APPENDICES

Appendix A: Clinical question and search strategies

Question ID	Question wording	Study type filters used	Databases and years
PHAR2a	What is the safety and efficacy of aspirin versus other antiplatelet agents for the treatment of patients with acute ischaemic stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR2b	What is the safety and efficacy of antiplatelet agents versus placebo for the treatment of patients with acute ischaemic stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR2c	What is the safety and efficacy of anticoagulants versus placebo for the treatment of patients with acute ischaemic stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR2d	What is the safety and efficacy of antiplatelet agents versus anticoagulants for the treatment of patients with acute ischaemic stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR3	What is the safety and efficacy of anticoagulants versus placebo or treatment as usual for the treatment of patients with acute venous stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR4	What is the safety and efficacy of anticoagulants versus antiplatelet agents for the treatment of patients with acute arterial dissection?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR5	For patients with acute warfarin associated haemorrhagic stroke, what is the safety and efficacy of i) vitamin K, ii) fresh frozen plasma, iii) prothrombin complex conjugate?	All study types	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR6	What is the safety and efficacy of anticoagulants versus antiplatelet agents or placebo for patients with acute stroke who may require anticoagulation for comorbidities (e.g. atrial fibrillation, prosthetic heart valve (mitral/aortic), deep vein thrombosis or pulmonary embolism)? What is the safety and efficacy of caval filters for deep vein thrombosis or pulmonary embolism?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PHAR7	What is the safety and efficacy of anticoagulants versus antiplatelet agents for the treatment of antiphospholipid syndrome in patients with acute ischaemic stroke?	All study types	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007

continued

Question ID	Question wording	Study type filters used	Databases and years
STAT1	a) For patients with acute stroke (including haemorrhagic stroke), what is the safety and efficacy of i) initiating statin therapy, ii) continuing statin therapy? b) Do patients on statins, and who subsequently have a stroke, have reduced mortality and morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
ADM1	In patients with suspected stroke, what are the benefits of being admitted to specialist care versus a non-specialised unit in terms of recovery time, morbidity and mortality?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
ADM2	Does rapid admission to an acute unit reduce mortality, morbidity and length of hospital stay?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
ASM1	What is the accuracy of a pre-hospital health professional assessment tool/checklist for identifying signs and symptoms of suspected stroke/TIA?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
ASM2	How accurately do scoring systems predict which patients with suspected TIA need to be referred urgently for specialist assessment?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
ASM3	In patients with a suspected minor stroke/TIA, does early versus late expert assessment reduce mortality or morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
IMAG1	After TIA, which modality (MRI or CT) should be used?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
IMAG2	Which patients with suspected TIA should be referred for urgent brain imaging?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
IMAG3	How quickly should brain imaging be performed following an acute stroke?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
IMAG4	Which patients with suspected stroke/TIA should be referred for urgent carotid imaging?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
NUTRI1	In patients with acute stroke a) what is the accuracy of i) bedside swallowing assessment, ii) videofluoroscopy, iii) fibreoptic endoscopic evaluation of swallowing, and b) how do the results of these assessments affect clinical outcomes?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007

continued

Question ID	Question wording	Study type filters used	Databases and years
NUTRI2	In patients with acute stroke who can take adequate fluids orally, does oral nutritional supplementation reduce mortality and morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
NUTRI2b	In patients with acute stroke, does fluid therapy reduce mortality and morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
NUTRI3	In patients with acute stroke who are unable to take adequate fluids orally, does a) early versus late initiation of tube feeding, or b) nasogastric (NG) (including nasal bridles) versus percutaneous endoscopically guided gastrostomy (PEG) (including radiologically inserted gastronomy tubes (RIGs)) reduce mortality and morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
PREV1	Does withdrawal or modification of oral intake prevent aspiration pneumonia after stroke?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
HYP1	What is the safety and efficacy of the interventions to control hyperglycaemia versus treatment as usual in patients with acute stroke?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
BP1	What is the safety and efficacy of measures to manipulate blood pressure versus treatment as usual in patients with acute stroke?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
OXY1	What is the safety and efficacy of supplemental oxygen therapy versus treatment as usual in patients with acute stroke?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
MOBIL1	Does early mobilisation versus treatment as usual reduce mortality and morbidity in patients with acute stroke?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
MOBIL2	Does placing patients with acute stroke in specific positions reduce mortality and morbidity?	Systematic reviews, RCTs, observational studies	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
REF1	Which patients with primary intracerebral haemorrhage should be referred for surgery?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
REF2	Which patients should be referred for decompressive hemicraniectomy?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007
REF3	Which patients with symptomatic carotid stenosis should be referred for urgent carotid interventional procedures (carotid endarterectomy and stenting)?	Systematic reviews, RCTs	Medline 1950–2007 Embase 1980–2007 Cinahl 1982–2007 Cochrane 1800–2007

NOTE: The final cut-off date for all searches was 31 October 2007.

Appendix B: Scope of the guideline and referral from the Department of Health

SCOPE

1 Guideline title

Stroke: national clinical guideline for diagnosis and initial management of acute stroke and transient ischaemic attack (TIA).

1.1 Short title

Stroke.

2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Chronic Conditions (NCC-CC) to develop a clinical guideline on acute stroke and TIA for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (DH). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines will support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

c) In parallel to the development of the Institute's acute stroke and TIA clinical guideline, the Royal College of Physicians' Intercollegiate Stroke Working Party will also be updating their guideline to focus on longer-term management and rehabilitation. The developers will work closely with the Intercollegiate Stroke Working Party to ensure continuity and to avoid any overlapping or gaps.

d) The DH has developed a National Stroke Strategy which was published in 2007. This addresses many of the issues regarding service models, structures and staffing. Where possible, this guideline will work closely with the Stroke Strategy Project Executive.

e) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Stroke is the third most common cause of death in the UK, and one of the most important causes of significant adult disability. Each year in the UK, approximately 120,000 people have a first stroke, 30% of whom die within a month. In addition, about 30,000 recurrent strokes occur. The risk of having a stroke before the age of 85 years is one in four for men, and one in five for women.

b) Stroke is a medical emergency and brain damage can be reduced if stroke is identified early enough.

c) Stroke and transient ischaemic attack (TIA) are very similar, the only difference being that the symptoms of TIA resolve completely within 24 hours, and stroke symptoms and signs persist. With refined sensitive imaging techniques, it has been clearly shown that many people who have experienced a TIA have sustained significant permanent cerebral damage. TIA is not, therefore, a benign condition. Stroke and TIA management depends upon accurate diagnosis of the underlying pathology and aetiology.

d) The risk of stroke within the first month after a TIA can be as high as 32% for some patient groups. With effective diagnosis, investigation and treatment, many strokes could be prevented.

e) The recent National Audit Office report 'Reducing brain damage: faster access to better stroke care' identified major problems with the consistent delivery of high-quality stroke care to all patients in England. Evidence clearly demonstrating that stroke is both a preventable and treatable disease has accumulated rapidly over recent years, but health services have been slow to reflect this.

f) The National Sentinel Audit in 2006 covering all hospitals in England, Wales and Northern Ireland showed that 78% of hospitals have a neurovascular clinic where only 35% of patients are seen within 7 days. Few hospitals had protocols agreed between the ambulance service and the acute Trust to ensure rapid transfer of patients with stroke to casualty, and access to brain scans remains difficult for some, particularly outside normal working hours.

g) The cost of stroke care is high, with an estimate in the National Audit Office report of £7 billion per year. Much of this is spent on providing longer-term healthcare, social services and financial support to people with residual disability. More effective acute treatment would save lives and money.

4 The guideline

a) The guideline development process is described in detail in two publications which are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the DH.

c) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.4.1 Groups that will be covered:

- Patients with transient ischaemic attacks (TIAs) or completed strokes, that is, an acute neurological event presumed to be vascular in origin and causing cerebral ischaemia, cerebral infarction or cerebral haemorrhage. This includes:
  - first and recurrent events
  - thrombotic and embolic events
  - primary intracerebral haemorrhage of any cause, including venous thrombosis.

4.4.2 Groups that will not be covered:

a) Specific issues relating to the general management of underlying conditions will not be considered, but the immediate management to reduce the extent of brain damage will be included.
b) Subarachnoid haemorrhage.
c) Children (16 and under).

4.2 Healthcare setting

Primary and secondary NHS healthcare settings, including referral to tertiary care.

- Pre-hospital emergency care settings, including ambulance services.

4.3 Clinical management

The purpose of the guideline is to describe the initial and early management (without specifying a fixed time) aimed at reducing the ischaemic brain damage, and in the case of TIAs, preventing subsequent stroke. This includes:

a) the rapid recognition of symptoms and diagnosis
b) initial and early management of stroke and TIA
c) diagnostic procedures aimed to delineate the nature and location of the pathology
d) treatment interventions that aim to minimise the pathology
e) management and maintenance of homeostasis (including fluids, nutrition and oxygen therapy)
f) initial and early pharmacotherapies including thrombolysis (note that guideline recommendations will normally fall within licensed indications; exceptionally, and only where clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use the 'Summary of product characteristics' to inform their decisions for individual patients).
g) management of complications where these are likely to affect the area of brain damage (for example, the early use of anticoagulants for venous thromboembolism in acute stroke)
h) non-pharmacological management, including the role of early mobilisation and positioning

i) indications for referral for specific interventions (for example, carotid angioplasty, carotid endarterectomy)
j) identification of people who need continuing or early anticoagulation.

4.4 Status

4.4.1 Scope

This is the final version of the scope. It has been out for consultation, modified in response to comments received and signed off by one of NICE's independent Guidelines Review Panels.

- Related NICE guidance:
  - 'Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events'. *NICE technology appraisal guidance* no. 90 (2005). Available from: www.nice.org.uk/TA090
  - 'Ischaemic stroke (acute) – alteplase'. *NICE technology appraisal guidance* no. 122 (2007). Available from: www.nice.org.uk/TA122

4.4.2 Development of guideline recommendations

The development of the guideline recommendations began in November 2006.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website: www.nice.org.uk/guidelinesmanual

5.1 Referral from the Department of Health

The Department of Health (DH) asked the Institute:

> 'To prepare a clinical guideline on the diagnosis and acute management of stroke and transient ischaemic attack, concentrating on initial treatment.'

Appendix C: Model to determine the cost effectiveness of immediate specialist assessment in a stroke unit compared to specialist assessment at a weekly clinic or no specialist assessment

▷ Questions:

ASM 1 What is the accuracy of a pre-hospital health professional assessment tool/checklist for identifying signs and symptoms of suspected stroke/TIA?

ASM 2 How accurately do scoring systems predict which patients with suspected TIA need to be referred urgently to a specialist assessment?

ASM 3 In patients with a suspected minor stroke/TIA, does early versus late expert assessment reduce mortality or morbidity?

ADM 2 Does rapid admission to a hyperacute stroke unit reduce mortality, morbidity and length of hospital stay?

▷ Background:

The risk of developing a stroke after hemispheric TIA can be as high as 30% within the first month, with the greatest risk being within the first 72 hours.* It is considered that effective management of patients with TIA or minor stroke requires identification of individuals at the highest risk and then appropriate early intervention.[195]

The ABCD^2 score aims to identify individuals at high risk of stroke and who may require emergency intervention. The score is based on known clinical predictors of stroke:

- Age
  - <60 years=0
  - ≥60=1
- BP
  - systolic ≤140 mmHg and/or diastolic ≤90 mmHg=0
  - systolic >140 mmHg and/or diastolic >90 mmHg =1
- clinical features
  - unilateral weakness=2
  - speech disturbance without weakness=1
  - other symptom=0

* National Pre-hospital Guidelines Group. 'The recognition and emergency management of suspected stroke and TIA: guidelines supplement'. London: RCP, 2007.

- duration of symptoms
  - <10 mins=0
  - 10 to 59 mins=1
  - ≥60 mins=2
- Presence of diabetes=1

The subgroup of patients with carotid stenosis accounts for the highest proportion of early recurrent strokes. Carotid endarterectomy reduces the risk of stroke in patients with recently symptomatic stenosis. For neurologically stable patients with TIA and minor stroke, benefit from endarterectomy is greatest if performed within 2 weeks of the event and falls rapidly with increasing delay.[196]

▷ Aim:

Population: patients with a TIA or minor stroke identified by a general practitioner (GP), in the accident and emergency (A&E) department or by an ambulance crew.

To evaluate the relative cost effectiveness of assessing TIA or minor stroke patients:
- immediately at a specialist stroke unit, or
- within 7 days at a weekly specialist stroke unit clinic, or
- by the patient's GP.

We assess cost effectiveness of each strategy not only for all minor stroke/TIA patients but also broken down by $ABCD^2$ score group.

▷ General methods:

The cost effectiveness of the different strategies was estimated using a simple decision analysis.

The NICE reference case was followed:
- Costs are measured from the perspective of the NHS and personal social services (PSS) perspective including the long-term care costs for stroke patients.
- Health outcome is measured from the perspective of the patient (not carer or family members).
- Health outcome is measured in terms of quality adjusted life years (QALYs), where one QALY is equal to one year of full health (or two years at half health etc.).
- A 3.5% discount rate was applied to both costs and effects. The discount rate reflects that people prefer to receive a benefit earlier and to incur a cost later, even in a world with zero inflation and no bank interest.[197]

Where appropriate, we have used data and assumptions from the HTA report on the effectiveness and cost effectiveness of carotid artery assessment by Wardlaw et al.[27]

▷ The model:

A decision tree is used to represent the model (see Figures C1, C2 and C3).

The decision model seeks to capture the following effects:
- Patients seen at a specialist clinic are more likely to be given appropriate medication and therefore will have strokes averted (in the first 90 days).

- Patients seen immediately will receive this medication sooner and therefore will have more strokes averted than those seen at weekly clinics.
- Patients seen at a specialist clinic will receive carotid artery ultrasound imaging (and subsequent carotid endarterectomy if stenosis >=50%), which will reduce the incidence of stroke (over 5 years). Whereas patients followed up by their GP do not receive imaging or surgery.
- Patients seen at a specialist clinic immediately will be more likely to receive endarterectomy within 2 weeks, when it is more effective, compared with patients who are seen at a weekly clinic. Furthermore, more patients will have a stroke before they have surgery.
- Carotid artery imaging is not perfectly accurate.
- Endarterectomy confers a risk of death in the short term.
- Specialist clinics are more costly than GP assessment. Costs of drugs over the lifetime will be increased. But these costs will be at least partly offset by cost savings from reduced stroke treatment over the lifetime.

The effect of different treatment strategies is first modelled in terms of effect on stroke incidence. Patients are then divided into whether or not the stroke was fatal and whether or not it left them dependent. Long-term quality adjusted life expectancy is estimated for each group and for the patients who do not experience a stroke. Similarly, lifetime healthcare costs are measured for each stroke outcome.

Patients in lower $ABCD^2$ score groups have a lower baseline risk of stroke and therefore have fewer strokes averted compared with patients in higher $ABCD^2$ score groups.

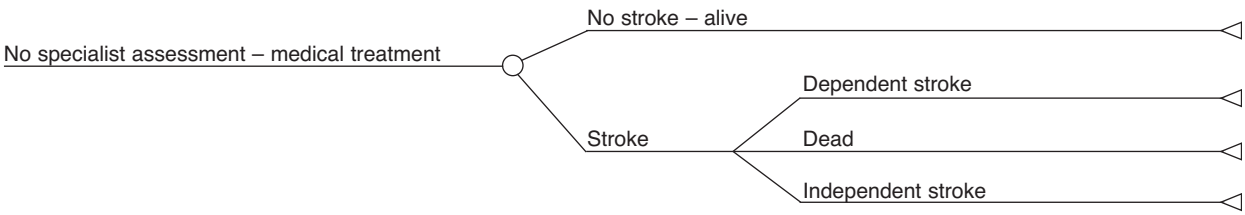

Figure C1: Decision tree arm for no specialist assessment

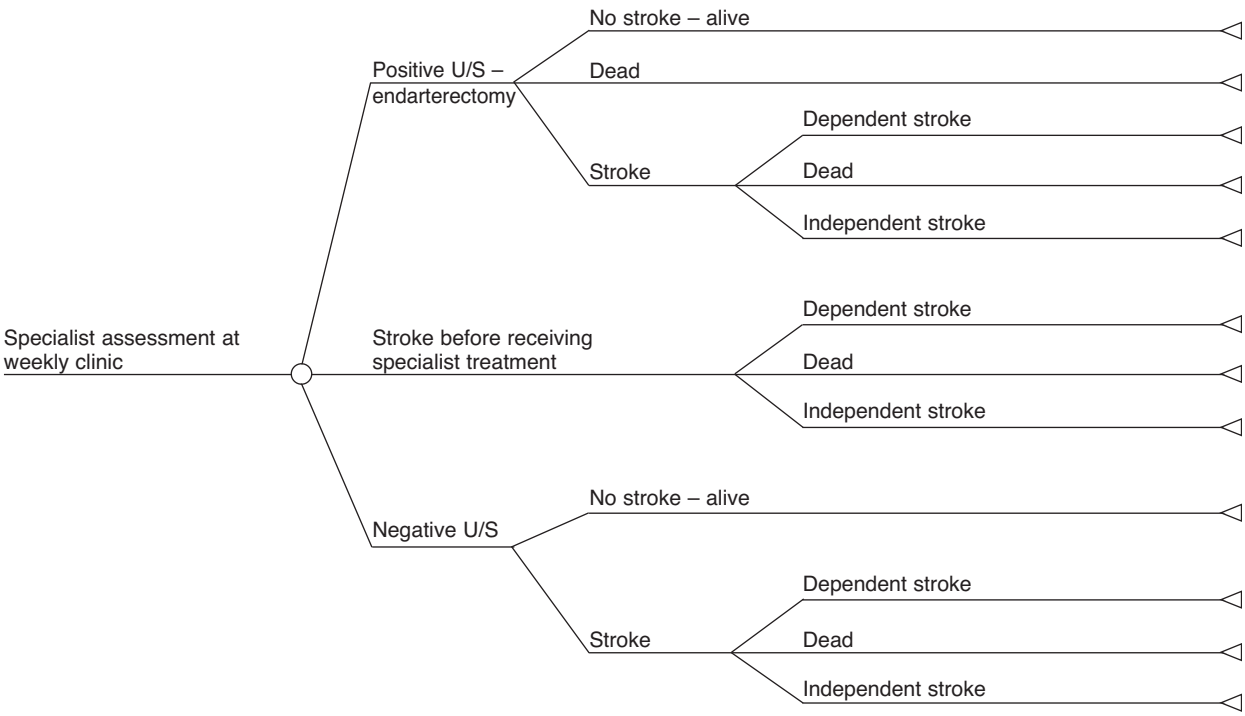

Figure C2: Decision tree arm for specialist assessment at a weekly clinic (the positive and negative scan results include true and false results)

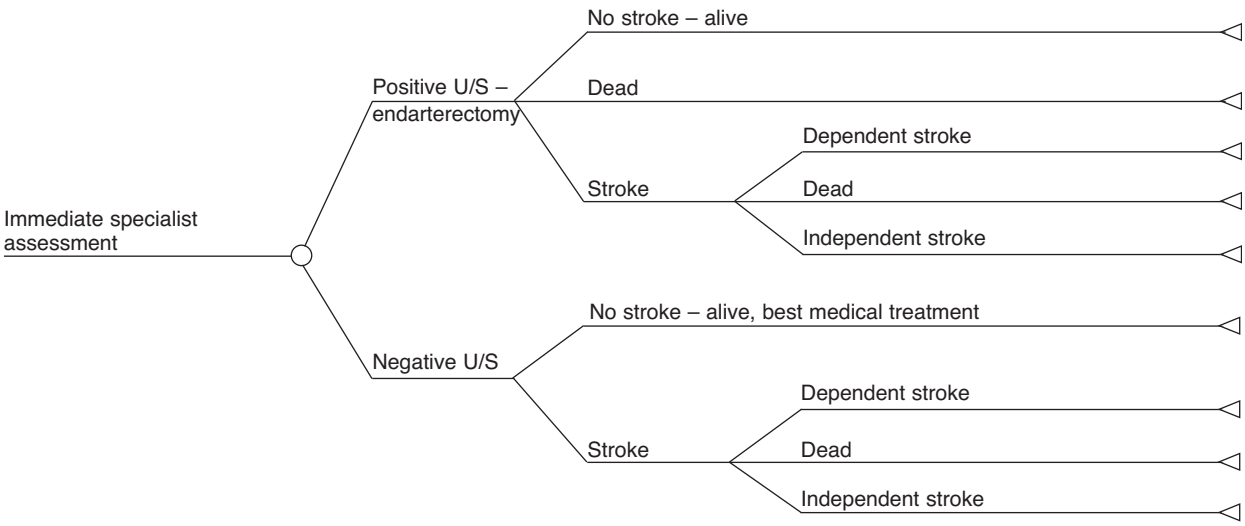

Figure C3: Decision tree arm for immediate specialist assessment (the positive and negative scan results include true and false results)

▷ Age/sex distribution of TIA and stroke mimics

The incidence of TIAs and minor strokes in a population of 500,000 people was reported in Wardlaw et al.[27] which used data from the Oxford Vascular Study (OXVASC).

Table C1 Wardlaw et al.[27] Expected number of TIAs and minor strokes per annum in a standard population of 500,000 people

	Age (years)				
	55–64	**65–74**	**75–84**	**≥85**	**Total**
Male	22.5 (5%)	66.3 (14%)	63.4 (13%)	25.7 (5%)	177.9 (36%)
Female	30.1 (6%)	65.3 (13%)	130.7 (27%)	86 (18%)	312.1 (64%)
All	52.3 (11%)	131.7 (27%)	194.2 (40%)	111.6 (23%)	490

The base case for this model assumes that all patients have a TIA or a minor stroke. The GDG felt this was unlikely to be the situation in practice as a high proportion of patients suspected as having a TIA would be discharged when found to have a TIA mimic. TIA mimics include epilepsy, migraines and brain tumours. Rates will vary according to the referral criteria of different centres. The TIA mimic rate has been estimated to be 50% using OXVASC data.[28] Although a fairly recent BMJ editorial suggested a TIA mimic rate of 30%.[198] We have added these results to the text. The impact of these additional patients will be explored by doubling the cost of initial assessment in each strategy to reflect a ratio of 1:1 of patients with actual TIA or minor stroke to those with stroke mimics who are discharged without further treatment for stroke prevention.

▷ Incidence of stroke after TIA

Johnston et al. (2007) reported the incidence of stroke up to 90 days after a TIA, by $ABCD^2$ score (Table C2). They had reviewed the evidence from six cohorts of patients from England and USA totalling 4,799 patients. The overall stroke rates were very similar for the UK and USA. The pooling was necessary to give greater precision to the estimates of stroke risk for the individual $ABCD^2$ groups. Taking the aggregate figures across all six cohorts, we estimated stroke rates (Table C2) for each $ABCD^2$ score group using the following formula:

$$m=(-1/t)\ln(S/S_0)$$

Where t is the number of days of follow-up since the TIA, S is the number of patients who survived the follow-up period without a stroke, and S_0 is the total number of patients in the group. To calculate the rate from 3–7 days the denominator, *S0*, is the number of patients who didn't have an event in the first 2 days. Similarly, to calculate the rate from 8–90 days the denominator, *S0*, is the number of patients who didn't have an event in the first 7 days.

Table C2 Stroke incidence after TIA, by ABCD^2 score

ABCD^2 score	All patients	Patients with stroke by day 2	Patients with stroke by day 7	Patients with stroke by day 90	Stroke rate days 1–2 (%)	Stroke rate days 3–7 (%)	Stroke rate days 8–90 (%)
0	47	0	0	0	0.00	0.00	0.00
1	191	0	0	4	0.00	0.00	0.03
2	543	7	8	17	0.65	0.30	0.04
3	847	10	12	29	0.59	0.29	0.04
4	1,165	41	60	93	1.79	1.10	0.11
5	994	48	68	118	2.47	1.49	0.17
6	852	72	101	145	4.41	2.77	0.29
7	160	10	17	35	3.23	2.41	0.37
All	**4,799**	**188**	**266**	**441**	**2.00**	**1.19**	**0.01**

▷ Accuracy of carotid ultrasound scan

It was assumed that all patients assessed at a specialist stroke unit will have a carotid ultrasound scan (U/S).

- If the scan is positive (carotid stenosis ≥50%), patients will have surgery (endarterectomy) in addition to medical treatment.
- If the carotid scan is negative (carotid stenosis <50%), patients will be treated with medical treatment alone.

Wardlaw et al.[27] reported that 10% of all patients with TIA had a carotid stenosis level of 50–99% (using NASCET criteria) which should be treated with surgery.

Table C3 Wardlaw et al.[27] Distribution of patients with TIA and minor stroke between stenosis bands

Stenosis level	% of all TIAs
70–99%	6
50–69%	4
0–49%, 100%	90

The sensitivities and specificities of U/S for detecting carotid stenosis were also reported by Wardlaw et al.[27] Surgery is recommended for patients with a stenosis level of ≥50%. Wardlaw et al. also reported the distribution of misdiagnosis by band, which is shown in Table C5.

Table C4 Sensitivity and specificity of ultrasound by stenosis level[27]

Stenosis	Sensitivity (95%CI)	Specificity (95%CI)
70–99%	0.89 (0.85 to 0.92)	0.84 (0.77 to 0.89)
50–69%	0.36 (0.25 to 0.49)	0.91 (0.87 to 0.94)
0–49%	0.83 (0.73 to 0.90)	0.84 (0.62 to 0.95)

Table C5 Misdiagnosis distribution for ultrasound by stenosis level[27]

	Actual stenosis band		
Misdiagnosed stenosis band	0–49%	50–69%	70–99%
0–49%	N/A	0.24	0.13
50–69%	0.36	N/A	0.87
70–99%	0.64	0.76	N/A

The associations between the ABCD^2 score and presence of carotid stenosis ≥50% were studied by Koton and Rothwell, but no clear relationship was found.[199] Wardlaw et al. reported a 0.53% relative risk of stroke in patients with stenosis level <70% compared to ≥70%.[27] By using this relative risk and keeping the proportion of patients with ≥70% stenosis constant in each group (6%), we were able to estimate stroke risk by both ABCD^2 score and stenosis level as follows:

Table C6 Baseline stroke risk, by ABCD^2 score and level of stenosis

	All (see Table C2)			Stenosis >=70			Stenosis <70		
ABCD^2 Score	Stroke rate days 1–2 (%)	Stroke rate days 3–7 (%)	Stroke rate days 8–90 (%)	Stroke rate days 1–2 (%)	Stroke rate days 3–7 (%)	Stroke rate days 8–90 (%)	Stroke rate days 1–2 (%)	Stroke rate days 3–7 (%)	Stroke rate days 8–90 (%)
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	0.00	0.00	0.03	0.00	0.00	0.05	0.00	0.00	0.02
2	0.65	0.30	0.04	1.16	0.54	0.07	0.62	0.29	0.04
3	0.59	0.29	0.04	1.06	0.52	0.08	0.56	0.27	0.04
4	1.79	1.10	0.11	3.21	1.97	0.20	1.70	1.04	0.10
5	2.47	1.49	0.17	4.43	2.67	0.31	2.35	1.42	0.17
6	4.41	2.77	0.29	7.91	4.97	0.52	4.19	2.63	0.27
7	3.23	2.41	0.37	5.78	4.31	0.66	3.06	2.28	0.35
All	**2.00**	**1.19**	**0.13**	**3.58**	**2.13**	**0.23**	**1.90**	**1.13**	**0.12**

▷ Effectiveness of carotid endarterectomy

Table C7 below gives the absolute risk reduction in stroke or death for patients having surgery compared to medical treatment by time to surgery and stenosis level.

Table C7 Absolute risk reduction per 100 patients with surgery in 5-year actuarial risk of ipsilateral carotid ischaemic stroke and any stroke or death within 30 days after trial surgery from the pooled analysis of the RCTs[45]

Factor	50 to 69% stenosis	≥70% stenosis
Time since last event (weeks)	Surgical vs medical (ARR; 95%CI)	Surgical vs medical (ARR; 95%CI)
<2	17/158 vs 34/150 (14.8; 6.2 to 23.4)	23/167 vs 54/149 (23.0; 13.6 to 32.4)
2 to 4 weeks	21/135 vs 20/110 (3.3; –6.3 to 13.0)	10/133 vs 24/105 (15.9; 6.6 to 25.2)

In the base case analysis, it was assumed that 80% of patients who were assessed immediately and had a stenosis level of ≥50% would have surgery within 2 weeks of their TIA. For patients having specialist assessment at a weekly clinic, only 25% were assumed to have surgery within 2 weeks. All other patients with a stenosis level of ≥50% would have surgery from 2 to 4 weeks after their TIA.

These were tested in a sensitivity analysis. For immediate assessment, 50% to 100% of surgery would take place within 2 weeks of TIA. For assessment at a weekly clinic, 0 to 50% of surgery would take place within 2 weeks of TIA.

▷ Effectiveness of medical treatment

The following data was based on the QRESEARCH database that was supplied for a modelling project being carried out in Birmingham. This data was drawn from 463 practices which use the EMIS clinical system (most common (>50%) primary care computer system).[200*] It shows that most patients are prescribed aspirin but only a small proportion of patients are prescribed appropriate combination medication post-TIA.

* QRESEARCH relies on GP Read codes and so is representative of people thought to have had a TIA in primary care – roughly half referred to specialist clinics with suspected TIA (OXVASC) are subsequently thought to have had a TIA.

Table C8 Prescriptions given by a GP at 1 month following a TIA (3,366 people were coded as suffering a TIA)

Drug (prescribed or over the counter)	N (%)
Antiplatelets/anticoagulants	
Aspirin	2,144 (64%)
Warfarin	171 (5%)
Statins	1,244 (37%)
Antihypertensives	
Thiazide	585 (17%)
Angiotensin-converting enzyme (ACEI)	672 (20%)
Angiotensin II receptor blocker (ARB)	174 (5%)
Combinations	
Antiplatelet agent/warfarin + statin + ACEI + thiazide†	153 (5%)
Antiplatelet agent/warfarin + statin + any hypertensive	742 (22%)

†gold standard

Wardlaw et al.[27] included relative risk reductions associated with various drugs given as treatment for TIA or minor stroke (Table C9). We assumed that all three groups would benefit from aspirin, but our baseline risk data (Tables C2 and C6) almost certainly already account for aspirin use. Our treatment effect is therefore a 15% reduction in the 90-day stroke risk for patients being assessed by specialists due to prescribing of modified release dipyridamole. Patients going immediately to the specialist clinic get this benefit from day 1, whereas patients being sent to the weekly clinic are assumed to get this effect from day 4.

Table C9 Wardlaw et al.[27] Risk of stroke in medically-treated patients by time after TIA or minor stroke and stenosis band

Time since initiation of medical therapy	Reduction in stroke risk (%)	Drugs assumed to affecting risks
<3 months	15	Modified release dipyridamole
<3 months	33	Aspirin and modified release dipyridamole
3–6 months	25	Aspirin and modified release dipyridamole
6–12 months	47	Aspirin, modified release dipyridamole and blood pressure-lowering drugs
1 year and beyond	55	Aspirin, modified release dipyridamole, blood pressure-lowering drugs and lipid-lowering drugs

▷ Stroke-related health status

The outcome of a stroke occurring less than 90 days after a first TIA (Table C10) was taken from the Express study (personal communication from Peter Rothwell). A low Rankin score (0–2) was considered an independent health state. A higher score (3–5) was considered a dependent state requiring long-term nursing care.

Table C10 Outcome of stroke within 90 days of first TIA

Dependent after stroke	11 (29%)
Independent after stroke	18 (47%
Dead	9 (24%)
All	**38 (100%)**

▷ Life Expectancy

The life expectancy was derived from data for the general population in England & Wales from the Office for National Statistics for 2003–2005. Based on the age-sex profile of patients (Table C1), the average life expectancy for a TIA patient who did not have a follow-up stroke within 90 days was estimated to be 10.8 years. It was assumed that a TIA patient who had a stroke which resulted in an independent health state would have half the life expectancy, 5.4 years. If the stroke resulted in a dependent health state, then their life expectancy would be a third, 3.6 years.

▷ Utilities

Utilities are the name given to generic measures of (health-related) quality of life measured on 0–1 scale. Health-related utilities scores are on a scale from 0 to 1, with 0 representing death and 1 representing perfect health. The utilities used in this model relate to each stroke-related health state and were taken from Wardlaw et al. [27]

Table C11 Utility scores for each outcome for the model[27]

	Utility score
Dependent after a stroke	0.31
Independent after a stroke	0.71
Fully recovered after TIA/no stroke at 90 days	0.88

Calculation of QALYs

For each stroke-related outcome the utility value was multiplied by the corresponding life expectancy to calculate the number of QALYs (Table C12). The QALYs were then discounted by 3.5% per year. Since we did not have data on stroke incidence up to 5 years for all patient groups, the QALYs gained attributable to averting strokes due to surgery were calculated separately but in the same manner (Table C13).

Table C12 Calculation of QALYs, based on stroke outcome within 90 days of TIA

Health state at 90 days	Utility	Life expectancy	QALYs	Discounted QALYs
Dependent after a stroke within 90 days	0.31	3.6	1.116	1.06
Independent after a stroke within 90 days	0.71	5.4	3.834	3.54
Fully recovered after TIA/no stroke at 90 days	0.88	10.8	9.504	8.05
Fatal stroke by 90 days/surgical death	0	0	0	0

Table C13 Calculation of QALYs gained from surgery, based on averting stroke up to 5 years

Type of stroke averted	LE*	LE* – no stroke	LYG**	Utility – no stroke	QALYs gained	Discounted QALYs gained
Dependent after a stroke	1.6	8.8	7.2	0.88	6.336	3.95
Independent after a stroke	3.5	8.8	5.3	0.88	4.664	2.66
Fatal stroke	0	8.8	8.8	0.88	7.744	6.31

LE, life expectancy; LYG, life years gained

▷ Costs

The cost of assessment at a stroke unit was taken from costs for a one-stop TIA clinic, which include staffing, overhead costs, imaging and labs.[201] A range of costs were collected from various centres in the UK, to be used to develop a new unit cost for the DH. The highest cost reported was used for immediate assessment (£410) and the mean cost was used for a weekly clinic (£316). These costs were varied in the probabilistic sensitivity analysis and the cost of immediate assessment at a stroke unit was doubled in a one-way sensitivity analysis. It was assumed that a patient who did not receive specialist assessment would have two GP consultations within the first month, at £25 per 10 minute consultation.[202]

Table C14 Costs of one-stop TIA clinics in the UK[201]

Specialist assessment costs	Mean
Immediate – daily clinic	£410
Weekly clinic	£316
GP clinic	£50

Table C15 Costs of surgery and stroke care by level of dependency[27]

	Mean (£)	Low (£)	High (£)
Cost of endarterectomy*	3,442	2,525	4,360
Dependent health state: stroke unit cost per patient for first year of treatment**	22,255	16,691	27,819
Dependent health state: cost per patient per year for subsequent years	11,292	8,469	14,115
Independent health state: stroke unit cost per patient for first year of treatment	3,716	2,787	4,645
Independent health state: cost per patient per year for subsequent years***	876	657	1,095

*cost per inpatient day £407 and average length of stay (LOS) in the hospital is 6 days
**mean LOS of 51 days inpatient, rehabilitation cost of £763 and average annual cost of £11,292 based on 1,854 first ever stroke patients from Scotland
***mean LOS of 14 days inpatient, rehabilitation cost of £40 and average annual cost of long-term care of £876

The most commonly prescribed drugs and their doses were taken from the Prescription Pricing Authority (PPA).[203] (Table C16)

Table C16 Most commonly cardiovascular prescribing taken from the Prescription Pricing Authority website[203]

		Used in base case analysis
Aspirin	75 mg	Yes
Simvastatin*	[40 mg]*	Yes
Atorvastatin	10 mg	
Modified release dipyridamole**	[2*200 mg]**	Yes
Clopidogrel	75 mg	
Lisinopril	10 mg	Yes
Bendrofluazide	2.5 mg	Yes
losartan	50 mg	
Perindopril*	20 mg	

* The dose of Simvastatin was thought to be too low by the GDG (15mg) and this was changed to 40mg.
** The GDG thought it was more likely that modified release dipyridamole would be prescribed in doses of 200mg, rather than 4 doses of 100mg a day as reported by the PPA.

For the base case analysis, it was assumed that patients assessed at the specialist clinic would be prescribed aspirin, a statin, an ace inhibiter and thiazide, all for life, plus modified release dipyridamole for 2 years. Whereas for the GP-assessed patients, only 14% would get this combination (minus modified release dipyridamole) and the rest would get only aspirin (based on the Oxford data – see Table C8 above).

Drug prices are shown in Table C17.

Table C17 Drug prices used in the model

BNF March 2007	(£)	Annual cost (£)
Aspirin (non-prop) 75mg 28-tabs	1.89	25
Bendroflumethiazide (non-prop) 2.5mg 28-tabs	1.15	15
Lisinopril (ACEi) (non-prop) 10mg 28 tabs	1.54	20
Simvastatin (non-prop) 40mg 28 tabs	3.40	44
Persantin Retard (modified release dipyridamole) (Boehringer Ingelheim), 200mg 60-cap	8.38	102

▷ Lifetime costs

Both drug costs and long-term care costs after stroke are calculated over the patient's lifetime (Table C18). The total costs differ between the alternative assessment strategies not only because assessment and surgery costs differ but also because stroke incidences will differ due to the different treatments given.

Table C18 Lifetime treatment costs,* by stroke-related health state

	Life expectancy	Lifetime costs	Discounted lifetime costs
Dependent after a stroke within 90 days	3.6	51,614	49,684
Independent after a stroke within 90 days	5.4	7,570	7,214
Fully recovered after a TIA/no stroke at 90 days (i.e. drug costs only)			
– GP assessment	10.8	798	674
– specialist assessment	10.8	1,327	1,152
Fatal stroke by 90 days/surgical death	0	0	0

* Not including the one-off costs of assessment and surgery

▷ Sensitivity analyses

One-way sensitivity analyses were carried out to test the robustness of the results to changes in the key parameters/assumptions.

▷ Results

The number of strokes, deaths and QALYs resulting from each strategy are presented in Table C19 – immediate specialist assessment had the least number of strokes and the most QALYs. GP care had the most strokes and least QALYs. The breakdown of costs is shown in Table C21 – weekly specialist assessment was most costly and GP care least costly.

Table C19 Base case results: events per 1,000 TIA patients

90-day outcome	Immediate specialist assessment	Weekly specialist assessment	GP care
Alive no stroke	837	831	814
Stroke	160	167	186
Dependent stroke	*46*	*48*	*54*
Independent stroke	*75*	*78*	*87*
Stroke death	*38*	*40*	*45*
Surgical death	3	3	0
All patients	1,000	1,000	1,000
Additional strokes averted by surgery beyond 90 days	17	12	0
QALYs	7,123	7,062	6,920

Table C20 Base case results: cost per 1,000 TIA patients

	Immediate specialist assessment (£)	Weekly specialist assessment (£)	GP care (£)
Assessment	410,000	301,508	50,000
Surgery	846,725	797,775	0
Drugs	964,621	957,201	548,797
Stroke care (independent)	821,591	855,484	954,681
Stroke care (dependent)	3,336,510	3,474,151	3,876,994
Stroke care (strokes averted by surgery)	–275,459	–186,662	0
Total cost	**6,103,988**	**6,199,458**	**5,430,472**

When all patients were assessed in the same way regardless of ABCD^2 score, immediate specialist assessment was the most cost-effective option. Immediate specialist assessment dominated weekly specialist assessment, it was more effective and less expensive than weekly specialist assessment.

Table C21 Base case results: cost effectiveness

	Mean QALYs	Mean Cost (£)	ICER (vs GP care) (£)	ICER (vs Weekly)
GP care	6.92	5,430		
Weekly specialist assessment	7.06	6,199	5,412	
Immediate specialist assessment	7.12	6,104	3,332	Immediate dominates

ICER=Incremental cost-effectiveness ratio (cost per QALY gained)

▷ Using the ABCD^2 score

The number of strokes averted in the first 90 days after TIA varied greatly by ABCD^2 score group (Table C1). However, immediate specialist assessment was still the most cost-effective strategy for all groups except 0 and 1 (Table C23). For group 0 the GP assessment was optimal and for group 1 it was either immediate assessment or GP care depending on whether the £20,000 or £30,000 per QALY threshold was used.

Table C22 Strokes by 90 days per 1,000 patients, by ABCD^2 score group

	Strokes per 1,000 patients		
ABCD^2 score	**Immediate specialist assessment**	**Weekly specialist assessment**	**GP care**
0	0	0	0
1	18	18	21
2	50	52	59
3	51	53	60
4	143	149	166
5	203	210	234
6	325	337	371
7	338	347	385
All	**160**	**167**	**186**

Table C23 Cost effectiveness by ABCD^2 score group

ABCD^2 score	ICER (weekly vs GP)	ICER (Immediate vs GP)	ICER (Immediate vs weekly)	Optimal strategy at £20,000 per QALY gained	Optimal strategy at £30,000 per QALY gained
0	50,625	31,397	1,231	GP	GP
1	27,819	20,579	1,231	GP	Immediate
2	18,014	11,849	Immediate dominates	Immediate	Immediate
3	17,286	11,662	Immediate dominates	Immediate	Immediate
4	6,398	3,989	Immediate dominates	Immediate	Immediate
5	3,630	2,120	Immediate dominates	Immediate	Immediate
6	1,108	269	Immediate dominates	Immediate	Immediate
7	652	149	Immediate dominates	Immediate	Immediate
All	**5,412**	**3,332**	**Immediate dominates**	**Immediate**	**Immediate**

ICER=Incremental cost-effectiveness ratio (£ per QALY gained)

▷ One-way sensitivity analyses

The results of the sensitivity analyses are presented in Tables C24 and C25.

Table C24 Results of one-way sensitivity analyses

	Immediate specialist assessment		Weekly specialist assessment		GP care	
Sensitivity analysis	**Mean cost (£)**	**Mean QALYs**	**Mean cost (£)**	**Mean QALYs**	**Mean cost (£)**	**Mean QALYs**
Base case	6,104	7.12	6,199	7.06	5,430	6.92
A	6,514	7.12	6,498	7.06	5,430	6.92
B	6,233	7.09	6,253	7.05	5,430	6.92
C	5,154	7.12	5,259	7.06	4,896	6.92
D	6,104	7.12	6,122	7.08	5,196	7.00
E	7,658	7.25	7,882	7.21	7,445	7.11
F	2,237	8.12	2,188	8.09	724	8.05
G	5,073	7.24	5,097	7.19	4,146	7.07

Table C25 Results of one-way sensitity analyses (continued)

Sensitivity analysis	ICER (weekly vs GP)	ICER (Immediate vs GP)	ICER (Immediate vs weekly)	Optimal strategy at £20,000 per QALY gained	Optimal strategy at £30,000 per QALY gained	Result by ABCD^2 score
Base case	5,412	3,332	Immediate dominates	Immediate	Immediate	See Table C23
A	7,524	5,360	264	Immediate	Immediate	No change
B	6,383	4,682	Immediate dominates	Immediate	Immediate	GP care is now optimal for groups 2 and 3
C	2,553	1,275	Immediate dominates	Immediate	Immediate	Immediate is now optimal for group 1
D	10,885	7,234	Immediate dominates	Immediate	Immediate	No change
E	4,403	1,503	Immediate dominates	Immediate	Immediate	No change
F	5,526	3,820	Immediate dominates	Immediate	Immediate	Immediate is now optimal for group 1
G	7,965	5,416	Immediate dominates	Immediate	Immediate	No change

ICER=Incremental cost-effectiveness ratio (£ per QALY gained)

▷ Sensitivity analysis A

The GDG commented that for every suspected TIA patient who has had a TIA or minor stroke, one patient will have had a TIA mimic.[200] It is difficult to estimate the consequences for these patients. To reflect this, the costs of specialist assessment were doubled assuming that for each patient treated for a TIA, the cost of another patient would be incurred who was discharged after assessment. This is a very conservative assumption since the model does not estimate the health gain (and possibly cost savings) attained by these patients from getting an improved diagnosis. Immediate specialist assessment remains the most cost-effective strategy for $ABCD^2$ scores 2–7 and overall.

Similarly, the addition of the cost of brain scan would also not affect which strategy is most cost effective.

▷ Sensitivity analysis B

In the base case analysis, it was assumed that the proportion of patients with stenosis was constant across the $ABCD^2$ score groups and that the absolute risk reduction from surgery was constant across the $ABCD^2$ score groups. However, it is possible that the risk reduction is smaller for patients in the lower $ABCD^2$ score groups. For this sensitivity analysis, we estimated the health gain using relative risk instead of absolute risk reductions (estimated from the same data – Table C7). The relative risk reductions (e.g. 65%RRR for stenosis >=70%) were applied to the 90-day stroke rates.

The benefits of endarterectomy in the base case analysis are based on 5-year follow-up of stroke risk. However, the ABCD score indicates only the risk in the short-term. The sensitivity analysis using relative risk reduction is based only on the 90-day stroke risk, and therefore underestimates the longer-term benefits. Hence, we believe that the sensitivity analysis is less plausible than the base case assumption.

▷ Sensitivity analysis C

In the base case analysis, patients undergoing specialist assessment are assumed to be prescribed a number of drugs and yet only the health effects of aspirin and dipyridamole are modelled. The model had a time horizon of 90 days for key events (strokes); unlike aspirin and dipyridamole, the other drugs are unlikely to influence stroke rates in the short term. Given our time constraints, we were unable to model the longer term health effects. However, for the key comparison of immediate versus weekly clinics, the health impact is not important since both sets of patients will receive the long-term benefit. In sensitivity analysis C, we calculate only the cost of aspirin and modified release dipyridamole for 90 days, as with the base case but the other drug costs are removed. The results of the model were largely unchanged.

▷ Sensitivity analysis D

In the base case, only patients receiving specialist assessment receive modified release dipyridamole. In this sensitivity analysis, we assume that 50% of patients receiving GP care are prescribed modified release dipyridamole. The cost-effectiveness results were largely unchanged.

▷ Sensitivity analysis E

We changed the life expectancy of a dependent stroke patient from 1/3 of normal to 2/3, and then the life expectancy of an independent stroke patient was changed from 1/2 of normal to 3/4. The cost-effectiveness results were largely unchanged.

▷ Sensitivity analysis F

We changed the life expectancy of a dependent stroke patient from 1/3 of normal to 1/6, and then the life expectancy of an independent stroke patient was changed from 1/2 of normal to 1/4. The cost-effectiveness results were largely unchanged.

▷ Sensitivity analysis G

We changed the probability of death after a first stroke to the lower confidence interval 11%. Similarly we changed the probability of dependency after a first stroke to the lower confidence limit 15%. The cost-effectiveness results were largely unchanged.

▷ Discussion

The most cost-effective strategy overall appears to be immediate specialist assessment. This strategy was optimal for all $ABCD^2$ score groups apart from 0 and 1, and the results appear to be robust to changes in key parameters.

Although the model includes costs for long-term nursing care for dependent stroke patients, informal care costs were not included since these are not within the NHS perspective. If they had been included, then immediate specialist assessment would appear even more cost effective.

The main driver for the cost effectiveness of immediate assessment appears to be getting patients on effective medication faster, which improves their outcomes.

The model is a simple representation, looking at only 90 days after the TIA for the effects of medical treatment and extrapolating from this to get long-term outcomes, and so caution should be applied when using these results. However, the results of this analysis reinforce the conclusions of other studies.

The Wardlaw et al. NHS HTA report[27] indicated that the net benefit of stroke prevention clinics was dependent on the speed with which patients could be investigated or treated. As the risk of stroke for TIA patients is high in the first month, treatment strategies which allow patients to be treated within this period appear to be cost effective.

The EXPRESS study, which was published after the development of this model, suggests that the impact of early specialist assessment on stroke risk might be greater still. This before and after cohort study found a relative reduction in stroke risk of about 80% for immediate specialist assessment compared to an appointment-based clinic.

Finally, a forthcoming report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D has constructed a similar cost-effective model comparing different assessment strategies.[28] It too found that same day clinics are cost effective compared with weekly clinics for every $ABCD^2$ score group.

In conclusion, referral of suspected TIA patients for immediate specialist assessment appears to be cost effective for all but the lowest risk patients because it supports timely prescribing of effective drugs and selection of patients for effective surgery.

Appendix D: GDG members' declaration of interests

Name and date of signature on declaration of interests form	Personal pecuniary interest	Personal family interest	Non-personal pecuniary interest	Personal non-pecuniary interest
ALLISON Rhoda	None	None	None	None
BARKER Julie	None	Husband works for Xansa-SBS who contract out financial functions of some NHS Trusts	None	None
BOWMASTER Alan	None	None	None	None
DAY Diana	None	None	None	None
FORD Gary	Honoraria from Boehringer Ingelheim, Astra Zeneca for educational activities and advisory boards.	Family ownership of GlaxoSmithKline shares	Research grants to institution or/and unrestricted educational grants from Boehringer Ingelheim, Lundbeck, and Astra Zeneca	Director UK Stroke Research Network
HATTON Steve	None	None	Company director at BPA/College of Paramedics	None
KORNER Joseph (Form signed on 15 November 2007)	None	None	None	None
LAMONT Peter	None	None	None	None
McMANUS Richard	None	None	In the last 5 years, Dr McManus has participated in research funded by: Pfizer, Sanofi – Aventis and A. Menarini Pharma and received funding to attend a research conference from MSD.	None
MORSE Mariane	None	None	None	None
POTTER John	Received lecture and research funding from various pharma companies more directly related to this GDG	None	None	None
RUDD Anthony	None	None	None	None
TYRRELL Pippa	None	None	None	None