

est maternal population. District F is a referral centre and its rate is raised by having cases referred from other districts. The invasive procedure rate for local women in district F averaged 5.4%. Thus about 1.4% of invasive procedures were performed on women referred from elsewhere.

## Discussion

We found no evidence that serum and nuchal translucency screening improves antenatal detection rates or reduces rates of invasive procedure. Our findings suggest that the recently announced government initiative to introduce universal serum screening from 2004 will not achieve its stated objectives. The current maternal age distribution observed in our study is different to that used in the demonstration projects; 15% of women who were pregnant during the study period were aged 35 years and over. As a consequence 58% of babies with Down's syndrome were born to women in this age group. This shows a return to levels seen in the 1950s and 1960s, when over 13% of childbearing women were aged 35 and over and more than half of

the children with Down's syndrome were born to women in this age group.<sup>2</sup> In districts with a higher proportion of older women the use of maternal age detects a high proportion of affected fetuses. The addition of routine anomaly scans, which are already offered in most UK health districts, also allows a large proportion of affected fetuses to be detected in younger women.

To avoid continuing the confusion that Down's screening currently causes in pregnant women, we believe that new screening methods should be offered only as part of a controlled study until their benefit is proved.

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- 1 Mutton DE, Alberman E, Ide R, Bobrow M. Results of first year (1989) of a national register of Down's syndrome in England and Wales. *BMJ* 1991;303:1295-7.
- 2 Adams MM, Erickson JD, Layde PM, Oakley GP. Down's syndrome. Recent trends in the United States. *JAMA* 1981;246:758-60.

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# A multicentre observational study of presentation and early assessment of acute stroke

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## Abstract

**Objective** To investigate delays in the presentation to hospital and evaluation of patients with suspected stroke.

**Design** Multicentre prospective observational study.

**Setting** 22 hospitals in the United Kingdom and Dublin.

**Participants** 739 patients with suspected stroke presenting to hospital.

**Main outcome measures** Time from onset of stroke symptoms to arrival at hospital, and time from arrival to evaluation by a senior doctor.

**Results** The median age of patients was 75 years, and 400 were women. The median delay between onset of symptoms and arrival at hospital was 6 hours (interquartile range 1 hour 48 minutes to 19 hours 12 minutes). 37% of patients arrived within 3 hours, 50% within 6 hours. The median delay for patients using the emergency service was 2 hours 3 minutes (47 minutes to 7 hours 12 minutes) compared with 7 hours 12 minutes (2 hours 5 minutes to 20 hours 37 minutes) for referrals from general practitioners ( $P < 0.0001$ ). Use of emergency services reduced delays to hospital (odds ratio 0.45, 95% confidence interval 0.23 to 0.61). The median time to evaluation by a senior doctor was 1 hour 9 minutes (interquartile range 33 minutes to 1 hour 50 minutes) but was undertaken in only 477 (65%) patients within 3 hours of arrival. This was not influenced by age, sex, time of

presentation, mode of referral, hospital type, or the presence of a stroke unit. Computed tomography was requested within 3 hours of arrival in 166 (22%) patients but undertaken in only 60 (8%).

**Conclusion** Delays in patients arriving at hospital with suspected stroke can be reduced by the increased use of emergency services. Over a third of patients arrive at hospital within three hours of stroke; their management can be improved by expediting medical evaluation and performing computed tomography early.

## Introduction

Stroke is a leading cause of death and long term disability and is associated with high costs.<sup>1 2</sup> Recent studies show that thrombolysis is an effective treatment in selected patients but needs to be undertaken within three hours and no later than six hours from the onset of symptoms.<sup>3-6</sup> Most guidelines emphasise the rapid assessment of patients with suspected stroke,<sup>7</sup> but this is not the case for most patients.<sup>8-10</sup> Studies in the United States have shown that underutilisation of emergency medical services and delays in hospital assessment are important impediments to thrombolysis,<sup>11-19</sup> which can be modified readily to improve the care of stroke.<sup>11-13</sup>

The uptake of thrombolysis has been more cautious in the United Kingdom than it has in North America and western Europe for two reasons.<sup>20 21</sup>

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Firstly, because meta-analysis of studies does not support the widespread use of thrombolytic therapy in the routine practice of stroke management in that benefit is marginal and mortality may be increased,<sup>5</sup> and secondly, because of the perception that most patients present too late to be eligible for treatment.<sup>22 23</sup> We aimed to investigate delays in the presentation to hospital and evaluation of patients with stroke in the United Kingdom and to identify measures that could improve their early management.

## Participants and methods

### Setting and patients

The study was conducted in 11 teaching hospitals and 11 district general hospitals in the United Kingdom and Dublin. Six teaching hospitals and five general district hospitals had a stroke unit. Thrombolysis was offered routinely at one hospital and as part of research at three hospitals. Consecutive patients with signs or symptoms suggestive of an acute stroke were included over a specified four week period.

### Data collection

Data at each hospital were collected by independent observers who were given formal training and standardised instructions on definitions and data collection techniques. The observers were alerted by triage staff on arrival of a patient with suspected stroke, regardless of time of day. They monitored patient management for the first three hours after arrival by using a structured format of prespecified variables considered to be important in stroke management. Clinical staff were not aware of the purpose of data collection or of the specific variables being monitored.

Time from onset of symptoms and time of arrival at hospital were recorded. The onset of stroke was defined as the time neurological deficit was first noticed by the patient or an observer. If symptoms were present on awakening, the onset of stroke was considered to be the time the patient fell asleep. For patients in whom time of onset was not documented, midnight on the day of onset was considered the onset time. The timing of various assessments and investigations (including computed tomography) after arrival at hospital was recorded. Delay to evaluation by a senior doctor was defined as the interval between the arrival time and evaluation by a doctor (senior house officer or a higher grade doctor on the admitting medical team) empowered to take decisions on specialist investigations and management. Information on the modes of referral was collected. These were classified as a 999 ambulance call by the patient or a relative (emergency services), a non-emergency referral by a general practitioner, a 999 ambulance call by a general practitioner (general practitioner plus 999), or other methods including arrival on own or by public transport.

## Results

### Patient characteristics

Overall, 739 patients were studied. The median age of patients was 75 years, with the largest proportion of patients being between 65 and 85 years (table 1). The most common type of stroke was ischaemic, accounting for 505 of the 565 (89%) patients with stroke in the

**Table 1** Descriptive characteristics of 739 patients with suspected stroke

Attribute	No (%) of patients
Median age (years; n=737):	75*
<55	80 (11)
55-64	96 (13)
65-74	192 (26)
75-84	255 (36)
≥85	114 (15)
Women (n=737)	400 (54)
Documented time of onset (n=646):	
00 00 to 05 59	59 (9)
06 00 to 11 59	242 (37)
12 00 to 17 59	164 (25)
18 00 to 23 59	181 (28)
Time of arrival at hospital (n=736):	
00 00 to 05 59	40 (5)
06 00 to 11 59	214 (29)
12 00 to 17 59	314 (43)
18 00 to 23 59	168 (23)
Mode of referral (n=736):	
Emergency services	320 (43)
General practitioner referrals	330 (45)
General practitioner referral plus emergency services	36 (5)
Others	50 (7)
Final diagnosis (n=739):	
Acute ischaemic stroke	405 (55)
Transient ischaemic attack	100 (14)
Intracerebral haemorrhage	49 (7)
Subarachnoid haemorrhage	11 (1.5)
Others	156 (21)
Not established	18 (2.5)

\*Interquartile range 66-82.

sample. Acute stroke was not the final diagnosis in nearly one in five patients suspected with a stroke on presentation (table 1). No significant differences were found between hospitals for patient characteristics, time of onset of symptoms, time of presentation, and the final diagnosis.

### Presentation to hospital

Most patients (95%) arrived at the hospital between 6 am and midnight, regardless of the time of onset of symptoms or mode of referral (table 1). The median delay between onset of symptoms and arrival at the hospital was six hours (interquartile range 1 hour 48 minutes to 19 hours 12 minutes). More than a third of the patients had arrived at hospital within three hours and nearly half within six hours of the onset of symptoms (table 2). The proportion of patients in different age groups did not vary significantly within different time intervals suggesting that older (≥75 years) patients were as likely to present to hospital early as younger patients. Overall, 43% (320 patients) of patients were brought by ambulance to the hospital after a 999 call to the emergency services by the patient or a relative (table 1). A similar proportion (45%) of patients consulted their general practitioner and were referred to hospital as non-urgent admissions. Overall, 81% (56 of 69) of the patients who arrived at hospital within an hour of the onset of symptoms were brought in by the emergency services compared with 7% (5 of 69) who first saw their general practitioner (figure). The median time between the onset of stroke and arrival at hospital for patients using the emergency service was 2 hours and 3 minutes (47 minutes to 7 hours and 12

minutes), which was significantly less than the 7 hours and 12 minutes (2 hours 5 minutes to 20 hours 37 minutes) for patients who first saw their general practitioner ( $P < 0.0001$ ). General practitioners used the emergency services for only 36 (5%) patients, in whom the median delay between onset of symptoms and presentation was 3 hours 47 minutes (2 hours 33 minutes to 6 hours 54 minutes).

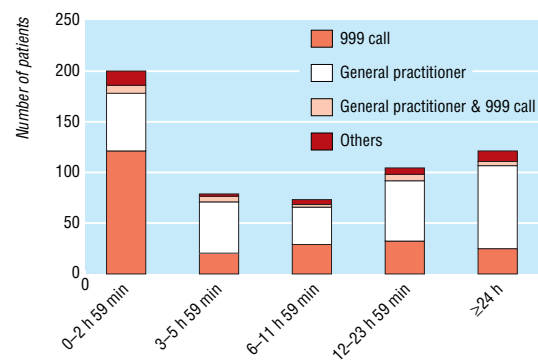
### Early assessment in hospital

A nurse recorded heart rate, blood pressure, temperature, and glucose concentrations in 634 (86%) patients within 15 minutes of arrival at hospital and in 688 (93%) patients within 30 minutes of arrival. In contrast, only 163 of 736 (22%) patients were seen within 15 minutes of arrival by a doctor from an emergency or assessment unit and 284 (38%) within 30 minutes of arrival (table 2). Evaluation by a senior doctor from the admitting medical team was undertaken in 477 (65%) patients within 3 hours of arrival at hospital. Of these patients, 26 (5%) were seen by a consultant, 115 (24%) by a specialist registrar, and 336 (70%) by a senior house officer. Computed tomography within 3 hours of arrival was requested in 166 (22%) patients but was undertaken in only 60 (8%). The interval between presentation to hospital and assessment by a senior doctor was not influenced by the age or sex of the patient, time of presentation, final stroke diagnosis, mode of referral, initial assessment by a doctor, academic status of hospital, or the presence of a stroke unit.

### Discussion

Around 37% of patients with suspected stroke present to hospital within three hours of the onset of symptoms and 50% within six hours of the onset of symptoms, similar to that reported in US studies.<sup>8-14</sup> Therefore thrombolysis may be a realistic option in the United Kingdom.

The study identified considerable delays in assessment of patients after arrival at hospital. Some of the delays in assessment may have resulted from the knowledge that the patient was stable after assessment by nursing staff (hence low priority) and compounded by the absence of established protocols for intervention for acute stroke in most hospitals. These factors may also be responsible for the low rate of early computed tomography; scanning was requested in less



Number of patients arriving within each time interval by mode of referral

**Table 2** Overall delay times. Values are numbers (percentages) of patients unless stated otherwise

Interval	Results
<b>Onset of symptoms to arrival (n=729)</b>	
Median time (interquartile range)	6 h (1 h 48 min to 19 h 12 min)
Time interval:	
0 to 2 h 59 min	271 (37)
3 to 5 h 59 min	93 (13)
6 to 11 h 59 min	85 (12)
≥12 h	280 (38)
<b>Arrival to initial assessment by emergency doctor (n=736)</b>	
Median time (interquartile range)	37 min (16 min to 1 h 12 min)*
Time interval:	
0-15 min	163 (22)
16-30 min	121 (16)
31-45 min	113 (15)
46-60 min	82 (11)
61-120 min	151 (20)
121-179 min	50 (7)
≥180 min	56 (8)
<b>Arrival to assessment by senior doctor (n=736)</b>	
Median time (interquartile range)	1 h 9 min (33 min to 1 h 50 min)*
Time interval:	
0-15 min	65 (9)
16-30 min	37 (5)
31-60 min	121 (16)
61-120 min	156 (21)
121-179 min	98 (13)
≥180 min	259 (35)

\*Median in 485 patients who arrived at emergency department within three hours of onset of stroke.

than a quarter of patients and undertaken in less than 10% within three hours of arrival. The existence of a stroke unit did not result in more patients being assessed early or the uptake of more computed tomography. However, all the hospitals had stroke specialists and probably provided better stroke services than the UK average.

The study highlights the needs of service development to improve the management of acute stroke. Efforts should be made at all levels (patient, ambulance services, general practitioners) to encourage the use of emergency services as the most direct means of reducing delays in getting to hospital and increasing the number of patients eligible for therapies. That nearly one in five patients with suspected stroke have non-stroke diagnoses emphasises the importance of early evaluation by a specialist and early involvement of specialist stroke services. Most importantly, the perception that delays in presentation prevent early specialist management of stroke in the United Kingdom is not justified, and there is a good case for bringing stroke practice in line with other developed countries.<sup>24</sup>

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### What is already known on this topic

Delay in presentation and assessment of patients with suspected stroke prevents the possible benefits from thrombolysis being achieved

Little is known about the presentation and early management of patients with acute stroke in the United Kingdom

### What this study adds

Most patients with suspected stroke in the United Kingdom arrive at hospital within six hours of the onset of symptoms

Not all patients are evaluated by a senior doctor within three hours of arrival at hospital and most do not undergo computed tomography

The potential for thrombolysis in patients with acute stroke can be improved significantly by greater use of emergency services and expediting evaluation and investigations by doctors

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- 1 American Heart Association. *Heart and stroke statistical update*. Dallas, TX: American Heart Association, 1999.
- 2 Hankey GJ, Warlow CP. Treatment and secondary prevention of stroke: evidence, costs and effects on individuals and populations. *Lancet* 1999;354:1457-63.

- 3 Grotta JC. Acute stroke therapy in the millennium: consummating the marriage between the laboratory and the bedside: the Feinberg lecture. *Stroke* 1999;30:1722-8.
- 4 Bath PM, Lees KR. ABC of arterial and venous disease: acute stroke. *BMJ* 2000;320:920-3.
- 5 Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolysis for acute ischaemic stroke. *Cochrane Library*. Issue 1. Oxford: Update software, 2000.
- 6 Lees KR. Thrombolysis. *Brit Med Bull* 2000;389-400.
- 7 Alberts MJ, Hademenos G, Latchaw RE, Jagoda A, Marler JR, Mayberg MR, et al. Recommendations for the establishment of primary stroke centers. *JAMA* 2000;283:3102-9.
- 8 Smith MA, Doliszny KM, Shahar E, McGovern PG, Arnett DK, Luepker RV. Delayed hospital arrival for acute stroke: the Minnesota stroke survey. *Ann Intern Med* 1998;129:190-6.
- 9 Katzan IL, Furlan AJ, Way LE, Farnk JJ, Harper DL, Hinchey JA, et al. A systematic audit of iv tPA in Cleveland area hospitals. *Stroke* 1999;30:266.
- 10 Evenson K, Rosamond W, Morris D. Prehospital and in-hospital delays in acute stroke care. *Neuroepidemiology* 2001;20:65-76.
- 11 Lacy C, Suh D, Bueno M, Kostis J, for the STROKE Collaborative Study Group. Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology (STROKE). *Stroke* 2001;32:63-9.
- 12 Schroeder E, Rosamond W, Morris D, Evenson K, Hinn A. Determinants of emergency medical services use in a population with stroke symptoms: the Second Delay in Accessing Stroke Healthcare (DASH II) Study. *Stroke* 2000;31:2591-6.
- 13 Morris DL, Rosamond W, Madden K, Schultz C, Hamilton S. Prehospital and emergency department delays after acute stroke. The Genentech Stroke Presentation Survey. *Stroke* 2000;31:2585.
- 14 Kothari R, Jauch E, Broderick J, Brott T, Sauerbeck L, Khoury J, et al. Acute stroke: delays to presentation and emergency department evaluation. *Ann Emerg Med* 1999;33:3-8.
- 15 Rosamond W, Gorton R, Hinn A, Hohenhaus S, Morris D. Rapid response to stroke symptoms: the Delay in Accessing Stroke Healthcare (DASH) Study. *Acad Emerg Med* 1998;5:45-51.
- 16 Menon SC, Pandey DK, Morganstern LB. Critical factors in determining access to acute stroke care. *Neurology* 1998;51:427-32.
- 17 Wester P, Radberg J, Lundgren B, Peltonen M, for the Seek-Medical-Attention-in-Time Study Group. Factors associated with delay admission to hospital and in-hospital delays in acute stroke and TIA. *Stroke* 1999;30:40-8.
- 18 Morris D, Rosamond W, Hinn A, Gorton R. Time delays in accessing stroke care in the emergency department. *Acad Emerg Med* 1999;6:218-23.
- 19 Bratina P, Greenberg L, Pasteur W, Grotta J. Current emergency department management of stroke in Houston, Texas. *Stroke* 1995;26:409-14.
- 20 Intercollegiate Working Party on Stroke. *National clinical guidelines on stroke*. London: Royal College of Physicians, 2000.
- 21 *Coronary Heart Disease/Stroke Task Force report*. Edinburgh: Scottish Executive, 2001.
- 22 Barer D, Main A, Lodwick R. Practicability of early treatment of acute stroke. *Lancet* 1992;339:1540-1.
- 23 Harper GD, Haigh RA, Potter JF, Castleden CM. Factors delaying hospital admission after stroke in Leicestershire. *Stroke* 1992;23:835-8.
- 24 Hacke W. A late step in the right direction for stroke care. *Lancet* 2000;356:869-70.

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## Dietary aflatoxin exposure and impaired growth in young children from Benin and Togo: cross sectional study

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Fetal and early childhood environment, including the nutritional status of the pregnant mother and the infant, are considered critical for growth and risk of disease in later life.<sup>1</sup> Many people in developing countries are not only malnourished but also chronically exposed to high levels of toxic fungal metabolites (mycotoxins). One family of mycotoxins, the aflatoxins, are carcinogenic and immunotoxic and cause growth retardation in animals.<sup>2</sup> Aflatoxins contaminate staple foods in West Africa, particularly maize and groundnuts, as a result of hot, humid storage conditions that promote fungal growth. High exposure to aflatoxins occurs throughout childhood in the region,<sup>3,4</sup> suggest-

ing that growth and development could be critically affected. We assessed exposure to aflatoxins in relation to anthropometric measures in children in Benin and Togo.

### Methods and results

We studied 480 children (aged 9 months to 5 years) from 16 villages in four geographic zones (four in each zone): Sudan savannah, north Guinea savannah, south Guinea savannah, and coastal savannah. The Ministries for Health in Benin and Togo gave ethical approval, and parents gave informed consent. We determined