

# Diagnostic accuracy of clinical tools for assessment of acute stroke: a systematic review

Daria Antipova (✉ [daria.antipova@abdn.ac.uk](mailto:daria.antipova@abdn.ac.uk))

University of Aberdeen <https://orcid.org/0000-0002-0267-1903>

Leila Eadie

University of Aberdeen Institute of Applied Health Sciences

Ashish Macaden

NHS Highland

Philip Wilson

University of Aberdeen Institute of Applied Health Sciences

---

## Research article

**Keywords:** acute cerebral ischaemia, clinical prediction rules, emergency care, intracerebral haemorrhage, large vessel occlusion, recanalization, stroke, scoring methods, thrombectomy, thrombolysis

**Posted Date:** July 12th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.11249/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published on September 4th, 2019. See the published version at <https://doi.org/10.1186/s12873-019-0262-1>.

# Abstract

**Introduction** Recanalisation therapy in acute ischaemic stroke is highly time-sensitive, and requires early identification of eligible patients to ensure better outcomes. Thus, a number of clinical assessment tools have been developed and this review examines their diagnostic capabilities. **Methods** Diagnostic performance of currently available clinical tools for identification of acute ischaemic and haemorrhagic strokes and stroke mimicking conditions was reviewed. A systematic search of the literature published in 2015-2018 was conducted using PubMed, EMBASE, Scopus and The Cochrane Library. Prehospital and in-hospital studies with a minimum sample size of 300 patients reporting diagnostic accuracy were selected. **Results** Twenty-five articles were included. Cortical signs (gaze deviation, aphasia and neglect) were shown to be significant indicators of large vessel occlusion (LVO). Sensitivity values for selecting subjects with LVO ranged from 23% to 99% whereas specificity was 24% to 97%. Clinical tools, such as FAST-ED, NIHSS, and RACE incorporating cortical signs as well as motor dysfunction demonstrated the best diagnostic accuracy. Tools for identification of stroke mimics showed sensitivity varying from 44% to 91%, and specificity of 27% to 98% with the best diagnostic performance demonstrated by FABS (90% sensitivity, 91% specificity). Hypertension and younger age predicted intracerebral haemorrhage whereas history of atrial fibrillation and diabetes were associated with ischaemia. There was a variation in approach used to establish the definitive diagnosis. Blinding of the index test assessment was not specified in about 50% of included studies. **Conclusions** A wide range of clinical assessment tools for selecting subjects with acute stroke has been developed in recent years. Assessment of both cortical and motor function using RACE, FAST-ED and NIHSS showed the best diagnostic accuracy values for selecting subjects with LVO. There were limited data on clinical tools that can be used to differentiate between acute ischaemia and haemorrhage. Diagnostic accuracy appeared to be modest for distinguishing between acute stroke and stroke mimics with optimal diagnostic performance demonstrated by the FABS tool. Further prehospital research is required to improve the diagnostic utility of clinical assessments with possible application of a two-step clinical assessment or involvement of simple brain imaging, such as transcranial ultrasonography.

## Rationale

Patients with acute stroke should have access to rapid assessment and early intervention with specialist care for optimal outcomes. Acute ischaemic stroke caused by a large vessel occlusion (LVO) is associated with high mortality rate of 80% [1] and can be optimally managed with intravenous (IV) thrombolysis followed by mechanical thrombectomy (MT). While IV thrombolysis can currently be provided in many general hospitals, MT can only be performed in specialised centres with neurointerventional facilities.

Recanalization therapy must be delivered within the first hours after symptom onset to improve functional outcome [2,3]. This requires a reliable triage system for early identification of subjects eligible for reperfusion therapy. It is also crucial to exclude intracranial haemorrhage and stroke-mimicking conditions before initiating therapy to avoid giving inappropriate or potentially life-threatening IV

thrombolysis. An ideal triage system could potentially be used in prehospital settings to determine both immediate care (particularly in remote areas) and transfer arrangements to appropriate hospital facilities.

An increasing number of studies assessing the diagnostic performance of clinical assessment tools has been seen in recent years. A systematic review of stroke recognition instruments in suspected stroke patients was performed by Rudd et al (2016) [4], and included studies that were published before 10 August 2015. The current review follows directly on from this date, and has been designed with the aim of answering the following questions:

1. What is the sensitivity and specificity of currently available clinical assessment tools for detecting subjects with ischaemic stroke due to LVO?
2. What is the sensitivity and specificity of currently available clinical assessment tools for diagnosing acute haemorrhagic stroke?
3. What is the sensitivity and specificity of currently available clinical assessment tools for differentiating between acute stroke and stroke-mimicking conditions?

## Methods

### *Protocol and registration*

The registered protocol can be accessed on PROSPERO, the international prospective register of systematic reviews:

[https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=112492](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=112492)

### *Eligibility criteria*

Inclusion and exclusion criteria are presented in Table 1.

Table 1. Review inclusion and exclusion criteria

### *Information sources*

A systematic search of the literature was conducted in October 2018, using a database-specific search strategy for each of the following electronic databases: *PubMed*, *EMBASE*, *Scopus* and *The Cochrane Library*.

### *Search strategy*

The search strategy included a combination of multiple iterations of MeSH and keyword terms relating to each component of the research questions as presented in Additional file 1.

The search was restricted to human studies, English language, adult participants, and publication years 2015-2018. This restricted publication date range was chosen to perform an updated analysis of the data available. A systematic review by Rudd et al (2016) included prospective studies and excluded retrospective studies, research within a known stroke population, tools that were exclusively used by ambulance dispatchers or with telecommunication systems [4]; however all of these were included in our systematic analysis.

### ***Study selection***

Titles of studies retrieved using the search strategy were screened by one of the review authors to identify studies that potentially met the inclusion criteria outlined in Table 1. The abstracts of those potentially eligible studies were independently assessed for eligibility by three review team members. Any disagreements between them over the eligibility of particular studies were resolved through discussion with a fourth reviewer.

Eligible papers were tabulated and used in the qualitative synthesis. Studies which reported diagnostic accuracy values such as sensitivity, specificity, and positive and negative predictive values were included in the quantitative meta-analysis.

### ***Data collection process***

A dedicated data extraction form was developed and used to collect relevant information from the included studies. The inclusion of information fields in the data collection form was guided by the review questions. The following components were assessed:

- study identification: name of the first author and publication year;
- setting for the application of the studied clinical tool: prehospital or in-hospital;
- inclusion/exclusion criteria for participants;
- sample size;
- name of the clinical assessment tool studied (where applicable);
- clinical information collected;
- background of personnel collecting and interpreting clinical information;
- diagnostic approach used to establish a final diagnosis;
- diagnostic accuracy values: true positive, true negative, false positive, false negative values, positive and negative predictive values, and/or positive and negative likelihood ratios, sensitivity and specificity.

As our analysis concerned only published data, no further data were sought from investigators.

### ***Risk of bias assessment in individual studies***

Two review authors qualitatively assessed included studies for a risk of bias and concerns regarding their applicability for each of three domains: patient selection, index test, and flow and timing, in accordance with the QUADAS-2 Tool quality assessment system [5]. A table summarising risk of bias and applicability concerns was constructed.

### ***Data synthesis***

The synthesis was performed in accordance with the Cochrane guidelines for diagnostic test accuracy reviews. The diagnostic accuracy data from each study were presented graphically by plotting sensitivities and specificities on a coupled column chart.

## **Results**

### ***Study selection***

The results of the study selection process are illustrated in Figure 1.

Figure 1. PRISMA flowchart. Outline of the study selection process using inclusion and exclusion criteria.

### ***Study characteristics***

The current review includes 25 new studies whereas adding to Rudd et al's review (2016) [4], which included 18 primary studies out of the total number of 5622 references identified. The main characteristics of the studies included in the current review are presented in Additional file 2.

In total, 25,642 cases were assessed across the included studies published between 2015-2018. Participants were recruited in the prehospital setting, or upon presentation to the hospital, or both. Of the included studies, 16/25 (64%) were retrospective.

### ***Risk of bias assessment in individual studies***

A summary of bias and applicability concerns is presented in Additional file 3.

All included studies recruited consecutive patients. Case-control methodology was avoided in all cases. Only studies with a high sample size of more than 300 participants according to Meader et al's (2014) classification [31] were considered for inclusion to ensure greater reliability of the study results. All included studies were analysed against the adequate blinding criterion.

In 13/25 (52%) papers it was not specifically mentioned or was judged to be unclear whether the results of clinical assessment (the index test) were interpreted independently from those tests that were used to make a final diagnosis (the reference test) [6,10,26,27,30,12,13,16,18,20,22–24].

The approach for establishing the final diagnosis was described in all included studies. Hospital discharge diagnosis was referred to as the gold standard in six papers, brain or cerebral vessel imaging alone in 14 cases, and five papers used clinical assessment together with imaging to establish the definitive diagnosis.

### ***Diagnostic accuracy of clinical tools in selecting subjects with LVO***

More than 20 different clinical assessment tools with optimal cut-offs for selecting subjects with ischaemic stroke due to LVO were analysed in this review (Table 2).

Table 2. Diagnostic accuracy values of clinical tools for selecting subjects with large vessel occlusion.

Sensitivity values ranged from 23% (NIHSS subitem LoC 1a) to 99% (NIHSS4, NIHSS6, a combination of reduced level of consciousness with inability to answer questions, facial weakness, arm weakness, sensation loss, and aphasia). Specificity ranged from 24% (OoH-NIHSS $\geq$ 1, CPSS1) to 97% (G-FAST=4). For simplicity, only those tools showing both sensitivity and specificity values 80% (an arbitrarily chosen threshold) were selected to be plotted (Figure 2).

Figure 2. Bar chart. Sensitivity and specificity values across the clinical tools for selecting subjects with large vessel occlusion.

It was suggested by Beume et al. (2018) [6] that cortical signs such as gaze deviation, aphasia or agnosia, and/or neglect were more accurate predictors of LVO than motor deficit alone (PPV 60%, NPV 94%). However, as demonstrated in Figure 2, FAST-ED4 (PPV 80%, NPV 100%), NIHSS10 (PPV 78%, NPV 99%), and RACE5 (PPV 81%, NP 99%) had the best diagnostic accuracy for selecting subjects with LVO. All three clinical assessment tools incorporate cortical signs as well as motor dysfunction.

The best sensitivity value of the combination of motor deficit and cortical signs incorporated into the Finnish Prehospital Stroke Scale (face drooping, limb weakness, speech difficulty, visual disturbance, and conjugate eye deviation) was for detection of proximal M1 occlusions (100%) and the lowest – for M2 and basilar artery – were 13% and 22%, respectively [22].

Moore et al. (2016) demonstrated that presence of all four components forming a combination of reduced consciousness level, lower limb weakness, dysarthria, and gaze deviation had sensitivity of 96% and specificity of 39% for LVO when compared with computed tomography angiography (CTA) [21]. Thus, those who do not have all four clinical features are less likely to have LVO, and therefore would not require CTA, decreasing the need for this test by about 32%. This approach might also contribute to decisions about immediate transfer to an endovascular centre for MT.

### ***Diagnostic accuracy of clinical tools in detecting acute haemorrhagic stroke***

The paper by Jin et al. (2016) [15] was the single eligible study for the present review that aimed to distinguish between two main subtypes of stroke – ischaemic stroke and haemorrhage. A total of 1989

cases from the Chinese population with suspected first-ever acute stroke were analysed. They proposed a discriminant function model based on the following clinical assessment findings: age above 65 years, past medical history of diabetes (DM), atrial fibrillation (AF), systolic blood pressure (SBP) above 180 mmHg, and vomiting at onset. It has shown a higher sensitivity but lower specificity for selecting subjects with ischaemic stroke (42-75.7% and 63.3-93.6%, respectively). Diagnostic accuracy values for haemorrhage were the opposite of the above: low sensitivity with higher specificity (58.5-93.6% and 42-79.2%, respectively). It has also been suggested that a history of AF and DM were more likely to be associated with ischaemic stroke, whereas high SBP and younger age were associated with haemorrhage.

### ***Diagnostic accuracy of clinical tools for differentiating between acute stroke and stroke-mimicking conditions***

There was a significant variation in diagnostic accuracy of tools designed for distinguishing between acute stroke and stroke mimics as shown in Figure 3.

Figure 3. Bar chart. Sensitivity and specificity values of clinical tools for differentiating between acute stroke and stroke-mimicking conditions.

Sensitivity values varied from 44% (LAPSS 1998) to 91% (sNIHSS-EMS). Specificity ranged from 27% (MPDS) to 98% (LAPSS 1998) (Table 3). FABS showed the best diagnostic accuracy values with 90% sensitivity and 91% specificity [11].

Table 3. Diagnostic accuracy values of clinical tools for selecting subjects with acute stroke and stroke-mimicking conditions.

The MPDS tool was developed to facilitate early identification of stroke or transient ischaemic attack by emergency medical dispatchers to enable early notification to receiving hospitals, and demonstrated satisfactory sensitivity of 86% but low specificity of 27% (PPV 20%, NPV 90%). Similarly, sNIHSS-EMS, which consisted of six NIHSS items selected as "suitable for prehospital use" [25] (level of consciousness, facial palsy, motor arm/leg, sensory, language and dysarthria), had the highest sensitivity value (91%) when compared with other clinical assessment tools but fairly low specificity (52%) (PPV 43%, NPV 93%). In contrast, LAPSS 1998 and LAPSS 2000 had the highest specificity (98% and 97%, respectively) but the lowest sensitivity (44% and 49%, respectively) values among the other tools [20,24].

The FABS tool was developed for identification of subjects with stroke-mimicking conditions and negative brain CT findings in the emergency department. The total score is calculated based on the absent risk factors for stroke (AF, hypertension, advanced age) and presence of sensory disturbance with no motor deficit. FABS showed the best overall diagnostic accuracy values of 90% sensitivity and 91% specificity (PPV 87%, NPV 93%) [11].

## **Discussion**

MT preceded by IV thrombolysis is considered the standard of care for patients with ischaemic stroke due to LVO, and can be given up to 16-24 hours from stroke onset according to the most recent guidelines [32]. Currently in the UK, patients with ischaemic stroke are eligible for IV thrombolysis within 4.5 hours from the last time they were known to be unaffected. Early initiation of reperfusion therapy is associated with better outcome [3] but this can be jeopardised by pre-, inter- and intra-hospital delays [33]. Therefore, a “drip and ship” theoretical model has been suggested as the optimal option, especially for areas with long transport times, as it involves direct transfer to a regional endovascular centre following early IV thrombolysis [34], however further evaluation is required.

A reliable triage system that could allow emergency transfer of patients eligible for MT directly to a regional centre with neurointerventional facilities could transform stroke care. It is therefore important to ensure reliable exclusion of stroke-mimicking conditions and intracranial haemorrhages as part of the patient selection process to avoid providing inappropriate treatment and associated complications. Thus, several clinical assessment tools have been designed for this purpose.

The present systematic review represents an update of Rudd et al’s review (2016) [4] with an extension of the data to 2018 analysed. It attempted to evaluate the diagnostic accuracy of clinical assessment tools for (1) selecting subjects with ischaemic stroke due to LVO who would benefit from a direct transfer to a regional endovascular centre; (2) differentiating between two main subtypes of stroke – ischaemic stroke and haemorrhage, and (3) distinguishing between acute stroke cases and stroke mimics.

All reviewed studies had a sample size of 300 consecutive participants or more [31] leading to higher reliability of reported findings. There were however some limitations found in the included studies. In about 50% of the analysed papers, it was unclear whether the index test was interpreted independently from the reference standard. Although the method used for establishing a final diagnosis was specified in all studies, there was a discrepancy between studies as in 15 cases imaging alone was referred to as gold standard, whereas in the remaining 10 papers it was a combination of clinical assessment and imaging findings / final diagnosis at discharge.

As proposed by Beume et al. (2018) [6], cortical signs such as aphasia or neglect are more accurate predictors of LVO than motor deficit alone. In contrast, the POMONA scale which includes only three items suggestive of cortical involvement: gaze deviation, expressive aphasia, and neglect, showed a low specificity of 50% but high sensitivity (98%) (PPV 21%, NPV 99%) [23]. However, adding motor deficit, for example, as assessed by FAST-ED, RACE or NIHSS scales, led to better diagnostic accuracy [9,14,15,21,25,27–32].

Modest diagnostic accuracy was seen in clinical assessment tools aiming to distinguish between acute stroke and stroke mimics. Sensitivity values varied from 44% to 91%, whereas specificity values were 27% to 98%. The FABS tool was designed specifically for detecting stroke mimics and included additional clinical information, such as atrial fibrillation compared to other well-established tools, for example, ROSIER. This scoring system demonstrated high sensitivity and specificity rates of about 90% (PPV 87%, NPV 93%) [11].

No studies included in the current systematic review aimed to select subjects with haemorrhagic stroke. A study by Jin et al. (2016) suggested however that clinical assessment findings such as hypertension and younger age were indicative of haemorrhage, whereas a history of AF and DM were more likely to be associated with ischaemic stroke [15].

There are a few limitations of currently available tools that possibly prevent them from being widely accepted. First, their specificity rates for LVO remain quite low, which could potentially lead to inappropriate transportation of patients at high cost [28]. Second, many studies were designed in such a way that patients with haemorrhage and/or stroke-mimicking conditions were excluded, which therefore would preclude these clinical tools from being applied to prehospital settings [6]. It might be beneficial to use an additional diagnostic tool in combination with clinical assessment that could provide valuable information and increase the accuracy of such a triage system.

An ideal clinical assessment tool would be a simple method that could be equally used in prehospital settings and in emergency department with high predictive values. It might be possible that a two-step approach using two different clinical assessment tools at the prehospital stage could be considered as an alternative option. The first step would be to select subjects with acute stroke who would benefit from reperfusion therapy and to exclude stroke mimicking conditions and acute intracranial haemorrhage. For this purpose, a tool with higher specificity should be considered, for example G-FAST [22]. A tool with very high specificity might allow prehospital thrombolysis to be offered to selected patients in remote areas in line with management of patients with S-T elevation myocardial infarction [35]. Thereafter, a decision on transferring subjects with suspected LVO to a specialised centre would be made on the basis of the clinical assessment score with high sensitivity value, such as NIHSS or a combination of clinical assessment findings as suggested by Moore et al. (reduced level of consciousness with inability to answer questions, facial weakness, arm weakness; sensation loss, and aphasia) [21,23,28]. However, this approach requires further validation.

Another possibility that could help increase triage accuracy is transcranial Doppler, which has been shown to detect occlusions in the major cerebral arteries with 68-100% sensitivity and 78-99% specificity [36–38]. It is a relatively inexpensive and readily portable diagnostic tool that takes on average not more than 15 minutes to complete an examination of the cerebral vessels [39], and can be used in prehospital settings, potentially with remote diagnostic support [40–42]. However, further assessment and validation of this proposed system is required.

## **Conclusion**

The diagnostic accuracy of clinical assessment tools published in 2015-2018 has been evaluated in the present systematic analysis. There were extensive data on clinical assessment findings that could assist in the diagnostic process. Diagnostic reliability of currently available tools varied across the studies. The best diagnostic performance was demonstrated by clinical assessment tools that incorporated both assessment of cortical signs and motor dysfunction, such as FAST-ED, RACE and NIHSS. There were limited data on clinical systems that can be used to differentiate between acute ischaemia and

haemorrhage. Diagnostic accuracy appeared to be modest for distinguishing between acute stroke cases and stroke mimics with the optimal diagnostic performance demonstrated by the FABS tool.

Further research is required to establish a novel triage system, possibly with the application of a two-step clinical assessment or a simple brain imaging modality, such as transcranial ultrasonography, to ensure diagnostic accuracy sufficient to guide management of patients in prehospital settings.

## List Of Abbreviations

AF – atrial fibrillation, DM – diabetes mellitus, IV – intravenous, LVO – large vessel occlusion, MT – mechanical thrombectomy, NPV – negative predictive value, PPV – positive predictive value, SBP – systolic blood pressure, Se – sensitivity, Sp - specificity.

## Declarations

### *Ethics approval and consent to participate*

Not applicable.

### *Consent for publication*

Not applicable.

### *Availability of data and materials*

Materials are available from the corresponding author upon request.

### *Competing interests*

The authors declare no competing interests.

### *Funding*

No specific funding was received for this work.

### *Authors' contributions*

All four authors were involved in the conceptualisation and development of the methodology. DA performed a complete literature search, assessment of full text of articles for eligibility and data extraction. Risk of bias assessment in individual studies was performed by DA and LE. DA performed a formal analysis of the collected data and writing of the original draft (including all tables and figures). DA finalised all drafts in consultation with LE, AM and PW. LE, AM and PW reviewed the manuscript and approved its final version.

### *Acknowledgements*

This work is part of a PhD project supported by the University of Aberdeen's Elphinstone Scholarship Programme. LE is funded by the European Space Agency SatCare grant.

The authors would like to thank Hannah Thomas and Emma Foster for the help with assessing full text of articles for eligibility for the current review.

## References

1. Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R. "Malignant" middle cerebral artery territory infarction: clinical course and prognostic signs. *Arch Neurol*. 1996;53:309–15.
2. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet (London, England)*. 2016;387:1723–31.
3. Saver JL, Fonarow GC, Smith EE, Reeves MJ, Grau-Sepulveda M V, Pan W, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. *JAMA*. 2013;309:2480–8.
4. Rudd M, Buck D, Ford GA, Price CI. A systematic review of stroke recognition instruments in hospital and prehospital settings. *Emerg Med J*. 2016;33:818–22.
5. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;155:529–36.
6. Beume L-A, Hieber M, Kaller CP, Nitschke K, Bardutzky J, Urbach H, et al. Large Vessel Occlusion in Acute Stroke. *Stroke*. 2018;49:2323–9.
7. Carrera D, Campbell BC V, Cortes J, Gorchs M, Querol M, Jimenez X, et al. Predictive Value of Modifications of the Prehospital Rapid Arterial Occlusion Evaluation Scale for Large Vessel Occlusion in Patients with Acute Stroke. *J Stroke Cerebrovasc Dis*. 2017;26:74–7.
8. Chen K, Schneider ALC, Llinas RH, Marsh EB. Keep it simple: vascular risk factors and focal exam findings correctly identify posterior circulation ischemia in "dizzy" patients. *BMC Emerg Med*. 2016;16:37.
9. Clawson JJ, Scott G, Gardett I, Youngquist S, Taillac P, Fivaz C, et al. Predictive Ability of an Emergency Medical Dispatch Stroke Diagnostic Tool in Identifying Hospital-Confirmed Strokes. *J Stroke Cerebrovasc Dis*. 2016;25:2031–42.
10. Demeestere J, Garcia-Esperon C, Lin L, Bivard A, Ang T, Smoll NR, et al. Validation of the National Institutes of Health Stroke Scale-8 to Detect Large Vessel Occlusion in Ischemic Stroke. *J Stroke Cerebrovasc Dis*. 2017;26:1419–26.

11. Goyal N, Tsivgoulis G, Male S, Metter EJ, Iftikhar S, Kerro A, et al. FABS: An Intuitive Tool for Screening of Stroke Mimics in the Emergency Department. *Stroke*. 2016;47:2216–20.
12. Gropen TI, Boehme A, Martin-Schild S, Albright K, Samai A, Pishanidar S, et al. Derivation and Validation of the Emergency Medical Stroke Assessment and Comparison of Large Vessel Occlusion Scales. *J Stroke Cerebrovasc Dis*. 2018;27:806–15.
13. Hastrup S, Damgaard D, Johnsen SP, Andersen G. Prehospital acute stroke severity scale to predict large artery occlusion: Design and comparison with other scales. *Stroke*. 2016;47:1772–6.
14. Heldner MR, Hsieh K, Broeg-Morvay A, Mordasini P, Bühlmann M, Jung S, et al. Clinical prediction of large vessel occlusion in anterior circulation stroke: mission impossible? *J Neurol*. 2016;263:1633–40.
15. Jin HQ, Wang JC, Sun YA, Lyu P, Cui W, Liu YY, et al. Prehospital identification of stroke subtypes in Chinese rural areas. *Chin Med J (Engl)*. 2016;129:1041–6.
16. Katz BS, McMullan JT, Sucharew H, Adeoye O, Broderick JP. Design and Validation of a Prehospital Scale to Predict Stroke Severity: Cincinnati Prehospital Stroke Severity Scale. *Stroke*. 2015;46:1508–12.
17. Kummer BR, Gialdini G, Sevush JL, Kamel H, Patsalides A, Navi BB. External Validation of the Cincinnati Prehospital Stroke Severity Scale. *J Stroke Cerebrovasc Dis*. 2016;25:1270–4.
18. Kuroda R, Nakada T, Ojima T, Serizawa M, Imai N, Yagi N, et al. The TriAGE+ Score for Vertigo or Dizziness: A Diagnostic Model for Stroke in the Emergency Department. *J Stroke Cerebrovasc Dis*. 2017;26:1144–53.
19. Lima FO, Silva GS, Furie KL, Frankel MR, Lev MH, Camargo ECS, et al. Field Assessment Stroke Triage for Emergency Destination: A Simple and Accurate Prehospital Scale to Detect Large Vessel Occlusion Strokes. *Stroke*. 2016;47:1997–2002.
20. Mao H, Lin P, Mo J, Li Y, Chen X, Rainer TH, et al. Development of a new stroke scale in an emergency setting. *BMC Neurol*. 2016;16:168.
21. Moore RD, Jackson JC, Venkatesh SL, Quarfordt SD, Baxter BW. Revisiting the NIH Stroke Scale as a screening tool for proximal vessel occlusion: Can advanced imaging be targeted in acute stroke? *J Neurointerv Surg*. 2016;8:1208–10.
22. Ollikainen JP, Janhunen H V, Tynkkynen JA, Mattila KM, Halinen MM, Oksala NK, et al. The Finnish Prehospital Stroke Scale Detects Thrombectomy and Thrombolysis Candidates-A Propensity Score-Matched Study. *J Stroke Cerebrovasc Dis*. 2018;27:771–7.
23. Panichpisal K, Nugent K, Singh M, Rovin R, Babygirija R, Moradiya Y, et al. Pomona Large Vessel Occlusion Screening Tool for Prehospital and Emergency Room Settings. *Interv Neurol*. 2018;7:196–203.

24. Purrucker JC, Hametner C, Engelbrecht A, Bruckner T, Popp E, Poli S. Comparison of stroke recognition and stroke severity scores for stroke detection in a single cohort. *J Neurol Neurosurg Psychiatry*. 2015;86:1021–8.
25. Purrucker JC, Härtig F, Richter H, Engelbrecht A, Hartmann J, Auer J, et al. Design and validation of a clinical scale for prehospital stroke recognition, severity grading and prediction of large vessel occlusion: The shortened NIH Stroke Scale for emergency medical services. *BMJ Open*. 2017;7.
26. Rodríguez-Pardo J, Fuentes B, Alonso de Leciñana M, Ximénez-Carrillo Á, Zapata-Wainberg G, Álvarez-Fraga J, et al. The Direct Referral to Endovascular Center criteria: a proposal for pre-hospital evaluation of acute stroke in the Madrid Stroke Network. *Eur J Neurol*. 2017;24:509–15.
27. Scheitz JF, Abdul-Rahim AH, Macisaac RL, Cooray C, Sucharew H, Kleindorfer D, et al. Clinical Selection Strategies to Identify Ischemic Stroke Patients with Large Anterior Vessel Occlusion: Results from SITS-ISTR (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry). *Stroke*. 2017;48:290–7.
28. Turc G, Maier B, Naggara O, Seners P, Isabel C, Tisserand M, et al. Clinical Scales Do Not Reliably Identify Acute Ischemic Stroke Patients With Large-Artery Occlusion. *Stroke*. 2016;47:1466–72.
29. Vanacker P, Heldner MR, Amiguet M, Faouzi M, Cras P, Ntaios G, et al. Prediction of Large Vessel Occlusions in Acute Stroke: National Institute of Health Stroke Scale Is Hard to Beat. *Crit Care Med*. 2016;44:e336-43.
30. Zhao H, Pesavento L, Coote S, Rodrigues E, Salvaris P, Smith K, et al. Ambulance clinical triage for acute stroke treatment paramedic triage algorithm for large vessel occlusion. *Stroke*. 2018;49.
31. Meader N, King K, Llewellyn A, Norman G, Brown J, Rodgers M, et al. A checklist designed to aid consistency and reproducibility of GRADE assessments: development and pilot validation. Vol. 3, *Systematic Reviews*. 2014. p. 82.
32. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2018;49:e46–110.
33. Sun C-HJ, Nogueira RG, Glenn BA, Connelly K, Zimmermann S, Anda K, et al. “Picture to puncture”: a novel time metric to enhance outcomes in patients transferred for endovascular reperfusion in acute ischemic stroke. *Circulation*. 2013;127:1139–48.
34. Holodinsky JK, Williamson TS, Demchuk AM, Zhao H, Zhu L, Francis MJ, et al. Modeling Stroke Patient Transport for All Patients With Suspected Large-Vessel Occlusion. *JAMA Neurol*. 2018;75:1477–86.

35. Pedley DK, Beedie S, Ferguson J. Mobile telemetry for pre-hospital thrombolysis: problems and solutions. *J Telemed Telecare*. 2005;11 Suppl 1:78–80.
36. Tsivgoulis G, Sharma VK, Lao AY, Malkoff MD, Alexandrov A V. Validation of transcranial Doppler with computed tomography angiography in acute cerebral ischemia. *Stroke*. 2007;38:1245–9.
37. Wada K, Kimura K, Minematsu K, Yasaka M, Uchino M, Yamaguchi T. Combined carotid and transcranial color-coded sonography in acute ischemic stroke. *Eur J Ultrasound*. 2002;15:101–8.
38. Tsivgoulis G, Sharma VK, Hoover SL, Lao AY, Ardelt AA, Malkoff MD, et al. Applications and advantages of power motion-mode Doppler in acute posterior circulation cerebral ischemia. *Stroke*. 2008;39:1197–204.
39. Gerriets T, Goertler M, Stolz E, Postert T, Sliwka U, Schlachetzki F, et al. Feasibility and validity of transcranial duplex sonography in patients with acute stroke. *J Neurol Neurosurg Psychiatry*. 2002;73:17–20.
40. Eadie L, Regan L, Mort A, Shannon H, Walker J, MacAden A, et al. Telestroke assessment on the move: prehospital streamlining of patient pathways. *Stroke*. 2015;46:e38-40.
41. Eadie L, Mulhern J, Regan L, Mort A, Shannon H, Macaden A, et al. Remotely supported prehospital ultrasound: A feasibility study of real-time image transmission and expert guidance to aid diagnosis in remote and rural communities. *J Telemed Telecare*. 2018;24:616-22.
42. Mort A, Eadie L, Regan L, Macaden A, Heaney D, Bouamrane M-M, et al. Combining transcranial ultrasound with intelligent communication methods to enhance the remote assessment and management of stroke patients: Framework for a technology demonstrator. *Health Informatics J*. 2016;22:691–701.

## Tables

Table 1. Review inclusion and exclusion criteria

Domain	Inclusion	Exclusion
Study type	Comparative observational studies	Case reports
	Prospective observational studies	Selected case series
	Cohort studies	Literature review
	Unselected case series	Conference proceedings
		Full text unavailable
Participants	Human	Non-human subjects
	Adults	Exclusively paediatric patients  Mixed paediatric and adult populations (where paediatric and adult groups are not possible to identify separately)
	Patients with ischaemic stroke (including patients with LVO), acute haemorrhagic stroke, and/or stroke-mimicking conditions and transient ischaemic attack	Exclusively patients with non-stroke conditions, such as sickle cell disease, arteriovenous malformation, traumatic brain injury, cerebral tumour, subarachnoid haemorrhage, vertigo etc.
	Sample size ≥ 300 participants[31]	Sample size < 300 participants
Setting	Prehospital and in-hospital	
Procedure	Use of a clinical assessment tool, including clinical scales, individual symptoms and signs designed for identification of patients with ischaemic stroke, including subjects with LVO, acute haemorrhagic stroke, and/or stroke-mimicking conditions	Exclusively assessing the diagnostic accuracy of a brain imaging modality for identification of patients with acute stroke and/or stroke-mimicking conditions
Aims/outcomes	Diagnostic accuracy of clinical tools designed for identification of patients with ischaemic stroke, including subjects with LVO, acute haemorrhagic stroke, and/or stroke mimicking conditions	Exclusively assessing the prognosis of functional disability caused by a stroke
	Diagnostic accuracy of clinical tools designed for differentiation between two main subtypes of stroke - ischaemic and haemorrhagic	Exclusively evaluating factors associated with misdiagnosis of stroke
		Exclusively diagnosing stroke patients with

		no assessment of clinical factors
Publication	2015 - 2018	Before January 2015
	In English	In languages other than English

Table 2. Diagnostic accuracy values of clinical tools for selecting subjects with large vessel occlusion.

Clinical assessment	Se	Sp	PPV	NPV	AUC
ACT-FAST [30]	0.85	0.93	0.53	0.99	0.90
aNIHSS 01 [28]	0.95	0.31	0.40	0.92	-
a-NIHSS item profile A 03 [14]	0.64	0.69	0.76	0.55	0.66
a-NIHSS item profile B 02 [14]	0.75	0.64	0.76	0.63	0.71
a-NIHSS item profile C 02 [14]	0.51	0.73	0.75	0.50	0.60
a-NIHSS item profile D 02 [14]	0.76	0.61	0.75	0.62	0.70
a-NIHSS item profile E 02 [14]	0.71	0.65	0.76	0.60	0.68
Aphasia; Neglect/gaze deviation [6]	0.91	0.70	0.60	0.94	0.77
Arm weakness [23]	0.96	0.41	0.18	0.99	0.68
Arm weakness; Leg weakness; Dysarthria [21]	0.92	0.44	0.28	0.96	-
Bernese score 1 05 [14]	0.73	0.79	0.85	0.66	0.76
Bernese score 2 02 [14]	0.71	0.80	0.84	0.64	0.74
Bernese score 3 02 [14]	0.67	0.86	0.88	0.63	0.75
Bernese score 4 01 [14]	0.67	0.83	0.86	0.63	0.74
Bernese score 5 03 [14]	0.77	0.83	0.87	0.70	0.79
CPSS 01 [28]	0.96	0.24	0.38	0.93	-
CPSS 02 [19,23]	0.56- 0.92	0.81- 0.85	0.40- 0.65	0.78- 0.99	0.75- 0.78
CPSS1 02 [14]	0.59	0.77	0.80	0.55	0.66
CPSS2 02 [14]	0.73	0.71	0.79	0.63	0.72
CPSSS 01 [14,17]	0.60- 0.86	0.80- 0.87	0.88	0.59	0.71
CPSSS 02 [13,16,17,25,28]	0.59- 0.83	0.40- 0.89	0.66- 0.77	0.77- 0.83	0.72- 0.80
CPSSS 03 [17]	0.51	0.93	-	-	-
CPSSS =4 [17]	0.25	0.96	-	-	-
C-STAT [22]	0.54	0.91	0.45	0.93	0.79
C-STAT 02 [12,27,30]	0.47- 0.85	0.68- 0.85	0.35- 0.40	0.88- 0.98	0.65- 0.85
DIRECT criteria [26]	0.74	0.92	0.43	0.98	0.91
EMSA 03 [12]	0.75	0.50	-	-	0.69
Expressive aphasia [23]	0.39	0.64	0.13	0.88	0.52
Facial weakness [23]	0.93	0.50	0.20	0.98	0.72
FAST=3 [27]	0.84	0.44	0.32	0.90	0.53
FAST-ED [22]	0.62	0.84	0.40	0.94	0.84

FAST-ED 03 [19]	0.71	0.78	0.62	0.84	0.76
FAST-ED 04 [12,19,25,30]	0.42- 0.96	0.82- 0.90	0.24- 0.80	0.82- 1.00	0.64- 0.91
FPSS [22]	0.54	0.91	0.47	0.93	0.85
Gaze deviation [23]	0.84	0.73	0.30	0.97	0.79
G-FAST 03 [22,27]	0.75- 0.89	0.39- 0.83	0.31- 0.39	0.92- 0.96	0.51- 0.85
G-FAST =4 [22]	0.36	0.97	0.59	0.91	
LAMS 04 [13,23,30]	0.57- 0.94	0.74- 0.85	0.28- 0.66	0.78- 0.99	0.70- 0.89
mNIHSS 05 [14]	0.78	0.76	0.85	0.69	0.78
mNIHSS 07 [28]	0.77	0.77	0.62	0.87	-
MPSS 03 [28]	0.84	0.65	0.54	0.89	-
Neglect [23]	0.88	0.69	0.28	0.98	0.79
Neglect/gaze deviation [23]	0.95	0.64	0.27	0.99	0.79
NIHSS 04 [23,28]	0.93- 0.99	0.24- 0.46	0.15- 0.46	0.93- 0.99	0.62
NIHSS 05 [28]	0.90	0.54	0.49	0.92	-
NIHSS 06 [12,19,23,28]	0.66- 0.99	0.39- 0.70	0.18- 0.55	0.85- 1.00	0.68- 0.72
NIHSS 07 [14,28]	0.81	0.72- 0.77	0.59- 0.84	0.72- 0.89	0.79
NIHSS 08 [23,25]	0.72- 0.98	0.48- 0.81	0.21- 0.71	0.82- 0.99	0.71
NIHSS 09 [12,25,28]	0.53- 0.81	0.72- 0.85	0.59- 0.75	0.81- 0.89	-
NIHSS 010 [19,23,25,28,29]	0.64- 0.98	0.56- 0.88	0.23- 0.78	0.80- 0.99	0.75- 0.84
NIHSS 014 [28]	0.61	0.88	0.72	0.82	-
NIHSS-8 [22]	0.63	0.89	0.44	0.94	0.84
NIHSS-8 08 [10]	0.81	0.75	0.52	0.92	0.82
NIHSS subitem - LoC (1a) [23]	0.23	0.81	0.14	0.88	0.52
NIHSS subitem - LoC (1b) [23]	0.60	0.56	0.16	0.91	0.58
NIHSS subitem - LoC (1c) [23]	0.49	0.68	0.17	0.91	0.59
NIHSS; Absence of prestroke handicap (mRS≤2); Hemineglect; AF; Female sex;	0.84	0.68- 0.71	0.41- 0.54	0.92- 0.94	0.84

Total score cut-off ¶16 [29]					
NIHSS symptom profile A or B [27]	0.76	0.65	0.40	0.90	0.68
OoH-NIHSS ≥1 [28]	0.96	0.24	0.38	0.93	-
PASS [22]	0.69	0.85	0.40	0.95	0.81
PASS ¶2 [13,23,25,27,30]	0.64- 0.96	0.59- 0.84	0.33- 0.74	0.81- 1.00	0.63- 0.89
Pomona ¶1 [23]	0.98	0.50	0.21	0.99	0.74
Pomona ¶2 [23]	0.86	0.71	0.71	0.97	0.79
RACE ¶3 [14]	0.74	0.80	0.85	0.67	0.77
RACE ¶5 [7,12,13,19,25-28,30]	0.46- 0.92	0.68- 0.91	0.27- 0.81	0.78- 0.99	0.67- 0.90
RACE V1 ¶4 [7]	0.85	0.56	-	-	0.81
RACE V2 ¶4 [7]	0.85	0.62	-	-	0.79
RACE V3 ¶3 [7]	0.89	0.48	-	-	0.78
RACE V4 ¶4 [7]	0.87	0.56	-	-	0.80
RACE V5 ¶4 [7]	0.83	0.57	-	-	0.79
RACE V6 ¶4 [7]	0.83	0.63	-	-	0.77
RACE V7 ¶3 [7]	0.87	0.51	-	-	0.76
Reduced level of consciousness with inability to answer questions; Leg weakness; Dysarthria; Gaze deviation [21]	0.96	0.39	0.27	0.98	-
Reduced level of consciousness with inability to answer questions; Facial weakness; Arm weakness; Sensation loss; Aphasia [21]	0.99	0.28	0.99	0.25	-
Reduced level of consciousness with inability to answer questions; Leg weakness; Neglect; Gaze deviation [21]	0.85	0.45	0.26	0.93	-
rNIHSS (profile A, B, C, D or E vs. profile F) [28]	0.83	0.61	0.51	0.88	-
ROSIER ¶4 [28]	0.79	0.76	0.61	0.88	-
sCPSSS (severe arm weakness, conjugate gaze deviation) ¶1 [17]	0.83	0.83			
sCPSSS ¶2 [17]	0.59	0.90			

sCPSSS =3 [17]	0.50	0.94			
sNIHSS-1 01 [14]	0.63	0.80	0.83	0.59	0.70
sNIHSS-1 02 [28]	0.66	0.81	0.63	0.83	
sNIHSS-5 02 [14]	0.76	0.77	0.84	0.68	0.76
sNIHSS-5 03 [25]	0.69	0.81	0.70	0.80	0.80
sNIHSS-5 04 [28]	0.72	0.80	0.63	0.85	-
sNIHSS-8 04 [14]	0.78	0.76	0.84	0.69	0.77
sNIHSS-8 06 [25,28]	0.64- 0.77	0.78- 0.88	0.63- 0.78	0.79- 0.88	0.82
sNIHSS-EMS 06 [25]	0.70	0.81	0.70	0.81	0.81
VAN [23]	0.95	0.56	0.23	0.99	0.77
Visual field defect [23]	0.88	0.75	0.33	0.98	0.82
3I-SS [13,22]	0.42- 0.50	0.92- 0.93	0.45- 0.77	0.77- 0.92	0.71- 0.78
3I-SS 01 [14]	0.73	0.78	0.83	0.65	0.75
3I-SS 02 [27]	0.65	0.72	0.42	0.87	0.71
3I-SS 04 [12,25,28]	0.19- 0.40	0.94- 0.95	0.74- 0.85	0.71- 0.74	0.65- 0.80

Abbreviations: NPV – negative predictive value; PPV – positive predictive value; Se – sensitivity; Sp – specificity.

Table 3. Diagnostic accuracy values of clinical tools for selecting subjects with acute stroke and stroke-mimicking conditions.

Clinical tool	Target condition	Se	Sp	PPV	NPV	AUC
CPSS [24]	Acute stroke	0.83	0.69	0.50	0.91	-
FABS <sup>3</sup> [11]	Stroke mimic	0.90	0.91	0.87	0.93	-
FAST [20,24]	Acute stroke	0.76-0.85	0.64-0.68	0.50-0.93	0.30-0.92	0.70
GZSS <sup>1.5</sup> [20]	Acute stroke	0.83	0.74	0.95	0.42	0.87
LAPSS [20]	Acute stroke	0.56	0.88	0.97	0.25	-
LAPSS 1998 [24]	Acute stroke	0.44	0.98	0.87	0.82	-
LAPSS 2000 [24]	Acute stroke	0.49	0.97	0.87	0.84	-
MASS [24]	Acute stroke	0.63	0.94	0.79	0.87	-
Med PACS [24]	Acute stroke	0.71	0.92	0.76	0.90	-
MPDS [9]	Acute stroke	0.86	0.27	0.20	0.90	-
ROSIER [20,24]	Acute stroke	0.78-0.80	0.71-0.79	0.59-0.94	0.34-0.91	0.77
sNIHSS-EMS [25]	Acute stroke	0.91	0.52	0.43	0.93	-
TriAGe+ <sup>10</sup> [18]	Acute stroke	0.78	0.72	0.57	0.87	0.78

Abbreviations: NPV - negative predictive value; PPV - positive predictive value; Se - sensitivity; Sp - specificity.

## Additional Material Legend

Additional file 1.docx Search strategy, table

Additional file 2.docx Characteristics of included studies, table

Additional file 3.docx Risk of bias and applicability concerns summary, table

## Figures

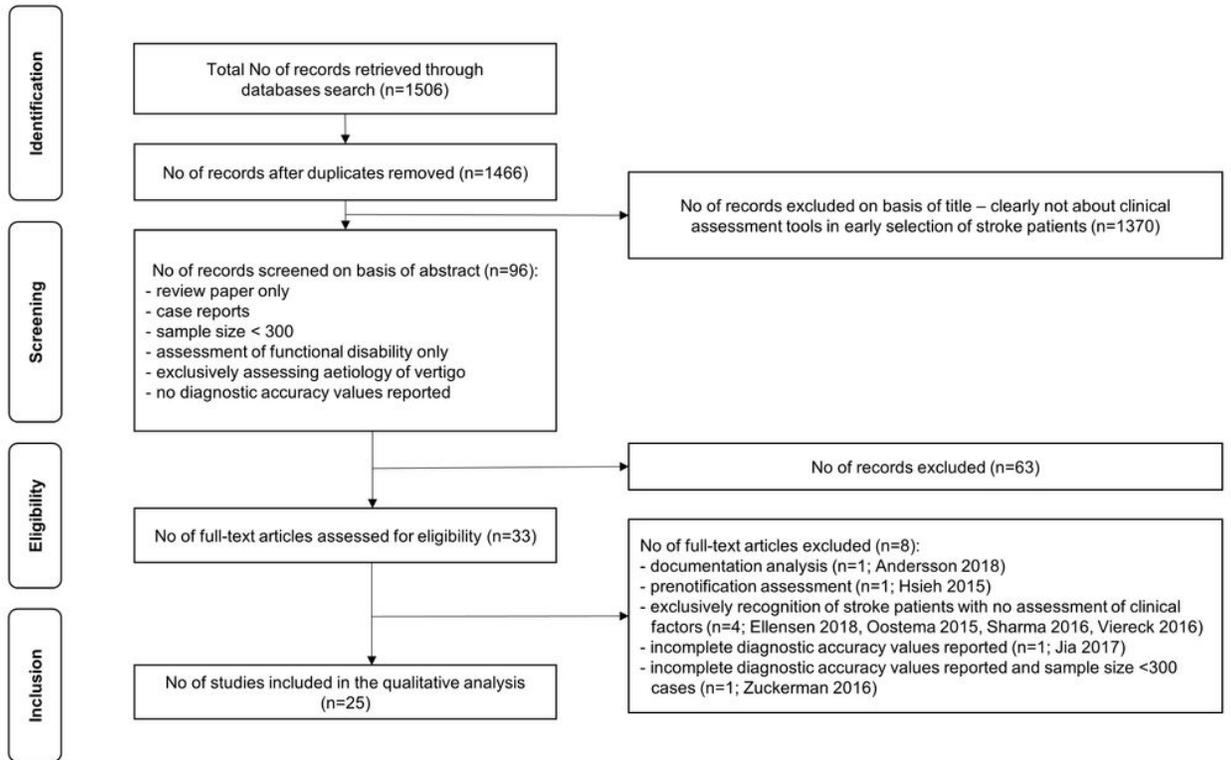
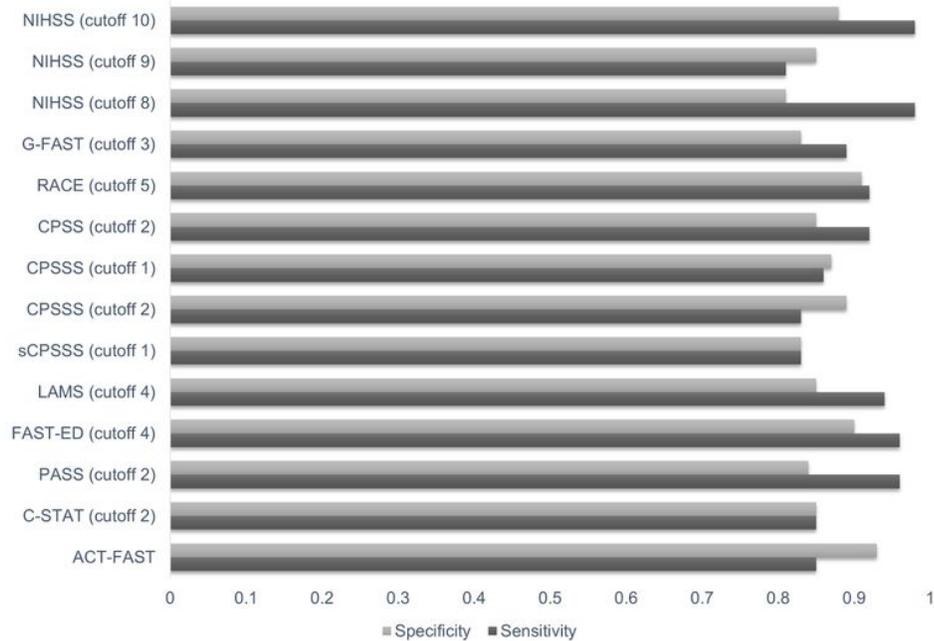


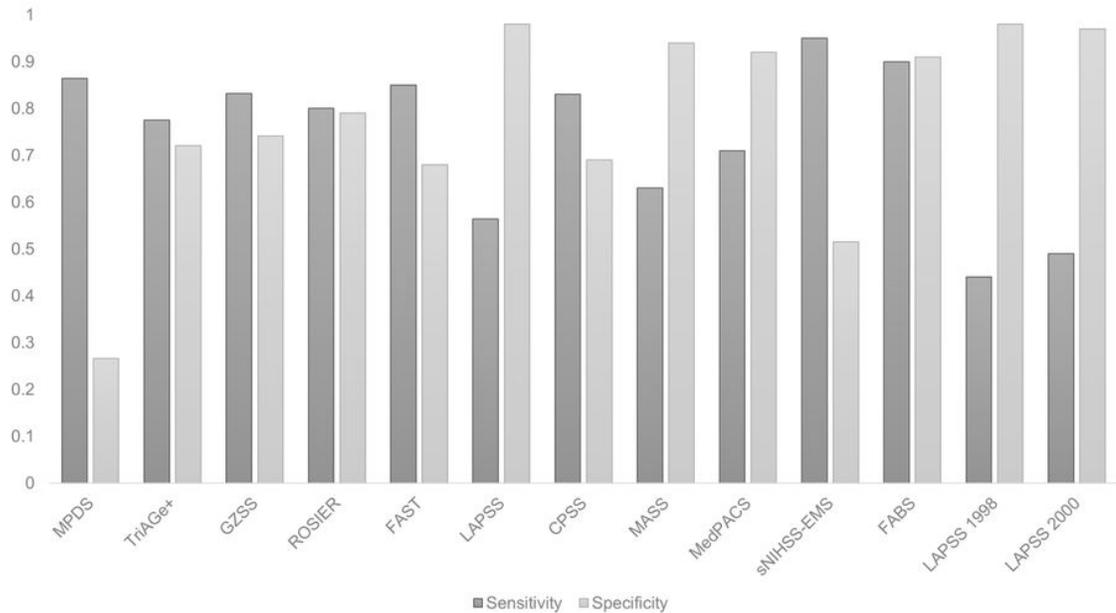
Figure 1

PRISMA flowchart. Outline of the study selection process using inclusion and exclusion criteria.



**Figure 2**

Bar chart. Sensitivity and specificity values across the clinical tools for selecting subjects with large vessel occlusion.



**Figure 3**

Bar chart. Sensitivity and specificity values of clinical tools for differentiating between acute stroke and stroke-mimicking conditions.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplement1.docx](#)
- [supplement2.docx](#)
- [supplement3.docx](#)
- [supplement3.doc](#)