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Characteristics of patients who had a stroke not initially identified during emergency prehospital assessment: a systematic review

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ABSTRACT

Background Around 25% of patients who had a stroke do not present with typical ‘face, arm, speech’ symptoms at onset, and are challenging for emergency medical services (EMS) to identify. The aim of this systematic review was to identify the characteristics of acute stroke presentations associated with inaccurate EMS identification (false negatives).

Method We performed a systematic search of MEDLINE, EMBASE, CINAHL and PubMed from 1995 to August 2020 using key terms: stroke, EMS, paramedics, identification and assessment. Studies included: patients who had a stroke or patient records; ≥18 years; any stroke type; prehospital assessment undertaken by health professionals including paramedics or technicians; data reported on prehospital diagnostic accuracy and/or presenting symptoms. Data were extracted and study quality assessed by two researchers using the Quality Assessment of Diagnostic Accuracy Studies V.2 tool.

Results Of 845 studies initially identified, 21 observational studies met the inclusion criteria. Of the 6934 stroke and Transient Ischaemic Attack patients included, there were 1774 (26%) false negative patients (range from 4 (2%) to 247 (52%)). Commonly documented symptoms in false negative cases were speech problems (n=107; 13%–28%), nausea/vomiting (n=94; 8%–38%), dizziness (n=86; 23%–27%), changes in mental status (n=51; 8%–25%) and visual disturbance/impairment (n=43; 13%–28%).

Conclusion Speech problems and posterior circulation symptoms were the most commonly documented symptoms among stroke presentations that were not correctly identified by EMS (false negatives). However, the addition of further symptoms to stroke screening tools requires valuation of subsequent sensitivity and specificity, training needs and possible overuse of high priority resources.

BACKGROUND

Worldwide, each year approximately 20 million people experience a stroke, of whom 5 million will die and 5 million will be disabled by their stroke.¹ Accurate, early recognition is necessary to maximise benefits of hyperacute treatment with intravenous thrombolysis and/or mechanical thrombectomy, where indicated and early specialist multidisciplinary care.^{2,3} With up to 70% of patients who had a stroke accessing the emergency medical services (EMS),⁴ the efficiency of the ‘stroke chain of survival’ relies heavily on the accuracy and

Key messages

What is already known on this subject?

- The sensitivity of prehospital screening tools for strokes ranges from 44 – 97%, partly due to the fact that about 25% of patients present with less common stroke symptoms.
- Prehospital recognition of stroke can be challenging. There is currently no consensus about whether to screen for additional symptoms, and which symptoms should be included in this expanded screening.

What this study adds?

- In this systematic review of studies on prehospital stroke recognition, between 2% and 52% of all stroke presentations transported by emergency medical services are not identified in the prehospital setting.
- Amongst stroke presentations that are not correctly identified by the EMS (false negatives), speech problems and posterior circulation symptoms including: nausea/vomiting, dizziness and visual disturbance/impairment were the most commonly documented characteristics.
- As some of these symptoms are very non-specific, adding further symptoms to stroke screening tools requires further evaluation of sensitivity and specificity, training needs, and possible overuse of high priority resources

timeliness of EMS identification of stroke symptoms and the ability to distinguish between stroke and non-stroke cases.

The use of screening tools to identify stroke by the EMS is recommended internationally including in guidelines for Australia, New Zealand, Europe and the USA. The majority of prehospital screening tools feature assessments for the most common stroke symptoms, as first reported in the Cincinnati Prehospital Stroke Scale (CPSS), also known as the Face Arm Speech Test (FAST).⁵ However, the accuracy of prehospital screening tools varies: sensitivity is reported ranging from 44% to 97% and specificity from 13% to 92%.⁶ The diverse nature of less common stroke symptoms such as visual disturbance, confusion and loss of balance can make correct identification challenging, particularly as up to 25% of patients who had a stroke



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do not present with symptoms commonly featured in screening tools.⁷

To date, there has not been an overview describing which symptoms are most common among patients who are not identified by the EMS, and there is currently no consensus about whether to assess symptoms with reduced specificity for stroke. Without screening tools and training to improve the identification of patients with less common stroke symptoms, inequity of available stroke care for patients will remain, particularly for patients with posterior stroke.⁸ The aim of this systematic review was to identify the characteristics of acute stroke presentations associated with inaccurate EMS identification (false negatives). Research objectives were to identify what proportion of patients who had a stroke are not identified by EMS/prehospital tools, to examine any differences in outcomes between false negative cases and those which are correctly identified, and to explore which symptoms are most commonly present in false negative cases.

METHODS

Search strategy and study selection

A search strategy was developed (online supplemental file 1), including the Medical Subject Heading terms stroke, EMS, paramedics, recognition and screening. The search strategy was adapted to search MEDLINE, EMBASE, CINAHL and PubMed from 1995 to August 2020. Studies were included from any country if published in English, with no restrictions on study design or quality.

Inclusion criteria: studies including patients who had a stroke (either actual patients ≥ 18 years or their records, any stroke type); studies including patients screened by health professionals including paramedics or technicians within the prehospital setting; data reported on prehospital diagnostic accuracy and/or symptoms present.

Exclusion criteria: non-stroke populations, studies including only stroke mimics, studies utilising prehospital screening tools to identify large vessel occlusion.

Review methods

Citations were screened independently by two researchers on title and then abstract. Any articles that met the inclusion criteria were read in full. Disagreements over the inclusion of any articles were discussed by members of the project steering group (SPJ, JMEG and CM). Backward and forward citation searches were performed to identify further studies and to test the quality of the search strategy.

Assessment of risk of bias in included studies

Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies V.2 (QUADAS-2) tool,⁹ comprising four domains: patient selection, index test, reference standard and flow and timing. We added the signalling question 'is data collected prospectively or retrospectively' within the patient selection domain. Any retrospective studies were categorised as high risk for the patient selection domain.

Data extraction and management

We designed a data extraction form that summarised the following characteristics: (1) Study detail (author, year of publication, study type, screening completed by, timing of data collection, screening tool used); (2) Patient characteristics (population, sample size, age, sex, stroke type, signs and symptoms of patients missed by the EMS recorded in prehospital and/or hospital

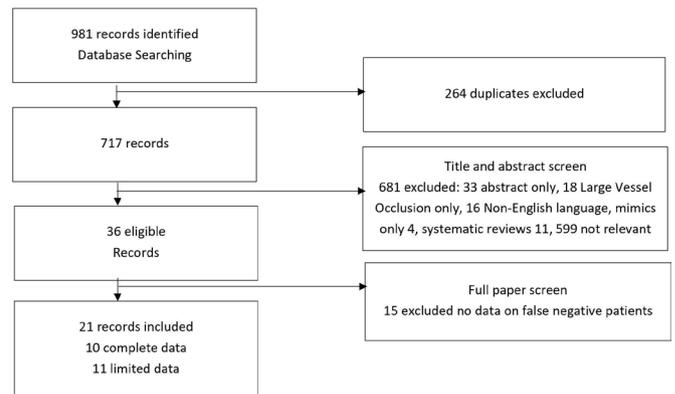


Figure 1 Flow diagram.

records, hospital diagnosis of stroke); and (3) Study quality (patient selection, risk of bias and applicability).

The accuracy of data extraction was checked by a second independent extractor for all included studies. We contacted study authors for missing data but at the time of writing had not received any responses. The protocol for the review was registered on PROSPERO.¹⁰ The reporting of this review is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.¹¹

Analysis

A priori it had been intended to perform a meta-analysis but due to heterogeneity between study settings, designs and screening tools used, the included studies have been described narratively. Results are reported as presented in the original studies, and no additional secondary analyses have been undertaken.

Results

The search strategy initially identified 845 articles. Following screening of the title, abstract or complete article, 21 studies met the inclusion criteria (see figure 1). Across all 21 studies, the number of included stroke patients totalled 6934, ranging from 35 to 997. Studies took place in the following countries: 10 in the USA^{5 12–20}; 3 in the UK^{21–23}; 3 in Australia^{24–26}; 2 in China,^{27 28} 2 in Sweden^{29 30} and 1 in Canada.³¹ Of the 21 included studies, 11 reported limited data and included no information on age, sex or symptoms.

Study quality

The studies' overall quality can be seen in online supplemental file 2. Six studies were identified as having a low risk of bias across 4 domains of the QUADAS-2,^{12 24 26–28 31} although only four reported symptom data.^{12 24 26 27} The majority of studies had a low risk of bias in terms of the screening tool used, confirmed diagnosis of stroke or non-stroke, flow and timing of emergency screening and final diagnosis. Fourteen studies had a high risk of selection bias, 12 due to retrospective designs^{13–18 22 23 26 29–31}; others due to select patient groups including: only patients who were transported to a specialist centre,²¹ participants defined by paramedic impression only¹⁹ and a convenience sample of patients presenting to the ED or inpatient neurology services.⁵

False negative cases

In all 21 studies, the number of false negative patients totalled 1774 (26%), ranging from 4 (2%) to 247 (52%). Only 10 of the 21 studies reported any further patient information. Details of the 10 studies with presentation of data describing a complete

Table 1 Study characteristics of 10 detailed studies

Screening Tool/Author (Year)	CPSS; Kothari et al (1999) ⁵	FAST* Smith et al (1999) ¹⁵	LAPSS; Kidwell et al (2000) ¹²	MASS; Bray et al (2005) ²⁴	No tool Mosley et al (2007) ²⁵	MASS; Bray et al (2010) ²⁶	LAPSS; Chen et al (2013) ²⁷	CPSS; Brandler et al (2015) ¹⁸	EMS protocol; Andersson et al (2018) ²⁹	CPSS; Oostema et al (2019) ²⁰
Total no of stroke patients	49	81	36	73	187	199	997	750	454	186
Total no of false negative stroke patients	13 (8)	32 (40)	4 (2)	7 (10)	44 (23)	8 (4)	215 (22)	282 (38)	218 (48)	45 (24)
Mean age	63.7	NS	NS	NS	75	76.5	45 (21%)>45	NS	76.1	82
Female n (%)	9 (69)	NS	NS	NS	25 (57)	4 (50)	NS	NS	106 (49)	28 (62)
Stroke type (%)	10 (77) Posterior circulation stroke 3 (23) Anterior circulation stroke	PICH 7 (22) Ischaemic stroke 25 (78)	NS	NS	NS	4 (50) Posterior circulation stroke 3 (38) PICH 1 (12) TIA	NS	NS	PICH 31 (14) Ischaemic stroke 172 (79) SAH 15 (7)	NS
Population	Stroke and non-stroke from ED and the inpatient neurology service	Confirmed and suspected stroke	Confirmed, suspected and non-stroke	Suspected stroke	Suspected stroke	Confirmed and suspected stroke	Confirmed, suspected and non-stroke	Suspected stroke	Confirmed stroke	Confirmed and suspected stroke
Study Type	Observational study	Observational study	Observational study	Observational study	Observational study	Cross-sectional observational study	Observational study	Observational study	Observational study	Observational study
Screening completed by	Physicians, paramedics and technicians	Paramedics	Paramedics	Paramedics	Paramedics	Paramedics	Paramedics	Paramedics	Ambulance technicians and nurses	Paramedics
Timing of data collection	Prospective	Retrospective	Prospective	Prospective	Prospective	Retrospective	Prospective	Retrospective	Retrospective	Prospective
Data collection period	NS	6 months	7 months	12 months	6 months	5 months	7 months	24 months	12 months	12 months

*FAST (language, visual field, motor strength and gait)
CPSS, Cincinnati Prehospital Stroke Scale; ED, Emergency Department; EMS, emergency medical service; FAST, Face Arm Speech Test; LAPSS, Los Angeles Prehospital Stroke Scale; MASS, Melbourne Ambulance Stroke Screen; NS, not stated; PICH, primary intracerebral haemorrhage; SAH, subarachnoid haemorrhage.

suspected stroke cohort are summarised in table 1. Symptom data are presented in table 2 and details of the remaining 11 studies in table 3. Of these 10 studies, the number of included stroke patients totalled 3012 of whom 868 (29%) were false negative, ranging from 4 (2%) to 282 (38%). Only five studies reported mean age or sex: in these studies, the mean age was 74.7 years and 57% of participants were female. Four studies reported specific stroke types, with the majority of false negative patients having ischaemic strokes, followed by primary intracerebral haemorrhage (41, 15%) and subarachnoid haemorrhage (15, 6%).

Use of prehospital screening tools

A range of stroke screening tools were used: the CPSS (five studies)^{5 13 14 18 20}; the FAST (three studies)^{22 23 30}; the Los Angeles Prehospital Stroke Scale (LAPSS) (two studies)^{12 27}; the Melbourne Ambulance Stroke Screen (two studies).^{24 26} One study used each of the following: Cincinnati Stroke Triage Assessment Tool¹⁹; the Ontario Prehospital Stroke Screening Tool³¹; LAPSS and CPSS¹⁷; Medic Prehospital Assessment for Code Stroke and CPSS¹⁶; Recognition of Stroke in the Emergency Room (ROSIER) and FAST²¹; ROSIER and CPSS.²⁸

Symptoms experienced by the false negative stroke patients

From the data available, it was not possible to determine whether symptoms were recorded by the EMS or identified later in hospital. In 10 studies reporting symptom data for false negative patients, the most commonly recorded were: speech problems (n=107; 13%–28%)^{20 25 26 29}; nausea/vomiting (n=94; 8%–38%)^{18 20 26 29}; dizziness (n=86; 23%–27%)^{5 18 20 26}; visual disturbance/impairment (visual loss, diplopia or blurring) (n=43; 13%–29%)^{5 20 24 29} and changes in mental status (n=51; 8%–25%).^{5 15 18 20 26}

Acute clinical outcomes in false negative cases

Of the 21 studies in total, only 8 (38%) reported any information in relation to management and treatment pathways. Five of these were undertaken between 1997 and 2009,^{5 12 26 31} all of which stated that false negative patients had minimal or atypical symptoms and would not have been candidates for thrombolysis based on protocols at the time. Three further studies took place between 2010 and 2019.^{20 23 29} In these studies, EMS-recognised strokes had significantly faster door-to-CT times (34.6 vs 84.7 min; p<0.001), but this did not translate into significantly higher rates of thrombolysis delivery (14.9% vs 4.4%; p=0.074). When patients were FAST-positive or a prealert was made, the median time from hospital arrival to CT request and scan was 39 and 57 min and 26 and 39 min, respectively, compared with medians of 120 and 155 min for FAST negative patients and 125 and 185 min for patients arriving at hospital without a prealert.²³ One study reported that a pre-alert was made for only 11% of patients who had a stroke who were not identified by the EMS compared with 70% of stroke patients who were identified (p<0.001).²⁹ Patients for whom the EMS did not identify stroke nor pre-alert the receiving centre had the longest time from ambulance call to first medical assessment in the Emergency Department (ED) at 87 min (68–147) and 52 min (45–73), respectively.²⁵

DISCUSSION

This is the first review that has systematically synthesised the research evidence identifying the signs and symptoms of patients who had a stroke who were not initially identified by the EMS.

Table 2 Frequency (%) of all symptoms reported for false negative stroke patients

	Kothari <i>et al</i> (1999) ⁵	Smith <i>et al</i> (1999) ¹⁵	Kidwell <i>et al</i> (2000) ¹²	Bray <i>et al</i> (2005) ²⁴	Mosley <i>et al</i> (2007) ²⁵	Bray <i>et al</i> (2010) ²⁶	Chen <i>et al</i> (2013) ²⁷	Brandler <i>et al</i> (2015) ¹⁸	Andersson <i>et al</i> (2018) ²⁹	Oostema <i>et al</i> (2019) ²⁰
Symptoms n (%)										
Facial droop	–	–	–	–	4 (9)	–	–	–	27 (12)	–
Arm weakness/drift	–	–	–	–	14 (32)	–	–	–	–	–
Leg weakness/drift	–	–	1 (25)	–	–	–	–	–	–	–
Arm/leg weakness/drift	–	–	–	–	–	–	–	–	69 (32)	–
Facial droop or arm weakness	–	–	–	–	–	–	81 (38)	–	–	–
Speech problems	–	–	–	–	10 (23)	1 (13)	–	–	61 (28)	35 (78)
Visual disturbance/impairment	2 (15)	–	–	2 (29)	–	–	–	–	28 (13)	11 (6)
Ataxia	3 (23)	–	–	–	–	2 (25)	–	–	–	13 (30)
Dizziness	3 (23)	–	–	–	–	2 (25)	–	77 (27)	–	4 (9)
Vertigo	3 (23)	–	–	–	–	–	–	–	96 (44)	7 (16)
Nausea or vomiting	–	–	–	–	–	3 (38)	–	22 (8)	64 (29)	5 (12)
Sensory deficit	–	–	–	–	–	–	–	–	–	–
Headache	–	–	–	–	–	1 (13)	–	40 (14)	40 (18)	9 (21)
Unilateral weakness	4 (31)	–	–	–	–	–	–	–	–	22 (48.9)
Mental status changes	1 (8)	6 (19)	–	–	–	2 (25)	–	34 (12)	–	8 (19)
Change in conscious level	–	2 (6)	–	–	–	1 (13)	–	–	–	–
Hypoglycaemia	–	–	–	1 (14)	–	–	–	–	–	–
Seizure	–	2 (6)	–	–	–	–	–	12 (4)	–	–
Quadriplegia	–	–	–	–	–	–	–	6 (2)	–	–
Bilateral weakness	–	–	2 (50)	–	–	–	–	–	–	–
Weakness other	–	–	–	–	–	–	–	91 (32)	–	–
Ophthalmoplegia	–	–	1 (25)	–	–	–	–	–	–	–
Fever	–	–	–	–	–	1 (13)	–	–	–	–
Incontinence	–	–	–	–	–	2 (25)	–	–	–	–
Fall	–	–	–	–	–	2 (25)	–	–	–	–

Across 21 studies, 26% of patients who had a stroke were not recognised by the EMS, ranging from between 2% and 52% of stroke presentations not identified in the prehospital setting. It should be noted that study quality and size varied considerably, with even studies using the same screening tools reporting substantial differences in the proportion of false negative patients.^{13 14}

EMS identification of patients who had a stroke enables patients to access the stroke pathway at the earliest opportunity, which expedites, where indicated, a prealert to the receiving hospital and subsequent transfer to a specialist centre. Research suggests that patients who had a stroke who are prealerted to the receiving hospital have significantly reduced times from onset to hospital arrival and specialist assessment, leading to higher thrombolysis rates and better outcomes.²³

Although a total of 30 different stroke symptoms were reported across 10 studies, the most common symptoms among false negative patients were speech problems, nausea/vomiting, dizziness, changes in mental status and visual disturbance/impairment. While in some cases, individual patient presentations can hinder assessment, it is surprising that patients who had a stroke with speech problems are so often misidentified by the EMS, especially given that speech problems are the most commonly reported stroke symptom of patients and callers to the EMS for suspected stroke.^{26 32 33} In studies using prehospital screening tools, the majority of tools, including the widely used FAST test, include assessment of speech (excluding LAPSS and C-STAT). It may be challenging to identify milder speech problems, especially in patients presenting with confusion or where the history is not clear, in the prehospital setting. It is also possible that for some patients in the included studies, their speech problems

were not present on initial assessment and evolved only after hospital admission.

Nausea/vomiting occurs in around 20% of acute stroke patients, most frequently in those with vertebrobasilar stroke. One ambulance service in the UK has recently added nausea/vomiting to their prehospital screening tool for stroke, which also includes vertigo, visual problems and ataxia.³⁴ The impact of this on the specificity of EMS stroke identification is unknown but may be considerable given that nausea/vomiting is a common symptom across a range of acute illnesses.

Dizziness is one of the most commonly reported symptoms in cerebellar stroke, occurring in up to three-quarters of patients. The term dizziness is non-specific but may be used to describe vertigo and presyncope. Although other focal neurological symptoms may accompany dizziness, dizziness alone presents in fewer than 1% of all patients who had a stroke.³⁵ In a recent retrospective analysis of National Institutes of Health Stroke Scale data, the addition of balance (defined as gait imbalance or leg weakness) and visual symptoms (visual loss and diplopia) to FAST symptoms would have improved recognition of stroke from 86% to 96% ($p < 0.0001$).³⁶ Similarly, in another study, the addition of ataxia or visual symptoms to the FAST would have increased sensitivity from 61% to 80% ($p < 0.001$) and 82% ($p < 0.001$), respectively³⁷; and in a further study of patients with posterior circulation stroke, FAST combined with ataxia and visual disturbance or blindness would have improved sensitivity from 70% to 84%.²² However, these studies preclude any estimate of specificity because they were limited to patients with confirmed stroke^{22 36 37}; further, sample sizes were small²³ and retrospective designs were used.^{22 37} In a further study aiming to increase sensitivity to posterior circulation stroke, balance and

Table 3 Study characteristics of 11 limited detail studies

Screening Tool; Author (Year)	CPSS; Ramanujam et al (2008) ¹³	CPSS; Frendl et al (2009) ¹⁴	OPSS; Chenkin et al (2009) ³¹	FAST; Huwez and Caswell (2011) ²²	FAST; Sheppard et al (2013) ²³	MedPACS vs CPSS; Studnek et al (2013) ¹⁶	ROSIER and FAST; Fothergill et al (2013) ²¹	CPSS and LAPSS; Asimos et al (2014) ¹⁷	FAST; Berglund et al 2014 ²⁰	ROSIER vs CPSS; Mingfeng et al (2012) ²⁸	C-STAT; McMullan et al (2018) ¹⁹
No of total stroke patients	477	154	229	35 posterior stroke	141	MedPACS 123; CPSS 94	ROSIER 27; FAST 21	CPSS 663; LAPSS 805	233	ROSIER 379 CPSS 383	158
No of total false negative stroke patients	247 (52)	18 (2)	27 (12)	11 (31)	35 (25)	MedPACS 48 (39); CPSS 39 (42)	ROSIER 6 (22); FAST 6, (29)	CPSS 130 (20); LAPSS 209 (26)	27 (12)	ROSIER 38 (10); CPSS 43 (11)	22 (14)
Mean age	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Female (%)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Population	Suspected stroke or TIA	Suspected stroke or TIA	Suspected stroke or TIA	Confirmed stroke	Confirmed stroke	Suspected stroke or TIA	Suspected stroke or TIA	Suspected stroke or TIA in the ED	Suspected stroke or TIA	Suspected stroke or TIA	Suspected stroke or TIA
Study Type	Observational study	Observational study	Observational study	Case note review	Case note review	Case note review	Observational study	Observational study	Observational study	Observational study	Observational study
Screening completed by	EMS (recorded data)	EMS (recorded data)	EMS (recorded data)	EMS (recorded data)	EMS (recorded data)	EMS (recorded data)	EMS	EMS (recorded data)	EMS (recorded data)	Emergency physician in the pre-hospital setting	EMS
Timing of data collection	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Prospective	Retrospective	Retrospective	Prospective	Prospective
Data collection period	12 months	NS	12 months	NS	9 months	6 months	14 months	26 months	6 months	18 months	6 months

CPSS, Cincinnati Prehospital Stroke Scale; C-STAT, Cincinnati Stroke Triage Assessment Tool; EMS, emergency medical service; FAST, Face-Arm-Speech Test; MedPACS, Medic-Prehospital Assessment for Code Stroke; NS, not stated; OPSS, Ontario Prehospital Stroke Screening; ROSIER, Recognition of Stroke in the Emergency Room; ROSIER, Recognition of Stroke in the Emergency Room; TIA, transient ischaemic attack.

eyes were added to the FAST (BEFAST). The Balance component of the BEFAST scale was scored by finger-to-nose testing and the Eyes component by assessing for diplopia using finger tracking. However, the addition of these additional symptoms did not improve stroke recognition.³⁸ Stroke-related visual problems also occur commonly during posterior circulation stroke but are challenging to recognise for both health professionals and patients and only around 20% of patients who had a stroke presenting predominantly with visual symptoms contact the EMS. While EMS identification of visual disturbance/impairment may be feasible, agreement would be needed around which visual problems should be assessed, how and by whom.

Five studies reported changes in mental status, ranging from 8% to 25%.^{5 15 18 20 26} Mental status was largely undefined in these studies but may include a range of symptoms: confusion, delirium, altered orientation and memory are more common in older patients, those with pre-existing cognitive impairments and underlying infections. While changes in mental status occur in up to one-third of patients who had a stroke, stroke is a rare cause (<3%) of isolated changes in mental status.

Although limited data were reported regarding patient eligibility for thrombolysis, recent research suggests that EMS-recognised strokes are more likely to be prealerted to hospital²⁹; are assessed more rapidly in the ED²⁵; have faster door-to-CT times^{20 23} and a greater likelihood of thrombolysis.²⁰ Further research is needed to explore the impact of a missed prehospital diagnosis on eligibility for time-dependent stroke treatments and on patient outcomes.

There were a number of limitations of the studies included. The majority of studies involved the validation or performance of prehospital stroke screening tools, entailed specialist training, and were mainly undertaken in selected groups of patients with confirmed or suspected stroke/TIA. Therefore, screening might only have been completed in patients for whom the EMS clinician already had a high index of suspicion for stroke and their subsequent labelling of stroke was determined by a clinical protocol. It was not clear in any of the studies whether symptom data had been recorded by the EMS or whether symptoms had been completely missed by the EMS and only recorded in hospital. Fourteen of the 21 included studies were at high risk of selection bias mainly due to retrospective data collection, which may have resulted in not all relevant patient symptoms being recorded; the majority of studies were conducted in single EMS and hospital centres. Study quality and size varied considerably and there was a lack of reported data, limiting the generalisability of study findings. Only four studies reported stroke type. Of these, although three studies reported symptoms for all false negative patients, these were not reported by stroke subtype. It is unknown whether false negatives have the same proportion of ICH and ischaemic strokes as the standard stroke population, or whether there are factors to do with symptom recognition which made affect this balance, for example, change in conscious level. A further limitation of the review was the inclusion only of studies that were published in English. Although we contacted authors for further information, at the time of writing no responses had been received. Some studies were excluded where the characteristics of false negative patients and patients with stroke mimics were not reported separately. As this review focused on the emergency assessment of stroke patients in prehospital settings, there may be other studies not included in this review that have reported data on false negative stroke patients. Eleven further papers reported the numbers of false negative patients but very little other data. Previous research has highlighted the failure of studies to identify and report false negative stroke patients,

particularly in studies which involve the selection and transportation of patients to specialist stroke centres.³⁹ It is important that future research studies which include false negative patients report more detail about this population to further understand their characteristics, the symptoms they experienced and any impact on patient outcomes.

While it may not be possible for EMS personnel to identify all stroke patients without reducing specificity, ongoing research in selected patients is exploring the use of point-of-care diagnostics. A range of diagnostic techniques are currently in development, but none are currently used routinely in practice.⁴⁰ Therefore, the recognition of suspected patients who had a stroke with the triaging of patients who present with stroke mimics and associated overuse of high priority EMS resources will continue to be challenging for the EMS.

CONCLUSIONS

Stroke presentations that are most frequently missed by the EMS commonly include symptoms of: speech problems, nausea/vomiting, dizziness, changes in mental status and visual disturbance/impairment. However, the addition of further symptoms to stroke screening tools would require evaluation of their sensitivity and specificity, any associated training needs, and the impact on EMS resource use. Despite the inclusion of speech symptoms in most prehospital screening tools, this symptom is often overlooked and the reasons for this may need to be explored further.

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Contributors SPJ: design and methodology, data collection, assessing risk of bias, data analysis, writing-up, full checking of final draft. JEB: design and methodology, writing-up, full checking of final draft. JMEG: design and methodology, assessing risk of bias, writing-up, full checking of final draft. CM: design and methodology, data collection, data analysis, assessing risk of bias, writing-up, full checking of final draft. GM: design and methodology, writing-up, full checking of final draft. CP: design and methodology, writing-up, full checking of final draft. CLW: design and methodology, writing-up, full checking of final draft.

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Search Strategy:

1. exp cerebrovascular accident/
2. stroke.mp.
3. cerebrovascular accident.mp.
4. 1 or 2 or 3
5. exp cerebrovascular accident/di [Diagnosis]
6. exp stroke/di
7. 5 or 6
8. (recogni\$ or identi\$ or strati\$ or screen\$).mp.
9. 4 and 8
10. 7 or 9
11. ambulance/
12. air medical transport/
13. exp emergency care/
14. emergency medical services/
15. emergency health service/
- 16 paramedics/
17. emergency medical technicians/
18. emergency/
20. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
21. 10 and 20

Online Supplementary File 2. Quality Assessment of Diagnostic Accuracy Studies version 2 of included studies

Study author (year)	Patient selection	Index test	Reference standard	Flow and timing
Andersson et al. (2018)	High	Not applicable	Not applicable	Not applicable
Asimos et al. (2014)	High	Low	Low	Low
Berglund et al. (2014)	High	Low	Low	Low
Brandler et al. (2015)	High	Low	Low	Low
Bray et al. (2005)	Low	Low	Low	Low
Bray et al. (2010)	High	Low	Low	Low
Chen et al. (2013)	Low	Low	Low	Low
Chenkin et al. (2009)	Low	Low	Low	Low
Fothergill et al. (2013)	High	Low	Low	Low
Frendl et al. (2009)	High	Low	Low	Low
Huwez Caswell (2013)	High	Unclear	Unclear	Unclear
Kidwell et al. (2000)	Low	Low	Low	Low
Kothari et al. (1999)	High	Low	Low	Low
McMullen et al. (2017)	High	Low	Unclear	Unclear
Mingfeng et al. (2014)	Low	Low	Low	Low
Mosley et al. (2007)	Low	Not applicable	Not applicable	Not applicable
Oostema et al. (2015)	Low	Low	Low	Low
Ramanujam (2008)	High	Low	Low	Low
Sheppard et al. (2013)	High	Low	Low	Low
Smith et al. 2009	High	Not applicable	Not applicable	Not applicable
Studnek et al. 2013	High	Low	Low	Low