Accuracy of clinical stroke scores for distinguishing stroke subtypes in resource poor settings: A systematic review of diagnostic test accuracy

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ABSTRACT

Background: Stroke is the second leading cause of death globally. Computerized tomography is used to distinguish between ischemic and hemorrhagic subtypes, but it is expensive and unavailable in low and middle income countries. Clinical stroke scores are proposed to differentiate between stroke subtypes but their reliability is unknown. **Materials and Methods:** We searched online databases for studies written in English and identified articles using predefined criteria. We considered studies in which the Siriraj, Guy's Hospital, Besson and Greek stroke scores were compared to computerized tomography as the reference standard. We calculated the pooled sensitivity and specificity of the clinical stroke scores using a bivariate mixed effects binomial regression model. **Results:** In meta-analysis, sensitivity and specificity for the Siriraj stroke score, were 0.69 (95% CI 0.62-0.75) and 0.83 (95% CI 0.75-0.88) for ischemic stroke and 0.65 (95% CI 0.56-0.73) and 0.88 (95% CI 0.83-0.91) for hemorrhagic stroke. For the Guy's hospital stroke score overall sensitivity and specificity were 0.70 (95% CI 0.53-0.83) and 0.79 (95% CI 0.68-0.87) for ischemic stroke and 0.54 (95% CI 0.42-0.66) and 0.89 (95% CI 0.83-0.94) for hemorrhagic stroke. **Conclusions:** Clinical stroke scores are not accurate enough for use in clinical or epidemiological settings. Computerized tomography is recommended for differentiating stroke subtypes. Larger studies using different patient populations are required for validation of clinical stroke scores.

Key words: Besson score, Guy's hospital stroke score, Greek stroke score, Siriraj stroke score, stroke

Introduction

Stroke is the second leading cause of death globally and is associated with up to 5.54 million deaths every year, two thirds of which occur in resource poor countries (RPC).[1] It has two main subtypes, ischemic and hemorrhagic. For optimal management, a distinction must be made between the subtypes since the therapy is different.[2] Ischemic stroke warrants institution of thrombolytic and/or antiplatelet therapy while in hemorrhagic stroke, hemostatic therapy may be given.[3] Ideally, either thrombolytic or hemostatic therapy should be given soon after the onset of stroke in order to improve outcome.[4]

Non-contrast computed tomography (CT) scan is the gold standard for distinguishing stroke sub-types.[5,6] It is cheaper than magnetic resonance imaging (MRI), but is still expensive and inaccessible for most resource poor settings. To overcome these difficulties and to enhance clinical bedside diagnosis, clinical stroke scores have been developed. The most commonly used ones include the Guy's hospital score (GHSS),[7] the Besson score,[8] the Greek stroke score[9] and the Siriraj stroke score (SSS).[10] In developing these scores, clinical variables that could potentially distinguish ischemia from hemorrhage in patients with acute stroke were used.

While these scores are not more accurate than neuro-imaging, they are simple, cheap and practical. However, their true accuracy and value in the diagnosis of stroke in resource poor settings remains unknown. We

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report a systematic review examining the evidence on the accuracy of clinical stroke scores in distinguishing between stroke subtypes, particularly within low and middle income countries (LAMICs).

Materials and Methods

Search strategy

We searched the following databases for both published and unpublished studies in the English language over the period 1983-2013: PubMed, EMBASE, Cochrane central register of controlled trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, Virtual health library, System for Information on Grey literature in Europe (SIGLE), Scientific Electronic Library Online (SciELO), MedNar and ProQuest. The following terms were used to generate a search: Stroke, Acute stroke, Brain ischemia, Cerebral hemorrhage, Cerebral infarction, Siriraj stroke score, Clinical stroke score, Guy's hospital stroke score, Allen score, Besson score, Greek stroke score.

Inclusion and exclusion criteria

We considered studies of diagnostic test accuracy from LAMICs that included patients admitted to hospital with a diagnosis of acute stroke according to the WHO criteria[2] and in which the index tests (Siriraj, Guy's Hospital, Besson and Greek stroke scores) and reference test (CT-Scan) were interpreted independently of one another on the same group of participants. Table 1 provides more details on each score. Due to a difference

in the prevalence of hemorrhagic stroke and stroke risk factors,[11,12] we did not consider studies from high income countries (HICs). Details on the calculation of test scores have been described previously.[7-10] Studies that evaluated two or more of these scores simultaneously were also included. Only studies that reported on the sensitivity and specificity of stroke scores compared to CT scan diagnosis were included however, studies that did not report on sensitivity and specificity but had sufficient information to calculate these were also considered.

Assessment of methodological quality

Papers selected for review were assessed independently for methodological validity prior to inclusion in the review using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria. Disagreements were resolved through discussion. We considered a representative spectrum of patients to be female or male patients of all ages presenting with mild, moderate or severe stroke symptoms, with or without a previous history of stroke. In the assessment of disease progression bias, 15 days was considered an appropriate period between onset of stroke and administration of the reference standard. This period helps to avoid interpreting resolving hemorrhages as infarcts and accommodates the lack of the sensitivity of CT scan in early ischemic stroke.

Data extraction

A data extraction form was designed and used to collect details from included studies. For each study, the

Table 1: Comparison of clinical stroke scores

Score	Country of origin	No. of variables	Formula	Interpretation
Siriraj stroke score	Thailand	5	Number of points=2.5* (level of consciousness)	>+1 Hemorrhage
			+2* (vomiting)	<−1 Infarction
			+2* (headache within 2 hours of onset)	+1 to −1 Equivocal
			+0.1* (diastolic blood pressure)	
			−3* (atheroma markers)	
			−12 (constant)	
Guys Hospital stroke score	United Kingdom	13	Number of points=Apoplectic onset+Level of consciousness+Plantar responses+(Diastolic blood pressure (24 hours after admission) ×0.17)+Atheroma markers+History of hypertension+Previous event (Transient ischemic attack)+Heart disease+Constant (−12)	<4 Infarction >24 Hemorrhage 4 to 24 Equivocal
Greek stroke score	Greece	4	Number of points=6* (Neurogical deterioration within 3 hours from admission)	< 3 Infarction
			+ 4* (vomiting)	>11 Hemorrhage
			+ 4* (white blood cells>12000)	3 to 11 Equivocal
			+ 3* (decreased level of consciousness)	
Besson score	France	8	Number of points=(2*alcohol consumption)+(1.5*plantar response both extensor)+(3*headache)+(3*history of hypertension)−(5*history of transient ischemic attack)−(2*peripheral arterial disease)−(1.5*history of hyperlipidemia)−(2.5* atrial fibrillation on admission)	<1 Infarction >1 Hemorrhage

* - Multiplication sign

following data were obtained: Author information, year of publication, study site, setting, study design, number and characteristics of patients (age, sex, ethnicity), reference standard, index test (s), information on clinicians who administered scores and clinicians who interpreted the reference standard i.e. background specialty. Sensitivity and specificity, number of patients with equivocal scores, true positive (TP), false positive (FP), true negative (TN) and false negative (FN) data for each test were taken directly from source papers. If this was not possible, they were calculated from provided data. Extracted data was then entered in a separate form and transferred to a spreadsheet.

Data synthesis

We derived indices of diagnostic performance from the data presented in each study for each index test. We constructed 2 × 2 contingency tables of true positive, false positive, false negative and true negative cases with CT scan as the independent variable and index test as the dependent variable and calculated sensitivity and specificity with 95% confidence interval (95% CI) for each stroke score in each study. However, since exclusion of indeterminate test results may result in overestimation of accuracy, we included equivocal test results in our calculations where these were reported. Because ischemic and hemorrhagic stroke have different management strategies we tabulated results for ischemic stroke separately from those for hemorrhagic stroke for each index test and generated separate forest plots of test performance for ischemic and hemorrhagic strokes.

Since included studies had a similar spectrum of patients and the threshold value used for the index tests was the same in all the studies, we performed a meta-analysis of the index test results using a bivariate mixed effects binomial regression model. Summary estimates for sensitivity, specificity, positive and negative likelihood ratios (LR) as well as diagnostic odds ratio were generated. Positive and negative predictive values were not calculated since they are dependent on prevalence of stroke subtypes which was different across included studies. We assessed heterogeneity graphically using forest plots and statistically using the quantity I^2. Analysis was performed on STATA v11.0 (Stata Corp., TX) using the 'midas' command and Review Manager Software version 5.[13]

Results

Study selection

A total of 115 relevant papers were identified in the literature search of which 39 were retrieved for

further examination. Three papers were retrieved from additional sources. Of the 42 papers retrieved for detailed examination, 22 were excluded and 20 papers were included in the review. Figure 1 outlines the study selection process.

Characteristics of included studies

Included studies were hospital-based diagnostic test accuracy studies conducted within a 20 year period (1991-2011) in Asia,[6,14-21] Eastern Europe[22,23] and Africa[24-32] (including north Africa.[27]) The aim in each study was evaluating the diagnostic performance of the index tests (SSS, GHSS and GSS) in distinguishing stroke sub-types among patients with acute stroke. CT scan was the documented reference standard in most studies. The SSS was evaluated in 18 studies while the GHSS was evaluated in 11 studies. The GSS was evaluated in three studies. No study evaluated the BS.

Two studies[29,31] were retrospective in design while the rest were prospective studies. The patient spectrum was mainly adult patients with acute stroke. In a number of studies, patients were only included if they had a CT scan performed. Reasons for lack of CT scan in patients who did not have the investigation were not elaborated in most studies. Further, many studies did not report characteristics of excluded patients for comparison with those included.

Overall, a total of 3638 patients from LAMICs were evaluated. Participants were of age range 14-87 years. Only two studies reported the severity of stroke among included patients.[14,25] Prevalence of hemorrhagic stroke (including SAH) ranged from 17.3% to 68.9% (median prevalence 37.85%; IQR 30.25%-48.76%) while prevalence of ischemic stroke ranged from 31% to 82.7% (median prevalence 58.75%; IQR 52.82%-68.5%). In five studies[14,17,22,27,30] equivocal results were excluded from the estimation of diagnostic performance of the index tests.
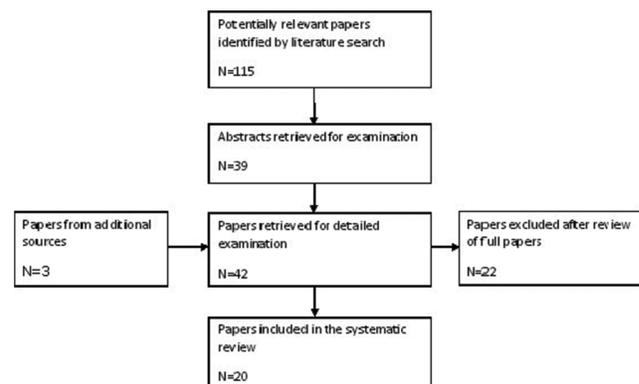

Figure 1: Flow diagram of study selection

The main outcomes reported in the studies were test sensitivity and specificity. However, positive and negative predictive values as well as likelihood ratios were reported in a number of studies. About half of the studies recommended the scores for use in the absence of CT scan for both clinical and epidemiological studies. Overall, the studies recommend larger and better designed studies for validation of the scores in addition to refining them. Table 2 presents a summary of the characteristics of included studies.

Methodological quality of included studies

Overall, studies included in the review were of sound quality despite incomplete reporting in some of them. Spectrum bias, disease progression bias, partial verification bias, differential verification bias and incorporation bias were adequately minimized. Blinding of index test and reference standard results was poorly reported across studies. All studies reported indeterminate results although not all of them included these results in the assessment of test performance.

Meta-analysis results
Accuracy of the Siriraj stroke score
Sensitivity of the test for ischemic stroke ranged from 0.30 to 0.85 while specificity ranged from 0.36 to 0.97. Overall, sensitivity for the test was 0.69 (95% CI 0.62-0.75) and specificity was 0.83 (95% CI 0.75-0.88) for ischemic stroke. There was significant statistical heterogeneity observed (I^2 = 90.25 for sensitivity and I^2 = 86.30 for specificity). The positive likelihood ratio (+LR) was 4 (95% CI 2.7-5.8) while the negative likelihood ratio (-LR) was 0.38 (95% CI 0.31-0.47).The test's diagnostic odds ratio (DOR) was 10 (95% CI 6-17).

Sensitivity for hemorrhagic stroke ranged from 0.33 to 0.87 while specificity ranged from 0.65 to 0.99. Overall, sensitivity for the test was 0.65 (95% CI 0.56-0.73) and specificity was 0.88 (95% CI 0.83-0.91) for hemorrhagic stroke. There was substantial heterogeneity observed (I^2 = 86.35 for sensitivity and I^2 = 83.86 for specificity). The +LR was 5.2 (95% CI 3.5-7.7) while the -LR was 0.40 (95% CI 0.31-0.51).The test's DOR was 13 (95% CI 7-23). Figures 2 and 3 show forest plots of sensitivity and specificity for the SSS for both ischemic and hemorrhagic stroke respectively for included studies from LAMICs.

Accuracy of the Guys hospital stroke score
Sensitivity for ischemic stroke ranged from 0.25 to 0.93 while specificity ranged from 0.50 to 0.97. Overall, sensitivity for the test was 0.7 (95% CI 0.53-0.83) and specificity was 0.79 (95% CI 0.68-0.87) for ischemic stroke. There was significant heterogeneity observed (I^2 = 97.33

for sensitivity and I^2 = 89.23 for specificity). The +LR was 3.4 (95% CI 2.4-4.7) while the –LR was 0.38 (95% CI 0.25-0.58). The DOR was 9 with a 95% CI of 5-15.

Sensitivity for hemorrhagic stroke ranged from 0.20 to 0.84 while specificity ranged from 0.48 to 1.00. Overall, sensitivity for the test was 0.54 (95% CI 0.42-0.66) and specificity was 0.89 specific (95% CI 0.83-0.94) for hemorrhagic stroke. There was significant heterogeneity observed (I^2 = 86.69 for sensitivity and I^2 = 90.92 for specificity). The + LR was 5.2 (95% CI 3.2-8.4) while the -LR was 0.51 (95% CI 0.40-0.66). The DOR was 10 (95% CI 5-19). Figures 2 and 3 show forest plots of sensitivity and specificity for the GHSS for both ischemic and hemorrhagic stroke for included studies from LAMICs.

Accuracy of the Greek stroke score
Statistical pooling of results was not undertaken due to the small number of studies evaluating this test. Sensitivity for ischemic stroke ranged from 0.39 to 0.64 while specificity ranged from 0.63 to 0.88. Sensitivity for hemorrhagic stroke ranged from 0.11 to 0.44 while specificity ranged from 0.63 to 0.96. There was graphical heterogeneity observed. Figures 2 and 3 show forest plots of sensitivity and specificity for the GSS for both ischemic and hemorrhagic stroke for included studies from LAMICs.

Discussion

Adequate management of acute stroke requires early distinction of ischemic stroke from hemorrhagic stroke. Before starting anticoagulant, antiplatelet or thrombolytic therapy for ischemic stroke, hemorrhagic stroke must be accurately ruled out. CT scan is sensitive for hemorrhagic stroke while MRI has been shown to have high sensitivity for early ischemic stroke.[33,34] However, both are expensive and unavailable in resource poor settings.[11]

We identified 18 studies that validated the SSS in LAMICs from Africa, Asia and Eastern Europe. Only about half of these recommended the score for either clinical or epidemiological use. Overall, we found the test to have a sensitivity of 0.63 (95% CI 0.54-0.72) and specificity of 0.88 (95% CI 0.82-0.91) for hemorrhagic stroke. Since the exclusion of hemorrhage in patients with acute stroke is important before starting anticoagulant therapy for those with ischemic stroke, the SSS is not sufficiently sensitive to exclude hemorrhage. Also, the likelihood ratios for the test for hemorrhagic stroke show that it only very minimally changes the post-test probability of having hemorrhage. Further, in order to be sufficiently

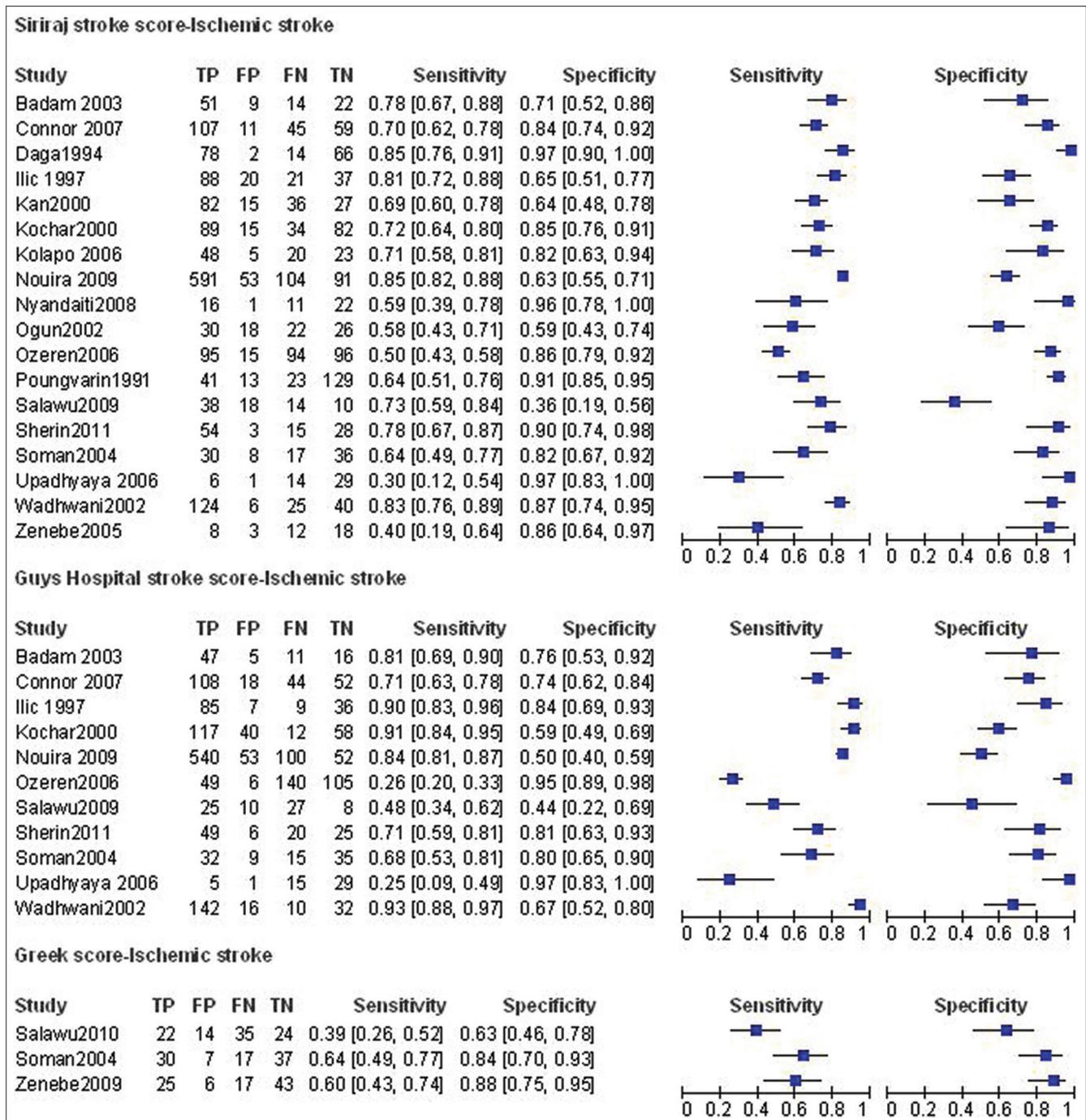## Table 2: Characteristics of included studies from low and middle income countries

Author/year (site)	Entry criteria	Participants	Index test (s)	Findings
Badam 2003 (India)[14]	Suspected stroke. Excluded those presenting >24 hours after stroke onset, SAH*, those with incomplete data, death before CT scan or alternative diagnosis on CT scan	134 patients (73 male). Mean age 57.3 years (SD 15.5 years). Range 14-75 years	SSS† GHSS‡	The SSS discriminated hemorrhage from infarction with a sensitivity of 78.5% (95% CI: 66.5, 87.7) and specificity of 71% (95% CI: 52, 85.8)
				For the GHSS used in distinguishing between infarction and hemorrhage the sensitivity was 81% (95% CI: 68.6, 90.1), specificity 76.2% (95% CI: 52.8, 91.8)
Connor 2007 (South Africa)[25]	All cases of stroke (new or recurrent) admitted to hospital. SAH and ICH§ combined	329 black patients (160 male). Mean age 48 years. 222 patients had CT scans and enough data to calculate scores	SSS GHSS	Neither score offered much advantage over clinician assessment with sensitivity 0.60 and 0.34, specificity 0.88 and 0.95 for intracranial hemorrhage in the SSS and GHSS, respectively; sensitivity 0.70 and 0.71, specificity 0.84 and 0.74, respectively, for ischemic stroke
Daga 1994 (India)[15]	Stroke based on clinical course. TIA‖, SAH and head injury excluded	160 patients (104 male). Mean age 60 years	SSS GHSS	The SSS had a predictive accuracy of 80% for hemorrhage and 83% for infarction. The GHSS gave a predictive accuracy of 66% for hemorrhage and 69% for infarction
Ilic 1997 (Serbia)[22]	Consecutive patients with clinical diagnosis of acute supratentorial stroke syndrome according to WHO **definition	188 patients. Mean age 67.11 years. Male: Female ratio 1.65:1	SSS GHSS	Sensitivity, specificity, PPV††, NPV‡‡ and accuracy for the SSS were 0.649, 0.863, 0.627, 0.88 and 0.786 and 0.833, 0.895, 0.924, 0.8 and 0.883 for the GHSS. A combination of both scores had a sensitivity, specificity, PPV, NPV and accuracy of 0.95, 0.89, 0.85, 0.97 and 0.92
Kan 2000 (Malaysia)[16]	Acute stroke according to WHO criteria. SAH excluded	160 patients (102 male). Age range 25-87 years. Mean age 60.3 years	SSS	Sensitivity, specificity and PPV for the SSS for infarct was 69.5%, 64.3%, 84.5% and 50%, 90.7% and 65.6% for hemorrhage. Overall accuracy was 64.4%
Kochar 2000 (India)[17]	Stroke according to WHO criteria. TIA, SAH and head injury excluded	240 patients. No age/sex distribution	SSS GHSS	Sensitivity, specificity, PPV, NPV and diagnostic gain for the SSS were 73%, 85%, 85%, 71%, and 30% for infarction and 85%, 73%, 71%, 85% and 27% for hemorrhage. Corresponding figures for the GHSS were 91%, 60%, 77%, 82% and 18% for infarction and 60%, 91%, 82%, 77% and 41% for hemorrhage respectively
Kolapo 2006 (Nigeria)[26]	Clinical diagnosis of stroke and brain CT scan within 14 days. Excluded patients <16 years, stroke >14 days and other causes of neurological deficit and recurrent stroke	96 patients (64 male). Mean age 54 years (SD 9 years). Age range 19-84 years	SSS	The correlation between SSS, headache, vomiting, loss-of-consciousness and CT diagnosis achieved statistical significance, whereas atheroma markers and diastolic blood pressure did not. The SSS has an overall predictive accuracy of 80%
Nouira 2009 (Tunisia)[27]	Patients >45 years with acute stroke according to WHO. Excluded those with previous severe neurological disorders and those on anticoagulants	1023 patients (516 male). Mean age 67 years (infarction) and 69 years (hemorrhage)	SSS GHSS	The area under the ROC*** curve was higher for the SSS compared with the GHSS (0.780 versus 0.702; P_.04). Using the original cut-off points, SSS had a sensitivity for the diagnosis of hemorrhage of 60% and a specificity of 95%; the corresponding values for the GHSS were 55% and 70%, respectively
Nyandaiti 2008 (Nigeria)[28]	Patients with stroke. Excluded those <16 years, with recurring stroke, with stroke>14 days and with other causes of neurological deficits	50 patients (70% male). Age range 24-77 years. Mean age 52.5 years	SSS	Sensitivity and predictive value of the SSS were 76.2% and 93% for infarction and 94.4% and 85% for hemorrhagic stroke. Overall accuracy was 84.6%
Ogun 2002 (Nigeria)[29]	Patients with stroke according to WHO and with adequate data to compute scores	96 patients (67 male). Mean age 60 years (SD 4.3 years). Age range 51-69 years	SSS	Sensitivity, specificity, PPV and NPV for the SSS were 50%, 62.5%, 55%, 62.5% for cerebral hemorrhage and 58%, 55%, 62.5%, 55% for cerebral infarction. Overall accuracy was 54.2%
Ozeren 2006 (Turkey)[23]	Acute stroke	300 patients. Ischemic stroke (110 male, mean age 63.07 years). Hemorrhagic stroke (67 male, mean age 62.23 years)	SSS GHSS	Diagnostic sensitivities of the SSS for ischemic stroke and intracerebral hemorrhage were 90.5% and 71.2% with an overall predictive accuracy of 84.1%. The PPVs for ischemic stroke and intracerebral hemorrhage were 86.4% and 78.7% respectively
				Diagnostic sensitivities of the GHSS for ischemic stroke and intracerebral hemorrhage were 57% and 92.8% with an overall predictive accuracy of 74.6%. The PPVs for ischemic stroke and intracerebral hemorrhage were 89.1% and 67.5% respectively

Contd...

Table 2: Contd...

Author/year (site)	Entry criteria	Participants	Index test (s)	Findings
Poungvarin 1991 (Thailand)[18]	Patients with supratentorial hemorrhage of infarction	206 patients. No age/sex distribution	SSS	Diagnostic sensitivities of the SSS for cerebral hemorrhage and cerebral infarction were 89.3% and 93.2% respectively, with an overall predictive accuracy of 90.3%
Salawu 2009 (Nigeria)[24]	Acute stroke according to WHO, age>18 years and stroke duration<14 days. Excluded recurrent stroke, SAH, TIA and tumor	95 patients. 62 male (mean age 58.75 years). 33 female (mean age 52.1 years)	SSS GHSS	Sensitivity, specificity, positive predictive value and negative predictive value for cerebral hemorrhage was 0.64, 0.48, 0.4 and 0.71 for GHSS and 0.35, 0.73, 0.4 and 0.68 for SSS
Salawu 2010 (Nigeria)[30]	Acute stroke according to WHO, age>18 years and stroke duration<14 days. Excluded recurrent stroke, SAH, TIA and tumor	95 patients. 62 male (mean age 58.75 years). 33 female (mean age 52.1 years)	GSS§§	The sensitivity, specificity, positive and negative predictive values for GSS were 0.538, 0.50, 0.389 and 0.647 respectively. Its overall accuracy was 51.4%
Sherin 2011 (Pakistan)[19]	Acute stroke as per WHO presenting within 7 days of onset. No age limit, CT scan within 2 weeks of stroke onset. Excluded those with stroke onset>1week, death/ discharge within 24 hours of admission, no CT scan done, SAH, patients on anticoagulant therapy and patients with bilateral motor weakness	100 patients (55 male). Mean age 60.5 years	SSS GHSS	The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the GHSS were 38.70%, 91.30%, 66.67%, 76.82% respectively for cerebral hemorrhage and 71.1%, 80.64%, 89.09% and 55.56% respectively for cerebral infarction, with overall predictive accuracy of 61%
				The sensitivity, specificity, PPV and NPV of SSS were 67.74%, 94.2%, 84% and 86.67% respectively for cerebral hemorrhage and 78.26%, 90.32%, 94.73% and 65.11% respectively for cerebral infarction, with overall predictive accuracy of 75%
Soman 2004 (India)[20]	Patients with neurodeficit >24 hours and CT scan showing supratentorial infarct of hemorrhage. Excluded SAH, patients with stroke due to other causes and those with insufficient data to calculate scores	91 patients. No age/sex distribution reported	SSS GHSS GSS	Sensitivity, Specificity, positive predictive value, negative predictive value for the GHSS were 0.5 (95% CI: 0.34,0.58), 0.94 (95% CI: 0.86,0.98), 0.81 (95% CI: 0.56,0.95), 0.78 (95% CI: 0.71,0.81)
				Sensitivity, Specificity, positive predictive value, negative predictive value for the SSS were 0.75 (95% CI: 0.63,0.84), 0.81 (95% CI: 0.71,0.89), 0.77 (95% CI: 0.65,0.86), 0.78 (95% CI 0.69,0.86)
				Sensitivity, Specificity, positive predictive value, negative predictive value for the GSS were 0.42 (95% CI: 0.23,0.53), 0.93 (95% CI: 0.87,0.98), 0.71 (95% CI: 0.39,0.91), 0.81 (95% CI: 0.75,0.85) respectively
Upadhyaya 2006 (India)[21]	Patients with diagnosis of acute stroke as defined by WHO. Excluded patients with previous stroke, SAH, post-ictal paralysis and trauma	50 patients (27 male)	SSS GHSS	The sensitivity, specificity and positive predictive value for the SSS were 85.71%, 96.30%, 85.71% for infarction and 96.30%, 85.71%, 96.29% for hemorrhage respectively, whereas the corresponding figures for Guy's Hospital stroke score were 100%, 95.45%, 83.34% for infarction and 95.45%, 100%, 100% for hemorrhage respectively
Wadhwani 2002 (India)[6]	Acute stroke and CT scan. Excluded patients with stroke due to other reasons, SAH and those who presented >72 hours after onset	200 patients (119 male). Mean age not reported	SSS GHSS	Sensitivity of the SSS was 92.54% for infarction and 87% for hemorrhage with an overall accuracy of 91.11%. the GHSS had a sensitivity of 93.42% for infarction and 66.66% for hemorrhage with an overall accuracy of 87%
Zenebe 2005 (Ethiopia)[31]	Clinical diagnosis of stroke and available CT scan. SAH excluded	41 patients. No age/sex distribution reported	SSS	Sensitivity and PPV for the SSS for hemorrhage was 77% and 67% and for infarction was 61.5% and 72.7%. The score's overall accuracy was 69.2%
Berhe 2009 (Ethiopia)[32]	Stroke according to WHO criteria excluding those with SAH and those without CT scan and with stroke due to other causes	91 patients. No age/sex distribution reported	GSS	The sensitivity, specificity, positive and negative predictive values were 0.778 (95% CI, 0.573-0.906), 0.893 (95% CI, 0.706-0.972), 0.875 (95% CI, 0.665-0.967), 0.806 (95% CI, 0.619-0.919), respectively. Its overall accuracy was 83.6%

*Subarachnoid hemorrhage, †Siriraj stroke score, ‡Guy's Hospital stroke score, §Intracerebral hemorrhage, ‖Transient ischemic attack, **World Health Organization, ††Positive predictive value, ‡‡Negative predictive value, §§Greek stroke score, ***Receiver operator characteristics, SSS - Siriraj stroke score, GHSS - Guy's hospital score, WHO - World Health Organization, CT - Computed tomography, CI - Confidence interval, PPV - Positive predictive value, NPV - Negative predictive value, TIA - Transient ischemic attack, SAH - Subarachnoid hemorrhage, ICH - Intracerebral Hemorrhage

Siriraj stroke score-Ischemic stroke

Study	TP	FP	FN	TN	Sensitivity	Specificity
Badam 2003	51	9	14	22	0.78 [0.67, 0.88]	0.71 [0.52, 0.86]
Connor 2007	107	11	45	59	0.70 [0.62, 0.78]	0.84 [0.74, 0.92]
Daga1994	78	2	14	66	0.85 [0.76, 0.91]	0.97 [0.90, 1.00]
Ilic 1997	88	20	21	37	0.81 [0.72, 0.88]	0.65 [0.51, 0.77]
Kan2000	82	15	36	27	0.69 [0.60, 0.78]	0.64 [0.48, 0.78]
Kochar2000	89	15	34	82	0.72 [0.64, 0.80]	0.85 [0.76, 0.91]
Kolapo 2006	48	5	20	23	0.71 [0.58, 0.81]	0.82 [0.63, 0.94]
Nouira 2009	591	53	104	91	0.85 [0.82, 0.88]	0.63 [0.55, 0.71]
Nyandaiti2008	16	1	11	22	0.59 [0.39, 0.78]	0.96 [0.78, 1.00]
Ogun2002	30	18	22	26	0.58 [0.43, 0.71]	0.59 [0.43, 0.74]
Ozeren2006	95	15	94	96	0.50 [0.43, 0.58]	0.86 [0.79, 0.92]
Poungvarin1991	41	13	23	129	0.64 [0.51, 0.76]	0.91 [0.85, 0.95]
Salawu2009	38	18	14	10	0.73 [0.59, 0.84]	0.36 [0.19, 0.56]
Sherin2011	54	3	15	28	0.78 [0.67, 0.87]	0.90 [0.74, 0.98]
Soman2004	30	8	17	36	0.64 [0.49, 0.77]	0.82 [0.67, 0.92]
Upadhyaya 2006	6	1	14	29	0.30 [0.12, 0.54]	0.97 [0.83, 1.00]
Wadhwani2002	124	6	25	40	0.83 [0.76, 0.89]	0.87 [0.74, 0.95]
Zenebe2005	8	3	12	18	0.40 [0.19, 0.64]	0.86 [0.64, 0.97]

Guys Hospital stroke score-Ischemic stroke

Study	TP	FP	FN	TN	Sensitivity	Specificity
Badam 2003	47	5	11	16	0.81 [0.69, 0.90]	0.76 [0.53, 0.92]
Connor 2007	108	18	44	52	0.71 [0.63, 0.78]	0.74 [0.62, 0.84]
Ilic 1997	85	7	9	36	0.90 [0.83, 0.96]	0.84 [0.69, 0.93]
Kochar2000	117	40	12	58	0.91 [0.84, 0.95]	0.59 [0.49, 0.69]
Nouira 2009	540	53	100	52	0.84 [0.81, 0.87]	0.50 [0.40, 0.59]
Ozeren2006	49	6	140	105	0.26 [0.20, 0.33]	0.95 [0.89, 0.98]
Salawu2009	25	10	27	8	0.48 [0.34, 0.62]	0.44 [0.22, 0.69]
Sherin2011	49	6	20	25	0.71 [0.59, 0.81]	0.81 [0.63, 0.93]
Soman2004	32	9	15	35	0.68 [0.53, 0.81]	0.80 [0.65, 0.90]
Upadhyaya 2006	5	1	15	29	0.25 [0.09, 0.49]	0.97 [0.83, 1.00]
Wadhwani2002	142	16	10	32	0.93 [0.88, 0.97]	0.67 [0.52, 0.80]

Greek score-Ischemic stroke

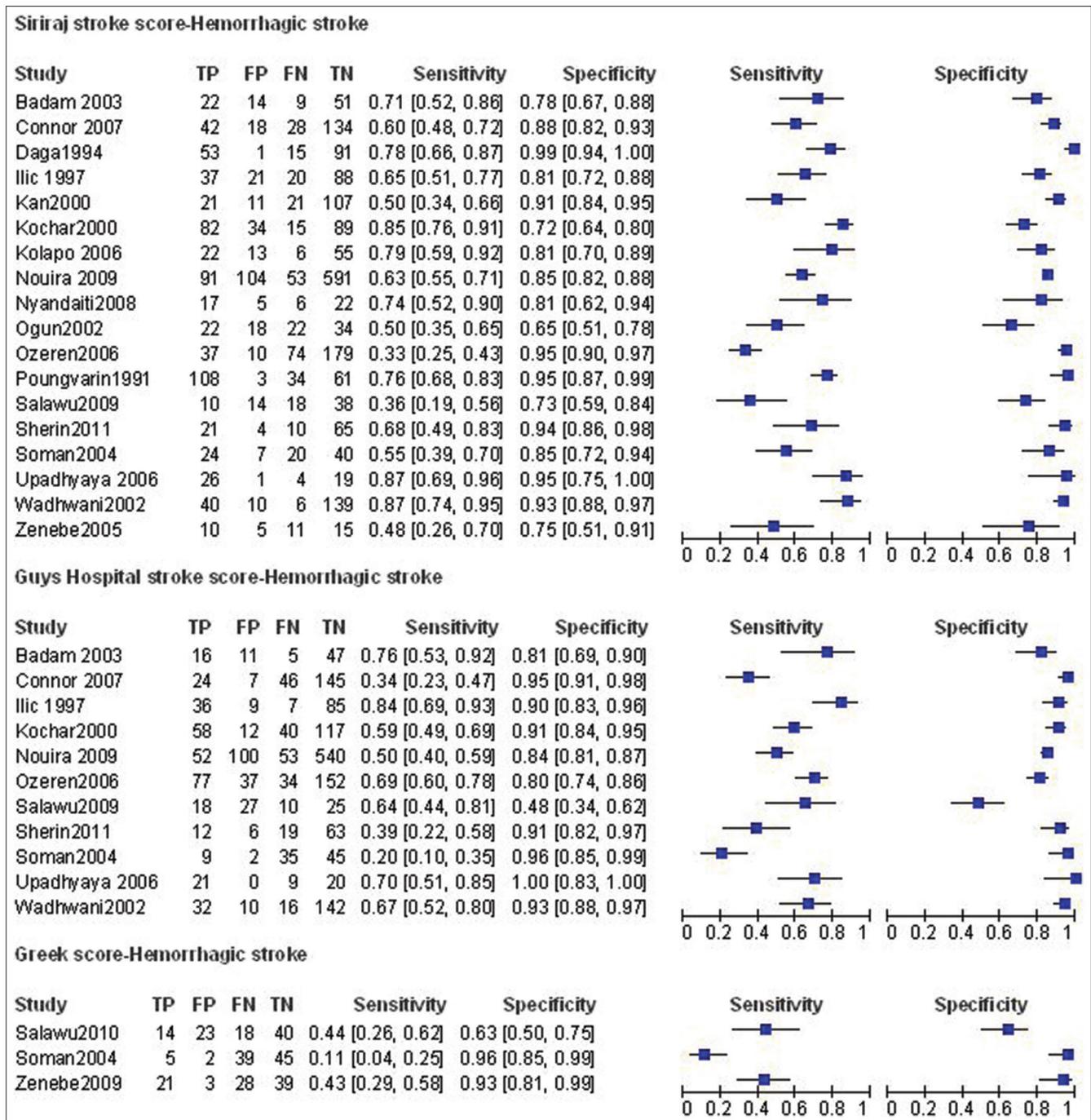| Study	TP	FP	FN	TN	Sensitivity	Specificity
Salawu2010	22	14	35	24	0.39 [0.26, 0.52]	0.63 [0.46, 0.78]
Soman2004	30	7	17	37	0.64 [0.49, 0.77]	0.84 [0.70, 0.93]
Zenebe2009	25	6	17	43	0.60 [0.43, 0.74]	0.88 [0.75, 0.95]

Figure 2: Coupled forest plots of sensitivity and specificity for stroke scores for studies from LAMICs (Ischemic stroke)

sure of the presence of ischemic stroke to guide on management, the clinical score needs to be specific enough to rule in ischemia. The SSS has a specificity of 0.82 (95% CI 0.74-0.88) for ischemic stroke and a positive likelihood ratio of 3.9 (95% CI 3.4-7.7). These estimates suggest that the score is not accurate enough for clinical or epidemiological use.

The poor accuracy of the SSS in LAMICs may be attributable to various factors. First, most studies had small sample sizes. Secondly, the SSS was developed in a country with a very high prevalence of hemorrhagic stroke relative to other countries and thus its accuracy may differ from its initial validation result. The inclusion of equivocal test results in our calculations may also explain the poor accuracy. However, this inclusion is necessary so as to give a true picture of the test's accuracy.

The Guy's hospital stroke score was developed on a predominantly young population which is known

Siriraj stroke score-Hemorrhagic stroke

Study	TP	FP	FN	TN	Sensitivity	Specificity
Badam 2003	22	14	9	51	0.71 [0.52, 0.86]	0.78 [0.67, 0.88]
Connor 2007	42	18	28	134	0.60 [0.48, 0.72]	0.88 [0.82, 0.93]
Daga1994	53	1	15	91	0.78 [0.66, 0.87]	0.99 [0.94, 1.00]
Ilic 1997	37	21	20	88	0.65 [0.51, 0.77]	0.81 [0.72, 0.88]
Kan2000	21	11	21	107	0.50 [0.34, 0.66]	0.91 [0.84, 0.95]
Kochar2000	82	34	15	89	0.85 [0.76, 0.91]	0.72 [0.64, 0.80]
Kolapo 2006	22	13	6	55	0.79 [0.59, 0.92]	0.81 [0.70, 0.89]
Nouira 2009	91	104	53	591	0.63 [0.55, 0.71]	0.85 [0.82, 0.88]
Nyandaiti2008	17	5	6	22	0.74 [0.52, 0.90]	0.81 [0.62, 0.94]
Ogun2002	22	18	22	34	0.50 [0.35, 0.65]	0.65 [0.51, 0.78]
Ozeren2006	37	10	74	179	0.33 [0.25, 0.43]	0.95 [0.90, 0.97]
Poungvarin1991	108	3	34	61	0.76 [0.68, 0.83]	0.95 [0.87, 0.99]
Salawu2009	10	14	18	38	0.36 [0.19, 0.56]	0.73 [0.59, 0.84]
Sherin2011	21	4	10	65	0.68 [0.49, 0.83]	0.94 [0.86, 0.98]
Soman2004	24	7	20	40	0.55 [0.39, 0.70]	0.85 [0.72, 0.94]
Upadhyaya 2006	26	1	4	19	0.87 [0.69, 0.96]	0.95 [0.75, 1.00]
Wadhwani2002	40	10	6	139	0.87 [0.74, 0.95]	0.93 [0.88, 0.97]
Zenebe2005	10	5	11	15	0.48 [0.26, 0.70]	0.75 [0.51, 0.91]

Guys Hospital stroke score-Hemorrhagic stroke

Study	TP	FP	FN	TN	Sensitivity	Specificity
Badam 2003	16	11	5	47	0.76 [0.53, 0.92]	0.81 [0.69, 0.90]
Connor 2007	24	7	46	145	0.34 [0.23, 0.47]	0.95 [0.91, 0.98]
Ilic 1997	36	9	7	85	0.84 [0.69, 0.93]	0.90 [0.83, 0.96]
Kochar2000	58	12	40	117	0.59 [0.49, 0.69]	0.91 [0.84, 0.95]
Nouira 2009	52	100	53	540	0.50 [0.40, 0.59]	0.84 [0.81, 0.87]
Ozeren2006	77	37	34	152	0.69 [0.60, 0.78]	0.80 [0.74, 0.86]
Salawu2009	18	27	10	25	0.64 [0.44, 0.81]	0.48 [0.34, 0.62]
Sherin2011	12	6	19	63	0.39 [0.22, 0.58]	0.91 [0.82, 0.97]
Soman2004	9	2	35	45	0.20 [0.10, 0.35]	0.96 [0.85, 0.99]
Upadhyaya 2006	21	0	9	20	0.70 [0.51, 0.85]	1.00 [0.83, 1.00]
Wadhwani2002	32	10	16	142	0.67 [0.52, 0.80]	0.93 [0.88, 0.97]

Greek score-Hemorrhagic stroke

Study	TP	FP	FN	TN	Sensitivity	Specificity
Salawu2010	14	23	18	40	0.44 [0.26, 0.62]	0.63 [0.50, 0.75]
Soman2004	5	2	39	45	0.11 [0.04, 0.25]	0.96 [0.85, 0.99]
Zenebe2009	21	3	28	39	0.43 [0.29, 0.58]	0.93 [0.81, 0.99]

Figure 3: Coupled forest plots of sensitivity and specificity for stroke scores for studies from LAMICs (Hemorrhagic stroke)

to have a higher prevalence of hemorrhagic stroke compared to an older population. The authors did not endorse its use for clinical management but suggested it may be used for epidemiological studies. The score has been validated in LAMICs with differing conclusions. In this review, 11 studies evaluated the GHSS. Specificity for ischemic stroke was 0.76 (95% CI 0.64-0.85) with a positive likelihood ratio of 2.9 (95% CI 2.2-3.9). These estimates are not sufficient enough to confirm ischemic stroke and commence anticoagulant therapy. Sensitivity

for hemorrhagic stroke was 0.49 (95% CI 0.38-0.61) which shows poor accuracy for ruling out hemorrhage. In addition to its poor diagnostic accuracy, the GHSS is cumbersome and may not be practical in resource poor settings.

Three studies from LAMICs evaluated the Greek score and due to this small number, we did not include them in meta-analysis. The score was developed in Greece and is simple to use. It was found to be very accurate in its

initial validation study. Overall, the score showed poor diagnostic performance in this review. It is probable that the higher prevalence of hemorrhagic stroke in resource poor settings affected its accuracy.

We found a high prevalence of hemorrhagic stroke among studies from LAMICs included in this review (median prevalence 37.85%; IQR 30.25%-48.76%). This is in keeping with other reports of higher prevalence of hemorrhagic stroke in patients from poorer countries.[11,12] One author attributes this to inadequate control of blood pressure as well as a high occurrence of aneurysms and arteriovenous malformations in poorer countries.[11] Another author suggests that the dramatic presentation of hemorrhagic stroke inclines clinicians to request for CT scan hence the higher prevalence.[12] We propose that both scenarios may contribute.

Our review has various strengths. Firstly, the included studies had an appropriate spectrum of patients. Secondly, in all the included studies, the stroke scores and reference standards were performed on the same patient population and the whole sample received verification with the reference standard. Thus, partial verification bias and differential verification bias were adequately avoided. Thirdly, the time between administration of stroke scores and reference standards was short enough to avoid disease progression bias. In our estimation of diagnostic performance indices, we included equivocal test scores so as to avoid bias in the estimates.

There were a number of weaknesses. First, there was poor reporting of blinding across all studies, thus the bias attributable to this could not be determined. Secondly, included studies may have had selection bias as some studies excluded patients without CT scan results. While reasons for this exclusion were not elaborated in a majority of the reports, it is possible that in LAMICs, cost of CT scan was a hindrance to access as was shown in one of the studies.[26] Thirdly, a majority of studies did not report on the severity of stroke among included patients. This is of particular interest since the scores' performance may vary with stroke severity. Finally, some causes of stroke e.g. sickle cell disease and rheumatic heart disease are of significance in the pediatric age group.[11] However, no study assessed the utility of the scores in this group.

In conclusion, we do not find the SSS, GHSS and GSS to be of sufficient accuracy to warrant routine use (clinical or epidemiological). The GHSS is cumbersome and may not be practical in resource poor settings. While the GSS is simple to use, few studies from around the globe have evaluated it. The SSS has been widely validated but it

may need to be modified to suit different populations. We recommend the continued use of CT scan for differentiating stroke subtypes in the absence of a sufficiently accurate clinical stroke score and advice on investment in neuroimaging equipment for use in resource poor settings. Further, larger studies in which the cost of CT scan does not influence patient selection are required for validation of the SSS, GHSS and GSS especially in resource poor countries. Newer scores using patient populations from each region may be warranted.

Acknowledgements

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