thrombosis (DVT) (non-ambulatory) who received DVT prophylaxis by end of hospital day two, including pneumatic compression, warfarin sodium or heparin sodium
Performance measures at discharge	
Discharge Antithrombotics	Antithrombotic therapy prescribed at discharge
Anticoagulation for Atrial Fibrillation	Anticoagulation prescribed at discharge for patients with atrial fibrillation or atrial flutter documented during the hospitalization
LDL 100	Lipid lowering agent prescribed at discharge if Low-density lipoprotein (LDL) ⩾100 mg/dL
Antihypertension for hypertension disease:	Antihypertension medication prescribed at discharge for patients with history of hypertension disease or hypertension

	disease documented during the hospitalization
Hypoglycemic therapy for diabetes mellitus:	Hypoglycemic medication prescribed at discharge for patients with history of diabetes mellitus or diabetes mellitus documented during the hospitalization
Smoking Cessation	Smoking cessation intervention (counseling or medication) prior to discharge for current or recent smokers

* Eligible patients are those without any medical contraindications (e.g., treatment intolerance, excessive risk of adverse reaction, patient/family refusal, or terminal illness/comfort care only) documented as reasons for nontreatment for each of the applicable measures. Also excludes patients who are discharged to hospice, or another short-term general hospital, leave against medical advice before the end of hospital day two. For acute performance measures except for rt-PA measure, excludes patients who died before the end of hospital day two. The acute rt-PA measure excludes patients with missing or erroneous onset, arrival or treatment times, those who began IV t-PA at an outside hospital, or who initiated IV t-PA after 180 minutes from onset. For performance measures at discharge, excludes patients who died during hospitalization. As for six performance measures from Get With The Guideline-Stroke (GWTG-Stroke), we employed the same criteria as the Get With The Guideline-Stroke (GWTG-Stroke).

Risk-standardized Mortality (RSM) Rates

RSM rates were calculated using a multivariate hierarchical regression model in accordance with the AHA/ASA recommendations for risk adjustment of ischemic stroke outcomes to compare hospital performance.[7] The first level of the hierarchical model included patient characteristics. These patient's variables were divided into three categories: (1) demographics and clinical features: age, gender, health insurance type (urban basic medical insurance schemes for urban and governmental employees and urban residents, new rural cooperative medical schemes for rural residents, commercial insurance, and self-payment), transport to hospital by emergency medical service, and NIHSS score at admission; (2) vascular risk factors: hypertension, diabetes mellitus, dyslipidaemia, AF, coronary artery disease, previous myocardial infarction, congestive heart failure, valvular heart disease, history of stroke/TIA, peripheral vascular disease, current smoking, and excessive alcohol consumption; (3) other pre-existing comorbid conditions: chronic obstructive pulmonary disease, hepatic cirrhosis, peptic ulcer, previous gastrointestinal bleeding, Alzheimer's disease/dementia, cancer, DVT/pulmonary embolus, renal dialysis, pre-stroke dependence (mRS ≥3), and blood glucose at admission. The second level included hospital-specific random intercepts that allow for different baseline mortality rates between hospitals. The hospital RSM rates were obtained as the ratio of "predicted" to expected mortality, multiplied by the unadjusted mortality rate for the total population.[14 15] The expected outcome for each hospital was the number of deaths expected at the hospital if the hospital's patients were treated at a "reference" hospital. The predicted hospital outcome was the number of expected mortalities at the "specific" hospital and not at a reference hospital. To ensure the stability of the measure, hospitals with fewer than 20 patients in the denominator of a measure were excluded.

Statistical analyses

Numbers (percentages) were used to describe categorical variables, and median values with interquartile ranges (IQRs) were reported for continuous variables. The correlations of individual performance measures, as well as performance measures and stroke outcomes, were evaluated using Pearson correlation coefficients. We reported both the relevant correlation coefficients and the percentage of the hospital-specific variation in RSM rates was explained; i.e., the squares of the correlation coefficients as indicators of the strength of the associations.[16]

All tests were two-tailed, and statistical significance was determined at the α level of 0.05 in univariate and multivariate analyses. Statistical analysis was performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Study hospitals and patient baseline characteristics

Among 14,526 eligible patients diagnosed with acute ischemic stroke from 132 hospitals throughout China, complete 1-year follow-up information was available for 12,173 patients (83.8%). We excluded 12 hospitals with fewer than 20 patients in the denominator of a measure. Finally, 120 hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis. Hospital and patient baseline characteristics were described in Table 2. Among 120 hospitals, 62 (51.67%) hospitals were teaching hospitals and 70 (58.33%) were from eastern regions. The median hospital bed size was 1200 (range, 700–1861) and annual stroke volume was 430 (range, 310–601). Among 12,027 patients, 7407 (61.59%) were men, and the median age was 67 (range, 57–75) years. Common vascular risk factors included hypertension, previous stroke/ TIA, smoking history, and diabetes. The median NIHSS score was 4 (range, 2–9).

Variability in performance measures

The overall composite score was 63.3% among the 120 hospitals. However, the composite score for each hospital varied considerably among the CNSR (Table 3). The hospitals in the highest quartile (quartile 4) had a median (IQR) composite score of 85.1% (82.2%–89.9%), compared with 50.9% (44.2%–58.1%) for those in the lowest quartile (quartile 1).

Table 3 also shows the variability in adherence to individual guideline-recommended performance measures among patients without contraindications. Within acute interventions, early antithrombotics showed the lowest degree of variance, although the difference between the first and third quartiles remained significant. In contrast, there were twofold to threefold differences in the use of IV rt-PA for 2 Hour, DVT prophylaxis, anticoagulant for AF and lipid-lowering medication for LDL ≥100 mg/dl.

Table 2. Baseline characteristics of patients with acute ischemic stroke among China National Stroke Registry

	Level	N (%)
Patient characteristics		
Total		12 027
Demographics		
Age, yr	Median (IQR)	67 (57-75)
Gender	Male	7 407(61.59)
	Female	4 620(38.41)
Insurance scheme	UBMIS	7 311(60.79)
	NRCMS	2 027(16.85)

	Commercial	397(3.30)
	Self-payment	2 292(19.06)
Transport to hospital by EMS	Yes	1 901(15.81)
NIHSS at admission	Median (IQR)	4 (2-9)
Vascular risk factors		
Previous stroke/TIA	Yes	4 088(33.99)
Diabetes	Yes	2 593(21.56)
Hypertension	Yes	7 672(63.79)
Dyslipidemia	Yes	1 344(11.17)
CHD/previous MI	Yes	1 748(14.53)
Atrial fibrillation	Yes	892(7.42)
PVD	Yes	76(0.63)
Ever Smoking	Yes	4 779(39.74)
Heavy drinking	Yes	1 873(15.57)
Pre-existing comorbid condition		
Congestive heart failure	Yes	250(2.08)
Valvular Heart Disease	Yes	288(2.42)
Chronic obstructive pulmonary disease	Yes	138(1.15)
Hepatic cirrhosis	Yes	41(0.34)
Peptic ulcer disease	Yes	336(2.81)
Previous gastrointestinal bleeding	Yes	184(1.54)
Dementia/Alzheimer's disease	Yes	156(1.30)

Cancer	Yes	215(1.80)
Deep venous thrombosis/Pulmonary embolus	Yes	77(0.64)
Renal Dialysis	Yes	9(0.08)
Pre-stroke dependence (mRS>2)	Yes	1 120(9.31)
Glucose on admission (≥7.5mmol/L)	Yes	2 328(19.72)
Hospital characteristics		
Total		120
Hospital size		
Beds	Median (IQR)	1 200 (700, 1 861)
Hospital type		
Teaching	Yes	62(51.67)
Annual stroke discharges	Median (IQR)	430 (310,601)
Geographic region		
East	Yes	70 (58.33)
Middle	Yes	26 (21.67)
West	Yes	24 (20.0)

IQR, interquartile range; UBMIS, urban basic medical insurance scheme; NRCMS, new rural cooperative medical scheme; EMS, emergency medical service; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; CHD, coronary artery disease; MI, myocardial infarction; PVD, peripheral vascular disease; mRS, modified Rankin scale.

Table 3. Hospital performance measures and RSM rates

Measures	25th Percentile	Median	75th Percentile
Composite score	59.05%	65.65%	72.75%
Acute interventions			
IV rt-PA for 2 Hour	0.00%	0.00%	25.00%
Early antithrombotics	73.21%	80.68%	88.24%
DVT prophylaxis	33.33%	59.22%	70.00%
Discharge interventions			
D/C antithrombotics	64.89%	77.00%	85.15%
Anticoagulation for AF	0.00%	14.29%	26.97%
Lipid-lowering drug for LDL ≥100 mg/dl	25.00%	41.89%	61.72%
Antihypertensive Medication	45.46%	61.37%	75.00%
Antidiabetic Medication	53.15%	67.03%	79.58%
Smoking cessation	50.55%	70.87%	83.33%
RSM rate			
30-day	4.91%	5.41%	6.17%
1-year	12.77%	13.55%	14.48%

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; D/C, discharge; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

Correlations of performance measures

The correlations between two individual hospital performance measures varied widely (Table 4). We found moderate correlation (Pearson correlation coefficient ≥0.40; P <0.001 for all) for all pairwise comparisons between antithrombotic at discharge and early antithrombotics, lipid-lowering drugs for LDL ≥100 mg/dl, antihypertensive medication, antidiabetic medication, and smoking cessation at discharge; and between antidiabetic medication and antihypertensive medication and smoking cessation at discharge. Other hospital performance measures had a modest correlation or no correlation with each other (Pearson correlation coefficient <0.40 for all).

Association of performance measures with hospital-level RSM rates

The median 30-day and 1-year RSM rate (IQR) was 5.41% (4.91%–6.17%) and 13.55% (12.77%–14.48%), respectively (Table 3).

Several performance measures showed a statistically significant, but modest, correlation with 30-day and 1-year RSM rates, including antithrombotics at discharge (Pearson correlation coefficients = 0.21 and 0.33, respectively), antihypertensive medication (Pearson correlation coefficients = 0.24 and 0.37, respectively) and antidiabetic medication (Pearson correlation coefficients = 0.33 and 0.36, respectively) (P <0.001 for all) (Table 4). These performance measures individually explained between 4.38% and 10.59% of hospital-level variation in 30-day RSM rates, and between 10.58% and 14.01% of hospital-level variation in 1-year RSM rates (Table 5).

The hospital-level composite score had a modest correlation with 30-day and 1-year RSM rates (Pearson correlation coefficients = 0.23 and 0.34, respectively) (Table 4), and explained 5.24% and 11.80% of the hospital-level variation in 30-day and 1-year RSM rates, respectively (Table 5).

Table 4. Correlation coefficients for performance measures and hospital RSM rate (30-day and 1-year)

	Acute interventions			Discharge interventions						
	IV rt-PA for 2 Hour	Early antithrombotics	DVT prophylaxis	Antithrombotics	Anticoagulation for AF	Lipid-lowering drug for LDL ≥100 mg/dl	Antihypertensive Medication	Antidiabetic Medication	Smoking cessation	Composite score
Acute interventions										
IV rt-PA for 2 Hour	1.00									
Early antithrombotics	-0.06	1.00								
DVT prophylaxis	-0.02	0.28*	1.00							
Discharge interventions										
Antithrombotics	0.06	0.40*	0.07	1.00						
Anticoagulation for AF	-0.02	0.00	0.07	0.27*	1.00					
Lipid-lowering drug for LDL ≥100 mg/dl	0.07	0.03	-0.06	0.45*	0.22*	1.00				
Antihypertensive Medication	0.09	0.12	-0.05	0.64*	0.20*	0.27*	1.00			
Antidiabetic Medication	0.18*	0.17	0.05	0.79*	0.14	0.39*	0.71*	1.00		
Smoking cessation	0.14	0.25*	0.02	0.43*	0.19*	0.13	0.37*	0.42*	1.00	

Composite score	0.10	0.55*	0.27*	0.89*	0.29*	0.50*	0.70*	0.77*	0.58*	1.00
Risk-standardized 30-day mortality rate	-0.13	-0.01	-0.15	-0.21*	-0.09	-0.22*	-0.24*	-0.33*	0.05	-0.23*
Risk-standardized 1-year mortality rate	-0.09	-0.08	-0.15	-0.33*	-0.10	-0.13	-0.37*	-0.36*	-0.07	-0.34*

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

*P<0.05.

Table 5. Variance in 30-day and 1-year RSM rates explained by each performance measure and composite measure

	30-day RSM rate	1-year RSM rate
Measures	% variance explained	% variance explained
Acute interventions		
IV rt-PA for 2 Hour	1.77%	0.84%
Early antithrombotics	0.02%	0.59%
DVT prophylaxis	2.28%	2.25%
Discharge interventions		
D/C antithrombotics	4.31%	10.58%
Anticoagulation for AF	0.86%	0.95%
Lipid-lowering drug for LDL ≥100 mg/dl	4.66%	1.64%
Antihypertensive Medication	5.98%	14.01%
Antidiabetic Medication	10.59%	13.09%
Smoking cessation	0.24%	0.43%
Composite score	5.24%	11.80%

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; D/C, discharge; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

DISCUSSION

The present study found that ischemic stroke care was suboptimal in China and there were various correlations among hospital performance measures. The hospital-level composite score had a modest correlation with 30-day and 1-year RSM rates. This finding suggested hospital performance measures cannot reliably infer short- and long- term mortality rates after acute ischemic stroke. Our results underscored that the current performance measures of stroke care provided complementary, but not redundant, information with the measures of 30-day and 1-year mortality.

The relationship between performance measures and stroke outcomes still exists uncertainty. Some studies have indicated the use of performance measures was associated with lower short-term mortality or better functional outcomes.[17-19] However, the link between stroke performance measures and outcome was not straightforward in certain other studies.[20-23] There were several probable reasons for the modest correlation between hospital-level performance measures and risk-standardised mortality in the present study. First, although clinical trials have shown a significant relationship between process interventions and outcomes,[24 25] the guideline-recommended performance measures were not mainly designed to be a substitute for overall short- and long-term hospital mortality. Second, there was relative little variation across hospitals in some performance measures, such as early antithrombotics after admission, which limited the ability to discriminate between hospitals based on their performance on this measure. Additionally, some performance measures, such as intravenous thrombolysis, may had a greater effect regarding stroke-related disability than that in stroke-related mortality.[26] Finally, hospital mortality rates, even risk-standardised ones, were likely affected by many factors independent of the performance measures of stroke care quality. These included severity of stroke, patients' or their family's

preference, economic level and clinical strategies that may contribute to a hospital's performance outcomes.[27]

The present study also demonstrated a significant correlation between certain guideline-recommended performance measures for acute ischemic stroke care, indicating the hospitals that perform well in one performance measure were likely to perform well in the others. However, other performance measures were less strongly correlated with each other. This finding implies different performance measures reflect separate components of quality in acute ischemic stroke care. Our work indicated that hospital performance rankings were likely to be substantially affected by the performance measures under selection. A broad range of performance measures appears necessary to comprehensively reflect hospital care practices.

Our study had several strengths. First, to date, the CNSR was the largest stroke database in China. Hospitals participating in the CNSR encompassed different regions and had good representativeness. Second, we used newer RSM methods based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.[7] Third, baseline characteristics of patients, such as age, gender, vascular risk factors, comorbid conditions, and stroke severity (NIHSS) were adjusted in calculating the RSM in accordance with the American Heart Association/American Stroke Association (AHA/ASA).[7 27] Additionally, besides short-term RSM, our study also analysed long-term RSM.

However, our study also had some limitations. First, our study was observational and non-randomised. The association between care processes and stroke outcomes did not necessarily prove causality and may be confounded by previously discussed factors. Second, our outcome was mortality; other outcomes, such as stroke recurrence and functional outcomes, were also vital to

patients and should be assessed in future studies.[23] Third, it remains unclear whether this process–outcome link for a given set of performance measures may vary over time. Future research need to determine the stability of the process-outcome relationship as quality improvement efforts drive broader care adoption. Finally, there were several differences between stroke healthcare delivery systems in China and in other countries. The results reported herein came from the Chinese healthcare system and therefore may not necessarily be generalisable to other countries.

CONCLUSIONS

The quality of process care for ischemic stroke was suboptimal in China, and there were various correlations in hospital performance among the individual metrics. Although the guideline-recommended performance measures were important in pursuing improved acute ischemic stroke outcomes, the relationship between performance measures and hospital short- and long-term risk-adjusted mortality rates was modest. Much broader measures needed to be used as a means of assessing and helping improve the quality of hospital-level stroke care.

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Contributorship Statement

XMZ and ZXL analyzed the data and wrote the manuscript. XLB, LPL, CXW, HL, JB, QY and DW analyzed and interpretated the data. ZXL, CJW, YJ, XMY and XMZ performed research. YJW, YLW, ZXL, YX and ZQZ conceived, designed and supervised the study.

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Competing interests

None.

Ethics approval

Approval was obtained from the Central Institutional Review Board at Beijing Tiantan Hospital.

Provenance and peer review

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	✓ **Page 3** (*a*) Indicate the study's design with a commonly used term in the title or the abstract
		✓ **Page 3** (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	✓ **Page 5** Explain the scientific background and rationale for the investigation being reported
Objectives	3	✓ **Page 5** State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	✓ **Page 5** Present key elements of study design early in the paper
Setting	5	✓ **Page 6** Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	✓ **Page 5** (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	✓ **Page 7-10** Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	✓ **Page 7-10** For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	✓ **Page 21** Describe any efforts to address potential sources of bias
Study size	10	✓ **Page 10** Explain how the study size was arrived at
Quantitative variables	11	✓ **Page 11** Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	✓ **Page 11** (*a*) Describe all statistical methods, including those used to control for confounding
		✓ **Page 11** (*b*) Describe any methods used to examine subgroups and interactions
		✓ **Page 11** (*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	✓ **Page 11** (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		✓ **Page 11** (b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	✓ **Page 11** (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		✓ **Page 11** (b) Indicate number of participants with missing data for each variable of interest
		✓ **Page 11** (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	✓ **Page 16** Report numbers of outcome events or summary measures over time
Main results	16	✓ **Page 17-19** (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which

		confounders were adjusted for and why they were included
		✓ **Page 12-15** (*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	✓ **Page 16-19** Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	✓ **Page 20** Summarise key results with reference to study objectives
Limitations	19	✓ **Page 21** Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	✓ **Page 20-21** Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	✓ **Page 21-22** Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	✓ **Page 23** Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: the China National Stroke Registry

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Title pages

Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: the China National Stroke Registry

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Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: the China National Stroke Registry

ABSTRACT

Objectives: Evidence-based performance measures were increasingly used to evaluate hospital quality of stroke care, but their impact on stroke outcome has not been verified. We aimed to evaluate the correlation between hospital performance measures and outcomes among acute ischemic stroke patients in Chinese population.

Methods: Data was derived from 120 hospitals participating in the China National Stroke Registry between September 2007 and August 2008. Adherence to 9 evidence-based performance measures was examed, and the composite score of hospital performance measures was calculated. Primary stroke outcomes were hospital-level, 30-day and 1-year risk-standardized mortality (RSM). Association of hospital individual performance measures and composite score with stroke outcomes was assessed by using Spearman correlation coefficients.

Results: The overall composite score of performance measures was 63.3%. The correlations coefficients between individual performance measures ranged widely from 0.01 to 0.66. The composite score was modestly associated with 1-year RSM (Spearman correlation coefficients, 0.34; $P<0.05$), however, no association was observed between the composite score and the 30-day RSM. The composite score explained only 2.53% and 10.18% of hospital-level variation in 30-day and 1-year RSM for acute stroke patients.

Conclusions: The adherence to evidence-based performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance

measures. The association of hospital performance measures with hospital-level 1-year RSM mortality rates was modest.

Article summary

Strengths and limitations of this study:

1. As the largest stroke database in China, hospitals participating in the China National Stroke Registry encompassed different regions and had good representativeness.
2. We used newer risk-standardized mortality methods based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.
3. Our study was observational and non-randomised. The association between hospital performance measures and stroke outcomes did not necessarily prove causality.

INTRODUCTION

Stroke remains to be the leading cause of mortality in China and was responsible for ≈1.9 million deaths.[1] Although evidence-based guidelines for stroke and transient ischemic attack (TIA) care have been developed and updated over time,[2-4] there were variations and deficiencies in how these guidelines were applied.[5-7] To reduce the national stroke burden, several national organizations developed a set of evidence-based hospital performance measures to quantify and promote the quality of stroke care.[7-9]

Evidence-based hospital performance measures evaluated the structure, process and outcome of stroke care, and provided a metric that could be tracked, reported and improved.[10] Evidence-based hospital performance measures were also increasingly used for certification for stroke centres,[11] public reporting[12] and remuneration for performance.[13] Despite substantial improvement in stroke care quality was observed in China, gaps in adherence to the evidence-based hospital performance measures still exist. In addition, although measuring outcomes after stroke has important policy implications,[14] there has been limited evidence demonstrating the association between adherence to performance measures and better patient outcomes.[15]

Using data from the China National Stroke Registry (CNSR), we sought to determine whether evidence-based hospital performance measures were associated with short- and long-term outcomes in acute ischemic stroke patients in China. Specifically, we (1) reported the hospital variation in adherence to evidence-based performance measures, (2) assessed the correlation between each individual performance measures, and (3) quantified the association between performance measures and hospital-level, risk-standardised, 30-day and 1-year mortality among acute ischemic stroke patients in China.

METHODS

CNSR overview

The CNSR was the first nationwide, hospital-based, prospective stroke registry of quality assessment in China. It was sponsored by the Ministry of Health of the People's Republic of China to establish a national stroke database for evaluating stroke care quality and outcomes, and conducted between September 2007 and August 2008. The study design of CNSR has been described previously.[16] Briefly, the criteria used for hospital selection included: (1) having at least one stroke neurologist, (2) at least two sites were included from each of the 31 provinces and municipalities in mainland China, (3) commitment to participate voluntarily and (4) ability to conduct research.[16 17] The CNSR recruited consecutive patients older than 18 years and diagnosed with ischemic stroke, transient ischemic attack (TIA), intracerebral haemorrhage, or subarachnoid haemorrhage within 14 days of the index event. We collected patients' demographics, adherence to performance measures in hospitals, and status at discharge, 90-day, 6-month and 1-year follow-up after symptom onset. The study was approved by the Central Institutional Review Board of Beijing Tiantan Hospital. Written informed consent was acquired from the patient or legally authorised representative.

Data collection

Hospitals' characteristics were surveyed. According to annual report on health statistics of China,[18] hospitals were divided into three regions: eastern, central and western. Academic status was defined as a hospital affiliated with a specific university. Hospital bed size was the number of total inpatient beds per site. Annual stroke discharge was the number of discharged patients diagnosed with stroke per year per hospital.

Trained research coordinators at each hospital reviewed medical records daily to identify, obtain informed consent, and enrol consecutive patients in accordance with the procedures indicated in a

standard data collection manual. The key variables in the CNSR were assessed, including: (1) demographic characteristics and medical history; (2) pre-stroke modified Rankin scale (mRS), and National Institutes of Health Stroke Scale (NIHSS) at admission, vascular risk factors, and clinical care during hospitalization and (3) 30-day and 1-year all-cause mortality after stroke. Patients who survived to discharge, or their authorised caregivers, were contacted via telephone by trained research personnel who used standardised scripts for follow-up at 90 days, 6 months and 1 year after stroke symptom onset[16]. Specific death events and dates were recorded in detail, and 30-day and 1-year all-cause mortality after stroke were confirmed.

Performance Measures

We evaluated nine hospital performance measures, including seven "core" measures for acute ischemic stroke as recommended by the American Heart Association/American Stroke Association (AHA/ASA) Get With The Guidelines-Stroke (GWTG-Stroke)[7] and two additional evidence-based secondary prevention metrics.[4] These seven core performance measures included (1) intravenous tissue-type plasminogen activator (tPA) in patients who arrive within 2 hours after symptom onset and treated within 3 hours (IV rt-PA < 2 Hour), (2) antithrombotic medication within 48 hours of admission (early antithrombotics), (3) deep vein thrombosis (DVT) prophylaxis within 48 hours of admission for nonambulatory patients (DVT prophylaxis), (4) antithrombotic medication, (5) anticoagulation for atrial fibrillation (AF) , (6) medications for lowering low-density lipoprotein (LDL) ≥100 mg/dL, (7) smoking cessation. The two additional performance measures were antihypertensive medication for patients with hypertension and hypoglycemia medication for diabetes mellitus. Details of the performance measures were described in the Table 1.

Adherence to hospital-level individual performance measures was calculated as the proportion of

patients who received the indicated care from among all the patients who were eligible for the indicated care. The overall hospital performance measures was measured as the composite score, which was calculated by the total number of interventions actually performed among all eligible patients at a hospital, divided by the total number of recommended interventions in all eligible patients.[19] Although the composite score was analysed as a continuous variable, hospitals were also divided, for descriptive purposes, into quartiles based on this continuous variable. To ensure the stability of the measure, hospitals with fewer than 20 patients in the denominator of a measure were excluded.

Table 1. Specifications of evidence-based performance measures

Performance measure of ischemic stroke care	Performance measure definition for eligible patients*
Acute performance measures	
IV rt-PA < 2 Hour	Intravenous recombinant tissue plasminogen activator (IV rtPA) in patients who arrive within 2 hours after initial symptom onset and treated within 3 hours
Early Antithrombotics	Antithrombotic therapy prescribed within 48 hours of hospitalization, including antiplatelet or anticoagulant therapy
DVT Prophylaxis	Patients at risk for deep vein thrombosis (DVT) (non-ambulatory) who received DVT prophylaxis by end of hospital day two, including pneumatic compression, warfarin sodium or heparin sodium
Performance measures at discharge	

Discharge Antithrombotics	Antithrombotic therapy prescribed at discharge
Anticoagulation for Atrial Fibrillation	Anticoagulation prescribed at discharge for patients with atrial fibrillation or atrial flutter documented during the hospitalization
LDL 100	Lipid lowering agent prescribed at discharge if Low-density lipoprotein (LDL) ⩾100 mg/dL
Antihypertension for hypertension disease:	Antihypertension medication prescribed at discharge for patients with history of hypertension disease or hypertension disease documented during the hospitalization
Hypoglycemic therapy for diabetes mellitus:	Hypoglycemic medication prescribed at discharge for patients with history of diabetes mellitus or diabetes mellitus documented during the hospitalization
Smoking Cessation	Smoking cessation intervention (counseling or medication) prior to discharge for current or recent smokers

* Eligible patients are those without any medical contraindications (e.g., treatment intolerance, excessive risk of adverse reaction, patient/family refusal, or terminal illness/comfort care only) documented as reasons for nontreatment for each of the applicable measures. Also excludes patients who are discharged to hospice, or another short-term general hospital, leave against medical advice before the end of hospital day two. For acute performance measures except for rt-PA measure, excludes patients who died before the end of hospital day two. The acute rt-PA measure excludes patients with missing or erroneous onset, arrival or treatment times, those who began IV t-PA at an outside hospital, or who initiated IV t-PA after 180 minutes from onset. For performance measures at

discharge, excludes patients who died during hospitalization. As for seven performance measures from Get With The Guideline-Stroke (GWTG-Stroke), we employed the same criteria as the Get With The Guideline-Stroke (GWTG-Stroke).

Risk-standardized Mortality (RSM) Rates

RSM rates were calculated using a multivariate hierarchical regression model in accordance with the AHA/ASA recommendations for risk adjustment of ischemic stroke outcomes to compare hospital performance.[15] The first level of the hierarchical model included patient characteristics. These patient's variables were divided into three categories: (1) demographics and clinical features: age, gender, health insurance type (urban basic medical insurance schemes for urban and governmental employees and urban residents, new rural cooperative medical schemes for rural residents, commercial insurance, and self-payment), transport to hospital by emergency medical service, and NIHSS score at admission; (2) vascular risk factors: hypertension, diabetes mellitus, dyslipidaemia, AF, coronary artery disease, previous myocardial infarction, congestive heart failure, valvular heart disease, history of stroke/TIA, peripheral vascular disease, current smoking, and excessive alcohol consumption; (3) other pre-existing comorbid conditions: chronic obstructive pulmonary disease, hepatic cirrhosis, peptic ulcer, previous gastrointestinal bleeding, Alzheimer's disease/dementia, cancer, DVT/pulmonary embolus, renal dialysis, pre-stroke dependence (mRS ≥3), and blood glucose at admission. The second level included hospital-specific random intercepts that allow for different baseline mortality rates between hospitals. The hospital RSM rates were obtained as the ratio of "predicted" to expected mortality, multiplied by the unadjusted mortality rate for the total population.[20 21] The expected outcome for each hospital was the number of deaths expected at the hospital if the hospital's patients were treated at a "reference" hospital. The predicted hospital outcome was the number of expected mortalities at the "specific" hospital and not at a reference hospital.

Statistical analyses

Numbers (percentages) were used to describe categorical variables, and median values with interquartile ranges (IQRs) were reported for continuous variables. The correlations of individual performance measures, as well as performance measures and stroke outcomes, were evaluated using Spearman correlation coefficients. The bonferroni correction was performed in the multiple comparisons. The inter-class correlation (ICC) of 30-day and 1-year RSM rate were calculated. We also reported both the relevant correlation coefficients and the percentage of the hospital-specific variation in RSM rates was explained; i.e., the squares of the correlation coefficients as indicators of the strength of the associations.[22]

All tests were two-tailed, and statistical significance was determined at the α level of 0.05 in univariate and multivariate analyses. Statistical analysis was performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Study hospitals and patient baseline characteristics

Among 14,526 eligible patients diagnosed with acute ischemic stroke from 132 hospitals throughout China, complete 1-year follow-up information was available for 12,173 patients (83.8%). We excluded 12 hospitals with fewer than 20 patients in the denominator of a measure. Finally, 120 hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis. Hospital and patient baseline characteristics were described in Table 2. Among 120 hospitals, 62 (51.67%) hospitals were teaching hospitals and 70 (58.33%) were from eastern regions. The median hospital bed size was 1200 (IQR, 700–1861) and annual stroke volume was 430 (IQR, 310–601). Among 12,027 patients, 7407 (61.59%) were men, and the median age was 67 (IQR, 57–75) years. Common

vascular risk factors included hypertension, previous stroke/ TIA, smoking history, and diabetes. The median NIHSS score was 4 (IQR, 2–9).

Variability in performance measures

The overall composite score was 63.3% among the 120 hospitals. However, the composite score for each hospital varied considerably among the CNSR (Table 3). The hospitals in the highest quartile (quartile 4) had a median (IQR) composite score of 85.1% (82.2%–89.9%), compared with 50.9% (44.2%–58.1%) for those in the lowest quartile (quartile 1).

In table 3, we showed hospital rates (median and IQR) for each process measure as well as 30-day and1-year RSM rates. Within acute interventions, early antithrombotics showed the lowest degree of variance, although the difference between the first and third quartiles remained significant. In contrast, there were twofold to threefold differences in the use of IV rt-PA < 2 Hour, DVT prophylaxis, anticoagulant for AF and lipid-lowering medication for LDL ≥100 mg/dl.

Table 2. Baseline characteristics of patients with acute ischemic stroke among China National Stroke Registry

	Level	N (%)
Patient characteristics		
Total		12 027
Demographics		
Age, yr	Median (IQR)	67 (57-75)
Gender	Male	7 407(61.59)
	Female	4 620(38.41)
Insurance scheme	UBMIS	7 311(60.79)
	NRCMS	2 027(16.85)
	Commercial	397(3.30)
	Self-payment	2 292(19.06)
Transport to hospital by EMS	Yes	1 901(15.81)
NIHSS at admission	Median (IQR)	4 (2-9)
Vascular risk factors		
Previous stroke/TIA	Yes	4 088(33.99)
Diabetes	Yes	2 593(21.56)
Hypertension	Yes	7 672(63.79)
Dyslipidemia	Yes	1 344(11.17)
CHD/previous MI	Yes	1 748(14.53)
Atrial fibrillation	Yes	892(7.42)
PVD	Yes	76(0.63)
Ever Smoking	Yes	4 779(39.74)

Heavy drinking	Yes	1 873(15.57)
Pre-existing comorbid condition		
Congestive heart failure	Yes	250(2.08)
Valvular Heart Disease	Yes	288(2.42)
Chronic obstructive pulmonary	Yes	138(1.15)
Hepatic cirrhosis	Yes	41(0.34)
Peptic ulcer disease	Yes	336(2.81)
Previous gastrointestinal bleeding	Yes	184(1.54)
Dementia/Alzheimer's disease	Yes	156(1.30)
Cancer	Yes	215(1.80)
Deep venous thrombosis/Pulmonary	Yes	77(0.64)
Renal Dialysis	Yes	9(0.08)
Pre-stroke dependence (mRS>2)	Yes	1 120(9.31)
Glucose on admission	Yes	2 328(19.72)
Hospital characteristics		
Total		120
Hospital size		
Beds	Median (IQR)	1 200 (700, 1 861)
Hospital type		
Teaching	Yes	62(51.67)
Annual stroke discharges	Median (IQR)	430 (310,601)
Geographic region		
East	Yes	70 (58.33)
Middle	Yes	26 (21.67)

West	Yes	24 (20.0)

IQR, interquartile range; UBMIS, urban basic medical insurance scheme; NRCMS, new rural cooperative medical scheme; EMS, emergency medical service; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; CHD, coronary artery disease; MI, myocardial infarction; PVD, peripheral vascular disease; mRS, modified Rankin scale.

Table 3. Hospital performance measures and RSM rates

Measures	Median (IQR, %)
Composite score	65.65 (59.05-72.75)
Acute interventions	
IV rt-PA < 2 Hour	0.00 (0.00-25.00)
Early antithrombotics	80.68 (73.21-88.24)
DVT prophylaxis	59.22 (33.33-70.00)
Discharge interventions	
Discharge antithrombotics	77.00 (64.89-85.15)
Anticoagulation for AF	14.29 (0.00-26.97)
LDL 100	41.89 (25.00-61.72)
Antihypertensive Medication	61.37 (45.46-75.00)
Antidiabetic Medication	67.03 (53.15-79.58)
Smoking cessation	70.87 (50.55-83.33)
RSM rate	
30-day	5.41 (4.91-6.17)
1-year	13.55 (12.77-14.48)

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

Correlations of performance measures

The correlations between two individual hospital performance measures varied widely (Table 4). After bonferroni correction (P< 0.001), we found moderate correlation (Spearman correlation coefficients ≥0.40; P <0.001 for all) for all pairwise comparisons between antithrombotic at discharge and lipid-lowering drugs for LDL ≥100 mg/dl, antihypertensive medication, and antidiabetic medication; and between antidiabetic medication and antihypertensive medication and smoking cessation at discharge. Other hospital performance measures had a modest correlation or no correlation with each other (Spearman correlation coefficient <0.40 for all).

Association of performance measures with hospital-level RSM rates

The median 30-day and 1-year RSM rate (IQR) was 5.41% (4.91%–6.17%) and 13.55% (12.77%–14.48%), respectively (Table 3). The ICC of 30-day RSM rate was 0.065, and the ICC of 1-year RSM rate was 0.041.

Several performance measures showed a statistically significant, but modest, correlation with 1-year RSM rates, including antithrombotics at discharge (Spearman correlation coefficients= 0.32), antihypertensive medication (Spearman correlation coefficients= 0.30) and antidiabetic medication (Spearman correlation coefficients= 0.31) (P< 0.05 for all) (Table 4). No correlations were observed between all performance measures and 30-day RSM rates. These performance measures individually explained between 0.04% and 5.02% of hospital-level variation in 30-day RSM rates, and between 0.08% and 10.05% of hospital-level variation in 1-year RSM rates (Table 5).

The hospital-level composite score had a modest correlation with 1-year RSM rates (Spearman correlation coefficients= 0.32), however, no correlation was observed between the composite score and the 30-day RSM rate (Spearman correlation coefficients= 0.16). The composite score explained

2.53% and 10.18% of the hospital-level variation in 30-day and 1-year RSM rates, respectively (Table 5).

Table 4. Correlation coefficients for performance measures and hospital RSM rate (30-day and 1-year)

	Acute interventions			Discharge interventions						
	IV rt-PA < 2 Hour	Early antithrombotics	DVT prophylaxis	Antithrombotics	Anticoagulation for AF	Lipid-lowering drug for LDL ≥100 mg/dl	Antihypertensive Medication	Antidiabetic Medication	Smoking cessation	Composite score
Acute interventions										
IV rt-PA < 2 Hour	1.00									
Early antithrombotics	0.01	1.00								
DVT prophylaxis	0.08	0.23	1.00							
Discharge interventions										
Antithrombotics	0.01	0.34*	0.03	1.00						
Anticoagulation for AF	-0.01	0.04	0.19	0.16	1.00					
LDL 100	0.08	0.13	0.07	0.44*	0.26*	1.00				
Antihypertensive Medication	-0.02	0.08	-0.09	0.59*	0.12	0.27*	1.00			
Antidiabetic Medication	0.04	0.10	0.07	0.66*	0.17	0.31*	0.64*	1.00		

Smoking cessation	-0.01	0.34*	0.01	0.34*	0.25*	0.13	0.21	0.26*	1.00	
Composite score	0.05	0.48*	0.24	0.79*	0.32*	0.69*	0.60*	0.62*	0.47*	1.00
Risk-standardized 30-day mortality rate	-0.16	-0.02	-0.06	-0.16	0.04	-0.09	-0.17	-0.22	-0.04	-0.16
Risk-standardized 1-year mortality rate	-0.12	-0.03	-0.11	-0.32*	-0.07	-0.22	-0.30*	-0.31*	-0.02	-0.32*

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

*P<0.001.

Table 5. Variance in 30-day and 1-year RSM rates explained by each performance measure and composite measure

	30-day RSM rate	1-year RSM rate
Measures	% variance explained	% variance explained
Acute interventions		
IV rt-PA < 2 Hour	2.43%	1.32%
Early antithrombotics	0.04%	0.08%
DVT prophylaxis	0.38%	1.14%
Discharge interventions		
Discharge antithrombotics	2.59%	10.05%
Anticoagulation for AF	0.14%	0.45%
LDL 100	0.76%	4.67%
Antihypertensive Medication	2.99%	9.24%
Antidiabetic Medication	5.02%	9.49%
Smoking cessation	0.18%	0.06%
Composite score	2.53%	10.18%

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

DISCUSSION

The present study found that ischemic stroke care was suboptimal in China and there were various correlations among hospital performance measures. The hospital-level composite score had a modest correlation with 1-year RSM rate, however, no correlation was observed between the composite score and 30-day RSM rate. This finding suggested hospital performance measures cannot reliably infer short- and long- term mortality rates after acute ischemic stroke. Our results underscored that the current performance measures of stroke care provided complementary, but not redundant, information with the measures of 30-day and 1-year mortality.

When compared our data with the GWTG-Stroke in America, we found that ischemic stroke care was suboptimal in China. The GWTG-Stroke program was developed by the AHA/ASA as a national stroke registry and performance improvement program with the primary goal of improving the quality of care and outcomes for stroke and TIA in America.[7 14] The comparison showed that many hospital performance measures in China were far down from the GWTG-Stroke,[14 23] including the composite score (63.3% in 2007 CNSR versus 94.0% in 2007 GWTG-Stroke), IV rt-PA < 2 Hour (14.1% in 2007 CNSR versus 72.8% in 2007 GWTG-Stroke), early antithrombotics (80.3% in 2007 CNSR versus 97.0% in 2007 GWTG-Stroke), DVT Prophylaxis (59.6% in 2007 CNSR versus 89.5% in 2007 GWTG-Stroke), discharge antithrombotics (71.0% in 2012 CNSR versus 98.9% in 2007 GWTG-Stroke), anticoagulation for atrial fibrillation (19.7% in 2007 CNSR versus 98.4% in 2007 GWTG-Stroke), lipid-lowering drug for low-density lipoprotein ⩾100 mg/dL (42.6% in 2012 CNSR versus 88.3% in 2007 GWTG-Stroke), and smoking cessation (63.3% in 2007 CNSR versus 93.6% in 2007 GWTG-Stroke). Financial burden, lacking of stroke center certification and stroke education might become the main reasons.

The relationship between performance measures and stroke outcomes still exists uncertainty. Some studies have indicated the use of performance measures was associated with lower short-term mortality or better functional outcomes.[24-26] However, the link between stroke performance measures and outcome was not straightforward in certain other studies.[27-30] There were several probable reasons for the modest correlation between hospital-level performance measures and risk-standardised mortality in the present study. First, although clinical trials have shown a significant relationship between process interventions and outcomes,[31 32] the evidence-based performance measures were not mainly designed to be a substitute for overall short- and long-term hospital mortality. Second, there was relative little variation across hospitals in some performance measures, such as early antithrombotics after admission, which limited the ability to discriminate between hospitals based on their performance on this measure. Additionally, some performance measures, such as intravenous thrombolysis, may had a greater effect regarding stroke-related disability than that in stroke-related mortality.[33] Finally, hospital mortality rates, even risk-standardised ones, were likely affected by many factors independent of the performance measures of stroke care quality. These included severity of stroke, patients' or their family's preference, economic level and clinical strategies that may contribute to a hospital's performance outcomes.[34]

The present study also demonstrated a significant correlation between certain evidence-based performance measures for acute ischemic stroke care, indicating the hospitals that perform well in one performance measure were likely to perform well in the others. However, other performance measures were less strongly correlated with each other. This finding implies different performance measures reflect separate components of quality in acute ischemic stroke care. Our work indicated

that hospital performance rankings were likely to be substantially affected by the performance measures under selection. A broad range of performance measures appears necessary to comprehensively reflect hospital care practices.

Our study had several strengths. First, to date, the CNSR was the largest stroke database in China. Hospitals participating in the CNSR encompassed different regions and had good representativeness. Second, we used newer RSM methods based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.[15] Third, baseline characteristics of patients, such as age, gender, vascular risk factors, comorbid conditions, and stroke severity (NIHSS) were adjusted in calculating the RSM in accordance with the American Heart Association/American Stroke Association (AHA/ASA).[15 34] Additionally, besides short-term RSM, our study also analysed long-term RSM.

However, our study also had some limitations. Firstly, our study was observational and non-randomised. The association between care processes and stroke outcomes did not necessarily prove causality and may be confounded by previously discussed factors. Secondly, our outcome was mortality; other outcomes, such as stroke recurrence and functional outcomes, were also vital to patients and should be assessed in future studies.[30] Thirdly, the hospital performance measures, stroke outcomes, and the link between them might vary over time (such as prolonged time frame to perform thrombolysis). Future research need to determine the stability of the process-outcome relationship as quality improvement efforts drive broader care adoption. Forthly, our data was collected between 2007 and 2008, therefore the interpretation of our data might be limited. Future research was needed to comfirm our results. Finally, there were several differences between stroke

healthcare delivery systems in China and in other countries. The results reported herein came from the Chinese healthcare system and therefore may not necessarily be generalisable to other countries.

CONCLUSIONS

The quality of process care for ischemic stroke was suboptimal in China, and there were various correlations in hospital performance among the individual metrics. Although the evidence-based performance measures were important in pursuing improved acute ischemic stroke outcomes, the relationship between performance measures and hospital long-term risk-adjusted mortality rates was modest. Much broader measures were needed to be used as a means of assessing and helping improve the quality of hospital-level stroke care.

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Contributorship Statement

XMZ and ZXL analyzed the data and wrote the manuscript. XLB, LPL, CXW, HL, JB, QY and DW analyzed and interpretated the data. ZXL, CJW, YJ, XMY and XMZ performed research. YJW, YLW, ZXL, YX and XQZ conceived, designed and supervised the study.

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Competing interests

None.

Ethics approval

Approval was obtained from the Central Institutional Review Board at Beijing Tiantan Hospital.

Provenance and peer review

Not commissioned; externally peer reviewed.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	✓ **Page 3** (*a*) Indicate the study's design with a commonly used term in the title or the abstract
		✓ **Page 3** (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	✓ **Page 5** Explain the scientific background and rationale for the investigation being reported
Objectives	3	✓ **Page 5** State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	✓ **Page 5** Present key elements of study design early in the paper
Setting	5	✓ **Page 6** Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	✓ **Page 5** (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	✓ **Page 7-10** Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	✓ **Page 7-10** For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	✓ **Page 21** Describe any efforts to address potential sources of bias
Study size	10	✓ **Page 10** Explain how the study size was arrived at
Quantitative variables	11	✓ **Page 11** Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	✓ **Page 11** (*a*) Describe all statistical methods, including those used to control for confounding
		✓ **Page 11** (*b*) Describe any methods used to examine subgroups and interactions
		✓ **Page 11** (*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	✓ **Page 11** (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		✓ **Page 11** (b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	✓ **Page 11** (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		✓ **Page 11** (b) Indicate number of participants with missing data for each variable of interest
		✓ **Page 11** (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	✓ **Page 16** Report numbers of outcome events or summary measures over time
Main results	16	✓ **Page 17-19** (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which

		confounders were adjusted for and why they were included
		✓ **Page 12-15** (*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	✓ **Page 16-19** Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	✓ **Page 20** Summarise key results with reference to study objectives
Limitations	19	✓ **Page 21** Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	✓ **Page 20-21** Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	✓ **Page 21-22** Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	✓ **Page 23** Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

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Secondary Subject Heading:	Evidence based practice
Keywords:	Hospital performance, Ischemic stroke, Quality and outcomes, Mortality

Title pages

Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

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Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

ABSTRACT

Objectives: Evidence-based performance measures were increasingly used to evaluate the hospital quality of stroke care, but their impact on stroke outcomes has not been verified. We aimed to evaluate the correlations between hospital performance measures and outcomes among acute ischemic stroke patients in Chinese population.

Methods: Data was derived from a prospective cohort, which included 120 hospitals participating in the China National Stroke Registry between September 2007 and August 2008. Adherence to 9 evidence-based performance measures was examined, and the composite score of hospital performance measures was calculated. Primary stroke outcomes were hospital-level, 30-day and 1-year risk-standardized mortality (RSM). Associations of individual performance measures and composite score with stroke outcomes were assessed by using Spearman correlation coefficients.

Results: One hundred and twenty hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis. Among 12,027 patients, 61.59% were men, and the median age was 67 years. The overall composite score of performance measures was 63.3%. The correlation coefficients between individual performance measures ranged widely from 0.01 to 0.66. No association was observed between the composite score and 30-day RSM. The composite score was modestly associated with 1-year RSM (Spearman correlation coefficients, 0.34; $P<0.05$). The composite score explained only 2.53% and 10.18% of hospital-level variation in 30-day and 1-year RSMs for acute stroke patients.

Conclusions: The adherence to evidence-based performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance measures. The hospital performance measures had no correlations with 30-day RSM rate and modest correlations with 1-year RSM rate.

Article summary

Strengths and limitations of this study:

1. As the largest stroke database in China, hospitals participating in the China National Stroke Registry encompassed different regions and had good representativeness.
2. We used the newer risk-standardized mortality method based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.
3. Our study was observational and non-randomised. The association between hospital performance measures and stroke outcomes did not necessarily prove causality.

INTRODUCTION

Stroke remains to be the leading cause of mortality in China and was responsible for around 1.9 million deaths in 2013.[1] Although evidence-based guidelines for stroke and transient ischemic attack (TIA) have been developed and updated over time,[2-4] there were variations and deficiencies in how these guidelines were applied.[5-7] To reduce the national stroke burden, several national organizations have developed a set of evidence-based hospital performance measures to quantify and promote the quality of stroke care.[7-9]

Evidence-based hospital performance measures evaluated the structure, process and outcome of stroke care, and provided a metric that could be tracked, reported and improved.[10] Evidence-based hospital performance measures were also increasingly used for certification of stroke centres,[11] public reporting[12] and remuneration for performance.[13] Although there has been substantial improvement in stroke care quality in China, gaps still exist in adherence to the evidence-based hospital performance measures. In addition, although measuring outcomes after stroke has important policy implications,[14] there has been limited evidence demonstrating the association between adherence to performance measures and better patient outcomes.[15]

The China National Stroke Registry (CNSR) was a national hospital-based, prospective stroke registry, which encompassed different regions and had good representativeness.[16] CNSR thoroughly investigated all indicators related to the quality of stroke care, including evidence-based acute performance measures and performance measures at discharge. Thus, it could reflect the real situation of stroke care in China. Using data from the CNSR, we sought to determine whether evidence-based hospital performance measures were associated with short- and long-term outcomes in acute ischemic stroke patients in China. Specifically, we (1) reported the hospital variations in adherence to evidence-based performance measures, (2) assessed the correlations between each

individual performance measures, and (3) quantified the associations between the performance measures and hospital-level, risk-standardised, 30-day and 1-year mortalities among acute ischemic stroke patients in China.

METHODS

CNSR overview

The CNSR was the first nationwide, hospital-based, prospective stroke registry of quality assessment in China, which conducted between September 2007 and August 2008. It was sponsored by the Ministry of Health of the People's Republic of China to establish a national stroke database to evaluate the stroke care quality and outcomes. The study design of CNSR has been described previously.[16] Briefly, the criteria used for hospital selection included: (1) having at least one stroke neurologist, (2) at least two sites were included from each of the 31 provinces and municipalities in mainland China, (3) commitment to participate voluntarily and (4) ability to conduct research.[16 17] The CNSR recruited consecutive patients older than 18 years and diagnosed with ischemic stroke, TIA, intracerebral haemorrhage, or subarachnoid haemorrhage within 14 days of the index event. We collected patients' demographics, adherence to performance measures during hospitalization, and status at discharge, 90-day, 6-month and 1-year follow-up after symptom onset. The study was approved by the Central Institutional Review Board of Beijing Tiantan Hospital. Written informed consent was acquired from the patient or the legally authorised representative.

Data collection

Hospitals' characteristics were surveyed. According to annual report on health statistics of China,[18] hospitals were divided into three regions: eastern, central and western. Academic status was defined as being affiliated with a specific university or not. Hospital bed size was the number of total

inpatient beds per site. Annual stroke discharge was the number of discharged patients diagnosed with stroke per year of each participating hospital.

Trained research coordinators at each hospital reviewed medical records daily to identify, obtain informed consent, and enrol consecutive patients in accordance with the procedures indicated in a standard data collection manual. The key variables in the CNSR were assessed, including: (1) demographic characteristics and medical history; (2) pre-stroke modified Rankin scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) at admission, vascular risk factors, and clinical care during hospitalization; and (3) 30-day and 1-year all-cause mortalities after stroke. Patients or their authorised caregivers were contacted via telephone by trained research personnel with standardised scripts for follow-up at 90 days, 6 months and 1 year after stroke symptom onset.[16] Specific death events and dates were recorded in detail, and 30-day and 1-year all-cause mortalities after stroke were confirmed.

Performance Measures

We evaluated nine hospital performance measures, including seven "core" measures for acute ischemic stroke as recommended by the American Heart Association/American Stroke Association (AHA/ASA) Get With The Guidelines-Stroke (GWTG-Stroke)[7] and two additional evidence-based secondary prevention metrics.[4] These seven core performance measures included (1) intravenous tissue-type plasminogen activator (tPA) in patients who arrived within 2 hours after symptom onset and treated within 3 hours (IV rt-PA < 2 hour), (2) antithrombotic medication within 48 hours of admission (early antithrombotics), (3) deep vein thrombosis (DVT) prophylaxis within 48 hours of admission for nonambulatory patients (DVT prophylaxis), (4) antithrombotic medication, (5) anticoagulation for atrial fibrillation (AF) , (6) medications for lowering low-density lipoprotein

(LDL) ≥100 mg/dL, (7) smoking cessation. The two additional performance measures were antihypertensive medication for patients with hypertension and hypoglycemia medication for diabetes mellitus. Details of the performance measures were described in Table 1.

Adherence to hospital-level individual performance measures was calculated as the proportion of patients who received the indicated care among all the patients who were eligible for the indicated care. The overall hospital performance measures were measured as the composite score, which was calculated by the total number of interventions actually performed among all eligible patients at a hospital, divided by the total number of recommended interventions in all eligible patients.[19] Although the composite score was analysed as a continuous variable, hospitals were also divided, for descriptive purposes, into quartiles based on this continuous variable. To ensure the stability of the measure, hospitals with fewer than 20 patients in the denominator of any measures were excluded.

Table 1. Specifications of evidence-based performance measures

Performance measures of ischemic stroke care	Definition of performance measures for eligible patients*
Acute performance measures	
IV rt-PA < 2 hour	Intravenous recombinant tissue plasminogen activator (IV rtPA) in patients who arrived within 2 hours after initial symptom onset and treated within 3 hours
Early antithrombotics	Antithrombotic therapy prescribed within 48 hours of hospitalization, including antiplatelet or anticoagulant therapy
DVT prophylaxis	Patients at risk for deep vein thrombosis (DVT) (non-ambulatory) who received DVT prophylaxis by end of hospital day two, including pneumatic compression, warfarin sodium or heparin sodium
Performance measures at discharge	
Discharge antithrombotics	Antithrombotic therapy prescribed at discharge
Anticoagulation for atrial fibrillation	Anticoagulation prescribed at discharge for patients with atrial fibrillation or atrial flutter documented during hospitalization
LDL 100	Lipid lowering agent prescribed at discharge if low-density lipoprotein (LDL) ⩾100 mg/dL
Antihypertensive therapy for hypertension	Antihypertension medication prescribed at discharge for patients with a history of hypertension or hypertension documented during hospitalization

Hypoglycemic therapy for diabetes mellitus	Hypoglycemic medication prescribed at discharge for patients with a history of diabetes mellitus or diabetes mellitus documented during hospitalization
Smoking cessation	Smoking cessation intervention (counseling or medication) prior to discharge for current or recent smokers

* Eligible patients were those without any medical contraindications (e.g., treatment intolerance, excessive risk of adverse reaction, patient/family refusal, or terminal illness/comfort care only) and documented as reasons for nontreatment for each of the applicable measures. We also excluded patients who were discharged to hospice, or another short-term general hospital, or against medical advice before the end of hospital day two. For acute performance measures except for rt-PA measure, we excluded patients who died before the end of hospital day two. For the acute rt-PA measure, we excluded patients with missing or erroneous onset, arrival or treatment times, those who began IV t-PA at an outside hospital, or who initiated IV t-PA after 180 minutes from onset. For performance measures at discharge, we excluded patients who died during hospitalization. As for seven performance measures from the Get With The Guideline-Stroke (GWTG-Stroke), we employed the same criteria as the Get With The Guideline-Stroke (GWTG-Stroke).

Risk-standardized Mortality (RSM) Rates

RSM rates were calculated using a multivariate hierarchical regression model in accordance with the AHA/ASA recommendations for risk adjustment of ischemic stroke outcomes to compare hospital performance.[15] The first level of the hierarchical model included patient characteristics. These patient's variables were divided into three categories: (1) demographics and clinical features: age, gender, health insurance type (urban basic medical insurance schemes for urban and governmental employees and urban residents, new rural cooperative medical schemes for rural residents, commercial insurance, and self-payment), transport to hospital by emergency medical service, and NIHSS score at admission; (2) vascular risk factors: hypertension, diabetes mellitus, dyslipidaemia, AF, coronary artery disease, previous myocardial infarction, congestive heart failure, valvular heart disease, history of stroke/TIA, peripheral vascular disease, current smoking, and excessive alcohol consumption; (3) other pre-existing comorbid conditions: chronic obstructive pulmonary disease, hepatic cirrhosis, peptic ulcer, previous gastrointestinal bleeding, Alzheimer's disease/dementia, cancer, DVT/pulmonary embolus, renal dialysis, pre-stroke dependence (mRS ≥3), and blood glucose at admission. The second level included hospital-specific random intercepts that allow for different baseline mortalities between hospitals. The hospital RSM rates were obtained as the ratio of "predicted" to expected mortality, multiplied by the unadjusted mortalities for the total population.[20 21] The expected outcome for each hospital was the number of deaths expected at the hospital if the hospital's patients were treated at a "reference" hospital. The predicted hospital-level outcome was the number of expected mortalities at the "specific" hospital and not at a reference hospital.

Statistical analyses

Numbers (percentages) were used to describe categorical variables, and median values with interquartile ranges (IQRs) were reported for continuous variables. The correlations of individual performance measures, as well as performance measures and stroke outcomes, were evaluated using Spearman correlation coefficients. The bonferroni correction was performed in the multiple comparisons. The inter-class correlation (ICC) of 30-day and 1-year RSM rates were calculated. The relevant correlation coefficients and the percentage of the hospital-specific variations in RSM rates were explained using the squares of the correlation coefficients as indicators of the strength of the associations.[22]

All tests were two-tailed, and statistical significance was determined at the α level of 0.05 in univariate and multivariate analyses. Statistical analysis was performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

Patient and Public Involvement

Stroke remains to be the leading cause of mortality in China,[1] which seriously affects the quality of patients' lives and brings huge burden to them. A number of national guidelines were bought out to improve the quality of stroke care and to reduce stroke mortality.[7-9] By exploring the association of hospital performance measures to improve stroke care with all-cause mortality, we hope to figure out whether improving stroke care quality could affect patients' mortality and improve patients' prognosis.

The CNSR recruited consecutive patients older than 18 years and diagnosed with ischemic stroke within 14 days of stroke onset from 132 hospitals throughout China between September 2007 and August 2008. The results of our study would be disseminated through the follow-ups of patients in CNSR, and through one of our projects of the national education of cerebrovascular diseases.

RESULTS

Study hospitals and patient baseline characteristics

Among 14,526 eligible patients diagnosed with acute ischemic stroke from 132 hospitals throughout China, complete 1-year follow-up information was available for 12,173 patients (83.8%). We excluded 12 hospitals with fewer than 20 patients in the denominator of any measures. Finally, 120 hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis. Hospital and patient baseline characteristics were described in Table 2. Among 120 hospitals, 62 (51.67%) hospitals were teaching hospitals and 70 (58.33%) were from eastern regions. The median hospital bed size was 1200 (IQR, 700–1861) and annual stroke volume was 430 (IQR, 310–601). Among 12,027 patients, 7,407 (61.59%) were men, and the median age was 67 (IQR, 57–75) years. Common vascular risk factors included hypertension, previous stroke/ TIA, smoking history, and diabetes. The median NIHSS score was 4 (IQR, 2–9).

Variability in performance measures

The overall composite score was 63.3% among the 120 hospitals. However, the composite score for each hospital varied considerably among the CNSR (Table 3). The hospitals in the highest quartile (quartile 4) had a median (IQR) composite score of 85.1% (82.2%–89.9%), compared with 50.9% (44.2%–58.1%) for those in the lowest quartile (quartile 1).

In table 3, we showed hospital rates (median and IQR) for each process measure as well as 30-day and1-year RSM rates. For acute interventions, the early antithrombotics showed the lowest degree of variance, although the difference between the first and third quartiles remained significant. In contrast, there were twofold to threefold differences in the use of IV rt-PA < 2 hour, DVT prophylaxis, anticoagulant for AF and lipid-lowering medication for LDL ≥100 mg/dl.

Table 2. Baseline characteristics of patients with acute ischemic stroke in the China National Stroke Registry

	Level	N (%)
Patient characteristics		
Total		12027
Demographics		
Age, yr	Median (IQR)	67 (57-75)
Gender	Male	7407(61.59)
	Female	4620(38.41)
Insurance scheme	UBMIS	7311(60.79)
	NRCMS	2027(16.85)
	Commercial	397(3.30)
	Self-payment	2292(19.06)
Transport to hospital by EMS	Yes	1901(15.81)
NIHSS at admission	Median (IQR)	4 (2-9)
Vascular risk factors		
Previous stroke/TIA	Yes	4088(33.99)
Diabetes	Yes	2593(21.56)
Hypertension	Yes	7672(63.79)
Dyslipidemia	Yes	1344(11.17)
CHD/previous MI	Yes	1748(14.53)
Atrial fibrillation	Yes	892(7.42)
PVD	Yes	76(0.63)
Ever smoking	Yes	4779(39.74)

Heavy drinking	Yes	1873(15.57)
Pre-existing comorbid conditions		
Congestive heart failure	Yes	250(2.08)
Valvular heart disease	Yes	288(2.42)
Chronic obstructive pulmonary	Yes	138(1.15)
Hepatic cirrhosis	Yes	41(0.34)
Peptic ulcer disease	Yes	336(2.81)
Previous gastrointestinal bleeding	Yes	184(1.54)
Dementia/Alzheimer's disease	Yes	156(1.30)
Cancer	Yes	215(1.80)
Deep venous thrombosis/Pulmonary	Yes	77(0.64)
Renal dialysis	Yes	9(0.08)
Pre-stroke dependence (mRS>2)	Yes	1120(9.31)
Glucose on admission	Yes	2328(19.72)
Hospital characteristics		
Total		120
Hospital size		
Beds	Median (IQR)	1200 (700, 1 861)
Hospital type		
Teaching	Yes	62(51.67)
Annual stroke discharges	Median (IQR)	430 (310,601)
Geographic region		
East	Yes	70 (58.33)
Middle	Yes	26 (21.67)

West	Yes	24 (20.0)

IQR, interquartile range; UBMIS, urban basic medical insurance scheme; NRCMS, new rural cooperative medical scheme; EMS, emergency medical service; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; CHD, coronary artery disease; MI, myocardial infarction; PVD, peripheral vascular disease; mRS, modified Rankin scale.

Table 3. Hospital performance measures and RSM rates

Measures	Median (IQR, %)
Composite score	65.65 (59.05-72.75)
Acute interventions	
IV rt-PA < 2 hour	0.00 (0.00-25.00)
Early antithrombotics	80.68 (73.21-88.24)
DVT prophylaxis	59.22 (33.33-70.00)
Discharge interventions	
Discharge antithrombotics	77.00 (64.89-85.15)
Anticoagulation for AF	14.29 (0.00-26.97)
LDL 100	41.89 (25.00-61.72)
Antihypertensive medication	61.37 (45.46-75.00)
Antidiabetic medication	67.03 (53.15-79.58)
Smoking cessation	70.87 (50.55-83.33)
RSM rate	
30-day	5.41 (4.91-6.17)
1-year	13.55 (12.77-14.48)

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

Correlations of performance measures

The correlations between two individual hospital performance measures varied widely (Table 4). After bonferroni correction (P< 0.001), we found moderate correlations (Spearman correlation coefficients ≥0.40; P <0.001 for all) for all pairwise comparisons between antithrombotic at discharge and lipid-lowering drugs for LDL ≥100 mg/dl, antihypertensive medication, and antidiabetic medication; and between antidiabetic medication and antihypertensive medication and smoking cessation at discharge. Other hospital performance measures had modest correlations or no correlations with each other (Spearman correlation coefficient <0.40 for all).

Association of performance measures with hospital-level RSM rates

The median 30-day and 1-year RSM rates (IQR) were 5.41% (4.91%–6.17%) and 13.55% (12.77%–14.48%), respectively (Table 3). The ICC of 30-day RSM rate was 0.065, and the ICC of 1-year RSM rate was 0.041.

All performance measures showed no correlations with 30-day RSM rate. Several performance measures showed statistically significant, but modest, correlations with 1-year RSM rate, including antithrombotics at discharge (Spearman correlation coefficients= 0.32), antihypertensive medication (Spearman correlation coefficients= 0.30) and antidiabetic medication (Spearman correlation coefficients= 0.31) (P< 0.05 for all) (Table 4). These performance measures individually explained between 0.04% and 5.02% of hospital-level variation in 30-day RSM rate, and between 0.08% and 10.05% of hospital-level variation in 1-year RSM rate (Table 5).

No correlation was observed between the hospital-level composite score and 30-day RSM rate (Spearman correlation coefficients= 0.16). Modest correlation was observed between the hospital-level composite score and 1-year RSM rate (Spearman correlation coefficients= 0.32). The

composite score explained 2.53% and 10.18% of the hospital-level variation in 30-day and 1-year RSM rates, respectively (Table 5).

Table 4. Correlation coefficients for performance measures and hospital RSM rates (30-day and 1-year)

	Acute interventions			Discharge interventions						
	IV rt-PA < 2 hour	Early antithrombotics	DVT prophylaxis	Antithrombotics	Anticoagulation for AF	Lipid-lowering drug for LDL ≥100 mg/dl	Antihypertensive medication	Antidiabetic medication	Smoking cessation	Composite score
Acute interventions										
IV rt-PA < 2 hour	1.00									
Early antithrombotics	0.01	1.00								
DVT prophylaxis	0.08	0.23	1.00							
Discharge interventions										
Antithrombotics	0.01	0.34*	0.03	1.00						
Anticoagulation for AF	-0.01	0.04	0.19	0.16	1.00					
LDL 100	0.08	0.13	0.07	0.44*	0.26*	1.00				
Antihypertensive medication	-0.02	0.08	-0.09	0.59*	0.12	0.27*	1.00			
Antidiabetic medication	0.04	0.10	0.07	0.66*	0.17	0.31*	0.64*	1.00		

Smoking cessation	-0.01	0.34*	0.01	0.34*	0.25*	0.13	0.21	0.26*	1.00	
Composite score	0.05	0.48*	0.24	0.79*	0.32*	0.69*	0.60*	0.62*	0.47*	1.00
Risk-standardized 30-day mortality rate	-0.16	-0.02	-0.06	-0.16	0.04	-0.09	-0.17	-0.22	-0.04	-0.16
Risk-standardized 1-year mortality rate	-0.12	-0.03	-0.11	-0.32*	-0.07	-0.22	-0.30*	-0.31*	-0.02	-0.32*

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

*P<0.001.

Table 5. Variance in 30-day and 1-year RSM rates explained by each performance measure and the composite measure

	30-day RSM rate	1-year RSM rate
Measures	% variance explained	% variance explained
Acute interventions		
IV rt-PA < 2 hour	2.43%	1.32%
Early antithrombotics	0.04%	0.08%
DVT prophylaxis	0.38%	1.14%
Discharge interventions		
Discharge antithrombotics	2.59%	10.05%
Anticoagulation for AF	0.14%	0.45%
LDL 100	0.76%	4.67%
Antihypertensive medication	2.99%	9.24%
Antidiabetic medication	5.02%	9.49%
Smoking cessation	0.18%	0.06%
Composite score	2.53%	10.18%

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

DISCUSSION

The present study found that ischemic stroke care was suboptimal in China and there were various correlations among hospital performance measures. The hospital-level composite score had no correlation with 30-day RSM rate and a modest correlation with 1-year RSM rate. This finding suggested hospital performance measures cannot reliably infer short- and long- term mortalities after acute ischemic stroke. Our results underscored that the current performance measures of stroke care provided complementary, but not redundant, information with the measures of 30-day and 1-year mortalities.

When compared our data with the GWTG-Stroke in America, we found that ischemic stroke care was suboptimal in China. The GWTG-Stroke program was developed by the AHA/ASA as a national stroke registry and performance improvement program with the primary goal of improving the quality of care and outcomes of stroke and TIA in America.[7 14] The comparison showed that many hospital performance measures in China were far down from the GWTG-Stroke,[14 23] including the composite score (63.3% in 2007 CNSR versus 94.0% in 2007 GWTG-Stroke), IV rt-PA < 2 hour (14.1% in 2007 CNSR versus 72.8% in 2007 GWTG-Stroke), early antithrombotics (80.3% in 2007 CNSR versus 97.0% in 2007 GWTG-Stroke), DVT prophylaxis (59.6% in 2007 CNSR versus 89.5% in 2007 GWTG-Stroke), discharge antithrombotics (71.0% in 2012 CNSR versus 98.9% in 2007 GWTG-Stroke), anticoagulation for AF (19.7% in 2007 CNSR versus 98.4% in 2007 GWTG-Stroke), lipid-lowering drug for LDL ≥100 mg/dL (42.6% in 2012 CNSR versus 88.3% in 2007 GWTG-Stroke), and smoking cessation (63.3% in 2007 CNSR versus 93.6% in 2007 GWTG-Stroke). Financial burden, lacking of stroke center certification and stroke education might be the main reasons.

The relationships between performance measures and stroke outcomes remained uncertainty. Some studies have indicated that the use of performance measures was associated with lower short-term mortality and better functional outcomes.[24-26] However, the links between these stroke performance measures and outcomes were not clear in other studies.[27-30] There were several probable reasons for the modest correlations between hospital-level performance measures and RSMs in the present study. Firstly, although clinical trials have shown significant relationships between performance measures and outcomes,[31 32] the evidence-based performance measures were not mainly designed for overall short- and long-term hospital mortalities. Secondly, there was relative little variation across hospitals in some performance measures, such as early antithrombotics after admission, which limited the ability to discriminate between hospitals based on their performance on these measures. Additionally, some performance measures, such as IV, may have a greater effect regarding stroke-related disability than mortality.[33] Finally, hospital mortalities, even risk-standardised ones, were likely affected by many factors independent of the performance measures of stroke care quality, such as severity of stroke, patients' or their family's preference, economic level and clinical strategies that may contribute to a hospital's performance outcomes.[34]

The present study also demonstrated significant correlations between certain evidence-based performance measures for acute ischemic stroke care, indicating that hospitals performing well in one performance measure were more likely to perform well in other measures. However, other performance measures were less strongly correlated with each other. This finding implies different performance measures reflect separate components of quality in acute ischemic stroke care. Our work indicated that hospital performance rankings were likely to be substantially affected by the

performance measures under selection. A broader range of performance measures may be needed to comprehensively reflect the quality of stroke care.

Our study had several strengths. First, to date, the CNSR was the largest stroke database in China. Hospitals participating in the CNSR encompassed different regions and had good representativeness. Second, we used the newer RSM method based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.[15] Third, baseline characteristics of patients, such as age, gender, vascular risk factors, comorbid conditions, and stroke severity (NIHSS) were adjusted in calculating the RSMs in accordance with the American Heart Association/American Stroke Association (AHA/ASA).[15 34] Additionally, besides short-term RSM, our study also analysed long-term RSM.

However, our study also had some limitations. Firstly, our study was observational and non-randomised. The association between stroke care performance and stroke outcomes did not necessarily prove causality and may be confounded by previously discussed factors. Secondly, our outcome was mortality; other outcomes such as stroke recurrence and functional outcomes were also vital to patients, which should be assessed in future studies.[30] Thirdly, the hospital performance measures, stroke outcomes, and the relationships between them might vary over time (such as extended time window for thrombolysis). Future research need to determine the stability of the process-outcome relationship as quality improvement efforts would drive broader care adoption. Fourthly, our data were collected between 2007 and 2008, therefore the interpretation of our data might be limited. Future research is needed to confirm our results. Finally, there were several differences in stroke healthcare delivery systems between China and other countries. The results

reported herein came from the Chinese healthcare system and therefore may not necessarily be generalisable to other countries.

CONCLUSIONS

The adherence to evidence-based performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance measures. The hospital performance measures had no correlations with 30-day RSM rate and modest correlations with 1-year RSM rate. More measures are needed to assess and improve the quality of hospital-level stroke care in China.

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Contributorship Statement

XMZ and ZXL analyzed the data and wrote the manuscript. XLB, LPL, CXW, HL, JB, QY and DW analyzed and interpretated the data. ZXL, CJW, YJ, XMY and XMZ performed research. YJW, YLW, ZXL, YX and XQZ conceived, designed and supervised the study.

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Competing interests

None.

Ethics approval

Approval was obtained from the Central Institutional Review Board at Beijing Tiantan Hospital.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	✓ **Page 3** (*a*) Indicate the study's design with a commonly used term in the title or the abstract
		✓ **Page 3** (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	✓ **Page 5** Explain the scientific background and rationale for the investigation being reported
Objectives	3	✓ **Page 5** State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	✓ **Page 5** Present key elements of study design early in the paper
Setting	5	✓ **Page 6** Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	✓ **Page 5** (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	✓ **Page 7-10** Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	✓ **Page 7-10** For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	✓ **Page 21** Describe any efforts to address potential sources of bias
Study size	10	✓ **Page 10** Explain how the study size was arrived at
Quantitative variables	11	✓ **Page 11** Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	✓ **Page 11** (*a*) Describe all statistical methods, including those used to control for confounding
		✓ **Page 11** (*b*) Describe any methods used to examine subgroups and interactions
		✓ **Page 11** (*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	✓ **Page 11** (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		✓ **Page 11** (b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	✓ **Page 11** (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		✓ **Page 11** (b) Indicate number of participants with missing data for each variable of interest
		✓ **Page 11** (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	✓ **Page 16** Report numbers of outcome events or summary measures over time
Main results	16	✓ **Page 17-19** (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which

		confounders were adjusted for and why they were included
		✓ **Page 12-15** (*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	✓ **Page 16-19** Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	✓ **Page 20** Summarise key results with reference to study objectives
Limitations	19	✓ **Page 21** Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	✓ **Page 20-21** Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	✓ **Page 21-22** Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	✓ **Page 23** Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

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Title pages

Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

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Relationship between Hospital Performance Measures and Outcomes in Patients with Acute Ischemic Stroke: a Prospective Cohort Study

ABSTRACT

Objectives: Evidence-based performance measures have been increasingly used to evaluate the hospital quality of stroke care, but their impact on stroke outcomes has not been verified. We aimed to evaluate the correlations between hospital performance measures and outcomes among acute ischemic stroke patients in Chinese population.

Methods: Data was derived from a prospective cohort, which included 120 hospitals participating in the China National Stroke Registry between September 2007 and August 2008. Adherence to 9 evidence-based performance measures was examined, and the composite score of hospital performance measures was calculated. Primary stroke outcomes were hospital-level, 30-day and 1-year risk-standardized mortality (RSM). Associations of individual performance measures and composite score with stroke outcomes were assessed by using Spearman correlation coefficients.

Results: One hundred and twenty hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis. Among 12,027 patients, 61.59% were men, and the median age was 67 years. The overall composite score of performance measures was 63.3%. The correlation coefficients between individual performance measures ranged widely from 0.01 to 0.66. No association was observed between the composite score and 30-day RSM. The composite score was modestly associated with 1-year RSM (Spearman correlation coefficients, 0.34; $P<0.05$). The composite score explained only 2.53% and 10.18% of hospital-level variation in 30-day and 1-year RSMs for acute stroke patients.

Conclusions: The adherence to evidence-based performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance measures. The hospital performance measures had no correlations with 30-day RSM rate and modest correlations with 1-year RSM rate.

Article summary

Strengths and limitations of this study:

1. As the largest stroke database in China, hospitals participating in the China National Stroke Registry encompassed different regions and had good representativeness.
2. We used the newer risk-standardized mortality method based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.
3. Our study was observational and non-randomised. The association between hospital performance measures and stroke outcomes did not necessarily prove causality.

INTRODUCTION

Stroke remains to be the leading cause of mortality in China, which was responsible for around 1.9 million deaths in 2013.[1] Although evidence-based guidelines for stroke and transient ischemic attack (TIA) have been developed and updated over time,[2-4] there were variations and deficiencies in how these guidelines were applied.[5-7] To reduce the national stroke burden, several national organizations have developed a set of evidence-based hospital performance measures to quantify and promote the quality of stroke care.[7-9]

Evidence-based hospital performance measures evaluated the structure, process and outcome of stroke care, and provided a metric that could be tracked, reported and improved.[10] Evidence-based hospital performance measures have also been increasingly used for certification of stroke centres,[11] public reporting[12] and remuneration for performance.[13] Although there has been substantial improvement in stroke care quality in China, gaps still exist in adherence to the evidence-based hospital performance measures. In addition, although measuring outcomes after stroke has important policy implications,[14] there has been limited evidence demonstrating the association between adherence to performance measures and better patient outcomes.[15]

The China National Stroke Registry (CNSR) was a national hospital-based, prospective stroke registry, which encompassed different regions and had good representativeness.[16] CNSR thoroughly investigated all indicators related to the quality of stroke care, including evidence-based acute performance measures and performance measures at discharge. Thus, it could reflect the real situation of stroke care in China. Using data from the CNSR, we sought to determine whether evidence-based hospital performance measures were associated with short- and long-term outcomes in acute ischemic stroke patients in China. Specifically, we (1) reported the hospital variations in adherence to evidence-based performance measures, (2) assessed the correlations between each

individual performance measures, and (3) quantified the associations between the performance measures and hospital-level, risk-standardised, 30-day and 1-year mortalities among acute ischemic stroke patients in China.

METHODS

CNSR overview

The CNSR was the first nationwide, hospital-based, prospective stroke registry of quality assessment in China, which conducted between September 2007 and August 2008. It was sponsored by the Ministry of Health of the People's Republic of China to establish a national stroke database to evaluate the stroke care quality and outcomes. The study design of CNSR has been described previously.[16] Briefly, the criteria used for hospital selection included: (1) having at least one stroke neurologist, (2) at least two sites were included from each of the 31 provinces and municipalities in mainland China, (3) commitment to participate voluntarily and (4) ability to conduct research.[16 17] The CNSR recruited consecutive patients older than 18 years and diagnosed with ischemic stroke, TIA, intracerebral haemorrhage, or subarachnoid haemorrhage within 14 days of the index event. We collected patients' demographics, adherence to performance measures during hospitalization, and status at discharge, 90-day, 6-month and 1-year follow-up after symptom onset. The study was approved by the Central Institutional Review Board of Beijing Tiantan Hospital. Written informed consent was acquired from the patient or the legally authorised representative.

Data collection

Hospitals' characteristics were surveyed. According to annual report on health statistics of China,[18] hospitals were divided into three regions: eastern, central and western. Academic status was defined as being affiliated with a specific university or not. Hospital bed size was the number of total

inpatient beds per site. Annual stroke discharge was the number of discharged patients diagnosed with stroke per year of each participating hospital.

Trained research coordinators at each hospital reviewed medical records daily to identify, obtain informed consent, and enrol consecutive patients in accordance with the procedures indicated in a standard data collection manual. The key variables in the CNSR were assessed, including: (1) demographic characteristics and medical history; (2) pre-stroke modified Rankin scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) at admission, vascular risk factors, and clinical care during hospitalization; and (3) 30-day and 1-year all-cause mortalities after stroke. Patients or their authorised caregivers were contacted via telephone by trained research personnel with standardised scripts for follow-up at 90 days, 6 months and 1 year after stroke symptom onset.[16] Specific death events and dates were recorded in detail, and 30-day and 1-year all-cause mortalities after stroke were confirmed.

Performance Measures

We evaluated nine hospital performance measures, including seven "core" measures for acute ischemic stroke as recommended by the American Heart Association/American Stroke Association (AHA/ASA) Get With The Guidelines-Stroke (GWTG-Stroke)[7] and two additional evidence-based secondary prevention metrics.[4] These seven core performance measures included (1) intravenous tissue-type plasminogen activator (tPA) in patients who arrived within 2 hours after symptom onset and treated within 3 hours (IV rt-PA < 2 hour), (2) antithrombotic medication within 48 hours of admission (early antithrombotics), (3) deep vein thrombosis (DVT) prophylaxis within 48 hours of admission for nonambulatory patients (DVT prophylaxis), (4) antithrombotic medication, (5) anticoagulation for atrial fibrillation (AF) , (6) medications for lowering low-density lipoprotein

(LDL) ≥100 mg/dL, (7) smoking cessation. The two additional performance measures were antihypertensive medication for patients with hypertension and hypoglycemia medication for diabetes mellitus. Details of the performance measures were described in Table 1.

Adherence to hospital-level individual performance measures was calculated as the proportion of patients who received the indicated care among all the patients who were eligible for the indicated care. The overall hospital performance measures were measured as the composite score, which was calculated by the total number of interventions actually performed among all eligible patients at a hospital, divided by the total number of recommended interventions in all eligible patients.[19] Although the composite score was analysed as a continuous variable, hospitals were also divided, for descriptive purposes, into quartiles based on this continuous variable. To ensure the stability of the measure, hospitals with fewer than 20 patients in the denominator of any measures were excluded.

Table 1. Specifications of evidence-based performance measures

Performance measures of ischemic stroke care	Definition of performance measures for eligible patients*
Acute performance measures	
IV rt-PA < 2 hour	Intravenous recombinant tissue plasminogen activator (IV rtPA) in patients who arrived within 2 hours after initial symptom onset and treated within 3 hours
Early antithrombotics	Antithrombotic therapy prescribed within 48 hours of hospitalization, including antiplatelet or anticoagulant therapy
DVT prophylaxis	Patients at risk for deep vein thrombosis (DVT) (non-ambulatory) who received DVT prophylaxis by end of hospital day two, including pneumatic compression, warfarin sodium or heparin sodium
Performance measures at discharge	
Discharge antithrombotics	Antithrombotic therapy prescribed at discharge
Anticoagulation for atrial fibrillation	Anticoagulation prescribed at discharge for patients with atrial fibrillation or atrial flutter documented during hospitalization
LDL 100	Lipid lowering agent prescribed at discharge if low-density lipoprotein (LDL) ⩾100 mg/dL
Antihypertensive therapy for hypertension	Antihypertension medication prescribed at discharge for patients with a history of hypertension or hypertension documented during hospitalization

Hypoglycemic therapy for diabetes mellitus	Hypoglycemic medication prescribed at discharge for patients with a history of diabetes mellitus or diabetes mellitus documented during hospitalization
Smoking cessation	Smoking cessation intervention (counseling or medication) prior to discharge for current or recent smokers

* Eligible patients were those without any medical contraindications (e.g., treatment intolerance, excessive risk of adverse reaction, patient/family refusal, or terminal illness/comfort care only) and documented as reasons for nontreatment for each of the applicable measures. We also excluded patients who were discharged to hospice, or another short-term general hospital, or against medical advice before the end of hospital day two. For acute performance measures except for rt-PA measure, we excluded patients who died before the end of hospital day two. For the acute rt-PA measure, we excluded patients with missing or erroneous onset, arrival or treatment times, those who began IV t-PA at an outside hospital, or who initiated IV t-PA after 180 minutes from onset. For performance measures at discharge, we excluded patients who died during hospitalization. As for seven performance measures from the Get With The Guideline-Stroke (GWTG-Stroke), we employed the same criteria as the Get With The Guideline-Stroke (GWTG-Stroke).

Risk-standardized Mortality (RSM) Rates

RSM rates were calculated using a multivariate hierarchical regression model in accordance with the AHA/ASA recommendations for risk adjustment of ischemic stroke outcomes to compare hospital performance.[15] The first level of the hierarchical model included patient characteristics. These patient's variables were divided into three categories: (1) demographics and clinical features: age, gender, health insurance type (urban basic medical insurance schemes for urban and governmental employees and urban residents, new rural cooperative medical schemes for rural residents, commercial insurance, and self-payment), transport to hospital by emergency medical service, and NIHSS score at admission; (2) vascular risk factors: hypertension, diabetes mellitus, dyslipidaemia, AF, coronary artery disease, previous myocardial infarction, congestive heart failure, valvular heart disease, history of stroke/TIA, peripheral vascular disease, current smoking, and excessive alcohol consumption; (3) other pre-existing comorbid conditions: chronic obstructive pulmonary disease, hepatic cirrhosis, peptic ulcer, previous gastrointestinal bleeding, Alzheimer's disease/dementia, cancer, DVT/pulmonary embolus, renal dialysis, pre-stroke dependence (mRS ≥3), and blood glucose at admission. The second level included hospital-specific random intercepts that allow for different baseline mortalities between hospitals. The hospital RSM rates were obtained as the ratio of "predicted" to expected mortality, multiplied by the unadjusted mortalities for the total population.[20 21] The expected outcome for each hospital was the number of deaths expected at the hospital if the hospital's patients were treated at a "reference" hospital. The predicted hospital-level outcome was the number of expected mortalities at the "specific" hospital and not at a reference hospital.

Statistical analyses

Numbers (percentages) were used to describe categorical variables, and median values with interquartile ranges (IQRs) were reported for continuous variables. The correlations of individual performance measures, as well as performance measures and stroke outcomes, were evaluated using Spearman correlation coefficients. The bonferroni correction was performed in the multiple comparisons. The inter-class correlation (ICC) of 30-day and 1-year RSM rates were calculated. The relevant correlation coefficients and the percentage of the hospital-specific variations in RSM rates were explained using the squares of the correlation coefficients as indicators of the strength of the associations.[22]

All tests were two-tailed, and statistical significance was determined at the α level of 0.05 in univariate and multivariate analyses. Statistical analysis was performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

Patient and Public Involvement

No patients were involved in the planning of this study. Patients were recruited via the doctors and investigators at local hospitals in China. Once the study results have been published in a peer-reviewed journal, a summary of the main study findings will be distributed in Chinese language via the local doctors and investigators to the patients.

RESULTS

Study hospitals and patient baseline characteristics

Among 14,526 eligible patients diagnosed with acute ischemic stroke from 132 hospitals throughout China, complete 1-year follow-up information was available for 12,173 patients (83.8%). We excluded 12 hospitals with fewer than 20 patients in the denominator of any measures. Finally, 120 hospitals that recruited 12,027 patients with ischemic stroke were included in our analysis.

Hospital and patient baseline characteristics were described in Table 2. Among 120 hospitals, 62 (51.67%) hospitals were teaching hospitals and 70 (58.33%) were from eastern regions. The median hospital bed size was 1200 (IQR, 700–1861) and annual stroke volume was 430 (IQR, 310–601). Among 12,027 patients, 7,407 (61.59%) were men, and the median age was 67 (IQR, 57–75) years. Common vascular risk factors included hypertension, previous stroke/ TIA, smoking history, and diabetes. The median NIHSS score was 4 (IQR, 2–9).

Variability in performance measures

The overall composite score was 63.3% among the 120 hospitals. However, the composite score for each hospital varied considerably among the CNSR (Table 3). The hospitals in the highest quartile (quartile 4) had a median (IQR) composite score of 85.1% (82.2%–89.9%), compared with 50.9% (44.2%–58.1%) for those in the lowest quartile (quartile 1).

In table 3, we showed hospital rates (median and IQR) for each process measure as well as 30-day and1-year RSM rates. For acute interventions, the early antithrombotics showed the lowest degree of variance, although the difference between the first and third quartiles remained significant. In contrast, there were twofold to threefold differences in the use of IV rt-PA < 2 hour, DVT prophylaxis, anticoagulant for AF and lipid-lowering medication for LDL ≥100 mg/dl.

Table 2. Baseline characteristics of patients with acute ischemic stroke in the China National Stroke Registry

	Level	N (%)
Patient characteristics		
Total		12027
Demographics		
Age, yr	Median (IQR)	67 (57-75)
Gender	Male	7407(61.59)
	Female	4620(38.41)
Insurance scheme	UBMIS	7311(60.79)
	NRCMS	2027(16.85)
	Commercial	397(3.30)
	Self-payment	2292(19.06)
Transport to hospital by EMS	Yes	1901(15.81)
NIHSS at admission	Median (IQR)	4 (2-9)
Vascular risk factors		
Previous stroke/TIA	Yes	4088(33.99)
Diabetes	Yes	2593(21.56)
Hypertension	Yes	7672(63.79)
Dyslipidemia	Yes	1344(11.17)
CHD/previous MI	Yes	1748(14.53)
Atrial fibrillation	Yes	892(7.42)
PVD	Yes	76(0.63)
Ever smoking	Yes	4779(39.74)

Heavy drinking	Yes	1873(15.57)
Pre-existing comorbid conditions		
Congestive heart failure	Yes	250(2.08)
Valvular heart disease	Yes	288(2.42)
Chronic obstructive pulmonary	Yes	138(1.15)
Hepatic cirrhosis	Yes	41(0.34)
Peptic ulcer disease	Yes	336(2.81)
Previous gastrointestinal bleeding	Yes	184(1.54)
Dementia/Alzheimer's disease	Yes	156(1.30)
Cancer	Yes	215(1.80)
Deep venous thrombosis/Pulmonary	Yes	77(0.64)
Renal dialysis	Yes	9(0.08)
Pre-stroke dependence (mRS>2)	Yes	1120(9.31)
Glucose on admission	Yes	2328(19.72)
Hospital characteristics		
Total		120
Hospital size		
Beds	Median (IQR)	1200 (700, 1 861)
Hospital type		
Teaching	Yes	62(51.67)
Annual stroke discharges	Median (IQR)	430 (310,601)
Geographic region		
East	Yes	70 (58.33)
Middle	Yes	26 (21.67)

West	Yes	24 (20.0)

IQR, interquartile range; UBMIS, urban basic medical insurance scheme; NRCMS, new rural cooperative medical scheme; EMS, emergency medical service; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; CHD, coronary artery disease; MI, myocardial infarction; PVD, peripheral vascular disease; mRS, modified Rankin scale.

Table 3. Hospital performance measures and RSM rates

Measures	Median (IQR, %)
Composite score	65.65 (59.05-72.75)
Acute interventions	
IV rt-PA < 2 hour	0.00 (0.00-25.00)
Early antithrombotics	80.68 (73.21-88.24)
DVT prophylaxis	59.22 (33.33-70.00)
Discharge interventions	
Discharge antithrombotics	77.00 (64.89-85.15)
Anticoagulation for AF	14.29 (0.00-26.97)
LDL 100	41.89 (25.00-61.72)
Antihypertensive medication	61.37 (45.46-75.00)
Antidiabetic medication	67.03 (53.15-79.58)
Smoking cessation	70.87 (50.55-83.33)
RSM rate	
30-day	5.41 (4.91-6.17)
1-year	13.55 (12.77-14.48)

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

Correlations of performance measures

The correlations between two individual hospital performance measures varied widely (Table 4). After bonferroni correction (P< 0.001), we found moderate correlations (Spearman correlation coefficients ≥0.40; P <0.001 for all) for all pairwise comparisons between antithrombotic at discharge and lipid-lowering drugs for LDL ≥100 mg/dl, antihypertensive medication, and antidiabetic medication; and between antidiabetic medication and antihypertensive medication and smoking cessation at discharge. Other hospital performance measures had modest correlations or no correlations with each other (Spearman correlation coefficient <0.40 for all).

Association of performance measures with hospital-level RSM rates

The median 30-day and 1-year RSM rates (IQR) were 5.41% (4.91%–6.17%) and 13.55% (12.77%–14.48%), respectively (Table 3). The ICC of 30-day RSM rate was 0.065, and the ICC of 1-year RSM rate was 0.041.

All performance measures showed no correlations with 30-day RSM rate. Several performance measures showed statistically significant, but modest, correlations with 1-year RSM rate, including antithrombotics at discharge (Spearman correlation coefficients= 0.32), antihypertensive medication (Spearman correlation coefficients= 0.30) and antidiabetic medication (Spearman correlation coefficients= 0.31) (P< 0.05 for all) (Table 4). These performance measures individually explained between 0.04% and 5.02% of hospital-level variation in 30-day RSM rate, and between 0.08% and 10.05% of hospital-level variation in 1-year RSM rate (Table 5).

No correlation was observed between the hospital-level composite score and 30-day RSM rate (Spearman correlation coefficients= 0.16). Modest correlation was observed between the hospital-level composite score and 1-year RSM rate (Spearman correlation coefficients= 0.32). The

composite score explained 2.53% and 10.18% of the hospital-level variation in 30-day and 1-year RSM rates, respectively (Table 5).

Table 4. Correlation coefficients for performance measures and hospital RSM rates (30-day and 1-year)

	Acute interventions			Discharge interventions						
	IV rt-PA < 2 hour	Early antithrombotics	DVT prophylaxis	Antithrombotics	Anticoagulation for AF	Lipid-lowering drug for LDL ≥100 mg/dl	Antihypertensive medication	Antidiabetic medication	Smoking cessation	Composite score
Acute interventions										
IV rt-PA < 2 hour	1.00									
Early antithrombotics	0.01	1.00								
DVT prophylaxis	0.08	0.23	1.00							
Discharge interventions										
Antithrombotics	0.01	0.34*	0.03	1.00						
Anticoagulation for AF	-0.01	0.04	0.19	0.16	1.00					
LDL 100	0.08	0.13	0.07	0.44*	0.26*	1.00				
Antihypertensive medication	-0.02	0.08	-0.09	0.59*	0.12	0.27*	1.00			
Antidiabetic medication	0.04	0.10	0.07	0.66*	0.17	0.31*	0.64*	1.00		

Smoking cessation	-0.01	0.34*	0.01	0.34*	0.25*	0.13	0.21	0.26*	1.00	
Composite score	0.05	0.48*	0.24	0.79*	0.32*	0.69*	0.60*	0.62*	0.47*	1.00
Risk-standardized 30-day mortality rate	-0.16	-0.02	-0.06	-0.16	0.04	-0.09	-0.17	-0.22	-0.04	-0.16
Risk-standardized 1-year mortality rate	-0.12	-0.03	-0.11	-0.32*	-0.07	-0.22	-0.30*	-0.31*	-0.02	-0.32*

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

*P<0.001.

Table 5. Variance in 30-day and 1-year RSM rates explained by each performance measure and the composite measure

	30-day RSM rate	1-year RSM rate
Measures	% variance explained	% variance explained
Acute interventions		
IV rt-PA < 2 hour	2.43%	1.32%
Early antithrombotics	0.04%	0.08%
DVT prophylaxis	0.38%	1.14%
Discharge interventions		
Discharge antithrombotics	2.59%	10.05%
Anticoagulation for AF	0.14%	0.45%
LDL 100	0.76%	4.67%
Antihypertensive medication	2.99%	9.24%
Antidiabetic medication	5.02%	9.49%
Smoking cessation	0.18%	0.06%
Composite score	2.53%	10.18%

IV, intravenous; rt-PA, recombinant tissue-type plasminogen; DVT, deep vein thrombosis; AF, atrial fibrillation; LDL, low-density lipoprotein; RSM, risk-standardised mortality.

DISCUSSION

The present study found that ischemic stroke care was suboptimal in China and there were various correlations among hospital performance measures. The hospital-level composite score had no correlation with 30-day RSM rate and a modest correlation with 1-year RSM rate. This finding suggested hospital performance measures cannot reliably infer short- and long- term mortalities after acute ischemic stroke. Our results underscored that the current performance measures of stroke care provided complementary, but not redundant, information with the measures of 30-day and 1-year mortalities.

When comparing our data with the GWTG-Stroke in America, we found that ischemic stroke care was suboptimal in China. The GWTG-Stroke program was developed by the AHA/ASA as a national stroke registry and performance improvement program with the primary goal of improving the quality of care and outcomes of stroke and TIA in America.[7 14] The comparison showed that many hospital performance measures in China were far down from the GWTG-Stroke,[14 23] including the composite score (63.3% in 2007 CNSR versus 94.0% in 2007 GWTG-Stroke), IV rt-PA < 2 hour (14.1% in 2007 CNSR versus 72.8% in 2007 GWTG-Stroke), early antithrombotics (80.3% in 2007 CNSR versus 97.0% in 2007 GWTG-Stroke), DVT prophylaxis (59.6% in 2007 CNSR versus 89.5% in 2007 GWTG-Stroke), discharge antithrombotics (71.0% in 2012 CNSR versus 98.9% in 2007 GWTG-Stroke), anticoagulation for AF (19.7% in 2007 CNSR versus 98.4% in 2007 GWTG-Stroke), lipid-lowering drug for LDL ≥100 mg/dL (42.6% in 2012 CNSR versus 88.3% in 2007 GWTG-Stroke), and smoking cessation (63.3% in 2007 CNSR versus 93.6% in 2007 GWTG-Stroke). Financial burden, lacking of stroke center certification and stroke education might be the main reasons.

The relationships between performance measures and stroke outcomes remained uncertainty. Some studies have indicated that the use of performance measures was associated with lower short-term mortality and better functional outcomes.[24-26] However, the links between these stroke performance measures and outcomes were not clear in other studies.[27-30] There were several probable reasons for the modest correlations between hospital-level performance measures and RSMs in the present study. Firstly, although clinical trials have shown significant relationships between performance measures and outcomes,[31 32] the evidence-based performance measures were not mainly designed for overall short- and long-term hospital mortalities. Secondly, there was relative little variation across hospitals in some performance measures, such as early antithrombotics after admission, which limited the ability to discriminate between hospitals based on their performance on these measures. Additionally, some performance measures, such as IV, might have a greater effect regarding stroke-related disability than mortality.[33] Finally, hospital mortalities, even risk-standardised ones, were more likely affected by many factors independent of the performance measures of stroke care quality, such as severity of stroke, patients' or their family's preference, economic level and clinical strategies that might contribute to a hospital's performance outcomes.[34]

The present study also demonstrated significant correlations between certain evidence-based performance measures for acute ischemic stroke care, indicating that hospitals performing well in one performance measure were more likely to perform well in other measures. However, other performance measures were less strongly correlated with each other. This finding implied different performance measures reflected separate components of quality in acute ischemic stroke care. Our work indicated that hospital performance rankings were likely to be substantially affected by the

performance measures under selection. A broader range of performance measures may be needed to comprehensively reflect the quality of stroke care.

Our study had several strengths. First, to date, the CNSR was the largest stroke database in China. Hospitals participating in the CNSR encompassed different regions and had good representativeness. Second, we used the newer RSM method based on hierarchical models to account for variation in case numbers across hospitals or for intra-hospital clustering effects.[15] Third, baseline characteristics of patients, such as age, gender, vascular risk factors, comorbid conditions, and stroke severity (NIHSS) were adjusted in calculating the RSMs in accordance with the American Heart Association/American Stroke Association (AHA/ASA).[15 34] Additionally, besides short-term RSM, our study also analysed long-term RSM.

However, our study also had some limitations. Firstly, our study was observational and non-randomised. The association between stroke care performance and stroke outcomes did not necessarily prove causality and may be confounded by previously discussed factors. Secondly, our outcome was mortality; other outcomes such as stroke recurrence and functional outcomes were also vital to patients, which should be assessed in future studies.[30] Thirdly, the hospital performance measures, stroke outcomes, and the relationships between them might vary over time (such as extended time window for thrombolysis). Future research need to determine the stability of the process-outcome relationship as quality improvement efforts would drive broader care adoption. Fourthly, our data were collected between 2007 and 2008, therefore the interpretation of our data might be limited. Future research is needed to confirm our results. Finally, there were several differences in stroke healthcare delivery systems between China and other countries. The results

reported herein came from the Chinese healthcare system and therefore may not necessarily be generalisable to other countries.

CONCLUSIONS

The adherence to evidence-based performance measures for acute ischemic stroke was suboptimal in China. There were various correlations among hospital individual performance measures. The hospital performance measures had no correlations with 30-day RSM rate and modest correlations with 1-year RSM rate. More measures are needed to assess and improve the quality of hospital-level stroke care in China.

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Contributorship Statement

XMZ and ZXL analyzed the data and wrote the manuscript. XLB, LPL, CXW, HL, JB, QY and DW analyzed and interpretated the data. ZXL, CJW, YJ, XMY and XMZ performed research. YJW, YLW, ZXL, YX and XQZ conceived, designed and supervised the study.

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Competing interests

None.

Ethics approval

Approval was obtained from the Central Institutional Review Board at Beijing Tiantan Hospital.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement: No additional data are available.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	✓ **Page 3** (*a*) Indicate the study's design with a commonly used term in the title or the abstract
		✓ **Page 3** (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	✓ **Page 5** Explain the scientific background and rationale for the investigation being reported
Objectives	3	✓ **Page 5** State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	✓ **Page 5** Present key elements of study design early in the paper
Setting	5	✓ **Page 6** Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	✓ **Page 5** (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	✓ **Page 7-10** Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	✓ **Page 7-10** For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	✓ **Page 21** Describe any efforts to address potential sources of bias
Study size	10	✓ **Page 10** Explain how the study size was arrived at
Quantitative variables	11	✓ **Page 11** Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	✓ **Page 11** (*a*) Describe all statistical methods, including those used to control for confounding
		✓ **Page 11** (*b*) Describe any methods used to examine subgroups and interactions
		✓ **Page 11** (*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	✓ **Page 11** (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		✓ **Page 11** (b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	✓ **Page 11** (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		✓ **Page 11** (b) Indicate number of participants with missing data for each variable of interest
		✓ **Page 11** (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	✓ **Page 16** Report numbers of outcome events or summary measures over time
Main results	16	✓ **Page 17-19** (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which

		confounders were adjusted for and why they were included
		✓ **Page 12-15** (*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	✓ **Page 16-19** Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	✓ **Page 20** Summarise key results with reference to study objectives
Limitations	19	✓ **Page 21** Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	✓ **Page 20-21** Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	✓ **Page 21-22** Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	✓ **Page 23** Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.