SUPPLEMENTAL MATERIAL

Extended methods

Study design and setting

This study used a cohort design. It was conducted as part of a larger project for which the process of recruitment and data collection have been detailed elsewhere.[1] Briefly, consent was sought from patients with a suspected diagnosis of stroke who had been admitted to the acute stroke ward in two urban hospitals (West Midlands, UK). Both hospitals had an ethnically diverse catchment population and offered an acute stroke service; 24 hours a day at one site and in working hours (9:00am to 5:00pm, Monday to Friday) in the other. Patients from either hospital catchment who contacted the EMS were transported to hospital by a single ambulance service. A localised EMS protocol for the rapid transfer of suspected stroke patients was in place (figure s1; please see online supplemental material). This protocol requires EMS staff to assess and document five criteria (onset time, FAST status, consciousness, evidence of seizure and blood sugar levels) prior to sending a pre-alert message. This protocol does not require staff to document where onset time is unknown or unclear. A summary of the patient pathway for acute stroke in the UK is detailed in the online supplemental material (figure s2). At the time of the study, a 4.5 hour maximum time window for thrombolysis was in operation.[2]

Selection of participants

Patients under the care of participating consultant stroke physicians were approached for consent by a member of the research team during their stay on the acute stroke ward during a nine month period between 01/11/2010 and 31/07/2011. Informed consent was obtained from all patients to permit identifiable patient data to be collected (to allow for data linkage) and only those with capacity (or an available consultee) were approached. Those with a final diagnosis of stroke (defined in their hospital discharge letter) who followed the acute stroke care pathway were included in this analysis. Whilst it is acknowledged that stroke mimic patients (those who follow the acute care pathway for stroke but are not subsequently diagnosed with the disease) are also eligible for this analysis, they were not included because of difficulties defining and systematically capturing this population. Exclusion of these patients was deemed acceptable because the initial assessments they receive before and upon arrival in hospital (as studied here) are unlikely to differ from those received by patients included in the study as these are conducted in clinical practice without knowledge of final diagnosis.

Data collection

The records of all consenting patients were interrogated. Identifiable patient data were used to locate and link hospital and EMS records. Data relating to patient demographics, times to hospital and CT brain scan, pre-hospital care and route to hospital were extracted from both EMS and hospital records. Additional data variables, such as time of nurse triage in the emergency department, time to first assessment by the emergency department consultant or time to first contact with the stroke team were also sought; however, these data were not routinely recorded in all patient records. Thus, time of CT request and time of CT scan (which were reliably documented by the electronic CT scan booking system) were extracted and used as a 'proxy marker' for timely and effective care.

Missing data were reviewed with source data verification. The accuracy of the data collected was reliant on the accuracy with which it was documented. It was not possible to account for scenarios were assessments were conducted but not documented or where information about the patients was communicated verbally between healthcare professionals.

Statistical analysis

All statistical analyses were performed in SPSS version 18.0 (SPSS Inc., Chicago, USA). Descriptive statistics were used to describe the study population, the proportion of patients accessing acute stroke services via different routes and the proportion of patients with known onset time and recognised stroke who were pre-alerted.

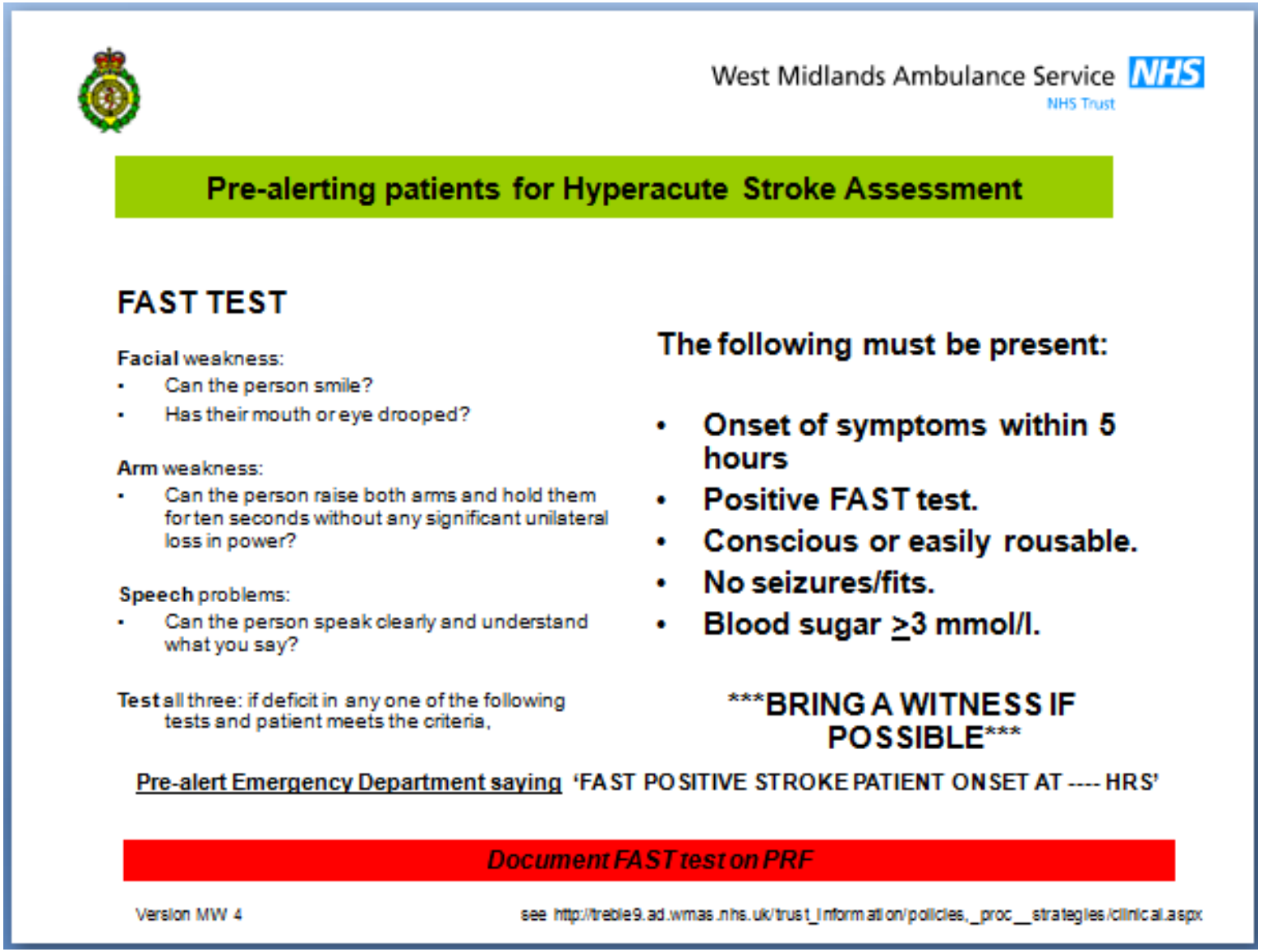
For patients arriving at hospital via the EMS, the association between pre-hospital assessments and time to CT request and scan were investigated. Specifically, we used proportional hazards modelling (Cox Regression) to investigate the association between three factors (recording of onset time by the EMS, FAST status [positive or negative/not recorded] or whether a pre-alert message was sent) and two outcome variables: time from arrival in hospital to CT request (primary outcome) and time from CT request to scan (secondary outcome). These outcome variables were chosen because they are accurately and routinely documented (automatically for every patient) and allow delineation of which part of the in-hospital service is being delayed; the initial decision making of the first attending hospital clinician or the CT scanning department. FAST negative patients were grouped with those where FAST was not documented for statistical purposes as it was assumed that these patients were similar in not presenting with typical stroke symptoms upon initial assessment.

Hazard ratios were adjusted for confounding variables which may have influenced the time to CT request and scan (or the decision to thrombolyse) upon arrival in hospital including: EMS recording of onset time, FAST status, patient age, route to hospital, hospital site, arrival in hospital within four hours of symptom onset, Glasgow Coma Score and whether the hospital was pre-alerted by EMS staff prior to arrival in the ED. These variables were chosen because they best represented the factors which might affect a decision to thrombolyse a patient from the data available in the medical records. It is acknowledged that other variables, such as National Institutes of Health Stroke Scale, could also be included in the model, however, these data were not routinely documented or available for every patient. In the absence of any established mathematical model describing the scenario examined here, factors were entered into the proportional hazards model as categorical variables using the backwards stepwise method. Full details of included variables and how they were coded can be found in tables s1 and s2 (please see online supplemental material).

The time from ambulance dispatch to key milestones on the stroke pathway was investigated specifically in patients who arrived within four hours of symptom onset (and therefore could be considered for thrombolysis if recognised and not contra-indicated). These times were compared in patients where onset time was/was not recorded by EMS staff, the FAST test was completed and positive/negative or a pre-alert message was/was not sent to the hospital.

Data are presented as means or medians (standard deviation [SD], inter-quartile range [IQR] or 95% confidence intervals [CI]), percentage of the recruited population (unless otherwise stated) and hazard ratios (95% confidence intervals), unadjusted and adjusted.

Figure s1. Local hospital pre-alert criteria



West Midlands Ambulance Service NHS
NHS Trust

Pre-alerting patients for Hyperacute Stroke Assessment

FAST TEST

Facial weakness:
- Can the person smile?
- Has their mouth or eye drooped?

Arm weakness:
- Can the person raise both arms and hold them for ten seconds without any significant unilateral loss in power?

Speech problems:
- Can the person speak clearly and understand what you say?

Test all three: if deficit in any one of the following tests and patient meets the criteria,

The following must be present:

- **Onset of symptoms within 5 hours**
- **Positive FAST test.**
- **Conscious or easily rousable.**
- **No seizures/fits.**
- **Blood sugar ≥3 mmol/l.**

BRING A WITNESS IF POSSIBLE

Pre-alert Emergency Department saying 'FAST POSITIVE STROKE PATIENT ONSET AT ---- HRS'

Document FAST test on PRF

Version MW 4

see http://treble9.ad.wmas.nhs.uk/trust_information/policies,_proc__strategies/clinical.aspx

Figure s2. Patient pathway for acute stroke in UK hospitals offering a stroke service 24 hours a day, 7 days a week

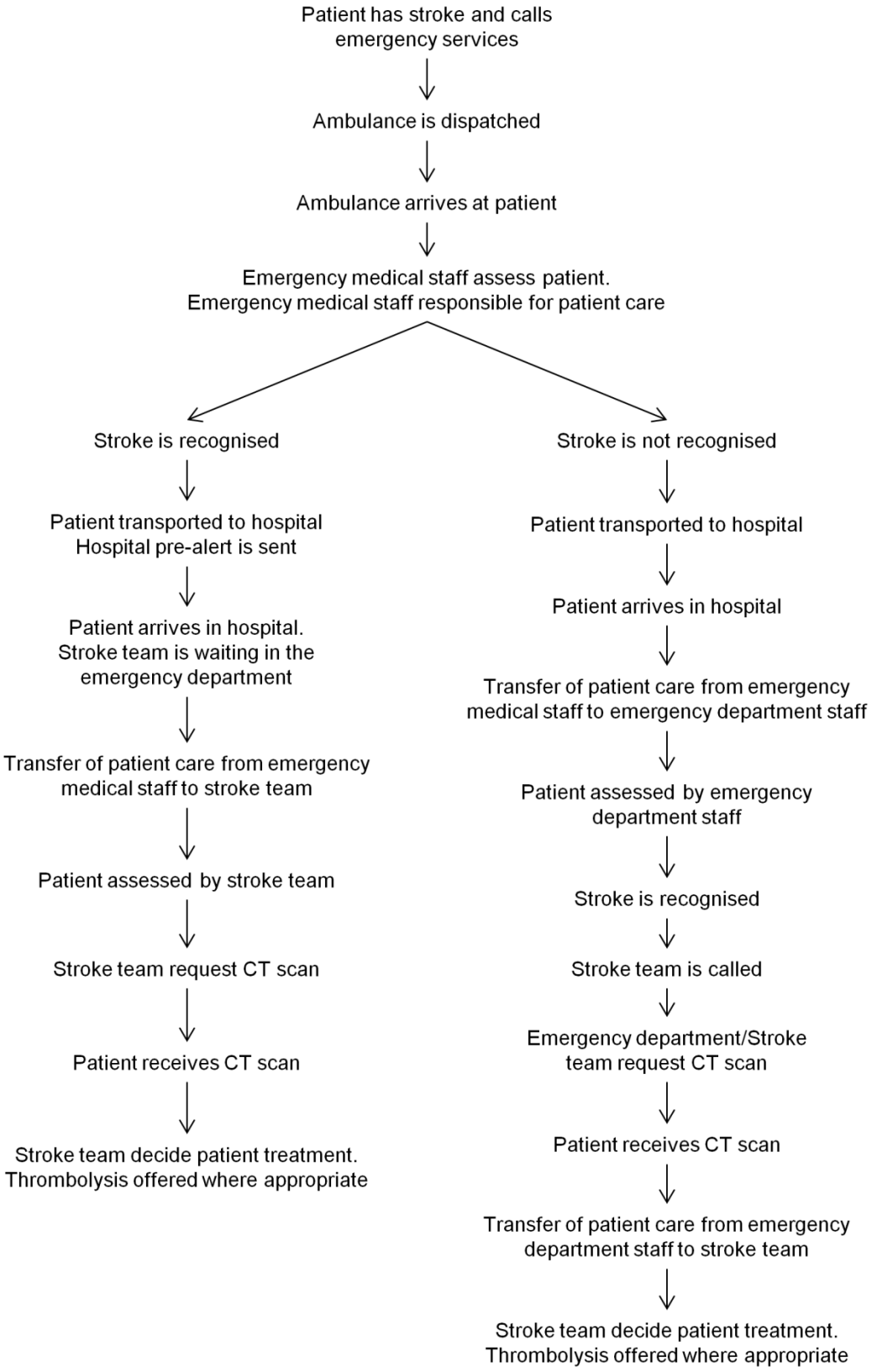


Table s1. Coding of variables considered in the proportional hazards modelling

Variable name	**Variable type**	**Variable coding**
Dependant variables		
Time to CT request (primary outcome)	Time (continuous)	Continuous (minutes)
Time to CT scan (secondary outcome)	Time (continuous)	Continuous (minutes)
Independent variables		
EMS recording of onset time	Categorical	Yes =1; No = 0
FAST status	Categorical	FAST+ = 1; FAST- or not done = 0
Hospital pre-alerted by EMS staff prior to arrival in the ED	Categorical	Yes =1; No = 0
Patient age	Categorical	Aged $\geq$80 years = 1; Aged <80 years = 0
Hospital site	Categorical	Hospital A = 1; Hospital B = 2; Hospital C = 3;
Arrival in hospital within four hours of symptom onset	Categorical	Yes =1; No = 0
Glasgow Coma Score	Categorical	Score of >8 (patient conscious) = 1; Score of $\leq$8 (patient unconscious) = 0
Route to hospital	Categorical	Ambulance = 1; General practitioner = 2; Called non-emergency healthcare provider (NHS direct) = 3; Patient transferred from another hospital for treatment = 4

CT = computed tomography; EMS = emergency medical service; FAST = face arm speech test; ED = emergency department

Table s2. Confounding variables considered in each proportional hazards model

Model	**Included confounding variables**	**Excluded confounding variables**	
		Non-significant (P > 0.2) difference from explanatory and outcome variables	**On the causal pathway between explanatory and outcome variables**
EMS recording of onset time – time to scan request	FAST status	Patient age, route to hospital, arrival in hospital within 4 hours of symptom onset, Glasgow Coma Score	Hospital pre-alerted by EMS staff prior to arrival in the ED
EMS recording of onset time – time to scan	Hospital site, route to hospital, patient age and FAST status	Arrival in hospital within 4 hours of symptom onset, Glasgow Coma Score	Hospital pre-alerted by EMS staff prior to arrival in the ED
FAST status – time to scan request	Arrival in hospital within 4 hours	EMS recording of onset time, patient age, route to hospital, Glasgow Coma Score	Hospital pre-alerted by EMS staff prior to arrival in the ED
FAST status – time to scan	Arrival in hospital within 4 hours, hospital site and route to hospital	EMS recording of onset time, patient age, Glasgow Coma Score	Hospital pre-alerted by EMS staff prior to arrival in the ED
Hospital pre-alerted prior to arrival – time to scan request	Arrival in hospital within 4 hours	EMS recording of onset time, FAST status, patient age, route to hospital, Glasgow Coma Score	n/a
Hospital pre-alerted prior to arrival – time to scan	FAST status	EMS recording of onset time, patient age, route to hospital, arrival in hospital within 4 hours of symptom onset, Glasgow Coma Score	n/a

EMS = emergency medical service; FAST = face arm speech test; ED = emergency department

References

1. Sheppard, J. P., Mellor, R. M., Bailey, S. M. et al. Protocol for an observation and implementation study investigating optimisation of the management of stroke and transient ischaemic attack (TIA). BMJ Open. 2012, 2:1-7.

2. Wahlgren, N., Ahmed, N., Davalos, A. et al. Thrombolysis with alteplase 3-4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. Lancet 2008, 372:1303-1309.