WORKING GROUP ON ACUTE PURCHASING

The Clinical and Cost-effectiveness of Computed Tomography in the Management of Transient Ischaemic Attack and Stroke

January 1997

GUIDANCE NOTE FOR PURCHASERS 97/01

Trent Development and Evaluation Committee

THE CLINICAL AND COST-EFFECTIVENESS OF COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF TRANSIENT ISCHAEMIC ATTACK AND STROKE (22.04.97)

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EXPERT ADVISORS TO TRENT DEC: Dr Ferguson, North Derbyshire Health Authority, Mr McCabe, ScHARR.

DECISION: The Committee commended the report as a useful document for outlining when CT scans should be undertaken. It considered it important that the information contained in the report should be disseminated to hospitals and general practitioners across the region. The guidelines for clinical application were supported by the Committee.

January 1997

THE CLINICAL AND COST-EFFECTIVENESS OF COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF TRANSIENT ISCHAEMIC ATTACK AND STROKE

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The Institute:

- provides advice and support to NHS staff on undertaking Health Services Research (HSR);
- provides a consultancy service to NHS bodies on service problems;
- provides training in HSR for career researchers and for health service professionals;
- provides educational support to NHS staff in the application of the results of research;
- disseminates the results of research to influence the provision of health care.

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FOREWORD

Individuals or small groups in each District Health Authority in Trent have historically considered evidence on the likely effectiveness of new procedures or therapies in conjunction with their cost, making judgements on whether these should be supported. Since all or most Health Authorities face the same issues, there tends to be repetition in analysis and this can be wasteful of scarce professional expertise.

There are national attempts to remedy this situation by providing information on the effectiveness of interventions and these are welcomed. There remains, however, a significant gap between the results of research undertaken and their incorporation into contracts.

Following a request from purchasers, a network has been established in the Trent Region to allow purchasers to share research knowledge about the effectiveness of acute service interventions and to determine collectively their purchasing stance.

ScHARR, which houses the Sheffield Unit of the Trent Institute for Health Services Research, facilitates a Working Group on Acute Purchasing. A list of interventions for consideration is recommended by the purchasing authorities in Trent and approved by the Purchasing Authorities Chief Executives (PACE) and the Trent Development and Evaluation Committee (DEC). A public health consultant from a purchasing authority leads on each topic and is assisted, as necessary, by a support team from ScHARR which provides help including literature searching, health economics and modelling. A seminar is then led by the consultant on the particular intervention where purchasers and provider clinicians consider research evidence and agree provisional recommendations on purchasing policy. The guidance emanating from the seminars is reflected in this series of Guidance Notes.

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EXECUTIVE SUMMARY

Stroke is a major cause of mortality and morbidity. It has been estimated that over 4% of NHS resources are devoted to the management of stroke, with long-term rehabilitation accounting for a significant proportion of the total amount. 'The Health of the Nation' document set a target of 40% reduction in the death rate for coronary heart disease and stroke in people under 65 and for stroke in people aged 65-74 by the year 2000.

There is significant scope for the secondary prevention of stroke through the long-term use of aspirin and oral anticoagulants. However, these treatments may lead to further problems if the initial stroke was haemorrhagic in nature. Computed Tomography (CT) scans of the head can be used to identify haemorrhagic strokes.

This paper uses published data on the benefits of secondary prevention in the management of ischaemic stroke, combined with data on the costs of CT scans in the Trent Region and drug costs from the Drug Tariff, to identify the additional costs and benefits of using CT scanning in the management of stroke compared to using a diagnostic clinical scoring system or assuming that all strokes are ischaemic.

The cost per life saved by scanning rather than using the clinical diagnosis scoring system ranges from £6,878 to £9,221, depending on the estimated effect of administering antiplatelet therapy to patients following a haemorrhagic stroke. Even at the upper end of this range, CT scanning in the management of stroke produces benefits at a cost which compares well with many procedures currently available within the NHS.

A purchasing strategy supporting the routine CT scanning of stroke patients likely to benefit from secondary prevention should be adopted. There should be a distinction between those patients requiring an urgent scan, and those requiring a scan as soon as reasonably possible within two weeks of the onset of symptoms i.e. before it becomes impossible to distinguish haemorrhagic from ischaemic strokes using a CT scan.

Such a policy is not only supported by the evidence of clinical and cost-effectiveness presented in this report, but is also consistent with the only existing professional guidelines for the management of acute stroke, published by the Royal College of Physicians and the King's Fund Forum.

1. INTRODUCTION

1.1 Computed Tomography in the Management of Transient Ischaemic Attack and Stroke

Stroke is a major cause of mortality and morbidity. In 1991 it was the cause of 12% of all deaths in England, and about half of all those who survive a stroke will be left significantly disabled.[1] Due to the resultant disability and need for prolonged rehabilitation, stroke accounts for 4.4% of total National Health Service (NHS) expenditure.[1]

'Health of the Nation'[2] targets call for :

- a reduction in the death rate for coronary heart disease and stroke in people under 65 by at least 40% by the year 2000 (baseline 1990); and
- a reduction in the death rate for stroke in people aged 65-74 by at least 40% by the year 2000 (baseline 1990).[1]

A transient ischaemic attack (TIA) is a marker of vascular disease and indicates that the patient is at risk of stroke and other serious vascular events.

A stroke may be ischaemic (85%) or haemorrhagic (15%). Haemorrhagic strokes can be further classified into either primary intracerebral haemorrhages - bleeding into the brain, or subarachnoid haemorrhages (SAH) - bleeding around the brain. Antiplatelet therapy and oral anticoagulants have proven benefit in terms of the management of TIA and long-term secondary prevention following an ischaemic stroke. There is no evidence of the effect of giving these treatments to patients with haemorrhagic strokes, but both are associated with haemorrhagic complications. Therefore, it is assumed that such treatment would have an adverse effect on outcome.

Computed Tomography (CT) scans of the head can be used to confirm the diagnosis of stroke, and to differentiate between ischaemic, haemorrhagic and non-stroke lesions. However, the overall clinical and cost-effectiveness of CT scanning in the management of TIA and stroke remains uncertain.

An agreement on the role of CT scanning is central to the development of shared care guidelines for the management of TIA and stroke.

1.2. Stroke and Transient Ischaemic Attack : Incidence and Prognosis

Table 1: Incidence of Stroke and Transient Ischaemic Attack per 100,000 Population per Year[3]

EVENT	INCIDENCE
STROKE:	
Cerebral infarction	202
Primary intracerebral haemorrhage	26
Subarachnoid haemorrhage	12
Total	**240**
TIA:	
Carotid territory	34
Other	8
Total	**42**

The overall 30 day case fatality rate following a first-ever stroke is 19%, but there is considerable variation by pathological type: [3,4,5,6,7,8,9,10]

Cerebral infarction	10%
Primary intracerebral haemorrhage	50%
Subarachnoid haemorrhage	46%

The overall one year mortality rate is 31%, varying by pathological type as follows:

Cerebral infarction	23%
Primary intracerebral haemorrhage	62%
Subarachnoid haemorrhage	48%

The proportion of all survivors assessed as being functionally independent at one year varies by pathological type as follows:

Cerebral infarction	65%
Primary intracerebral haemorrhage	68%
Subarachnoid haemorrhage	76%

The risk of stroke following a TIA is highest in the first year, at about 11%, falling to a constant rate of 5.5% per year thereafter. The risk of death is about 7% per year (one and a half times normal), mostly from stroke or myocardial infarction.

There is good evidence from OPCS data that the mortality rate from stroke has consistently fallen in this country over the past 20 years, although the rate of decline may now have slowed. The cause(s) of this decrease is much debated, however, with the expected increase in both the number and proportion of elderly people in the population, the overall incidence of stroke and TIA is likely to increase in the coming years.

1.3. The Management of Transient Ischaemic Attack and Stroke : Effective Therapeutic Interventions

1.3.1. Transient Ischaemic Attack

The appropriate management of hypertension (and possibly hypercholesterolaemia) is likely to reduce the risk of a future stroke, as will the cessation of smoking, but the effect of such strategies has not been quantified.[11]

Meta-analysis has indicated that antiplatelet drugs reduce the risk of future serious vascular events (stroke, myocardial infarction or vascular death) by about one quarter.[12] This equates to a three year benefit of about 40 vascular events avoided per 1,000 patients treated. Treatment should commence immediately and is probably required indefinitely.

Oral anticoagulation is indicated when a definite source of cardiac embolism has been identified, and for patients with atrial fibrillation. It is estimated that 90 serious vascular events will be prevented if 1,000 such patients are anticoagulated for one year.[13] Antiplatelet therapy has a less significant protective effect in this group of patients (40 events prevented

per 1,000 patients treated for one year), but can be used in those patients for whom an anticoagulant is contraindicated.

Finally, for those patients in whom further investigation reveals carotid stenosis of greater than 70%, carotid endarterectomy is generally more effective than medical treatment alone. Following surgery, there is a 5% reduction in the three year risk of any disabling or fatal stroke (or surgical death).[14]

1.3.2. Stroke

(i) *Haemorrhagic stroke*

In patients with a SAH, oral nimodipine (a calcium antagonist) reduces the incidence of cerebral ischaemia and poor outcome by about one third.[15] These patients need to be identified promptly so that neurosurgical intervention can be considered. Similarly, neurosurgical intervention may be required following a cerebellar stroke because of the risk of obstructive hydrocephalus.

(ii) *Ischaemic stroke - acute phase*

The International Stroke Trial Collaborative Group has recently published the results of a major, randomised trial of up to 14 days of antithrombotic therapy (aspirin and/or heparin) started as soon as possible after an acute ischaemic stroke.[16] At this stage the routine use of low or medium-dose subcutaneous heparin cannot be recommended, although further research may identify certain groups of patients who could benefit from such treatment. However, the early use of aspirin 300mg daily was associated with a reduction in the number of deaths or recurrent strokes (10 per 1,000 patients treated) in the first few weeks after the acute event. Although this benefit was not as great as anticipated, and was not maintained at six months, similar results have been reported by the Chinese Acute Stroke Trial[17]. The immediate use of aspirin should be considered, therefore, in all patients with acute ischaemic stroke, once the diagnosis has been confirmed.

A recent US study showed an improved clinical outcome at three months for patients with acute ischaemic stroke treated within three hours with the thrombolytic, tissue plasminogen activator (t-PA).[18] However, there was no significant reduction in mortality, and there was an increased incidence of symptomatic intracerebral haemorrhage in those treated with t-PA. The practical difficulties involved in treating such patients within three hours of the onset of stroke, and the equivocal results of previous studies of thrombolytic therapy (including trials

stopped because of unacceptable rates of intracerebral haemorrhage) dictate that the routine use of such treatment cannot be recommended at this stage. Again, future studies may identify discrete sub-groups of patients with ischaemic stroke who may benefit.

(iii) *Ischaemic stroke - longer term*

Antihypertensive treatment is likely to reduce the absolute risk of subsequent vascular events, but should be deferred for at least a few days after the onset of stroke.[19]

Long-term antiplatelet therapy should be offered to patients following an ischaemic stroke, as this has been shown to reduce the risk of future serious vascular events by about a quarter (a three year benefit of about 40 vascular events avoided per 1,000 patients treated).[12] As stated above, such treatment should be started as soon as possible after the onset of symptoms.

Anticoagulant therapy is indicated for those patients with minor ischaemic strokes who are in atrial fibrillation.[13] At present there is no evidence to support starting such treatment within two weeks of the onset of symptoms. Antiplatelet therapy is an alternative in those patients for whom an anticoagulant is contraindicated.

Finally, patients who make a good functional recovery following an ischaemic stroke in the territory of the internal carotid artery should be investigated with a view to a carotid endarterectomy being performed.[14]

1.4. Dangers of Inappropriate Treatment

There is little evidence on the dangers of inappropriate treatment, specifically, the treatment of haemorrhagic stroke with antiplatelet therapy (e.g. aspirin) or anticoagulant (e.g. warfarin).

Warfarin is certainly a known aetiological factor in the incidence of intracerebral haemorrhage in the general population. In a review of the evidence, Kase reported that warfarin was associated with bleeding complications in about 7-8% of patients.[20] Although intracerebral haemorrhage accounts for only 0.5-1.5% of all these bleeding events, the prognosis is very poor, and the risk increases with age. Overall, warfarin has been estimated to increase between 8-fold and 11-fold the risk of intracerebral haemorrhage, as compared with non-anticoagulated individuals with similar risk factor profiles. Therefore,

even in the absence of evidence of a deleterious effect (and it is difficult to envisage such evidence being collected), it is reasonable to assume that warfarin is contraindicated in patients with a haemorrhagic stroke.

Similarly, there is no evidence on the outcome in patients with a haemorrhagic stroke treated with antiplatelet therapy. However, there is circumstantial evidence from the work of the Antiplatelet Trialists' Collaboration.[12] In these studies, compared to controls, there was an increased incidence of haemorrhagic stroke in patients at risk of occlusive vascular disease who were treated with antiplatelet therapy. This increase was non-significant in those classified as 'high risk' patients, but significant in those patients classified as 'low risk', in whom the antiplatelet therapy was being used for the primary prevention of serious vascular events. In these 'low risk' patients, this increased incidence of haemorrhagic stroke largely accounted for the lack of a significant overall reduction in vascular mortality. Thus, it would appear that antiplatelet therapy is also contraindicated in patients with a haemorrhagic stroke, although the effect on outcome in these patients cannot be quantified.

2. USE OF COMPUTED TOMOGRAPHY IN THE MANAGEMENT OF TRANSIENT ISCHAEMIC ATTACK AND STROKE : SUMMARY OF EVIDENCE OF EFFECTIVENESS

2.1 Why Computed Tomography and not Magnetic Resonance Imaging?

Computed Tomography is generally assumed to be the 'gold-standard' diagnostic test for stroke, but there are certain reservations which accompany this assumption. CT is quick and largely non-invasive, and is extremely accurate in distinguishing haemorrhage from infarction even moments after the event (although the best time to detect small haemorrhages is probably at 24-48 hours). However, the density of haemorrhages declines with time, so that by 14-21 days the haematoma can be isodense with brain and thus invisible.[21] Also, 40-50% of diagnosed infarcts are not visualised until 48 hours after the event and, thus, a negative scan during this period cannot exclude a cerebral infarct.[22] Finally, the cerebellum and brain stem are not well evaluated by CT because the bony casing of the posterior fossa tends to obscure these structures.

Magnetic resonance imaging (MRI) certainly has the advantage over CT with respect to the identification of structures in the posterior fossa, but has a longer imaging time, which can introduce movement artifacts (a potential problem with restless stroke patients).

One recent study attempted to compare the performance of the two techniques in the early detection of ischaemic stroke or haemorrhage.[23] This was a prospective study of acute strokes, with patients receiving a baseline clinical assessment followed by baseline imaging studies (concurrent CT and MRI scans). The process was repeated at intervals of 24 hours, three to five days and three months. The study neurologists who performed the clinical assessment were blinded to the results of imaging, as were the study radiologists to the clinical findings. A total of 80 patients were recruited (the refusal rate was not reported) within 24 hours of the onset of symptoms; 68 of these being recruited within four hours. Seventy five of the patients recruited were cerebral infarcts and only five were due to haemorrhage; those patients with the clinical diagnosis of SAH were excluded from the study. Neither technique was significantly superior in the very early detection of either haemorrhage or infarction although, in the case of haemorrhage, this is not surprising given the small number. Significantly more baseline CT scans were reported as normal in those patients whose symptoms had resolved within 24 hours and whose scans, therefore, should not have shown evidence of an acute event.

Therefore, given also that CT is cheaper and much more readily available than MRI, it probably deserves to be regarded as the 'gold standard'.

2.2. How Can the Effectiveness of Computed Tomography be Assessed?

CT scanning of the head is the most widely used imaging technique in the evaluation of stroke.[24] However, there have been no randomised controlled trials or observational studies to compare the outcome of stroke, or TIA, patients receiving a CT scan with those not receiving a scan. A measure of effectiveness which can be assessed from the literature, however, is the 'yield' of a CT scan performed on these patients, defined as the proportion of the tests performed that detect a pathologically relevant or potentially treatable condition that influences management.[25]

2.3. Computed Tomography and Transient Ischaemic Attack

In the Oxfordshire Community Stroke Project, 512 patients with transient neurological symptoms either were referred by their GPs or presented at a hospital.[7] Following assessment by the study team, only 195 (38%) were classified with the clinical diagnosis of TIA, a further 46 (9%) were classified as possible TIAs, and the remainder were diagnosed as suffering from a wide variety of conditions including two meningiomas. Of the 195 TIAs, 184 were classified as incident TIAs, the remaining patients having had a previous TIA or stroke. Of the 184 incident TIAs, 120 (65%) received a CT scan.[26] The results were as follows:

- No intracranial (subarachnoid or primary intracerebral) haemorrhage reported;
- No structural lesion (tumour, aneurysm or arteriovenous malformation) reported;
- Ischaemic lesions reported in 32 scans (27%).

However, when the positive reports were compared with the clinical features, the ischaemic lesion was found to be situated in an area of the brain appropriate to the patients' symptoms in only 14 cases (12%). Also, there were no significant differences in the clinical features, the duration of the attacks or the prognosis of patients with and without ischaemic lesions on CT. However, the numbers were small and, therefore, this information, was of no additional value to the clinician.

Similar results were reported in a Finnish hospital-based study of acute cerebrovascular events,[27] although it might be assumed that patients with an atypical course to their disease might be over-represented in such a study. The CT results for the 51 patients with a presumed TIA were as follows:

- No intracranial haemorrhage reported;
- No structural lesion reported;
- Ischaemic lesions reported in 3 scans (6%);
- Non-specific lesions reported in 15 scans (29%) - largely local or generalised atrophy of varying severity.

None of the non-specific changes was felt to be of clinical relevance, and the relevance of the ischaemic lesions was not discussed.

Similarly, a prospective study of 469 consecutive patients considered for carotid endarterectomy was performed in the US over a five year period.[28] Of these, 237 (51%) were diagnosed as having suffered TIA, and all patients went on to receive a duplex scan of the carotid vasculature in the neck, a CT scan and a carotid arteriography. No intracranial haemorrhages or structural lesions were reported in any of the 469 scans. Ischaemic lesions were reported in 119 of the 469 scans (25%) but, unfortunately, this information was not provided separately for patients with TIA. However, the result of the CT scan did not influence the decision to proceed with surgery in any of the cases, and neither did the findings correlate with postoperative morbidity or mortality. It is impossible to know exactly how much emphasis the study team did place on the result of the CT scan, but the proportion of abnormal scans was certainly very similar in both the operative (23%) and non-operative (27%) groups.

The results from these studies suggest that there is no clinical benefit to be gained from routinely CT scanning patients with TIA as clinically diagnosed by a specialist. Significantly, intracranial haemorrhage was not reported in any of these studies in patients fulfilling the main criterion for diagnosing a TIA, namely that the symptoms resolved within 24 hours. This suggests that it is useful to maintain the distinction between TIA and minor ischaemic stroke, even if their management and prognosis are very similar, as the risk of a supposed ischaemic event actually being haemorrhagic appears to increase with symptoms of longer duration.

2.4 Computed Tomography and Stroke

In assessing the yield from the CT scanning of stroke patients, one option is to compare the results of such scans with the clinical diagnosis of those same patients. The evidence exists to enable this comparison to be made for the two issues central to the management of stroke: distinguishing stroke from non-stroke, and distinguishing haemorrhagic from ischaemic stroke.

2.4.1 Distinguishing Stroke from Non-stroke

After the first two years of the Oxfordshire Community Stroke Project, the referrals to the study team were evaluated.[29] For the 736 referrals of acute neurological deficit, the clinical diagnosis of the study team was as follows:

Clinically definite first stroke	325
TIA	74
Previous stroke	176
Referred in error	29
Clinically not stroke	132

Of the 325 'clinically definite first strokes', five non-stroke lesions (two subdural haematomas, two gliomas and one metastasis) were detected on CT scan (90% of patients receiving a scan). Of the 132 'clinically not strokes', the majority of whom did not receive a CT scan, three were reclassified as a first stroke following CT.

This gives a false positive rate of 1.5% and a false negative rate of 1% for the study neurologists in the clinical diagnosis of stroke, although these figures may have been higher if all patients had been scanned.

Similarly, in an Italian community-based study of stroke, of 379 patients diagnosed as 'clinically definite first strokes' by the study team, four (1%) were found to have a subdural haematoma or tumour on CT scan (false positives).[9] However, no figures were provided on the false negatives (those assessed as a non-stroke and subsequently diagnosed as a stroke following a CT scan).

In the Finnish hospital-based study (and therefore a selected population), the study neurologist had a false positive rate of 3.2% and false negative rate of 4.7% in diagnosing stroke compared to CT scan.[27]

These three studies all incorporated specialist assessment of suspected strokes, and it can reasonably be assumed that non-specialist assessment would result in higher false positive and false negative rates. Indeed, the incidence of non-stroke lesions detected by CT scanning in patients with suspected stroke has been reported to be as high as 16%.[21] The detection of non-stroke lesions on scans of suspected strokes is certainly an added bonus as, even though structural lesions such as subdural haematomas and tumours are likely to present again, if not detected by the scan, the prognosis will worsen with time.

2.4.2 Distinguishing Haemorrhagic from Ischaemic Stroke

Clinical scoring systems have been advocated for differentiating between haemorrhagic and ischaemic strokes when a CT scanner is unavailable. Two such systems have been evaluated in the literature, the Guy's Hospital score[30] (alternatively known as the Allen score) and the Siriraj stroke score.[31] Both these scores were developed to produce relative probabilities of haemorrhage and ischaemia for individual patients, and cut-off points can be used to classify strokes as 'probably haemorrhagic', 'probably ischaemic' or of 'uncertain pathology'. For the purposes of this work, these scoring systems can be regarded as standardised substitutes for thorough clinical assessment of acute stroke.

The Guy's Hospital score is of most interest as this system was developed for use in the UK, and Table 2 summarises the expected results of using this score in the clinical assessment of 1,000 acute strokes. The figures are based on a study by Celani et al, in which 15% of the strokes were subsequently confirmed as haemorrhagic following a CT scan (consistent with the community based studies of the epidemiology of stroke).[32]

TABLE 2: Outcome of the Use of the Guy's Hospital Score in the Clinical Assessment of 1,000 Acute Strokes

OUTCOME	GUY'S HOSPITAL SCORE Number	(95%CI)
Correctly Diagnosed Ischaemic Stroke	680	(620-740)
Wrongly Diagnosed Ischaemic Stroke (i.e. CT Shows Haemorrhage)	70	(37-103)
Correctly Diagnosed Haemorrhagic Stroke	43	(17-69)
Wrongly Diagnosed Haemorrhagic Stroke (i.e. CT Shows Ischaemia)	17	(0-34)
Uncertain Pathology	190	(139-241)

An estimate of the overall yield from the use of CT scanning in the assessment of the same 1,000 acute strokes can thus be made:

Yield = 1,000 - (680 + 43) = 277 = **27.7%.**

Thus, in 27.7% of cases a CT scan of the head would change the clinical diagnosis (or enable the diagnosis to be made) and alter the subsequent management of the patient.

The false positive rate in the clinical diagnosis of stroke has been estimated at 4%.[27,29] Thus, for every 1,000 suspected strokes, CT scanning would reveal 40 non-strokes. The effect of these non-strokes on the estimate of the yield cannot be calculated, but it is likely to increase it.

3. COST AND BENEFIT IMPLICATIONS OF ADOPTING INTERVENTION

As the studies identified in the literature review suggest that there is no clinical benefit to be gained from routinely scanning patients with TIA, there is no reason to conduct an economic evaluation of such a programme. However, there is good evidence that routinely scanning stroke patients will influence the subsequent management of a significant proportion of them, and evidence also exists on the effectiveness of the therapeutic interventions used in the management of ischaemic stroke.[12,13] These two sources of information can form the basis of an economic evaluation, together with the following data on costs:

Anticoagulant (warfarin 6mg daily, plus 8 INR tests at £1.64 each)	£34.11 per annum
Antiplatelet (aspirin 300mg daily)	£1.61 per annum
Non contrast CT scan of the head	£103.77
Transport for an outpatient CT scan (minimum charge for a health transport vehicle with two crew)	£30.00

Mean dose of warfarin and frequency and cost of INR tests taken from a review of the use of anticoagulants in primary care (personal communication, Framework for Appropriate Care Throughout Sheffield).
The drug costs are taken from the Drug Tariff.[33]
The CT scan and transport costs are the mean Extra-Contractual Referral (ECR) costs of these procedures within Trent.[34]

3.1 Assumptions Made in the Economic Evaluation

- In the absence of comparable data, the baseline outcome event rates for haemorrhagic strokes are assumed to be the same as for ischaemic strokes.[12,13]

- Aspirin has been shown to increase the risk of fatal haemorrhagic stroke by 0.25% over three years in patients with a previous ischaemic stroke.[12] The effect when given to patients with a previous haemorrhagic stroke can only be estimated, but the following options are considered:
    A. Same risk as when given to patient with ischaemic stroke - 0.25%
    B. Ten times the risk of giving it to patient with ischaemic stroke - 2.5%
    C. Twenty five times the risk of giving it to patient with ischaemic stroke - 6.25%

- It is also assumed that patients with a haemorrhagic stroke who receive aspirin do not experience the mortality/morbidity benefits observed in patients with an ischaemic stroke.

3.2 Estimates of the Cost per Life Saved for Various Scenarios

Baseline. 1,000 acute strokes - none scanned or treated with aspirin or warfarin.

1,000 acute strokes: - 850 ischaemic - 153 in atrial fibrillation (AF).[35]
- 150 haemorrhagic - 16 in AF.[35]

Expected number of deaths in the 3 years following the acute stroke = 164.

Scenario 1. 1,000 acute strokes - none scanned, but all treated with aspirin.

Costs incurred - the cost of the aspirin.

Table 3: Cost per Life Saved for Scenario 1

OUTCOME	OPTION A	OPTION B	OPTION C
Number of Deaths	149	152	158
Lives Saved with Respect to Baseline	15	12	6
Cost of Programme (£)	4,582	4,578	4,565
Undiscounted Cost Per Life Saved (£)	305	382	761
Discounted Cost Per Life Saved (£)*	308	382	772

*Costs and benefits (lives saved) discounted at a rate of 6% per annum (the rate currently recommended by the Treasury for use throughout the public sector).

Scenario 2. 1,000 acute strokes - all assessed using the Guy's Hospital score, and those classified as ischaemic treated with aspirin.

Costs incurred - the cost of the aspirin.

Table 4: Cost per Life Saved for Scenario 2

OUTCOME	OPTION A	OPTION B	OPTION C
Number of Deaths	151	153	156
Lives Saved with Respect to Baseline	13	11	8
Cost of Programme (£)	3,435	3,432	3,427
Undiscounted Cost Per Life Saved (£)	264	312	428
Discounted Cost Per Life Saved (£)	269	315	432

Scenario 3. 1,000 acute strokes - all scanned and treated with aspirin or warfarin as appropriate.

Costs incurred - the cost of the scans, aspirin and warfarin, and the transport costs for the 240 patients not admitted to hospital (Hospital Episode Statistics suggest that 76% of acute strokes are currently admitted to hospital in Trent).

Expected number of deaths in the 3 years following the acute stroke = 137.
Lives saved with respect to baseline = 27.
Cost of programme = £128,669.
Undiscounted cost per life saved = £4,766.
Discounted cost per life saved = £4,990.

In order to estimate the cost per life year saved in each scenario, a number of assumptions would have to be made with respect to the age at which the acute stroke occurred (not available from the Antiplatelet Trialists' Collaboration),[12] the persistence of benefits beyond the three year follow-up period and the life expectancy of this group of patients. Given the assumptions already made in the analysis, this was felt to be of limited value.

3.3 Estimates of the Cost per Serious Vascular Event Avoided for Each Scenario

Baseline. 1,000 acute strokes - none scanned or treated with aspirin or warfarin.

Expected number of outcome events in the 3 years following the acute stroke:

Non-fatal myocardial infarctions = 28.

Non-fatal strokes = 138.

Vascular deaths = 130.

Total number of serious vascular events = 296.

Scenario 1. 1,000 acute strokes - none scanned, but all treated with aspirin.

Table 5: Cost per Serious Vascular Event Avoided for Scenario 1

OUTCOME	OPTION A	OPTION B	OPTION C
Number of Non-Fatal Myocardial Infarctions	**20**	**20**	**20**
Number of Non-Fatal Strokes	**119**	**119**	**119**
Number of Vascular Deaths	**115**	**118**	**124**
Total Number of Serious Vascular Events	**254**	**257**	**263**
Serious Vascular Events Avoided with Respect to Baseline	**42**	**39**	**33**
Cost of Programme (£)	**4,582**	**4,578**	**4,565**
Undiscounted Cost Per Serious Vascular Event Avoided (£)	**109**	**117**	**138**
Discounted Cost Per Serious Vascular Event Avoided (£)	**109**	**117**	**138**

Scenario 2. 1,000 acute strokes - all assessed using the Guy's Hospital score, and those classified as ischaemic treated with aspirin.

Table 6: Cost per Serious Vascular Event Avoided for Scenario 2

OUTCOME	OPTION A	OPTION B	OPTION C
Number of Non-Fatal Myocardial Infarctions	**22**	**22**	**22**
Number of Non-Fatal Strokes	**123**	**123**	**123**
Number of Vascular Deaths	**118**	**120**	**123**
Total Number of Serious Vascular Events	**263**	**265**	**268**
Serious Vascular Events Avoided with Respect to Baseline	**33**	**31**	**28**
Cost of Programme (£)	**3,435**	**3,432**	**3,427**
Undiscounted Cost Per Serious Vascular Event Avoided (£)	**104**	**111**	**122**
Discounted Cost Per Serious Vascular Event Avoided (£)	**104**	**111**	**123**

Scenario 3. 1,000 acute strokes - all patients scanned and treated with aspirin or warfarin as appropriate.

Expected number of outcome events in the 3 years following the acute stroke:

Non-fatal myocardial infarctions = 19.

Non-fatal strokes = 92.

Vascular deaths = 102.

Total number of serious vascular events = 213.

Serious vascular events avoided with respect to baseline = 83.

Cost of programme = £128,669.

Undiscounted cost per serious vascular event avoided = £1,550.

Discounted cost per serious vascular event avoided = £1,621.

3.4. Summary of the Cost-effectiveness of Each Scenario

Table 7: Summary of the Cost-effectiveness of Each Scenario

SCENARIO	LIVES SAVED	UNDISCOUNTED (DISCOUNTED*) COST PER LIFE SAVED (£)	SERIOUS VASCULAR EVENTS AVOIDED	UNDISCOUNTED (DISCOUNTED*) COST PER SERIOUS VASCULAR EVENT AVOIDED (£)
One **1,000 Acute Strokes - None Scanned but All Treated with Aspirin:**				
Option A	**15**	**305 (308)**	**42**	**109 (109)**
Option B	**12**	**382 (382)**	**39**	**117 (117)**
Option C	**6**	**761 (772)**	**33**	**138 (138)**
Two **1,000 Acute Strokes - All Assessed Using GHS,+ and Those Classified as Ischaemic Treated with Aspirin:**				
Option A	**13**	**264 (269)**	**33**	**104 (104)**
Option B	**11**	**312 (315)**	**31**	**111 (111)**
Option C	**8**	**428 (432)**	**28**	**122 (123)**
Three **1,000 Acute Strokes - All Scanned And Treated with Aspirin or Warfarin as Appropriate**	**27**	**4,766 (4,990)**	**83**	**1,550 (1,621)**

***** Costs and benefits discounted at a rate of 6% per annum.
+ GHS : Guy's Hospital score

3.5. Sensitivity Analysis

The two variables that impact most on these analyses are:

1. The effect of aspirin when given to patients with a previous haemorrhagic stroke - a range of estimates has been provided based on differing assumptions as to the magnitude of this effect.

2. The cost of a non-contrast CT scan of the head - the mean ECR cost of this procedure was used in the analyses, but the actual cost ranged between £44.69 and £200 for the various providers within the Trent Region.[34]

Using this information, a range of estimates can be provided for Scenario 3:

Discounted cost per life saved = £2,682 to £8,220.

Discounted cost per serious vascular event avoided = £871 to £2,670.

3.6 Crude Estimate of the Net Cost of Each Scenario

The analysis presented earlier in this section uses gross costs. However, there is also potential for cost savings from vascular events avoided. Secondary care cost savings have, therefore, been calculated for each scenario, based on the number of serious vascular events avoided. These savings are purely notional, as no true savings can be made until a hospital ward closes or staffing levels are reduced, but the analyses do demonstrate the monetary value of some of the benefits arising from each scenario.

The following secondary care costs are again the mean ECR costs attributed to these diagnoses within the Trent Region.[34]

Acute myocardial infarction (uncomplicated) - £1,510
Stroke - £2,216
Vascular death - each death attributed to either an acute myocardial infarction or stroke (in the appropriate proportion for each scenario) and assumed to consume the same resources.

Table 8: Estimate of the Net Cost of Each Scenario

SCENARIO	COST OF PROGRAMME (£)	SERIOUS VASCULAR EVENTS AVOIDED: MI/STROKE/VD+	COST SAVINGS (£)	UNDISCOUNTED NET COST/ SAVING OF PROGRAMME (£)	DISCOUNTED NET COST/ SAVING OF PROGRAMME* (£)
One **1,000 Acute Strokes - None Scanned, but All Treated with Aspirin:**					
Option A	**4,582**	**8/19/15**	**84,286**	**79,704**	**75,736**
Option B	**4,578**	**8/19/12**	**78,266**	**73,688**	**70,120**
Option C	**4,565**	**8/19/6**	**66,224**	**61,659**	**58,694**
Two **1,000 Acute Strokes - All Assessed Using GHS, # and Those Classified as Ischaemic Treated with Aspirin:**					
Option A	**3,435**	**6/15/12**	**66,471**	**63,036**	**59,596**
Option B	**3,432**	**6/15/10**	**62,443**	**59,011**	**55,773**
Option C	**3,427**	**6/15/7**	**56,400**	**52,973**	**49,936**
Three **1,000 Acute Strokes - All Scanned and Treated with Aspirin or Warfarin as Appropriate**	**128,669**	**9/46/28**	**174,340**	**45,671**	**37,786**

+ MI: Myocardial Infarction VD: Vascular Death
* Costs and benefits discounted at a rate of 6% per annum.
# GHS : Guy's Hospital score

3.7 Marginal Analysis

In the absence of a CT scan, clinical assessment of an acute stroke would be followed by the use of aspirin in those classified as ischaemic (Scenario 2). Therefore, a marginal analysis comparing Scenario 3 against Scenario 2 is required to provide purchasers with an estimate of the cost-effectiveness of Scenario 3 compared to the 'next best' alternative. The discounted costs and benefits of the two scenarios are as follows:

	Cost (£)	Lives Saved with Respect to Baseline	Serious Vascular Events Avoided with Respect to Baseline
SCENARIO 3	127,734	25.6	78.8
SCENARIO 2:			
OPTION A	3,251	12.1	31.2
OPTION B	3,248	10.3	29.3
OPTION C	3,243	7.5	26.4

Thus, the discounted marginal costs and benefits of Scenario 3 compared to Scenario 2 are:

	Cost (£)	Lives Saved	Serious Vascular Events Avoided
OPTION A	124,483	13.5	47.6
OPTION B	124,486	15.3	49.5
OPTION C	124,491	18.1	52.4

This produces a discounted marginal cost per life saved of:

OPTION A	£9,221
OPTION B	£8,136
OPTION C	£6,878

and a discounted marginal cost per serious vascular event avoided of:

OPTION A	£2,615
OPTION B	£2,515
OPTION C	£2,376

3.8 Validity of the Economic Evaluation

In the absence of a randomised controlled trial or observational study comparing the outcome of stroke patients receiving a CT scan against those not receiving a scan, data had to be drawn from a number of sources. These data were far from ideal even where they existed, the following factors detracting from the internal validity of the analyses:

- The data on the effects of using antiplatelet therapy for the secondary prevention of ischaemic stroke were taken from the Antiplatelet Trialists' Collaboration.[12] The analyses

were performed on patients with a previous history of stroke or TIA and most patients were entered into trials several weeks after the index event. The effects of treatment for ischaemic stroke may have been distorted by the inclusion of TIAs although, in the trials with individual patient information available, there was no significant difference in the outcome of the two patient groups. In addition, the beneficial effects of treatment, and the risks of inappropriate treatment, may well be greater the earlier treatment is initiated.

- The analyses of the benefits of both antiplatelet and anticoagulant therapy covered periods of follow-up between two and three years, but it is likely that the beneficial effects persist beyond this point.

- The non-strokes detected by scanning suspected strokes (mainly subdural haematomas and tumours) may be treatable, but the impact this would have on the cost-effectiveness of routine scanning cannot be predicted. Similarly, the potential benefit of referring SAHs and cerebellar strokes to the neurosurgeons for possible intervention has not been incorporated in the analysis.

- The effects, both beneficial and detrimental, of giving antiplatelet therapy to patients with haemorrhagic strokes remain unknown and have only been estimated in the analyses.

- The primary and secondary care costs (and the longer-term community care costs) are not incorporated in the analyses, and the cost of suffering endured by patients and their carers has not been considered either.

In addition, there are a number of factors which will impact on the external validity or generalisability of the analyses:

- It has been assumed that there is some spare capacity for obtaining CT scans, and that additional capital investment is not required. If this is not the case, and with the cost of CT scanners varying from about £300,000 to £1 million, the cost of implementing Scenario 3 would rise significantly. However, a survey performed in 1992/93 of all UK hospital consultant geriatricians, general physicians and neurologists (84% response rate) reported that 74% of consultants had on-site CT scanning facilities and that 90% could obtain a CT scan for patients with a stroke within two weeks of the onset of symptoms.[36] The proportion of consultants with on-site CT scanning facilities will certainly

have increased over the past four years, although this will not necessarily have led to increased availability.

- The marginal costs and benefits of Scenario 3 will vary between areas, as the proportion of acute stroke patients currently receiving a CT scan varies between areas. In the published literature the proportion of all acute stroke patients admitted to hospital has ranged from 54% to 76%[10] and the proportion of those admitted who receive a CT scan has varied between 17% and 50%.[37,38] In addition, the cost benefit ratio may be less favourable than that anticipated if the cases with most to gain are those currently receiving a CT scan.

Finally, it is evident that discounting the costs and benefits at a rate of 6% per annum (as currently recommended by the Treasury) has little effect on either the absolute or relative cost-effectiveness of the various scenarios. This is not surprising, as discounting is only really of importance when the timing of costs and benefits varies greatly between scenarios and, in this instance, the period of interest is only three years.

4. OPTIONS FOR PURCHASERS AND PROVIDERS

A summary of the cost-effectiveness of Scenarios 1, 2 and 3 is provided in Table 7. To help put these data in context, the cost per life saved of a range of other interventions is provided below.[39]

Table 9: The Cost per Life Saved of Other Interventions

INTERVENTION	COST PER LIFE YEAR 1991
Opportunistic lipid screening in General Practice	£3,671
Nicotine gum compared to physician advice against cigarette smoking in primary care: men aged 35-39	£3,934
Coronary care unit provision for people experiencing MI	£4,974
Breast cancer screening for women aged 45 to 65	£8,417
Formal screening for cervical cancer	£9,070
Intensive care treatment for patients with multiple trauma	£9,977
Use of neonatal intensive care unit: BW 500 to 999g	£11,400
Kidney transplant with immunosuppressive therapy	£17,400
Haemodialysis	£27,000

All three scenarios compare very favourably to the above interventions in terms of the cost per life saved. Although no comparable costs per vascular event avoided were found in the literature, all three scenarios show putative net savings when the secondary care costs attributed to these events are taken into account (Table 8). The relative cost-effectiveness of the three scenarios is difficult to assess because of the lack of data relating to the effect of administering antiplatelet therapy to a patient with a haemorrhagic stroke.

Scenario 1 is certainly equitable, but not necessarily realistic. Clinicians are unlikely to be persuaded to treat all strokes empirically with antiplatelet therapy, in the knowledge that 15% will be haemorrhagic.

In Section 2.4 it was concluded that the clinical classification of stroke would be incorrect or indeterminate in 27.7% of cases. Even if Scenario 2 was modified to include CT scanning of those classified as indeterminate, the error rate would still be 8.7%. In addition, the potential benefits of an anticoagulant would be wasted, as extensive discussion with local clinicians

(GPs and hospital consultants) has not identified a single one who would prescribe anticoagulant therapy following a stroke without a CT scan.

Scenario 3 results in considerably more lives saved and vascular events avoided than any of the alternatives. Significantly, the marginal cost per life saved of Scenario 3 compared to Scenario 2 ranges from £6,878 to £9,221, depending on the estimated effect of administering an antiplatelet to patients following a haemorrhagic stroke (Section 3.7). This marginal analysis offers an estimate of the cost-effectiveness of Scenario 3 compared with the 'next best' alternative, and the results still compare very favourably with those presented in Table 9.

It is unrealistic to assume, however, that all strokes can, or should, be scanned. In the Oxfordshire Community Stroke Project, 6.5% of patients with an acute stroke had died before a scan could be arranged, 9.2% of patients were too ill and, in a further 2.4% of cases, either the patient or his/her relatives refused.[3] It is important to try to identify those patients likely to die early or suffer severe long-term disability, as a CT scan will cause unnecessary distress for the patient and his/her family, and there is no evidence that the severely disabled will benefit from long-term secondary prevention. The trials of such therapy excluded patients who had suffered disabling strokes.[12,13] Although disability fluctuates markedly over the first week, there is good evidence that the level of disability at one week is of prognostic importance, and other prognostic features predicting death or long-term disability (such as loss of consciousness, complete paralysis and urinary incontinence) are well established.[10]

In addition, a CT scan will not influence the subsequent management of those patients in whom antiplatelet and anticoagulant therapy are contraindicated.

5. DISCUSSION AND CONCLUSIONS

There is no evidence to support a policy of routinely scanning patients with a suspected TIA. However, many patients referred to a specialist as suspected TIAs will be suffering from other conditions. This supports the view that patients with transient neurological symptoms should be referred urgently to a neurovascular physician for assessment,[11] because of both the diagnostic uncertainty and the need for suitable interventions to be introduced immediately to gain the greatest benefit. Such a policy will need to be agreed and developed at a local level.

However, a purchasing strategy supporting the routine CT scanning of stroke patients likely to benefit from secondary prevention should be adopted. There should be a distinction, as indicated below, between those patients requiring an urgent scan, and those requiring a scan as soon as reasonably possible within two weeks of the onset of symptoms i.e. before it becomes impossible to distinguish haemorrhagic from ischaemic strokes. Priority should be given to scanning these patients, as the Stroke Trials have indicated at least short-term benefits following the early use of aspirin in patients with ischaemic strokes.[16,17] There are no age restrictions for these recommendations.

Table 10: Indications for a Computed Tomography Scan Following an Acute Stroke

URGENT SCAN INDICATED	SCAN INDICATED AS SOON AS POSSIBLE (BUT WITHIN TWO WEEKS)
• Patient with evolving, unstable signs • Patient already on antiplatelet, anticoagulant or thrombolytic therapy at the time of his/her stroke • Patient known to be suffering from a bleeding disorder • Patient with suspected cerebellar stroke • Patient with suspected SAH	• Patient being considered for treatment with antiplatelet, anticoagulant or thrombolytic therapy • Patient with uncertain diagnosis of stroke • Patient being considered for carotid endarterectomy

Patients for whom antiplatelet and anticoagulant therapy are contraindicated should not receive a CT scan, unless one of the above indications applies. Neither is it appropriate to scan (routinely) moribund patients. At this stage there is no evidence to support the routine scanning of those patients suffering a severely disabling stroke (as assessed at one week)

but, if sufficient resources are available, such patients should be scanned if drug treatment of an ischaemic stroke would be considered appropriate.

Such a policy is not only supported by the evidence of clinical and cost-effectiveness presented in this report, but is also consistent with the only existing professional guidelines for the management of acute stroke, published by the Royal College of Physicians[40] and the King's Fund Forum.[24]

The implications of such a policy will need to be addressed at a local level. This will involve an assessment of the additional cost of a change in practice (current practice within each area will need to be assessed to identify the baseline position), and the provision of GP access to scanners will need to be negotiated. To avoid unnecessary hospital admissions, such access will need to be provided, either directly or via an urgent outpatient appointment.

Finally, assuming recommendations to scan routinely those stroke patients likely to benefit from secondary prevention are adopted, the feasibility of establishing a stroke register, possibly across Trent, should be examined. The maintenance of such a register would be facilitated by a policy of scanning the majority of strokes, and it would be of immense value as an aid to future audit and research projects.

6. USE OF COMPUTED TOMOGRAPHY : SUMMARY MATRIX

PATIENT GROUP AND PROPOSED INTERVENTION	PATIENT CRITERIA (GUIDELINES NOT PROTOCOLS)	ESTIMATED FUTURE ACTIVITY	OPPORTUNITY FOR COST SAVING	AUDIT/RESEARCH ACTIVITY	EFFECTS THAT COULD BE EXPECTED IN RELATION TO STARTING POINT	COST-EFFECTIVENESS
All those presenting with a TIA.	No benefit from routine CT scanning.	N/A	N/A	N/A	N/A	N/A
All those presenting with an acute stroke who meet the agreed criteria will receive a CT scan of the head, and ischaemic strokes will be treated subsequently with antiplatelet or anticoagulant therapy as appropriate.	Criteria for an urgent CT scan: • Patient with evolving, unstable signs • Patient already on antiplatelet, anticoagulant or thrombolytic therapy at the time of his/her stroke • Patient known to be suffering from a bleeding disorder • Patient with suspected cerebellar stroke • Patient with suspected SAH Criteria for a CT scan within 2 weeks: • Patient being considered for treatment with antiplatelet, anticoagulant or thrombolytic therapy • Patient with uncertain diagnosis of stroke • Patient being considered for carotid endarterectomy Indications for not scanning: • Patients for whom antiplatelet and anticoagulant therapy are contraindicated • Patient is moribund	Incidence of acute stroke = 240 per 100,000 pop. pa. A high, but variable, proportion of these will meet the agreed criteria. The additional cost of the programme will vary widely between districts depending on the proportion of acute strokes currently admitted to hospital, and the proportion of those admitted who currently receive a CT scan.	1. Reduced hospital admissions for MI and stroke. 2. Reduced use of primary and community health services for the acute management and rehabilitation of MIs and strokes.	1. Adherence to guidelines. 2. Mortality in the 3 years following an acute stroke. 3. Hospital admissions for MI and stroke in the 3 years following an acute stroke. 4. Appropriate use of antiplatelet and anticoagulant therapy following an acute stroke. 5. Development of a stroke register for audit/research activity.	Compared to a policy of clinically assessing acute strokes and treating those classified as ischaemic with antiplatelet therapy: Between 14 and 18 lives saved and between 48 and 52 serious vascular events (non-fatal MIs and strokes, and vascular deaths) avoided per 1,000 acute strokes scanned.	Discounted cost per life saved of between £6,878 and £9,221. Discounted cost per serious vascular event avoided of between £2,376 and £2,615.

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