# What is the Optimum Model of Service Delivery for Transient Ischaemic Attack?

***Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation R&D (NCCSDO)***

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# *Executive Summary*

## Background

It is now well recognised that people who have a transient ischaemic attack (TIA) are at high risk of going on to have a stroke, and the risks of this happening are highest in the first few days following the event. There are several interventions, both medical and surgical, that can potentially substantially reduce this risk of stroke following a TIA. Therefore, it is relevant for health services to consider how best to provide services for patients who have had a TIA so as to ensure that they receive speedy diagnosis and prompt treatment to reduce the chance that they will have a stroke. National guidelines and policy recommend that the solution is to have patients seen rapidly by a specialist in an out-patient setting. It has been suggested that some patients at particularly high risk of stroke should be admitted to hospital so that if they do have a stroke, then they will receive prompt treatment to minimise the impact of that stroke (e.g. with thrombolysis). A further option is to encourage patients to contact the emergency services when they have symptoms. Alternatively, patients might be managed by their general practitioner.

## Aim

The aim of this research was to conduct mathematical modelling to determine what is the optimum pattern of service provision for people presenting with a transient ischaemic attack or minor stroke.

## About this study

In order to do this, it was necessary to gather data to populate the model. These data were obtained from the Oxford Vascular Study (OXVASC), the Newcastle Rapid Ambulance Protocol Study, the QRESEARCH general practice database, and the literature. From the OXVASC study, data were obtained on the incidence of TIA and minor stroke, and the risk of stroke following these events. The Newcastle data provided data on how long it took people to reach hospital when they attended via the emergency services. The QRESEARCH database provided data on the current management of TIA in general practice. The literature was used to determine the impact of treatments on reducing risks of subsequent stroke, accuracy with which GPs diagnose TIA, and to obtain costing data. In addition, we performed a patient survey to determine patient costs and patient preferences for different types of service.

The model comprised a discrete event simulation, programmed in Borland Delphi. It predicted what would happen under different patterns of service provision to people who present to the health service with symptoms suggestive of TIA or minor stroke. The model simulated 10 years of time for a population of 500,000. Current

practice was compared to different patterns of service provision, including daily rapid access clinics, twice weekly clinics and weekly clinics. It was assumed that the rapid access clinic would provide accurate diagnosis, rapid assessment for carotid endarterectomy where appropriate, and optimal medical management (blood pressure lowering; statin therapy; dual anti-platelet therapy; anticoagulation if atrial fibrillation). For each type of service provision, it tested what would happen if the referral threshold was changed according to predicted risk of stroke using the ABCD2 scoring system. It also modelled what would happen if high risk people were admitted to hospital, if greater use was made of emergency services, and if GPs improved their diagnosis and management. The principal outcome of the model was number of major strokes (i.e. strokes that lead to hospital admission) prevented and cost. This enabled incremental cost effectiveness ratios (ICERs) to be calculated.

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# Key findings

Daily rapid access clinics were more cost-effective than current practice. If a referral threshold was set at an ABCD2 score of 4 or more, then this would on average lead to 4 referrals per week, and prevent 4 strokes per year at an average cost of £27,000 per stroke. Referring all patients (approximately 16 per week) with possible TIAs was also cost-effective, with an ICER of £50,000 per major stroke prevented compared to the refer at ABCD2 score of 4 strategy. Admitting patients with high ABCD2 scores for three days observation was not cost-effective, with an ICER of over £1,000,000 per major stroke prevented as compared to referring all suspected cases to a daily rapid access clinic. Twice weekly and weekly clinics were less effective and less cost effective than daily clinics, but were cost effective compared to current practice. For example, referring to a twice weekly clinic with a threshold of ABCD2 score of 4 or more prevents 3.3 additional major strokes per year as compared to current practice at an ICER of £33,000 per stroke prevented. The conclusions of the model were unchanged if greater use was made of emergency ambulance services. However, it was not cost effective to encourage use of emergency ambulances to expedite rapid treatment of TIAs. If GPs initiated optimal medical management on seeing the patient, then it is only cost effective to use rapid access clinics if all patients are referred (regardless of whether the GP has made a diagnosis of TIA, or what the patient's ABCD2 score is). If GPs were better at diagnosis of TIA than suggested by the literature then the option of referring all suspected TIAs is no longer cost effective.

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# Conclusion

We estimate that to prevent a stroke that would lead to a hospital admission is on average the equivalent of saving about 4 QALYs. Therefore, around £80,000 per major stroke averted is likely to be considered cost-effective. Therefore, we drew the following conclusions for service provision from the simulation model:

Configuration of rapid access neurovascular clinics:

- Where possible, these should allow for same day referrals. Daily clinics are more cost effective than less frequent clinics (e.g. twice weekly or weekly). The referral threshold for these clinics can be varied according to clinic capacity using an ABCD2 score cut off between 4 and 7.

- On grounds of cost-effectiveness the optimal threshold would be to refer patients with suspected TIA with an ABCD2 score of 4 or more if capacity is limited to around 1 patient per day (serving a population of 500,000).If capacity is not limited, then it is cost effective to see all possible TIAs

- If daily clinics are not possible, twice or once weekly clinics are cost effective with a referral threshold of ABCD2 of 4 or more.
- Flexible clinics, i.e where staff can do other work when capacity is not required on a given day, are more cost-effective than fixed clinics.

In patient admission:

- We do not recommend in-patient admission to facilitate thrombolysis for patients at high risk of stroke because of high ABCD2 score

Use of emergency services:

We do not recommend that patients are encouraged to use 999 services where symptoms have resolved

# The Report

## 1: Introduction

The importance of early management of TIA and minor stroke was recognised in the 2004 National Clinical Guidelines for Stroke, which recommended that patients first seen in the community with TIA or stroke from which they have recovered should be assessed and investigated in a specialist service as soon as possible within 7 days. (Intercollegiate Stroke Working Party, June 2004). It is now recognised that there is significant potential for reducing stroke risk following transient ischaemic attack (TIA) if treatment is initiated promptly. This is reflected in the National Stroke Strategy that was published in December 2007, which recommended that high-risk TIA patients needed to be assessed by experts within 24 hours of experiencing symptoms, and that lower risk groups needed to be seen within seven days. (Department of Health, 2007).

This strategy is based upon key advances in our understanding of the epidemiology and treatment of TIA in recent years:

- The incidence of TIA is rising:
  The Oxford Vascular Study (OXVASC) has found that the age specific incidence has doubled over the last twenty years in comparison to data from the Oxford Community Stroke Project. (Rothwell, 2004a). Given the increased risk of TIA with increasing age, this represents a substantial increase in absolute numbers of people who have had such an event. Using modern definitions of TIA, the annual incidence is of the order of 0.7 per 1,000 (data on file from OXVASC). The incidence of presumptive diagnosis of TIA by a general practitioner is nearly twice this. (Hippisley-Cox, 2005). Thus, in a PCT of 100,000 population, it would be anticipated that 123 people would suffer an event per annum that a GP will label as a TIA. A similar number of patients will have an event labelled as a minor stroke.

- The risk of stroke after TIA is high:
  Currently, around 8% of people who have had a transient ischaemic attack (TIA) will go on to have a stroke within 7 days, and 12% within a month. (Coull, 2004; Lovett, 2003). Similarly, someone who has had a minor stroke has a 12% risk of a recurrence within 7 days, and a 15% risk within a month. Indeed, 16% of first strokes are preceded by a TIA, and about 30% of all strokes are recurrent events. (Rothwell, 2004a; Mant 2004a)

- A simple clinical score can differentiate between people at high early risk and lower risk following TIA:
  Rothwell et al found that a six point score, the ABCD score, based on simple clinical features (age, blood pressure, whether or not there was unilateral weakness or speech disturbance, and duration of symptoms), was highly predictive of 7 day risk of stroke following TIA. (Rothwell, 2005). A subsequent refinement of this score, the ABCD2 score, that incorporated whether the patient had diabetes, was validated in four independent groups of patients and found to be a better predictor than the ABCD score. (Johnston, 2007).The ABCD2 score gives a total between 0 and 7, and is scored as follows:
  - **A**ge ≥ 60, 1 point
  - **B**lood pressure ≥ 140/90 mmHg, 1 point
  - **C**linical features: unilateral weakness, 2 points; speech impairment without weakness 1 point.
  - **D**uration of symptoms: ≥ 60 mins, 2 points; 10-59 mins, 1 point

- **D**iabetes, 1 point.

Treatments can reduce this risk:
There is strong evidence that interventions can reduce the risk of stroke recurrence following TIA, including blood pressure lowering, cholesterol lowering, anti-platelet therapy, and carotid endarterectomy. (PROGRESS Collaborative group, 2001; Heart Protection Study Collaborative Group, 2002; Antithrombotic Trialists' Collaboration, 2002; Rothwell, 2003).While, with the exception of carotid endarterectomy and aspirin, there is a lack of evidence on the effect of early application of these treatments, recent observational studies suggest that early administration can be dramatic. A before and after study set in Oxfordshire found that changing the median delay to first prescription for treatment from 20 days to less than 1 day was associated with an 80% reduction of the risk of stroke at 90 days. (Rothwell, 2007). Similarly, introduction of a 24-hour access hospital clinic for suspected TIA in France was associated with an observed rate of stroke that was over 80% lower than the expected rate from applying the ABCD2 score. (Lavallée, 2007). Therefore, it is plausible that optimal management of TIA and minor stroke could lead to a significant reduction in stroke incidence, thereby reducing morbidity and mortality in the community and helping to meet government targets. (Secretary of State for Health, 1999; Department of Health 2001).

In the UK, there is variation in terms of both availability of these specialist services and what they provide. (Redfern, 2002). Many patients with a presumptive diagnosis of TIA continue to be managed entirely in primary care. (Mant, 2003a). On the other hand, a proportion of people with a TIA are assessed by emergency medical services while they still have symptoms, e.g. through dialling '999'.

Therefore, the strategy raises questions as well as answers. Should the emphasis be on the development of rapid access specialist clinics (analogous to rapid access chest pain clinics)? (Mant, 2004b). What is the trade off in terms of cost versus outcome if these clinics have the capacity to see all patients on the same day that they are referred, or if there is a maximum wait (e.g. 7 days)? What would be the impact if more patients with TIA were seen in hospital within a few hours of symptom onset (e.g. if health education campaigns alert people to the symptoms of stroke, and are encouraged to dial '999)? Alternatively, should GPs manage patients more actively, without referring all to specialist clinics?

A further issue is whether a single model of care should be applied to all patients with TIA or whether different models are more appropriate for different categories of patient. It may be that people with a low risk of recurrence may be managed appropriately in primary care, whereas people at high risk would benefit from urgent specialist assessment.

One way to answer this multiplicity of research questions in a single study is to perform mathematical modelling whereby 'what if' scenarios are constructed on the basis of what is already known. The purpose of such modelling is to work out the likely outcome of different patterns of service provision on the basis of the best available evidence. Here we report the development and results of one such mathematical model, the aim of which was to compare the predicted outcomes (in terms of strokes prevented, quality adjusted life years and cost) of different models of service provision for patients with transient ischaemic attack (TIA).

## *1.1 Structure of this report*

There were two phases to this research, which ran in parallel. Data collection for the model, and development of the model. The methods used to collect data and their results are given in chapter 3. Chapter 4 describes the construction of the model, and chapter 5 the results of the model. Chapter 6 discusses the findings of the research. While the focus is on discussing the results of the model, there is also discussion of the findings of some of the specific research that was carried out to collect data for the model, namely an analysis of routine general practice data, and a survey of patients with TIA. The concluding chapter makes recommendations for policy and research.

# 2:Aims and Objectives

## *2.1 Focus of this research*

This research focuses on the optimum management of patients who present to their GP with symptoms suggestive of a TIA or minor stroke. The distinction between these two conditions is arbitrary. Conventionally, using the WHO criteria, an event is classified as a TIA if the symptoms last for less than 24 hours, and a stroke if the symptoms last for over 24 hours. (Dennis, 1989). However, a proportion of TIAs by this definition are associated with infarcts on brain scans, while a proportion of people with stroke have normal scans. (Laloux, 1996). While the research is not directly concerned with the management of more severe stroke, there is overlap in that some patients with TIA have emergency admissions to hospital (the recommended treatment pathway for acute stroke).

## *2.2 Aim*

To compare the predicted outcomes (in terms of strokes prevented, quality adjusted life years and cost) of different models of service provision for patients with transient ischaemic attack (TIA) through the use of mathematical modelling.

## *2.3 Objectives*

1. To construct a discrete-event simulation model to compare four different patterns of service provision: current practice; enhanced primary care service; a '999' service; and a rapid access neurovascular clinic.

2. To populate the discrete-event simulation model with data from:

a. The ongoing Oxford Vascular Study

b. The Newcastle Rapid Ambulance Protocol study

c. The QRESEARCH general practice database

d. The literature

3. To undertake primary research to ascertain patient preferences with regard to the different types of model

4. To make recommendations regarding service delivery (where sensitivity analysis demonstrates that the results of the model are robust)

5. To make recommendations regarding primary research (where sensitivity analysis demonstrates that the results of the model vary according to the underlying assumptions)

# 3: Data inputs into the model

We populated the model with data from a variety of sources:

**1. The Oxford Vascular Study (OXVASC)**. OXVASC is an ongoing community based incidence study of stroke and TIA set in Oxfordshire. (Rothwell, 2004a) Its approach (intensive contact with approximately 90 GPs covering a population of just under 100,000 and early validation by a study clinician) results in very high and accurate ascertainment of TIAs and minor strokes in patients who are not admitted to hospital and who tend to be under-ascertained in hospital based incidence studies. OXVASC data was used to provide estimates of the incidence of TIA & minor stroke; their prognosis (time specific up to 3 months following the event); the proportion of people with TIA that see a GP and with what time lag; the accuracy of GP diagnosis of TIA and minor stroke. OXVASC is currently the only source of reliable population-based data on TIAs in the UK.

**2. The Newcastle Rapid Ambulance Protocol Study**. This was a prospective 18 month study of all referrals of patients with suspected acute stroke / TIA, including direct triage of patients by ambulance paramedics, to an acute stroke unit. (Nor, 2004). This was used to provide data on how quickly patients with TIA and minor stroke use '999' services.

**3. Analysis of routine general practice data exploiting the QRESEARCH database**. This dataset comprises 3.3 million current patients and 4 million past patients. (QRESEARCH, 2005). This was used to provide data on current practice in terms of their management (namely, drugs used, investigations, and whether referred). This complemented the epidemiological data from OXVASC data by providing data from a broader population base. It was also the principal source for ascertaining current practice.

**4. Patient survey.** This was required to identify costs incurred by patients, and information on patient preferences (which while not used to inform the model, was relevant for interpreting the results of the model). We established a patient advisory group comprising people who have had a history of TIA/ minor stroke. This group helped us to identify key themes. A short survey instrument was then developed and distributed to a TIA/ minor stroke population.

**5. Data from the literature.** We used the literature to obtain estimates of effectiveness for key interventions, where possible, in relation to timing after TIA/ minor stroke, impact of stroke on quality adjusted life years and costing studies. Systematic methods were employed to identify, appraise and extract data from relevant literature. (Centre for Reviews and Dissemination, 2001)

## *3.1 The Oxford Vascular Study*

OXVASC data was used in two ways. For some of the questions, the answers were available from existing publications, or from analyses being performed by the OXVASC investigators at the time that this research was being carried out. For other questions, the OXVASC database was analysed de novo.

### 3.1.1 Specific analyses of the OXVASC data set

These analyses were performed on OXVASC data from three full years (April 2002 to March 2005) of patients presenting to the OXVASC clinic with a TIA or minor stroke. This comprised 589 patients with TIA or minor stroke, and 277 patients with symptoms suggestive of TIA where the final diagnosis was non-cerebrovascular disease.

#### 3.1.1.1 What is the incidence of presentation with symptoms suggestive of TIA where final diagnosis is non-cerebrovascular disease?

For the model, we needed to know how many patients presented with symptoms suggestive of TIA that turned out to have an alternative diagnosis. These patients are referred to as 'TIA mimics'. Table 3.1 shows number of patients attending OXVASC study clinics referred as possible TIA where the final diagnosis was non-cerebrovascular over the three year time period.

**Table 3.1 Other clinic attenders (TIA mimics) in OXVASC by age and sex.**

| Age (years) | Men | Women | Total |
|---|---|---|---|
| < 35 | 3 | 9 | 12 |
| 35 - 44 | 16 | 10 | 26 |
| 45 - 54 | 14 | 20 | 34 |
| 55 - 64 | 32 | 22 | 54 |
| 65 - 74 | 28 | 31 | 59 |
| 75 - 84 | 33 | 35 | 68 |
| ≥ 85 | 9 | 15 | 24 |
| Total | 135 | 142 | 277 |

The OXVASC study population over this time period is shown in table overleaf.

**Table 3.2 OXVASC study population by age and sex.**

| Age (years) | Men | Women | Total |
|---|---|---|---|
| < 35 | 22581 | 20273 | 42854 |
| 35 - 44 | 7515 | 6411 | 13926 |
| 45 - 54 | 6092 | 5589 | 11681 |
| 55 - 64 | 4983 | 4776 | 9759 |
| 65 - 74 | 3443 | 3524 | 6967 |
| 75 - 84 | 1936 | 2615 | 4551 |
| ≥ 85 | 420 | 948 | 1368 |
| Total | 46970 | 44136 | 91106 |

Data are the means of the three mid-year populations in the study practices.

Thus, crude three-year incidence is 277/91106, which is 3 per 1,000, which equates to an annual incidence of 1 per 1,000.

#### 3.1.1.2 What are the characteristics of patients with TIA, minor stroke and TIA mimic?

For programming reasons it is necessary to assign a complete set of values to all patient characteristics, although some are only applicable to one or two of the three types of patient. A discrete event simulation model assigns patient characteristics on the basis of underlying probabilities. Therefore, the relevant presentation of these data is as probabilities. These underlying probabilities were obtained from the OXVASC data.

*a. Age and sex:*
Table 3.3 shows the probability that a patient will be of a given age group if they present with a TIA mimic, genuine TIA or stroke derived from the OXVASC data set. Table 3.4 shows these adjusted for age and sex distribution of the population of England and Wales.

**Table 3.3 Probability that a patient will be in a given age group if they present with TIA mimic, genuine TIA or stroke (OXVASC data)**

| | Actual condition | | |
|---|---|---|---|
| Age group | TIA mimic | Genuine TIA | Stroke |
| 20-25 | 0.0034 | 0.0034 | 0.0000 |
| 25-30 | 0.0069 | 0.0069 | 0.0000 |
| 30-35 | 0.0000 | 0.0000 | 0.0000 |
| 35-40 | 0.0000 | 0.0000 | 0.0100 |
| 40-45 | 0.0207 | 0.0207 | 0.0201 |
| 45-50 | 0.0069 | 0.0069 | 0.0201 |
| 50-55 | 0.0380 | 0.0380 | 0.0267 |
| 55-60 | 0.0551 | 0.0551 | 0.0368 |
| 60-65 | 0.0724 | 0.0724 | 0.0870 |
| 65-70 | 0.1414 | 0.1414 | 0.1404 |
| 70-75 | 0.1242 | 0.1242 | 0.1572 |
| 75-80 | 0.1655 | 0.1655 | 0.1572 |
| 80-85 | 0.1965 | 0.1965 | 0.1739 |
| 85-90 | 0.0897 | 0.0897 | 0.1037 |
| 90-95 | 0.0655 | 0.0655 | 0.0636 |
| 95-100 | 0.0138 | 0.0138 | 0.0033 |
| sum | 1 | 1 | 1 |

(TIA mimic assumed as for TIA.)

The probability that a patient will be male can be represented in the following formula:

Patient is male with probability $p$ depending on age group $j$ ($j$ = 4, …, 19), where

$$\log\left(\frac{p}{1-p}\right) = \alpha + \beta j,$$

and the parameters $\alpha$ and $\beta$ are given in the following table (OXVASC data):

| Parameter | value |
|---|---|
| $\alpha$ | 1.534 |
| $\beta$ | -0.121 |

*a1. Age and sex adjusted for general population*
Adjustments were comparing the OXVASC population with the general population of England and Wales. The age and sex breakdown is based on data from http://www.statistics.gov.uk/statbase/ssdataset.asp?vlnk=9398&More=Y accessed 4 June 2007.

**Table 3.4 Probability that a patient will be in a given age group if they present with TIA mimic, genuine TIA or stroke (adjusted for general population)**

| | Actual condition | | |
|---|---|---|---|
| Age group | TIA mimic | Genuine TIA | Stroke |
| 20-25 | 0.0029 | 0.0029 | 0.0000 |
| 25-30 | 0.0057 | 0.0057 | 0.0000 |
| 30-35 | 0.0000 | 0.0000 | 0.0000 |
| 35-40 | 0.0000 | 0.0000 | 0.0087 |
| 40-45 | 0.0172 | 0.0172 | 0.0173 |
| 45-50 | 0.0063 | 0.0063 | 0.0179 |
| 50-55 | 0.0329 | 0.0329 | 0.0231 |
| 55-60 | 0.0523 | 0.0523 | 0.0351 |
| 60-65 | 0.0696 | 0.0696 | 0.0829 |
| 65-70 | 0.1350 | 0.1350 | 0.1345 |
| 70-75 | 0.1193 | 0.1193 | 0.1496 |
| 75-80 | 0.1663 | 0.1663 | 0.1580 |
| 80-85 | 0.1971 | 0.1971 | 0.1749 |
| 85-90 | 0.1036 | 0.1036 | 0.1201 |
| 90-95 | 0.0757 | 0.0757 | 0.0740 |
| 95-100 | 0.0161 | 0.0161 | 0.0039 |

(TIA mimic assumed as for TIA.)

The adjustment of the formula for predicting sex, taking into account general population characteristics, is shown below:

Patient is male with probability $p$ depending on age group $j$ ($j$ = 4, …, 19), where

$$\log\left(\frac{p}{1-p}\right) = \alpha + \beta j,$$

and the parameters $\alpha$ and $\beta$ are given in the following table:

| Parameter | value |
|---|---|
| $\alpha$ | 1.439 |
| $\beta$ | -0.119 |

*b. Blood pressure*

Blood pressure data for systolic blood pressure is drawn from a normal distribution dependent on patient type as shown below. It is rounded to the nearest mmHg. For the purposes of the model, raised blood pressure is taken to be a systolic blood pressure of over 140mmHg (as per ABCD2 score).

| Patient type | Mean | S.D. | Source |
|---|---|---|---|
| TIA mimic | 140 | 30 | Assumption |
| Genuine TIA | 153.8 | 29.9 | OXVASC data |
| Stroke | 155.4 | 26.3 | OXVASC data |

*c. Clinical symptoms score*

This variable can take values 0=neither weakness nor speech disturbance, 1=speech disturbance without weakness, 2=any weakness. It is strictly only relevant for prognosis in the case of genuine TIAs. For programming convenience, it is set to value 0 for TIA mimics, and to value 2 for strokes. For genuine TIAs, C score is sampled from an age-dependent distribution. The probability $p_i$ of a C score of at most $i$ ($i$ = 0, 1) for a patient in age group $j$ ($j$ = 4, …, 19) is given by

$$\log\left(\frac{p_i}{1-p_i}\right) = \alpha_i + \beta j,$$

where the parameters $\alpha_i$ and $\beta$ were found by ordinal logistic regression from the OXVASC dataset, using only the TIA data, as follows:

| Parameter | Value |
|---|---|
| $\alpha_0$ | 0.336 |
| $\alpha_1$ | 1.278 |
| $\beta$ | -0.082 |

*d. Duration of symptoms score*

This variable can take values 0=0-9 mins, 1=10-59 mins, 2=60 mins or more. It is strictly only relevant for prognosis in the case of genuine TIAs. For programming convenience, it is set to value 0 for TIA mimics, and to value 2 for strokes. For genuine TIAs, D score is sampled from an age-dependent distribution. The probability $p_i$ of a D score of at most *i* (*i* = 0, 1) for a patient in age group *j* (*j* = 4, …, 19) is given by

$$\log\left(\frac{p_i}{1-p_i}\right) = \alpha_i + \beta j,$$

where the parameters $\alpha_i$ and $\beta$ were found by ordinal logistic regression from the OXVASC dataset, which only contained data on this parameter for TIA patients, as follows:

| Parameter | Value |
|---|---|
| $\alpha_0$ | -0.407 |
| $\alpha_1$ | 1.330 |
| $\beta$ | -0.093 |

*e. Total Cholesterol*

This is sampled from a normal distribution with mean 5.34 and standard deviation 1.24 (OXVASC data).

*f. Atrial Fibrillation status*

This variable can take values 0=no AF, 1=undiagnosed AF, 2=diagnosed AF. The OXVASC dataset contained information about AF status and whether on warfarin pre-event. Patients without AF were coded 0, although a small number of these were on warfarin. Those with AF were coded 1 or 2 according to warfarin status. The probability $p_i$ of a score of at most *i* (*i* = 0, 1) for a patient in age group *j* (*j* = 4, …, 19) is given by the formula:

$$\log\left(\frac{p_i}{1-p_i}\right) = \alpha_i + \beta j,$$

where the parameters $\alpha_i$ and $\beta$ were found by ordinal logistic regression from the OXVASC dataset (interpreted as described above) as follows:

| Parameter | Value |
|---|---|
| $\alpha_0$ | 4.894 |
| $\alpha_1$ | 6.383 |
| $\beta$ | -0.226 |

*g. Diabetes*

Diabetes is set with probability *p* depending on age group *j* (*j* = 4, …, 19), where

$$\log\left(\frac{p}{1-p}\right) = \alpha + \beta j,$$

and the parameters *α* and *β* are given in the following table (OXVASC data):

| Parameter | Value |
|---|---|
| *α* | -0.460 |
| *β* | -0.116 |

*h. Antiplatelet therapy pre-event*

The patient is already on antiplatelet therapy with probability *p* depending on age group *j* (*j* = 4, …, 19), where

$$\log\left(\frac{p}{1-p}\right) = \alpha + \beta j,$$

and the parameters *α* and *β* are given in the following table (OXVASC data):

| Parameter | Value |
|---|---|
| *α* | -2.591 |
| *β* | 0.162 |

*i. Statin pre-event*

The patient is already on statin with probability *p* depending on cholesterol level *x*, where

$$\log\left(\frac{p}{1-p}\right) = \alpha + \beta x,$$

and the parameters *α* and *β* are given in the following table (OXVASC data):

| Parameter | Value |
|---|---|
| *α* | 0.793 |
| *β* | -0.373 |

Note that patients with higher cholesterol are less likely to be on statin pre-event.

*j. Suitability for Carotid Endarterectomy*

OXVASC data was used to determine suitability for assessment for carotid endarterectomy. The presence of an entry for symptomatic stenosis was taken as indicating suitability for investigation. This applied only to patients for whom the territory was given as carotid, and not to all such patients: in other words, the absence of an entry for symptomatic stenosis in patients where the territory was carotid was taken as implying a contraindication for carotid endarterectomy. For the base case, it was assumed that only those with symptomatic stenosis from 70 to 99 percent are suitable for carotid endarterectomy.

Based on OXVASC data, the probability that a patient is suitable for assessment is 0.611, while the probability that the patient is suitable for carotid endarterectomy is set to 0.041. If the category from 50 to 69 percent is also included, then the probability that a patient is suitable for carotid endarterectomy increases to 0.070. These probabilities are not correlated with any other patient characteristic.

### 3.1.2 Data inputs from published Oxvasc analyses and how they were incorporated into the model

#### 3.1.2.1 Incidence of TIA and minor stroke, and 'TIA mimic'

The incidence of TIA comes from the OXVASC data. Published incidence of TIA from OXVASC was 0.6 per 1,000 standardised to the England & Wales population. (Rothwell, 2004a) Analysis of further data from OXVASC (unpublished – provided for this study) suggests incidence 0.7 per 1,000.

The incidence of minor stroke used for the model (a stroke that does not lead to significant disability or lead to hospital admission) is difficult to derive from the literature. In OXVASC, the incidence of minor stroke (defined as a Rankin score of 0-1 at 30 days) was found to be 0.55 per 1,000. We have assumed that approximately half (45%) of these minor stroke events will have resulted in hospital admission. This gives a total ratio of genuine cerebrovascular events (TIA and minor stroke) to non-cerebrovascular events of 1:1, which fits with our review of the literature that found that approximately half of patients referred by a GP to specialist neurovascular clinic with a query TIA/ minor stroke have actually had a cerebrovascular event (see section on accuracy of GP diagnosis of TIA below).

The incidence of TIA mimic (i.e people presenting with possible cerebrovascular symptoms whose final diagnosis is non-cerebrovascular) is given above – in section 3.1.1.1

The age and sex specific incidences of these events is shown in the table below:

**Table 3.5 Incidence of TIA mimic, genuine TIA, minor and major stroke**
(per 1,000 patients per year)
A.Observed incidence of stroke events – males

| Age group | TIA mimic | Genuine TIA | Minor Stroke | Major Stroke |
|---|---|---|---|---|
| < 35 | 0.01 | 0.01 | 0.00 | 0.00 |
| 35 – 44 | 0.22 | 0.22 | 0.27 | 0.00 |
| 45 – 54 | 0.33 | 0.33 | 0.38 | 0.35 |
| 55 – 64 | 1.14 | 1.14 | 1.40 | 0.37 |
| 65 – 74 | 3.39 | 3.39 | 5.03 | 1.43 |
| 75 – 84 | 6.71 | 6.71 | 7.92 | 1.50 |
| ≥ 85 | 10.32 | 10.32 | 14.29 | 5.44 |

B. Observed incidence of stroke events – females

| Age group | TIA mimic | Genuine TIA | Minor Stroke | Major Stroke |
|---|---|---|---|---|
| < 35 | 0.03 | 0.03 | 0.00 | 0.00 |
| 35 - 44 | 0.05 | 0.05 | 0.16 | 0.00 |
| 45 - 54 | 0.42 | 0.42 | 0.42 | 0.12 |
| 55 - 64 | 1.40 | 1.40 | 1.12 | 0.63 |
| 65 - 74 | 3.97 | 3.97 | 3.50 | 0.58 |
| 75 - 84 | 8.67 | 8.67 | 6.76 | 3.75 |
| ≥ 85 | 12.66 | 12.66 | 11.60 | 3.47 |

In order to achieve these incidences of the different diagnoses, the mean time between successive arrivals of a given patient type were set as follows:

| Event | Mean time between arrivals (hours) |
|---|---|
| TIA mimic | 17.6 |
| Genuine TIA | 25.1 |
| Minor stroke | 58.7 |

Summary:
*The population size is set at 500,000, with 1,000 people presenting per annum with symptoms suggestive of a TIA or minor stroke. This comprises 35% genuine TIAs, 15% minor strokes and 50% 'TIA mimics', and equates to an incidence of TIA of 0.7 per 1,000, an incidence of minor stroke of 0.3 per 1,000 and an incidence of TIA mimic of 1 per 1,000.*

#### 3.1.2.2 Initial patient action on getting symptoms of TIA

There are two aspects of patient actions to consider for the model. The first is the choice between contacting A&E or GP and the second is the time from onset to the first contact with A&E or the GP. The aim here is to produce a reasonable representation of reality without overcomplicating the model. The relevant data source is the OXVASC data set, and important summary information is reported in Giles *et al* (2006). (Giles, 2006).

Patient response is classified as emergency or non-emergency. Essentially, an emergency response is defined as one where the patient responds as soon as physically capable of so doing.

Programming code was added to the model to reproduce the Giles *et al* study with the modelled patient group. The results of the model were compared to the findings of Giles *et al* and the parameters of the model adjusted as necessary.

The baseline probability of an emergency response was taken according to ABCD score as follows:

| ABCD score | 0 to 3 | 4 | 5 | 6 |
|---|---|---|---|---|
| P(Emergency) | 0.3 | 0.5 | 0.55 | 0.6 |

This was then increased by 0.1 on Monday and Tuesday and decreased by 0.1 on Friday and Saturday. An across the board increase of 0.2 was used when the enhanced use of 999 services option was applied.

Only 20 percent of emergency responses involve a direct call to A&E. Others involve a call to GP. Emergency calls to GP are deflected to A&E if the patient is still

symptomatic. This is interpreted as applying to all strokes, and to 30 percent of TIAs for which the symptom duration is over 60 minutes.

The time taken to see an A&E doctor following onset of symptoms is based on an analysis of the Newcastle ambulance data set – see section 3.2 below.

$\gamma = 1.12$; $\lambda = 0.466$, where $\gamma$ and $\lambda$ represent parameters of a Weibull distribution.

In case of emergency contact with GP, the time to appointment is taken from the same distribution. This can be either a visit to the GP surgery or a GP home visit.

Non-emergency contact with GP is taken to be available only between 9.30am and 5.30pm on Monday to Friday. It is assumed that the earliest possible contact time for non-emergency contact is 5 hours after onset. First sampling the day on which contact is made, and then sampling the time for that day determine the actual contact time.

For day of non-emergency GP contact, the basic rule is that if the earliest possible contact time is before 2.00pm on any day, then it is equally likely that contact will be made on any of three days including that day. If the earliest possible contact time is after 2.00pm on any day, then it is equally likely that contact will be made on any of the next three days. If application of this basic rule gives contact on a Saturday or Sunday, then contact is postponed to the following Monday.

The time of day for non-emergency GP contact is sampled uniformly between 9.30am and 5.30pm where possible. The only exception is for same day contact when the earliest possible contact time is between 9.30am and 2.00pm. In that case the time is sampled uniformly between the earliest possible contact time and 5.30pm.

The following table gives some examples of the application of this rule:

**Table 3.6: Illustrations of how patient initial contact with GP was built into the model**

| Earliest possible contact time | Actual contact time |
|---|---|
| 4.00pm Tuesday | Equal probability of Wednesday, Thursday, or Friday of that week. Time sampled uniformly between 9.30am and 5.30pm. |
| 11.00am Friday | One-third probability between 11.00am and 5.30pm that Friday. Two-thirds probability between 9.30am and 5.30pm following Monday. |
| 11.00am Saturday | Uniformly between 9.30am and 5.30pm the following Monday. |

## *3.2 Newcastle Rapid Ambulance Protocol Study*

In Newcastle, in collaboration with the ambulance service, a database has been maintained to monitor what happens to suspected stroke patients who are brought to hospital under a rapid ambulance protocol. While the purpose of the rapid ambulance protocol is to fast track care for patients with acute stroke who might benefit from thrombolysis, a proportion of patients also went through the service that had non-cerebrovascular diagnoses and also TIA. It is the data on these latter groups of patients that are relevant to the generation of our model, since this gives us plausible data on how long it takes patients to be seen by a doctor if they use the '999' route which is one of the pathways being explored in the model. The data set has already been used to explore the accuracy of the Face Arm Speech Test (FAST), the stroke recognition instrument, by paramedics in the scene as compared to stroke physicians after admission. (Nor, 2004)

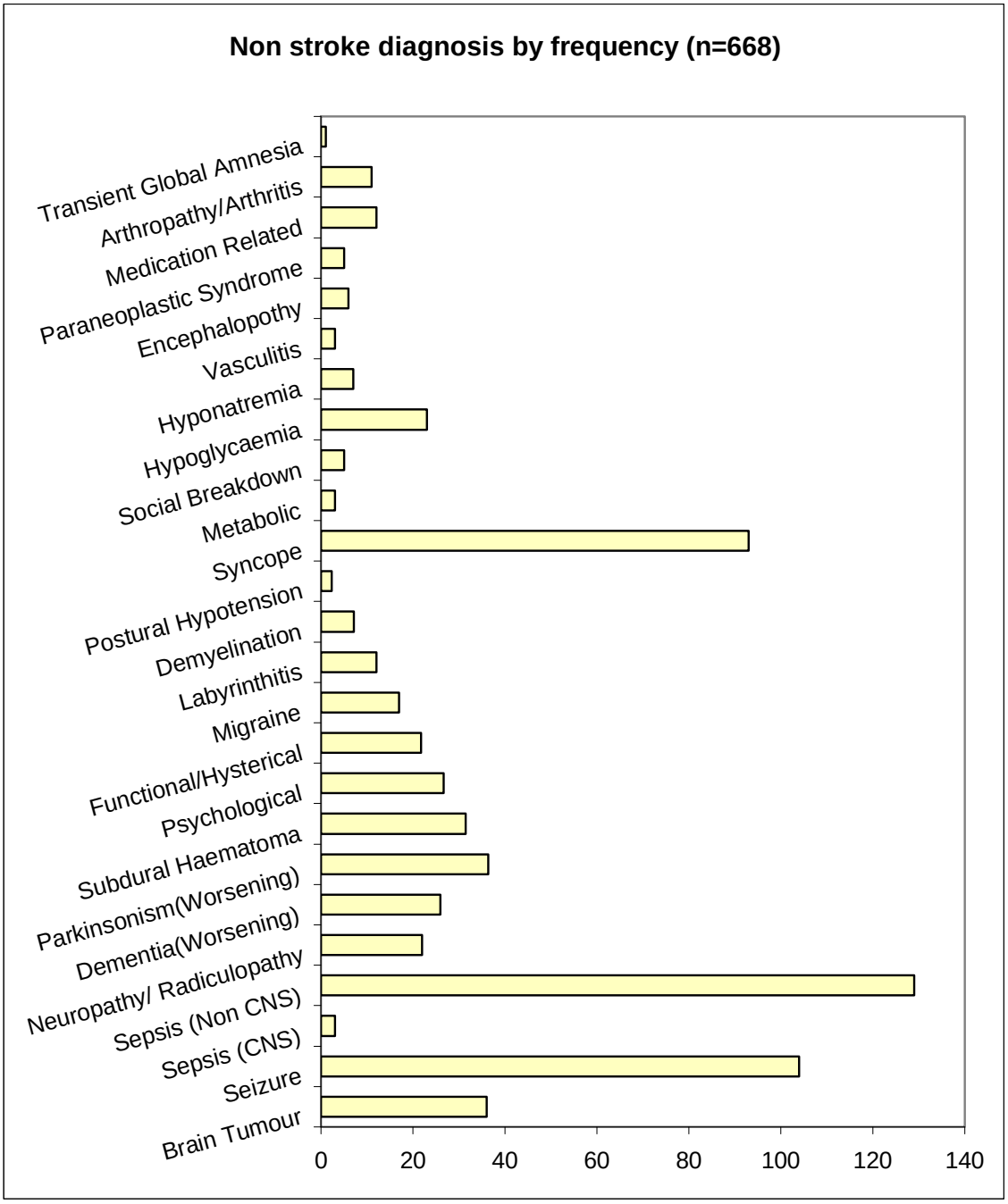
In addition to data on patients who attended A&E following a 999 call, the database also includes information on patients who attended A&E either as self-referrals, or referred by their GP.

For each patient, the computerised database captures time delay between paramedic and specialist stroke physician assessment as well as time between this set of initial set of assessments and formal admission. In addition, stroke subtypes by Oxford Community Stroke Project (OCSP) classifications were recorded. For patients with suspected stroke but who ultimately received a non-stroke diagnosis the diagnosis was specified.

### 3.2.1. What is the final diagnosis of patients sent to A&E with suspected stroke?

The mean age of this population was 71, with 47% male. 193 (11%) of the 1790 patients in the data set had a TIA, 945 (53%) had a stroke, 32 (2%) a sub-arachnoid haemorrhage. The remaining 620 patients had a non-cerebrovascular diagnosis, of which the commonest were sepsis, seizure and syncope. These are illustrated in figure 3.1

**Figure 3.1 Non-stroke diagnoses**

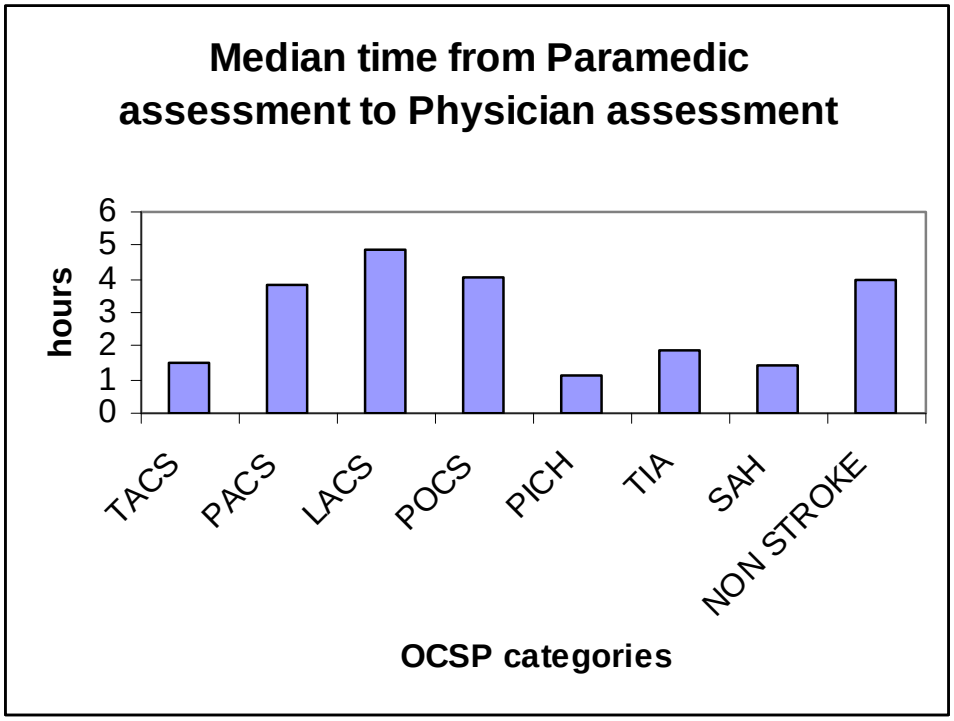


### 3.2.2 How long does it take people to get to hospital?

This was measured in two ways – the time lapse between being assessed by a paramedic and having a diagnosis made by a physician, and the time lapse between being assessed by a paramedic and getting to hospital.

Time delay between paramedic assessment and stroke diagnosis by a physician
For all diagnoses, the median time delay (n=1610) from the data was [IQR] 3.35 hours [1.15-10.72] – see figure 3.2.

**Figure 3.2 Time delay to seeing physician by diagnosis**

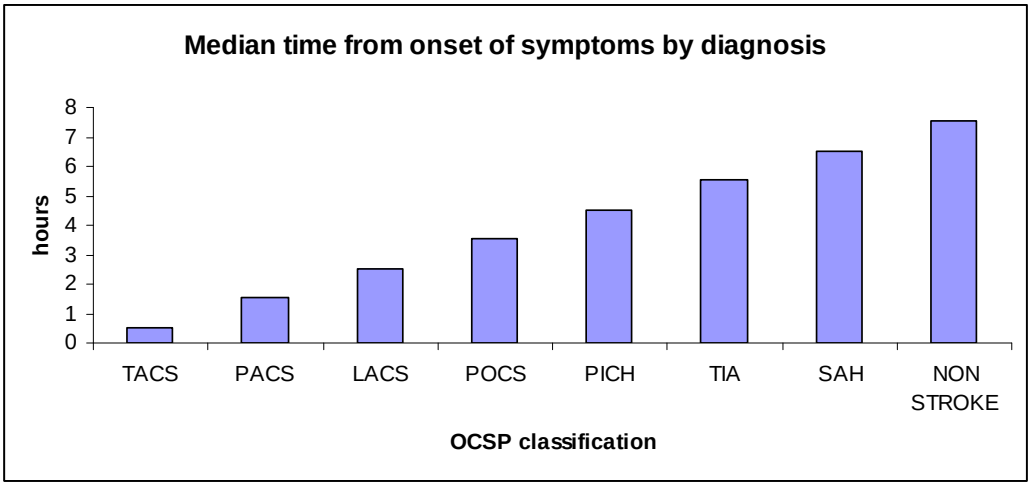



Stroke - TACS: total anterior circulation infarction
Stroke - PACS: partial anterior circulation infarction
Stroke - LCI: lacunar circulation infarction
Stroke – PCI: posterior circulation infarction
TIA – Transient ischaemic attack
SAH – Sub-arachnoid haemorrhage

Time delay between paramedic assessment and admission to hospital
For all diagnoses the median [IQR] time delay was 0.44 [0.17-0.99] hours (n=1587).

Time delay from onset of symptoms to admission
For all diagnoses the median [IQR] time delay was 6.72 [1.52-19.23] hours (n=1587).

**Figure 3.3 Time delay from onset of symptoms to admission**




Calculation for the model
From the Newcastle dataset, a formula was derived to approximate the time taken to see an A&E doctor for the model for patients who dialled 999:

$\gamma = 1.12$; $\lambda = 0.466$, where $\gamma$ and $\lambda$ represent parameters of a Weibull distribution.

## *3.3 Analysis of the QRESEARCH database*

The purpose of this analysis was to provide data from a large representative GP database as to what secondary prevention medications people are put on following a TIA under current practice and the average time delay before treatment is initiated.

### 3.3.1 Data on current practice from other sources

Rothwell and colleagues in Oxford found that premorbid blood pressure prior to an incident TIA (2002-4) was 147/80 mmHg with cholesterol of 5.6 mmol/l. (Rothwell, 2004a). Premorbid preventative medication included 38% receiving an antiplatelet agent, 46% were taking an antihypertensive and 22% a lipid-lowering drug. These data were gathered from a small cohort of less than 100 individuals suffering a TIA in the study period. Previous studies have shown that secondary prevention following TIA is sub optimal in terms of both blood pressure and lipid control as well as prescribed medication. Work using a GPRD cohort from 1992-6 showed that anti platelet medication was prescribed to between 30-45% of people following TIA. (Gibbs, 2001).

The National Sentinel Audit for Stroke currently only includes people admitted to or seen in hospital with Stroke or TIA. (Rudd, 2004). In 2001, of 7,884 patients whose pre-admission medication was known, 46% (3,666) were taking an anti-thrombotic drug. Anti-thrombotic therapy was given by the time of discharge in 91% (4,583/5,020) of applicable patients. By 2006, 100% of eligible patients were receiving antithrombotic therapy at discharge. (Rudd, 2004).

Data from Ontario describing post TIA management in an emergency room setting found that although 45% of people with TIA received neuro imaging, only 63% were prescribed antithrombotic medication before discharge. (Gladstone, 2004). A primary care based study from North Carolina found that primary care physicians changed (added to or started) antiplatelet medication in 47% of people presenting with TIA on the day of presentation. (Goldstein, 1995).

This study examines both process measures (risk lowering management) and outcome measures (risk factor control) before and up to a year after an index TIA in UK General Practices contributing to the QRESEARCH database. The results from these data inform the model with regard to baseline GP performance.

### 3.3.2 Methods

Data regarding demographic details, cerebrovascular risk factors and prescribed medication were extracted from the anonymised primary care records of people who were coded as suffering a first transient ischaemic attack between 1.4.2004 and 30.3.2005 in the disease registers of 463 practices contributing to the QRESEARCH database (see page 35 for list of Read Codes used). Eligible patients were registered at least 3 months before the date of their first TIA and had no evidence of a prior TIA or stroke before that date.

Eligible practices had used the EMIS clinical computer system at least six months before 1/4/2003. The last upload of data from the practice to QRESEARCH had to be later than 30/4/2006. QRESEARCH (www.qresearch.org) is a joint venture between Nottingham University and EMIS, a GP software supplier, which consists of a database containing the anonymised primary care records from patients

registered with participating practices from which datasets such as the one used in this study can be extracted.

Cases were followed up within the dataset from the date of their incident TIA until the first of the following occurred: patient has non-fatal stroke; patient dies; patient leaves practice; or TIA index date plus 12 months.

Outcome definitions: mortality and morbidity
*Death:* The patient is recorded (in the *date-of-death* field) as having died within one year of the TIA.

*Non-fatal stroke:* The patient has a first-ever Read-coded mention of stroke within one year of the TIA. Additionally, they must still have been alive one month after the stroke, and only the first such stroke was counted in each case.

Analysis
Analysis was performed using STATA 9 SE (Statacorp). Patients were censored at the time of deregistration (if before the end of the study) or at the end of the study period. Blood pressure control, cholesterol level and preventive medication prescription were evaluated in the 12 months before and after the index TIA. Paired comparisons of normally distributed data were made using paired t tests and paired comparisons of proportions were made using McNemar's test. In view of multiple testing a p value of $<0.01$ was chosen for significance.

A Kaplan-Meier analysis was used to estimate mortality and non-fatal stroke in the year following index TIA.

### 3.3.3 Results

3405 individuals suffered an index (first) TIA during the study of whom 3366 (99%) were alive one month after their index TIA and 3042 (89%) were still alive after one year (see table 3.7). At the time of the TIA, mean age was just over 72 and 56% were women. Mean age for women suffering a TIA was 73.6 compared to 70.9 for men.

**Table 3.7. baseline and follow up raw data**

| | 1 month Pre TIA | 1 month Post TIA | 12 months Post TIA |
|---|---|---|---|
| Population at Risk (n) | 3405 | 3366 | 3042 |
| Mean Age (SD) | 72.4 (13.4) | 72.3 (13.4) | 71.7 (13.1) |
| Sex (%Male) | 44.3% | 44.2% | 44.4% |
| Number (%) with BP measurement in last 12 months* | 2677 (79%) | N (93%) | 2885 (95%) |
| Number (%) with cholesterol measurement in last 12 months* | 1497 (44%) | N 1145(63%) | 2419 N (80%) |
| Number (%) receiving Antiplatelet or anticoagulants | 1312 (38%) | 2454 (72%) | 2430 (79%) |
| Number (%) receiving Lipid Lowering Therapy | 612 (17%) | 1255 (37%) | 1290 (42%) |
| Number (%) receiving Antihypertensive Medication | 1340 (39%) | 1635 (48%) | 1534 (50%) |
| Number (%) receiving combination of antiplatelet/anticoagulants, statin, Anti HT Rx | 370 (10%) | 742 (22%) | 879 (28%) |

* Any individual with a reading in the previous 12 months

#### 3.3.3.1 Risk Factors

Three thousand and forty two individuals were still present in the data set (ie had survived and not moved away from the contributing practices) one year after TIA. The systolic and diastolic blood pressure were evaluated in the 2297 (75%) individuals alive after 1 year with a result both before and after their TIA. Similarly, the total cholesterol was evaluated in the 1110 (36%) individuals alive after 1 year who had a result both before and after their TIA.

Blood Pressure

In the year prior to TIA, the majority (79%) of individuals had a blood pressure measurement recorded with a mean of 144/80mmHg for the last reading and 39% were receiving blood pressure lowering medication. One month following TIA, most (93%) had had a blood pressure check in the last year, which was sustained one year following TIA (95%). When only those individuals with both a blood pressure recorded in the year before and after TIA were included (=2297/3042 (82%) alive at one year), mean blood pressure fell from 145/80mmHg to 139/77mmHg, $t > 12$, $p < 0.0001$. (Table 3.8). The proportion with a last blood pressure in the previous year equal to or below 150/90 mmHg improved from 68% to 79% ($X^2 = 100$, $p < 0.0001$) and similarly for a target of 140/90 mmHg the proportion improved from 48% to 60% ($X^2 = 79$, $p < 0.0001$).

Cholesterol

In the year before TIA, 44% of individuals had total cholesterol measurement recorded in the previous year. This rose to 63% one month after TIA and 80% one year after TIA. When only those individuals with both a total cholesterol recorded in the year before and after TIA were included (=1164/3042 (38%) alive at one

year), mean total cholesterol fell from 5.3 mmol/l to 4.5 mmol/l, t = 18.3, p<0.0001 (table 3.8). The proportion at or below a target total cholesterol of 5 mmol/l improved from 44.3% to 76% ($X^2$ = 279, p<0.0001).

**Table 3.8: Paired blood pressure and cholesterol readings before and after TIA****

| | 1 month Pre TIA | 12 months Post TIA | difference | t | p |
|---|---|---|---|---|---|
| SBP* N=2297 | 145.3 (144.4, 146.1) | 139.1 (138.4, 139.9) | -6.1 (-7.0, -5.2) | 12.8 | <0.0001 |
| DBP* | 80.1 79.7, 80.6) | 77.0 (76.5, 77.4) | -3.2 (-3.7, -2.6) | 12.12 | <0.0001 |
| Target 150/90 | 1321 (67.6) | 1823 (79.4) | | $X^2$ = 100.2 | <0.0001 |
| Target 140/90 | 1103 (48.0) | 1368 (59.6) | | $X^2$ = 79.2 | <0.0001 |
| Total Cholesterol* N=1110 | 5.33 (5.24, 5.42) | 4.53 (4.46, 4.59) | 0.80 (0.72, 0.89) | -18.3 | <0.0001 |
| Target 5 mmol/l | 492 (44.3) | 844 (76.0) | - | $X^2$ = 279 | <0.0001 |

*Mean (95% CI)

**** In each case, only individuals alive at 1 year with the relevant reading in both the year before and year after TIA are included.**

### 3.3.2 Risk factor Management

Data are presented here for those people alive one year after suffering a TIA in order to allow comparison of prescribing both before and after the event. Baseline data are similar for the whole cohort compared to those alive at one year: for example baseline prescription of an antithrombotic or patient noted to be taking over the counter (OTC) aspirin was 1312/3405 (39%) of all those alive one month before TIA, compared to 1170/3042 (39%) when just those alive one year post TIA are considered.

Antithrombotic medication

Of those alive 12 months post TIA, prescription of antithrombotic medication or record of OTC aspirin was 1170/3042 (39%) before TIA compared to 2333/3042 (77%), $X^2$=1005, p<0.0001 after TIA. (table 3.9)

Antiplatelet medication

Aspirin alone was prescribed or noted to be taken OTC by 956/3042 (31%) pre TIA and 55% post. Aspirin and dipyridamole were prescribed pre TIA to 26/3042 (0.9%) vs 187/3042 (6%) post TIA. Similarly clopidogrel prescription increased from 41/3042 (1%) to 177/3042 (6%). In each case these differences were all highly statistically significant (table 3.9). Smaller but still statistically significant increases in prescription were see in dipyridamole alone and Antiplatelet PLUS warfarin. (All table 3.9)

Anticoagulant medication

Prescription of warfarin alone increased from 87/3042 (3%) to 156/3042 (5%), $X^2$ = 44, p<0.0001. (table 3.9)

**Table 3.9: Anti platelet / anticoagulant paired data**

| | 1 month Pre TIA (N=3042) | 12 months Post TIA (N=3042) | $X^2$** df=1 in each case | p |
|---|---|---|---|---|
| Aspirin OR other antiplat. OR warfarin | 1170 (39) | 2333 (77) | 1005 | <0.0001 |
| Aspirin alone | 956 (31) | 1680 (55) | 422 | <0.0001 |
| Aspirin AND dipyridamole | 26 (0.9) | 187 (6) | 142 | <0.0001 |
| Dipyridamole alone | 18 (0.6) | 41(1) | 12 | 0.0008 |
| Clopidogrel alone | 41 (1) | 177 (6) | 116 | <0.0001 |
| Aspirin/other antiplat. AND warfarin | 17 (0.6) | 71 (2) | 47 | <0.0001 |
| Warfarin alone | 87 (3) | 156 (5) | 44 | <0.0001 |
| | | | | |

*n(%) ** McNemar's test

Antihypertensive medication

Immediately before diagnosis of TIA, of the 50% of individuals with a last BP reading above 140 mmHg, 2/3 were not prescribed anti hypertensive medication. For a threshold of 160 mmHg, 18% had a last reading above this and 8% of all patients had a last blood pressure reading above 160 mmHg and no medication prescribed. After TIA, 39% of individuals had a last recorded BP reading of over 140 mmHg, of whom 56% were not prescribed blood pressure lowering medication (table 3.10).

Considering those alive after one year, the proportion of individuals prescribed any antihypertensive 1 month pre TIA was 1203/3042 (40%) compared with 1525/3042 (50%) twelve months later (table 3.8). After TIA, there were increases in the proportion of people prescribed one, two and three antihypertensives and the median number of antihypertensives increased from 0 (IQR 0,4) to 1 (0, 5), p<0.0001.

One month prior to TIA, 39% of women were prescribed an antihypertensive as were 40% of men. One year following TIA, 50% of women and 50% of men were receiving antihypertensive mediation.

*By Class*

There were large increases in the proportion prescribed ACE inhibitors and thiazide diuretics (absolute increases of 7% and 5% respectively) with smaller increases in Calcium Channel Blockers, Angiotensin Receptor Blockers and Beta Blockers. Little change was seen in the prescription of alpha blockers following TIA.

**Table 3.10: Use of anti-hypertensives in before and after TIA**

| | 1 month Pre TIA* (N=3042) | 12 months Post TIA* (N=3042) | $X^2$** df=1 in each case | p |
|---|---|---|---|---|
| Any antihypertensive | 1203 | 1525 | 128 | <0.0001 |

| | | | | |
|---|---|---|---|---|
| | (40) | (50%) | | |
| Number of antihypertensives n (%) | | | | |
| 0 | 1,839 (60) | 1,517 (50) | | |
| 1 | 658 (22) | 799 (26) | | |
| 2 | 381 (13) | 502 (17) | | |
| 3 | 133 (4) | 188 (6) | | |
| 4 | 29 (1) | 31 (1) | | |
| 5 | 2 | 5 | | |
| Median number of antihypertensives | 0 (0, 4) | 1 (0,5) | -12.3*** | <0.0001 |
| ACEI | 461 (15) | 674 (22) | 89 | <0.0001 |
| ARB | 152 (5) | 221 (7) | 29 | <0.0001 |
| Thiazide | 391 (13) | 537 (18) | 50 | <0.0001 |
| Calcium-channel blockers | 367 (12) | 459 (15) | 25 | <0.0001 |
| Beta-blockers | 483 (16) | 528 (18) | 5.6 | 0.018 |
| Alpha blocker | 91 (3) | 97 (3) | 0.4 | 0.59 |

*n(%) ** McNemar's test ***Wilcoxan Rank

Lipid Lowering medication

Lipid lowering prescription (both statins and fibrates) increased from 565/3042 (19%) pre TIA to 1280/3042 (42%) post TIA, the vast majority of which reflects increased statin prescription. Of those receiving a statin pre TIA who had a total cholesterol recorded in the previous year, 320/487 (66%) had a cholesterol below 5 mmol/l. Following TIA, of those with a cholesterol in the last year who were prescribed a statin, 928/1143 (81%) had a cholesterol below 5mmol/l. Of those people not prescribed a statin who had a cholesterol recorded, before suffering a TIA, 345/1010 (34%) had a cholesterol below 5 compared with 715/1262 (57%) following TIA.

The proportion of people receiving a statin at each level of last recorded statin increased following TIA compare to before (Figures 3.4 and 3.5).

One month before TIA 16% of women and 19% of men were prescribed a statin. One year after TIA, 690/1865 (41%) of women and 574/1357 (42%) of men were prescribed a statin.

**Figure 3.4: Recorded Total Cholesterol by Statin Prescription Pre TIA**

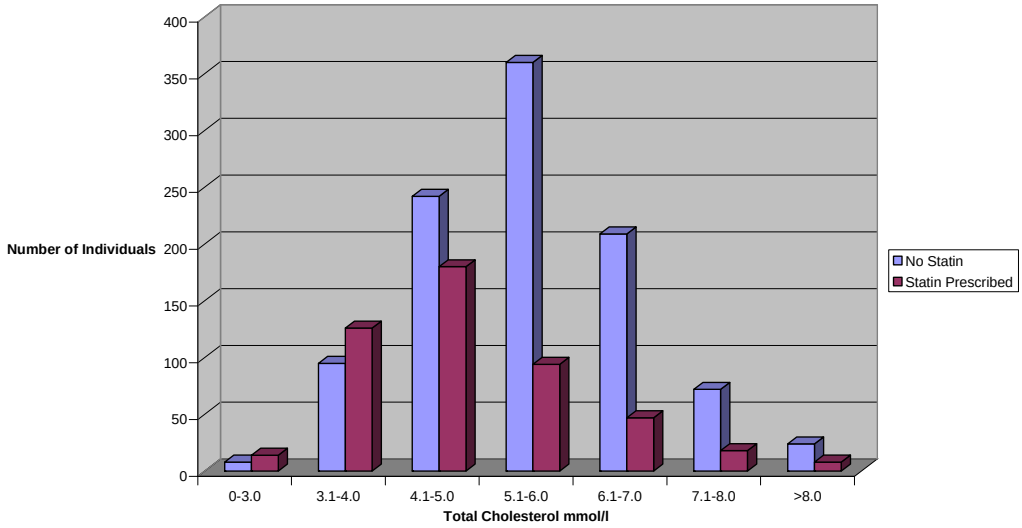
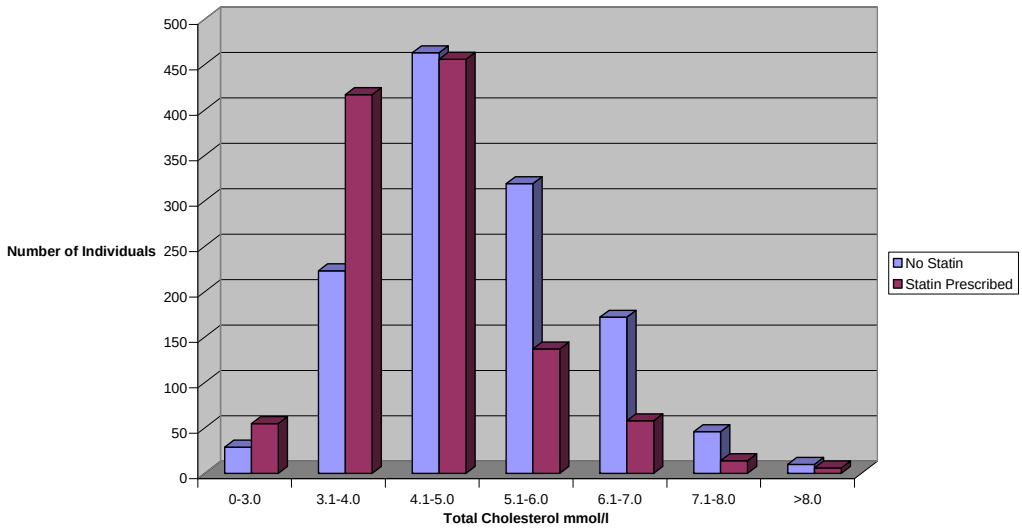



**Figure 3.5: Recorded Total Cholesterol by Statin Prescription Post TIA**




*By Class*

Following TIA, simvastatin prescription increased threefold and atorvatastatin prescription doubled with much smaller changes in other statins. The prescription of statins was correlated with cholesterol at 1 year with 65% of those with a total cholesterol below 3mmol/l prescribed a statin compared to only 25% of those with a cholesterol over 6 mmol/l (table 3.11).

**Table 3.11: Use of lipid lowering therapy before and after TIA**

| | 1 month Pre TIA* (N=3042) | 12 months Post TIA* (N=3042) | $X^2$** df=1 in each case | p |
|---|---|---|---|---|
| Statin / fibrate | 565 (19) | 1280 (42) | 494 | <0.0001 |
| Statin | 552 (18) | 1264 (42) | 489 | <0.0001 |
| Fibrate | 16 (0.5) | 19 (0.6) | 0.5 | 0.6 |
| Simvastatin | 344 (11) | 1017 (33) | 541 | <0.0001 |
| Atorvastatin | 234 (8) | 472 (16) | 161 | <0.0001 |
| Pravastatin | 41 (1) | 61 (2) | 8 | 0.005 |
| Fluvastatin | 21 (0.7) | 17 (0.6) | 1.1 | 0.4 |
| Rosuvastatin | 19 (0.6) | 33 (1) | 7 | 0.013 |

*n(%) ** McNemar's test

### 3.3.3 Survival Curves

Kaplein – Meier Survival curves were calculated for both death and non fatal stroke post TIA (figures 3.6 & 3.7). 220 (6.5%) people died in the first 12 months following TIA. One year after TIA, 3042 (89%) of individuals were still alive and registered. In terms of non fatal stroke, incidence was highest in the 1 month following TIA consisting of 306/493 (62%) of all non fatal strokes with a further 187 (38%) in the subsequent 11 months.

**Figure 3.6: Survival (months) following TIA**

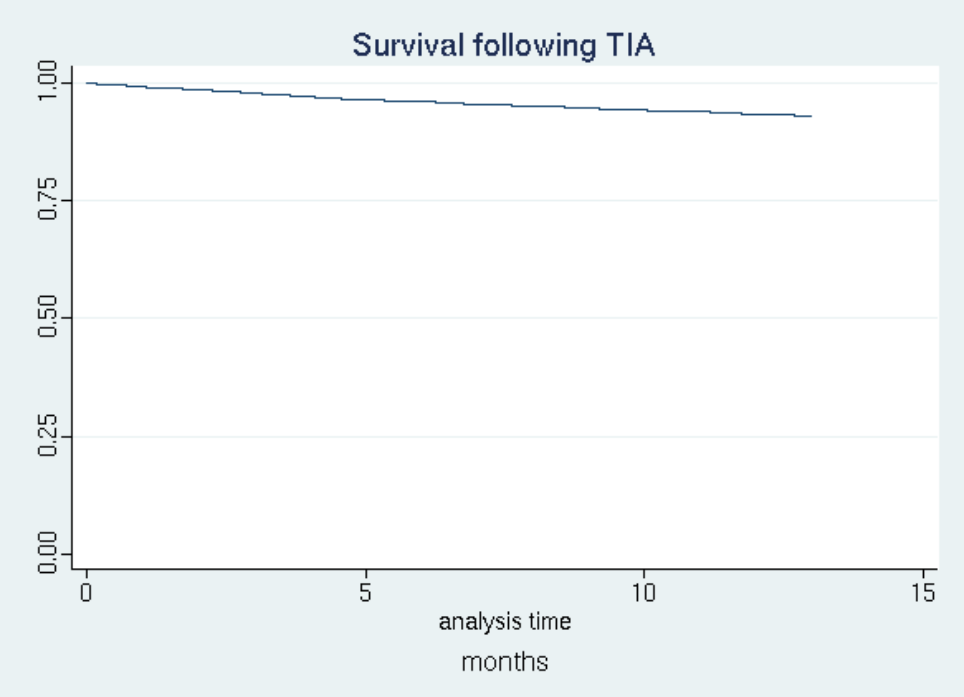


**Figure 3.7: Non fatal stroke following TIA**


### 3.3.4 Incorporating the QRESEARCH results into the model

**Table 3.12 Parameters defining standard GP treatment (derived from QRESEARCH analysis)**

| Parameter | Value |
|---|---|
| Probability of referral for CE assessment if suitable | 0.15 |
| Probability of antiplatelet monotherapy | 0.324 |
| Probability of antiplatelet dual | 0.089 |
| Probability of cholesterol test | 0.226 |
| Probability of immediate BP/AF | 0.59 |
| Probability of delayed BP/AF | 0.381 |
| Minimum time to delayed BP/AF | 7 days |
| Mean time to delayed BP/AF | 123 days |

For antiplatelet therapy, QRESEARCH data shows 65.5 percent on aspirin including 8.9 percent on dual treatment. In the starting population, 44.0 percent are on antiplatelet. After 8.9 percent of the population have been put on to dual therapy, 40.1 percent remain on monotherapy, with 51.0 percent on no therapy. To produce a total of 65.5 percent on aspirin, we must switch 16.5 percent of the population from no therapy to monotherapy. Thus the probability of being switched to monotherapy is 16.5/51.0 = 0.324.

For statin therapy, QRESEARCH data shows 40.4 percent on statin. In the starting population, 24.2 percent are already on statin and a further 71.8 percent are not on statin but have cholesterol over 3.5. To reach a target of 40.4 percent on statin, the proportion needed to convert is 18.0/71.8 = 0.226.

For time to blood pressure assessment, the proportion with missing BP over time was fitted to a curve of the form $A+Be^{-\lambda t}$. The value of *A* gives the proportion never tested, *B* gives the proportion with a delayed test and so $1-A-B$ gives the proportion tested immediately. The reciprocal of $\lambda$ is the mean time to testing in the case of a delayed test. The minimum time to testing is an assumption. It was assumed that AF testing would be at the same time as blood pressure.

## *3.4 Patient survey*

In order to ascertain the costs incurred by patients who have a TIA, and to identify patient preferences with regard to patterns of service delivery, a questionnaire survey was developed. Development was done in conjunction with a patient advisory group and was piloted on patients participating in the OXVASC study. The finalised questionnaire was then sent to patients from selected practices in the West Midlands and Hertfordshire.

West Midlands Multi-centred Research Ethics Committee (MREC) approval (MREC Ref: 06/MREC07/69) and Trust permission from the South Birmingham PCT Consortium and Hertfordshire PCT consortium were obtained for the questionnaire study.

### 3.4.1 Patient survey methods

Patient Advisory Group

A Patient Advisory Group (PAG) was established to advise on the content and structure of the questionnaire. Patients registered with a West Midlands practice and who had had a TIA were sent a letter inviting them to participate in the PAG. Those who expressed an interest were invited to attend a meeting at their surgery. The PAG comprised seven patients.

During the meeting the patients were asked to complete the draft questionnaire and then feedback their thoughts on both the structure and content. To ensure all possible courses of action were included in the questionnaire, patients also discussed what they did when they had their TIA. Comments, suggestions and feedback were incorporated into the survey. This was then sent to the PAG members who completed and returned the questionnaire to us with any further comments and/or suggestions. No further amendments were necessary at this point.

The PAG was also asked to comment on the information sheet and the covering letter that would accompany the questionnaire. All PAG members felt that these were clear, easily understood and contained all the information that people would need to enable them to decide whether or not to complete the questionnaire. Therefore, no changes were made to these in light of PAG feedback.

The Questionnaire

The questionnaire was split into four main areas: information about the patient; information about their TIA; questions about the type of service they would prefer; details about what they did and what costs they incurred when they had their TIA. It was sent together with the information sheet, covering letter from the patient's GP and a pre-paid envelope.

Pilot Questionnaire Distribution

The questionnaire was piloted on patients identified as having a recent TIA through the OXVASC study, with the aim of identifying any areas in the survey that were inconsistently or incorrectly completed. The questionnaire was distributed to patients 6 months post event. Approximately 25 OXVASC patients were sent a questionnaire.

Main Questionnaire Distribution

Practices in the South Birmingham Primary Care Trust and Hertfordshire Primary Care Trust consortiums were invited to participate in the questionnaire survey study.

Those practices agreeing to take part were asked to run a report on their clinical computer system to identify all patients who had been diagnosed as having a TIA in the preceding 12 months. The practice would then screen the list to ensure that any person where it would be inappropriate to send a questionnaire was excluded (for example: recently deceased; diagnosed with a terminal illness). Anonymised patient details (date of birth; gender; postcode; practice computer number) were sent to the study office at the University of Birmingham. Packs comprising a questionnaire, introductory letter, information sheet and prepaid envelope were then sent to the practices, who distributed the questionnaire to their patients. Completed questionnaires were returned to Birmingham University. A reminder was sent to all non-responders after one month.

Analysis

Analysis was carried out using SPSS software (v14.0). All analysis was done on the 104 patients who returned a completed questionnaire unless otherwise stated. P values have only been given where results were statistically significant. Missing data accounts for any proportions that do not total 100%.

### 3.4.2 Main questionnaire Results

Practices

19 practices in the West Midlands and Hertfordshire areas agreed to participate in the questionnaire survey study. Practices represent a range of characteristics, with single-handed practices right through to practices with 16 GPs participating. Practices were also a mix of urban/rural, and all levels of socio-economic status were included. (Socio-economic status was derived from the Index of Multiple Deprivation).

A total of 186 patients were identified as having had a TIA and were sent a questionnaire. There was a wide variation between practices in the number of eligible patients: the average per practice was 9.8 (range 2-22). Patient mean age was 78.8 years (range 35.5-100.2).

114 (61%) patients returned a questionnaire. However, 10 (5%) of patients returned a blank questionnaire: these were classed as non-responders for the analysis. 104 (56%) surveys were completed and returned.

Responders and Non-Responders

There were few significant differences between responders and non-responders. Patients from bigger practices were more likely to return a questionnaire, although there was no clear linear association, as patients from the largest practices (those with 9 or more GPs) were less likely to respond. The mean age of responders was 74.5 years (range 43.6-100.2), while non-responders were slightly older, with a mean age of 75.3 (range 35.5-97.1): this difference was not statistically significant. There was no difference in the response rates between men and women, or between the different practice socio-economic levels (see table 3.13).

**Table 3.13: Characteristics of responders versus non-responders**

| Characteristic | | Responders n (%) | P Value* |
|---|---|---|---|
| Size of practice (no. of GPs) | 1-4 | 37 (51%) | |
| | 5-6 | 28 (62%) | |
| | 7-8 | 22 (79%) | |
| | 9+ | 17 (43%) | 0.013 |
| Practice Index of Multiple Deprivation (quartile) | 1 (least deprived) | 31 (61%) | |
| | 2 | 41 (59%) | |
| | 3 | 10 (38.5%) | |
| | 4 | 22 (55%) | |
| Sex | M | 54 (62%) | |
| | F | 49 (62%) | |

* p value only given if statistically significant

Characteristics of Respondents

The mean age of respondents was 74.5 years (range 43.6-100.2). A reasonable balance of proportions between men and women was found. The patient completed the majority of questionnaires themselves, although the patient's carer returned a number. Very few patients were in paid employment: most patients were retired, although a few were unemployed or unable to work due to illness.

There was also a reasonable balance of proportions across the practice characteristics, with all the different practice sizes and deprivation levels having patients who returned completed questionnaires. (See table 3.14)

**Table 3.14: Characteristics of Respondents**

| Patient Characteristic | | Number (%) |
|---|---|---|
| Sex | Male | 54 (52) |
| | Female | 49(47) |
| Who completed questionnaire | Patient | 93 (89) |
| | Carer | 10 (10) |
| In Paid employment | Yes | 13 (12.5) |
| | Retired | 77 (74) |
| | Unemployed/Sick | 3 (3) |
| | Caring for relative | 6 (6) |
| **Practice Characteristic** | | |
| Size of practice (no. of GPs) | 1-4 | 37 (36) |
| | 5-6 | 28 (27) |
| | 7-8 | 22 (21) |
| | 9+ | 17 (16) |
| Index of Multiple Deprivation (quartile) | 1 (least deprived) | 31 (30) |
| | 2 | 41 (39) |
| | 3 | 10 (10) |
| | 4 | 22 (21) |

Information about the TIA

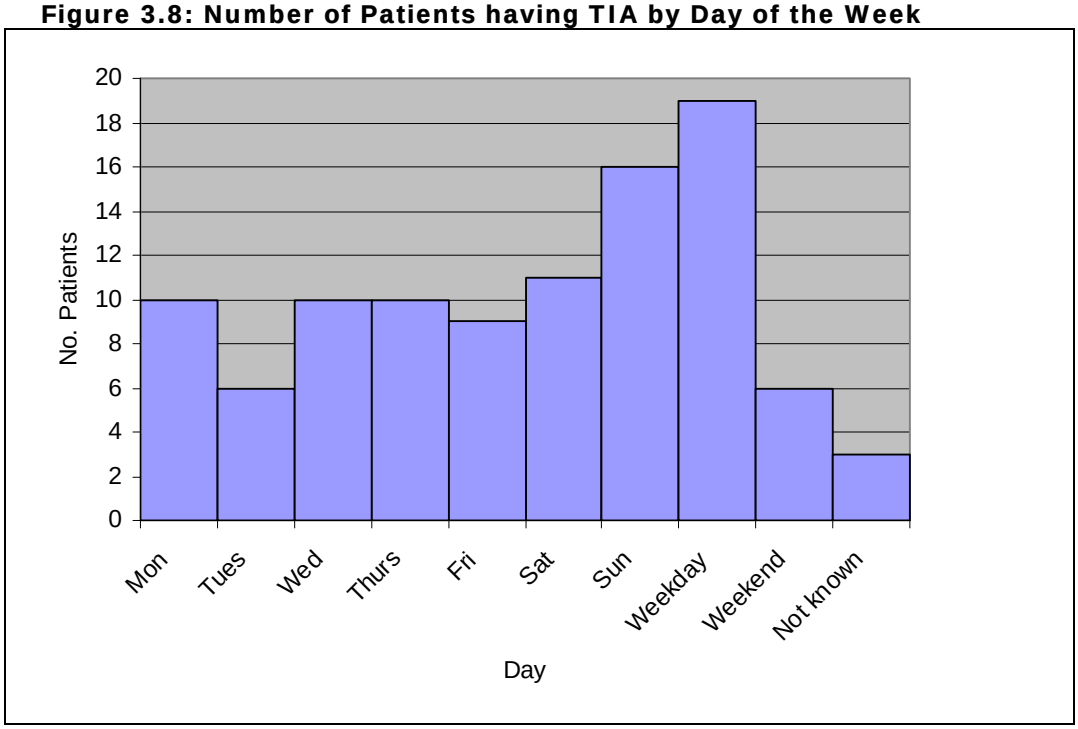
Patients were asked to indicate which day of the week that they had their TIA, and if they couldn't remember, to state whether it was a weekday or a weekend (see figure 3.8). For analysis, patients were grouped into whether they had their TIA

during the week or at the weekend (see table 3.15). Unsurprisingly, more people had their TIA during the week, although the proportion of people having their symptoms at the weekend was slightly higher than may be expected when taking the difference in number of days into account.

**Table 3.15: Day of TIA**

| Day of TIA | Number (%) |
|---|---|
| Weekday | 64(61.5) |
| Weekend | 33 (32) |
| Not known | 3 (3) |

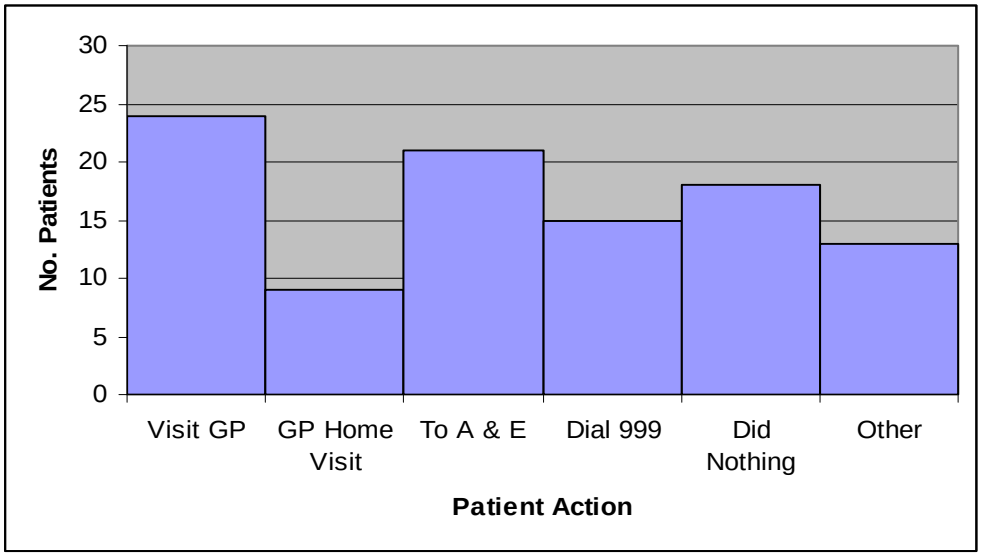
**Figure 3.8: Number of Patients having TIA by Day of the Week**




Patient Action at Time of TIA

Patients were also asked what they did when they experienced their symptoms, and patients report a variety of responses (figure 3.9). Most people visited their GP, although many chose to go to their local accident and emergency department. Nearly a fifth of people did nothing initially, although all subsequently sought help.

**Figure 3.9: Patient Action at Time of TIA**



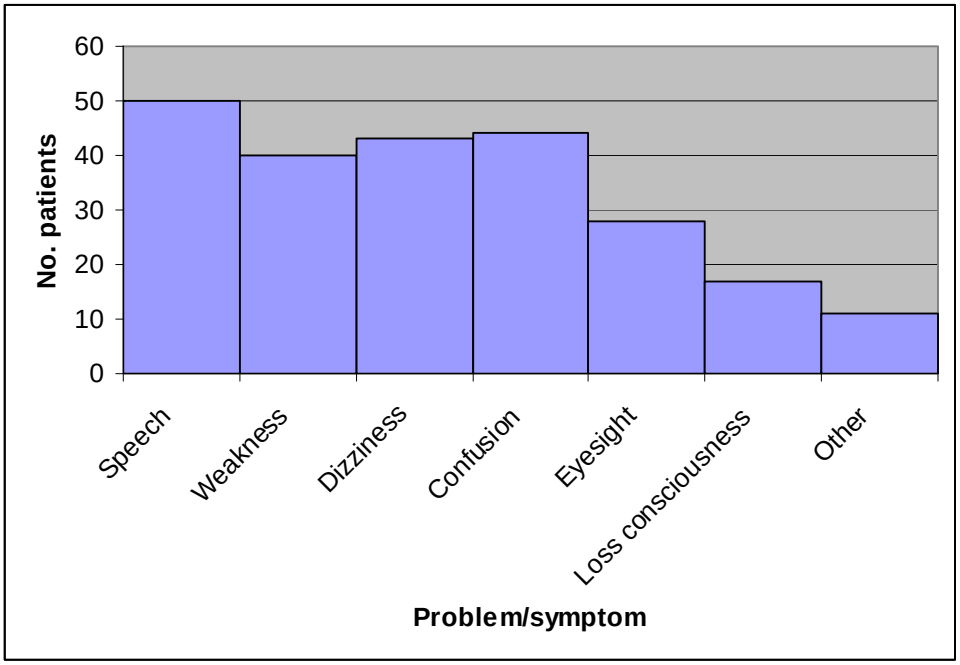

To look at whether people take different actions if they experience their symptoms at the weekend than they do if they are ill during the week, actions taken were grouped into: contacted GP (patients who visited their GP or requested a home visit); visited hospital (patients who visited A & E or dialled 999); or other (patients who contacted NHS Direct, saw an optician or went to a specialist eye hospital and patients who did nothing). Patients who had their TIA at the weekend were more likely to visit hospital than their GP. (See table 3.16)

**Table 3.16: Patient Action by Day of TIA**

| Day of TIA | Action taken | Number (%) | p value |
|---|---|---|---|
| Weekday | Contacted GP | 26 (41) | 0.025 |
| | Visited hospital | 17 (27) | |
| | Other | 20 (32) | |
| Weekend | Contacted GP | 6 (18) | |
| | Visited hospital | 17 (51.5) | |
| | Other | 10 (30) | |

It is also possible that the specific symptoms experienced influenced the action a patient took. The questionnaire asked patients to indicate what symptoms they suffered (see figure 3.10)

**Figure 3.10: Patient Reported Symptoms**




The most commonly reported symptom was problems with speech, with 48% of responders having suffered this. Many people also reported dizziness, weakness and confusion, and some suffered loss of consciousness. Patients who reported having 'other' symptoms described headaches, vomiting and difficulty with food. However, the type of symptom experienced by a patient did not influence what course of action they decided to take, with the exception of temporary loss of consciousness, which made people more likely to call 999 or visit A & E (see table 3.17).

**Table 3.17: Patient Action by Reported Symptom**

| Symptom | | Contacted GP Number (%) | Visited hospital Number (%) | Other Number (%) | p value* |
|---|---|---|---|---|---|
| Difficulty speaking | Yes | 15 (30) | 18 (36) | 17 (34) | |
| | No | 18 (36) | 18 (36) | 14 (28) | |
| Weakness/numbness | Yes | 14 (35) | 14 (35) | 12 (30) | |
| | No | 19 (32) | 22 (37) | 19 (32) | |
| Dizziness/giddiness | Yes | 15 (36) | 19 (45) | 9 (19) | |
| | No | 18 (31) | 17 (29) | 23 (40) | |
| Confusion | Yes | 12 (27) | 18 (41) | 13 (32) | |
| | No | 21 (37.5) | 18 (32) | 17 (30) | |
| Problem with eyesight | Yes | 7 (25) | 14 (50) | 7 (25) | |
| | No | 26 (36) | 22 (31) | 24 (33) | |
| Loss of consciousness | Yes | 2 (12) | 10 (59) | 5 (29) | 0.046 |
| | No | 31 (37) | 26 (31) | 26 (31) | |
| Other | Yes | 3 (27) | 4 (36) | 4 (36) | |
| | No | 30 (34) | 32 (36) | 27 (30) | |

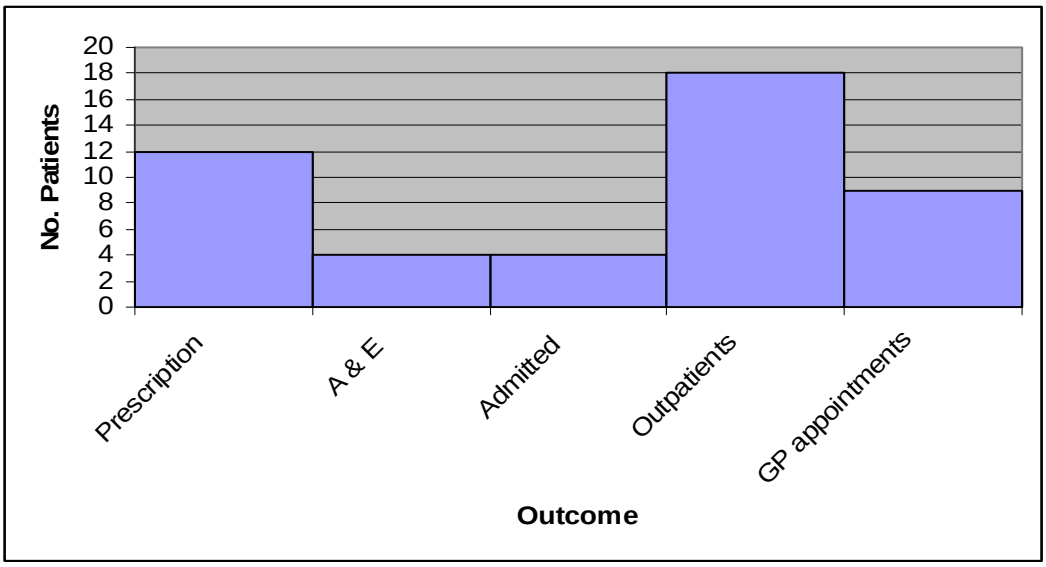
* p value only reported where significant

Patients who initially did not seek medical attention about their symptoms all subsequently sought advice. The average time lapse between TIA and seeking medical attention for this group was 263 hours (11 days), although there was wide variation in the delay (range 1 hour – 84 days). Slightly more women than men took no immediate action (10 (56%) versus 8 (44%)) but this was not a significant difference. Type of symptom did not influence whether or not a patient would seek medical advice, including loss of consciousness (2 patients who suffered this did not seek assistance). Most patients who did nothing subsequently visited their GP, although one patient did visit a consultant one week post TIA.

Patients who contacted a GP

Patients who either visited a GP or had a home visit from a locum (n=33) were asked to give details about the outcome of that appointment. The most frequent outcome was referral to hospital outpatients, although a number of people were sent to A & E or admitted to hospital. In a number of cases, the GP managed the patient themselves, giving them further appointments and/or prescriptions. (See figure 3.11)

**Figure 3.11: Outcome of GP Appointment***




*Does not total 33 as outcomes are not mutually exclusive

Patient Preference

Patients were asked to tell us about what kind of TIA service they would prefer. They were asked to rank 3 options: treatment by GP; treatment at A&E; urgent referral to a specialist.

The option of treatment by GP was ranked as the favourite option most often, with 42 (40%) of patients choosing this type of service; urgent referral to a specialist was cited by the fewest patients as being their preferred method of service provision. However, treatment by a specialist was given as second choice by the highest number of people. (See table 3.18)

Responses were allocated a score (1=favourite option; 2=second favourite option; 3=least favourite option) and a mean score for each response was calculated. Treatment by GP was still the favoured option (mean 1.78, Standard Deviation

(SD) 0.81); with hospital the second choice (mean 2.02, SD 0.85) and specialist treatment the least favoured option (mean 2.14, SD 0.76).

**Table 3.18: Patient Preference of Service Provision**

| | GP Number (%) | Hospital Number (%) | Specialist Number (%) |
|---|---|---|---|
| 1st Choice | 42 (40) | 29 (28) | 19 (18) |
| 2nd Choice | 29 (28) | 25 (24) | 34 (33) |
| 3rd Choice | 22 (21) | 31 (30) | 31 (30 |

Patient Costs

To identify what costs were incurred by patients when they had their TIA, people were asked how they travelled to their GP or hospital and how much they paid in fares or parking fees. These costs relate only to the initial visit to health services after TIA, and does not include costs incurred by further appointments or referral elsewhere. Therefore, costs incurred by patients having multiple trips to surgeries or hospitals would be higher.

Most patients travelled by car (57 (55%)) although 21 (20%) did go to hospital by ambulance. 8 (8%) people walked, and 6 (6%) went by public transport. The mean journey length (one way) was 4.65 miles (range 1-35), although that relates only to the 46 patients who provided an estimate of the distance. The mean cost in parking fees for those travelling by car was £1.43 (range £0 - £12.00). Only one patient who used public transport paid a fare (£5.50); other patients were presumably entitled to free use of public transport. The difference in mean costs for patients who visited their GP and those who went to hospital were tested; the mean for GP visits was £0.59 (SD 1.91) per visit, while the mean for a hospital visit was £1.63 (SD 3.1).

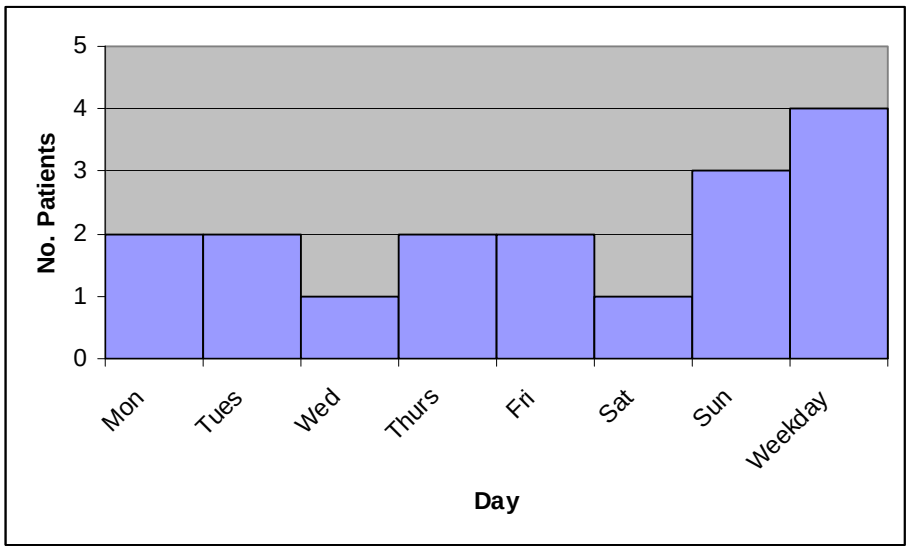
### 3.4.3 Pilot data results

No demographic data were collected about the OXVASC patients, as the aim of this phase of the study was to test the suitability of the questionnaire. Therefore, no response rate has been calculated and no description of the responder's characteristics has been given. However, the analysis performed on the main questionnaire has been repeated on the pilot patients.

18 people completed and returned a questionnaire. Seventeen questionnaires were completed by the patients themselves (for the remaining questionnaire it was not known who completed it). Six (33%) of people were in paid employment, while 10 (56%) of patients stated that they were retired. The remaining 2 (11%) people were carers for a relative.

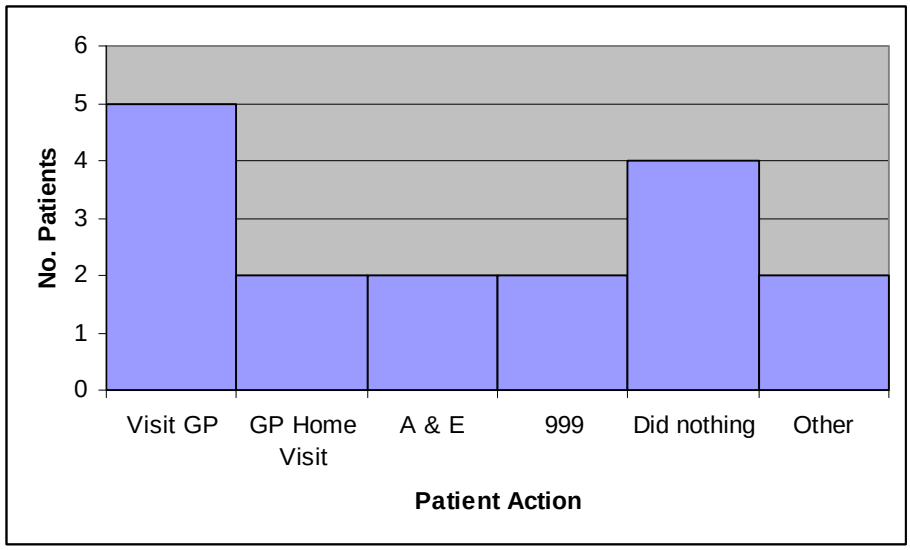
Again, patients were asked to indicate which day of the week that they had their TIA. (See figure 3.12) When grouped into whether they had their TIA during the week or at the weekend it was found that 13 (72%) of patients had their TIA during the week, and 4 (22%) at the weekend (for 1 patient time of TIA is unknown). Unlike the results found in the main questionnaire, for this group of patients the proportion of patients having a TIA at the weekend was slightly lower than might be expected.

**Figure 3.12: Number of Patients having TIA by Day of the Week – pilot data**




When asked what they did when they experienced their symptoms, the results showed a similar pattern to that of the main questionnaire. Again, most people visited their GP or their local hospital, and 22% of patients took no immediate action. (See figure 3.12). Patients who took 'other' action cited contacting NHS Direct or contacting a specialist eye hospital as the course of action followed.

**Figure 3.13: Patient Action at Time of TIA – pilot data**




Patients were again grouped into contacted GP, visited hospital, or other to determine whether or not day of the week influenced actions. A slightly different pattern was found than was found in the main questionnaire results, with a higher proportion of patients having a TIA at the weekend contacting their GP rather than going to hospital (see table 3.19).

**Table 3.19: Patient Action by Day of TIA – pilot data**

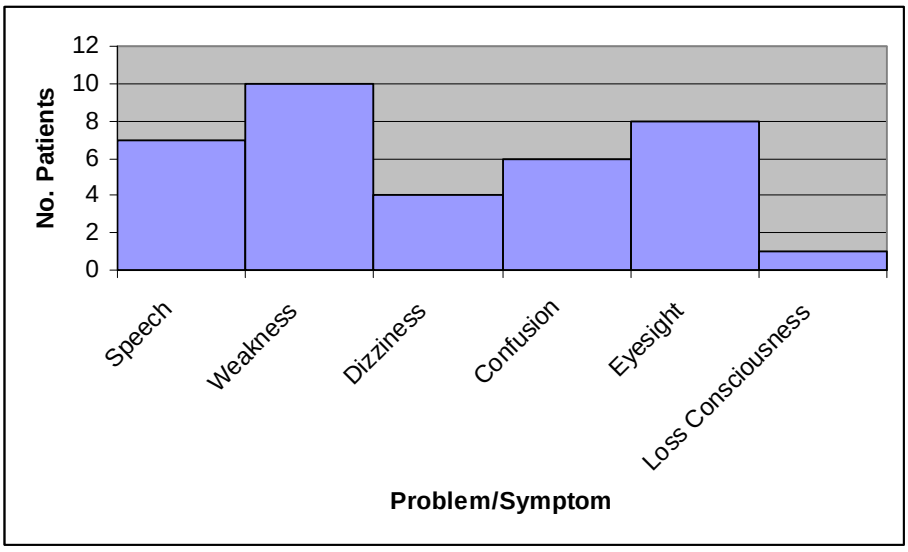
| Day of TIA | Action Taken | Number (%) |
|---|---|---|
| Weekday | Contacted GP | 3 (25) |
| | Visited Hospital | 3 (25) |
| | Other | 6 (50) |
| Weekend | Contacted GP | 3 (75) |
| | Visited Hospital | 1 (25) |
| | Other | 0 (0) |

People who did nothing initially all sought subsequent advice, but only two people gave an estimate of the time delay – 1-21 days. Type of symptom suffered had no influence on the course of action taken.

Patient Reported Symptoms

The most commonly reported symptom in this group of patients was weakness or numbness down one side of the body with 10 (56%) of patients having suffered this. Many people also reported having problems with their eyesight or difficulty with speech (see figure 3.14).

**Figure 3.14: Patient Reported Symptoms – pilot data**




Again, the type of symptom experienced by a patient did not influence what course of action they took.

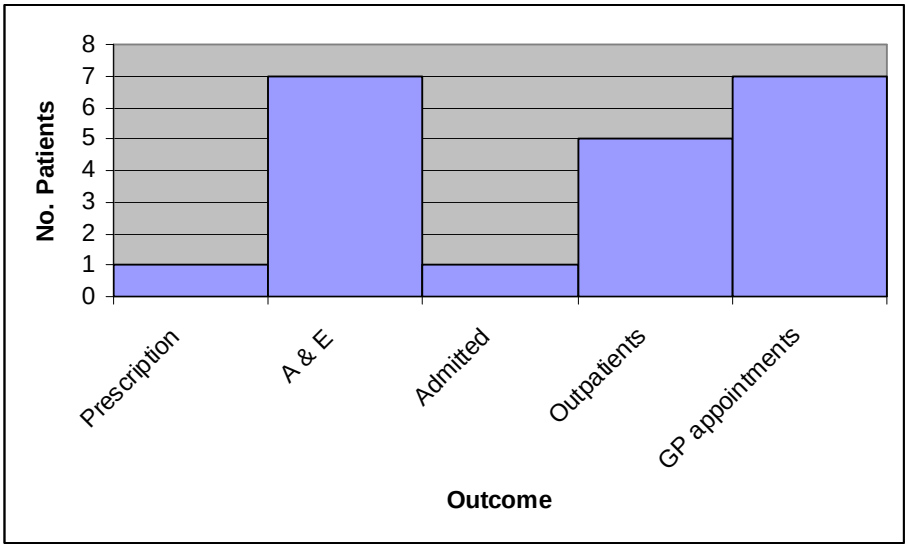
**Table 3.20: Patient Action by Reported Symptom – pilot data**

| Symptom | | Contacted GP Number (%) | Visited Hospital Number (%) | Other Number (%) |
|---|---|---|---|---|
| Difficulty speaking | Yes | 4 (57) | 2 (29) | 1 (14) |
| | No | 3 (30) | 2 (20) | 5 (50) |
| Weakness/Numbness | Yes | 4 (44) | 2 (22) | 3 (33) |
| | No | 3 (37.5) | 2 (25) | 3 (37.5) |
| Dizziness/Giddiness | Yes | 1 (33) | 0 (0) | 2 (67) |
| | No | 6 (43) | 4 (29) | 4 (29) |
| Confusion | Yes | 3 (50) | 2 (33) | 1 (17) |
| | No | 4 (36) | 2 (18) | 5 (45.5) |
| Problems with eyesight | Yes | 3 (37.5) | 1 (12.5) | 4 (50) |
| | No | 4 (36) | 2 (18) | 5 (45.5) |
| Loss of consciousness | Yes | 0 (0) | 0(0) | 1 (100) |
| | No | 7 (44) | 4 (25) | 5 (31) |

Patients who contacted a GP

Patients who either visited a GP or had a home visit from a locum (n=7) also provided information on the outcome of the appointment. In this population, all patients were both referred to A & E and given further GP appointments. Only 1 patient was given a prescription (see figure 3.15).

**Figure 3.15: Outcome of GP Appointment – pilot data***




* Does not total 7 as outcomes are not mutually exclusive.

Patient Preference

Analysis of the patient choice of which type of TIA service they prefer was carried out as for the main questionnaire. In this population, urgent referral to a specialist clinic was given as first choice by the most patients, with referral to hospital the favourite option of the fewest number of people. (See table 3.21)

**Table 3.21: Patient Preference of Service Provision – pilot data**

| | GP | Hospital | Specialist |
|---|---|---|---|

| | Number (%) | Number (%) | Number (%) |
|---|---|---|---|
| 1st Choice | 6 (33) | 3 (17) | 9 (50) |
| 2nd Choice | 7 (39) | 4 (22) | 5 (28) |
| 3rd Choice | 4 (22) | 10 (56) | 2 (11) |

The mean scores showed referral to specialist to be the favoured option (mean 1.56, SD 0.73), with treatment by GP as the second choice (mean 1.88, SD 0.78) and referral to hospital as the least favourite (mean 2.41, SD 0.80)

Patient Costs

Costs were estimated using the same method as used for the main questionnaire. Again, most people travelled by car (12 (67%)) with 4 (22%) going by ambulance and 1 (6%) person walking. No one used any form of public transport. 12 patients provided an estimate of journey distance (mean 6.3 miles, range 1-10 miles). The mean cost in parking fees for the 12 patients who travelled by car was £0.83 (range £0 - £4.00). The difference in mean costs for people who visited their GP and those who went to hospital were tested, with the mean for GP being £0.37 (SD 0.75) per visit, while the mean for a hospital visit was £1.00 (SD 2.0)

## *3.5 Data from the literature*

### 3.5.1. Accuracy of GP diagnosis of TIA / minor stroke

A review of the literature was carried out to identify studies that assessed accuracy of GP diagnosis of TIA. A summary of these studies is shown in table 3.19. Four sources (Gibbs, 2001; Martin, 1997; Ferro, 1996; Jempere, 1996) give a positive predictive value in the range 60-70%. Taking a PPV of 67% with a prevalence of 50% and sensitivity of 80% gives a specificity of 60%. The sensitivity of 80% was derived from the study by Quik van Milligen et al. (Quik-van Milligen, 1992).

Summary:
*The GP will make a diagnosis that the patient has or has not had a TIA/ minor stroke. The sensitivity and specificity of GP diagnosis is set at 80% and 60% respectively.*

**Table 3.22: summary of studies looking at accuracy of GP diagnosis of TIA**

| Paper | Setting | Method | Results |
|---|---|---|---|
| Ferro, 1996 | Portugal | A list of 20 neurological symptoms was distributed to 20 GPs and 22 neurologists who graded the compatibility of each diagnosis with a TIA diagnosis. At least 2 neurologists validated the TIA diagnoses made by GPs for patients under their care. | During the study period, the GPs diagnosed 103 TIAs and 52 (50%) were referred for neurological evaluation. Validation of diagnosis by GP was confirmed in 10 patients (19%); TIA diagnosis was incorrect in 42 patients. 26 (50%) patients had strokes and 16 (31%) had a noncerebrovascular disorder. |
| Dennis, 1989 | UK | Epidemiological study of the incidence of TIAs in patients registered with 50 GPs. GPs notified the Oxfordshire Family Practitioners Committee of all patients suspected of suffering a TIA and one of the authors further assessed each of the patients and carried out investigations to confirm the diagnosis. | Of 512 patients with supposed TIA referred by GPs, 195 (38%) did have a TIA and 317 (62%) had noncerebrovascular disorders. |
| Quik-van Milligen, 1992 | Holland | A questionnaire that included 10 TIA cases was mailed to a random sample of 10% of all GPs in the Netherlands. | 80% of cases were correctly diagnosed. |
| Jempere, 1996 | Spain | Epidemiological study of TIA and minor strokes. | GPs referred 193 patients with supposed TIA for neurological evaluation. 129 (67%) had a correct diagnosis and 64 (33%) were diagnosed with noncerebrovascular disorders. It is not mentioned how many minor strokes were labelled TIAs by the GPs. |
| Gibbs, 2001 | UK | The diagnosis made by a specialist was compared with the diagnostic code entered | For the 27 patients referred with a diagnostic code for TIA, the GP and specialist concurred exactly |

| | | | |
|---|---|---|---|
| | | onto the General Practitioner Research Database (GPRD) by the GP to determine how often they were in agreement, as a test of the validity of the diagnostic data entered onto the GPRD. | in 13 cases (48%). Therefore, the specialist gave an alternative diagnosis for 14 (52%) patients. |
| Tomasik, 2003 | Poland | A questionnaire including 3 pairs of TIA cases (3 cases of symptoms of transient monocular blindness (MB) and other 3 of hemispheral ischemia (HI)) was distributed to 100 GPs. 2 GPs with a specialist interest in vascular diseases rated the correctness of each diagnosis based on: correct = described as TIA, probably correct = description of vascular process but without specification and incorrect = no relationship with CV disease. | 89 GPs responded giving the following results for each of the 6 cases:<br>MB<br>HI<br>Correct: 18 (20%)<br>41 (46%)<br>Prob. Correct: 45 (51%) 11 (12%)<br>Incorrect: 26 (29%)<br>37 (42%)<br>Therefore, physicians confronted with TIA cases had difficulties diagnosing it. |
| Mant, 2003b | UK | Identification of prevalent cases of stroke through reviews of GP-based computer systems, population surveys and hospital-based routine information systems. | 118 patients had a diagnosis of TIA by a GP, but only in 34 (29%) of these was there evidence of confirmation of the diagnosis by a specialist. |
| Martin, 1997 | UK | The diagnosis of patients referred to the neurovascular clinic by the GPs was compared to that of the 2 neurologists. | The specialists confirmed the referral diagnosis of TIA in 200/332 (60%) patients. |

### 3.5.2 Optimal secondary prevention of stroke following TIA and minor stroke

This was derived from the National Clinical Guidelines for stroke and the NICE guidance on use of dual anti-platelet therapy following a cerebrovascular event. (Intercollegiate Stroke Working Party, June 2004; National Institute for Health & Clinical Excellence, 2005)

Optimal treatment is:

- warfarin for those diagnosed with AF;
- no antiplatelet therapy for those taking warfarin;
- antiplatelet dual therapy for all those not taking warfarin;
- statin if total cholesterol is greater than 3.5;
- antihypertensive if SBP is greater than 130mmHg;
- referral if suitable for assessment for carotid endarterectomy.

Note that we have not modelled any delay in the measurement of cholesterol.

If antihypertensive treatment is given, then it is assumed to lower the SBP by 9mmHg. (PROGRESS Collaborative group, 2001). If someone has a second event

after having received antihypertensive therapy, no further lowering of blood pressure is modelled.

### 3.5.3 What delays are there to carotid endarterectomy following GP referral?

The delays to carotid endarterectomy using the standard GP care were based upon the following:

***Carotid Endarterectomy***

| Parameter | Value | Source |
|---|---|---|
| Median delay referral to assessment | 24 days | Mehta, 2005 |
| Median delay assessment to surgery | 67 days | Mehta, 2005 |
| Probability of stroke at CE | 0.02 | VascularWeb, 2006 |

For patients who see a specialist whether in A&E or in a rapid access out-patient clinic, it is assumed that appropriate assessment for suitability for carotid endarterectomy is carried out at that time (i.e. there is no wait). However, the delay to surgery is still modelled on the Mehta et al data.

### 3.5.4 What is the impact of treatments on subsequent stroke risk?

The factors affecting the risk of stroke are as shown in table 3.20. For the risk of carotid endarterectomy, the data given by Rothwell *et al* (Rothwell, 2004b) were converted into odds ratios, which were interpreted as hazard ratios in the model. Data were given in four groups according to time from event. However, a common value has been used for groups in pairs.

**Table 3.23 Factors affecting risk of stroke**

| Parameter | Value | Source |
|---|---|---|
| RR for 9mmHg increase in SBP | 1.5 | MacMahon, 1994 |
| RR for AF no warfarin (v no AF) | 5 | Wolf, 1991 |
| RR for AF with warfarin (v no AF)* | 1.67 | M Aguilar |
| RR for antiplatelet mono (v no Rx) | 0.75 | Anti-thrombotic trialists' collaboration, 2002 |
| RR for antiplatelet dual (v mono) | 0.8 | ESPIRIT, 2006 |
| RR for statin | 0.84 | Cholesterol Treatment Trialists' Collaborators, 2005 |
| RR for diabetes | 2.5 | Ebrahim, 1999 |
| RR for carotid endarterectomy | | |
| - within 2 weeks of event | 0.28 | Rothwell, 2004b |
| - 2 to 4 weeks after event | 0.28 | |
| - 4 to 12 weeks after event | 0.54 | |
| - at least 12 weeks after event | 0.54 | |

*This figure is only applied after patients have been on warfarin for at least 72 hours. For the first 72 hours after initiating warfarin treatment, the risk for "AF no warfarin" is applied.

For convenience, the baseline risk is defined as applying to a patient with systolic blood pressure (SBP) of 148mmHg without AF or diabetes and on no relevant medication. The relative risks indicated above are then applied. To produce the correct overall incidence, it is necessary to determine the mean relative risk for

each age and sex group in the modelled population, and then divide the overall incidence by this mean relative risk to give the baseline incidence. This is then converted into a figure in mean hours to event. The mean relative risks were found to be as follows:

**Table 3.24: Calculated mean relative risks for a non-diabetic not in AF with SBP 148mmHg on no relevant medication**

| Age group | Males | Females |
|---|---|---|
| < 35 | 2.37 | 1.76 |
| 35 - 44 | 2.59 | 2.20 |
| 45 - 54 | 2.23 | 2.00 |
| 55 - 64 | 2.26 | 2.09 |
| 65 - 74 | 2.42 | 2.52 |
| 75 – 84 | 2.61 | 2.90 |
| ≥ 85 | 3.25 | 3.20 |

It is assumed that the risk factors applicable for stroke apply equally to genuine TIAs and strokes, but not to TIA mimics. Accordingly, the revised baseline risks (revised from table 3.5) are as shown in the table 3.25.

**Table 3.25 Adjusted incidence of TIA mimic, genuine TIA, minor and major stroke**
(per 1,000 patients per year)

Baseline incidence– males

| Age group | TIA mimic | Genuine TIA | Minor Stroke | Major Stroke |
|---|---|---|---|---|
| < 35 | 0.01 | 0.01 | 0.00 | 0.00 |
| 35 - 44 | 0.22 | 0.09 | 0.10 | 0.00 |
| 45 - 54 | 0.33 | 0.15 | 0.17 | 0.16 |
| 55 - 64 | 1.14 | 0.50 | 0.62 | 0.16 |
| 65 - 74 | 3.39 | 1.40 | 2.08 | 0.59 |
| 75 - 84 | 6.71 | 2.57 | 3.03 | 0.58 |
| ≥ 85 | 10.32 | 3.17 | 4.39 | 1.67 |

Baseline incidence– females

| Age group | TIA mimic | Genuine TIA | Minor Stroke | Major Stroke |
|---|---|---|---|---|
| < 35 | 0.03 | 0.02 | 0.00 | 0.00 |
| 35 - 44 | 0.05 | 0.02 | 0.07 | 0.00 |
| 45 - 54 | 0.42 | 0.21 | 0.21 | 0.06 |
| 55 - 64 | 1.40 | 0.67 | 0.53 | 0.30 |
| 65 - 74 | 3.97 | 1.58 | 1.39 | 0.23 |
| 75 - 84 | 8.67 | 2.99 | 2.33 | 1.29 |
| ≥ 85 | 12.66 | 3.95 | 3.62 | 1.08 |

### 3.5.6 What is the risk of subsequent events?

TIA mimic
The risk of TIA mimic is taken to be the same as the baseline risk, depending on age and sex only, regardless of all other patient attributes.

Genuine TIA
For risk of repeat genuine TIA, the baseline risk is modified by the risk factors for stroke. This applies following TIA mimic and (minor) stroke: there is a higher risk of repeat TIA following genuine TIA, which is currently modelled as a RR of 4.

Stroke
Following TIA mimic, the baseline risk is modified by the risk factors for stroke.

Following TIA, it is essential to account for the increased risk of stroke in the first few days after the TIA. From the OXVASC data, time to stroke following TIA appears to follow a Weibull distribution. This distribution may be defined by its survival curve

$S(t) = \exp(-\lambda t^{\gamma})$, where $t$ is time in days from the onset of the TIA.

The two parameters $\gamma$ and $\lambda$ are known respectively as shape and scale parameters. If $\gamma = 1$, then the distribution reduced to a (fixed risk) exponential distribution. If $\gamma < 1$, then the risk is reducing over time. This is the form that is required here.

We programmed a model with a fixed value of $\gamma$, and $\lambda$ dependent on ABCD score. The model allows $\lambda$ to be specified separately for each value of the ABCD score, but given the small number of events in the OXVASC data set it was appropriate to fit a model with a constant hazard ratio for each unit increase in ABCD score. Using this

approach, the maximum likelihood estimator of $\gamma$ was 0.298, with values of $\lambda$ as shown below:

| ABCD score | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| $\lambda$ | 0.0038 | 0.0045 | 0.0053 | 0.0062 | 0.0073 | 0.0085 | 0.0100 |

Following stroke, we again have a Weibull distribution, but the ABCD score is not used. The maximum likelihood estimators are $\gamma = 0.348$ and $\lambda = 0.0045$.

In all cases, it is assumed that for patients aged under 75, one half of repeat strokes are major strokes, while for patients 75 or over, two thirds of strokes are major strokes.

### 3.5.7 What is the mortality associated with minor stroke?

Applying the general mortality to the population entering the model with minor stroke gives one-year mortality of 0.055, compared to observed mortality of 0.137 using OXVASC data. The additional mortality here is modelled as stroke-related mortality.

The factors affecting the risk of stroke-related mortality are as shown in the following table. These are based on the relative risk of repeat stroke with the assumption that 20% are fatal.

**Table 3.26: Factors affecting risk of stroke related mortality**

| Parameter | Value |
|---|---|
| RR for 9mmHg increase in SBP | 1.1 |
| RR for AF no warfarin (v no AF) | 1.8 |
| RR for AF with warfarin (v no AF)* | 1.2 |
| RR for antiplatelet mono (v no Rx) | 0.95 |
| RR for antiplatelet dual (v mono) | 0.96 |
| RR for statin | 0.97 |
| RR for diabetes | 1.3 |
| RR for carotid endarterectomy | |
| - within 2 weeks of event | 0.86 |
| - 2 to 4 weeks after event | 0.86 |
| - 4 to 12 weeks after event | 0.91 |
| - at least 12 weeks after event | 0.91 |

*This figure is only applied after patients have been on warfarin for at least 72 hours. For the first 72 hours after initiating warfarin treatment, the risk for "AF no warfarin" is applied.

The relative risks are applied to a baseline risk of one additional death per 4900 days at risk (incorporated into the model as a risk per hour). This was calibrated so that the number of stroke-related deaths was approximately equal to 1.5 times the number of other cause deaths in the stroke population.

With regard to thrombolysis, we did not model the benefit of thrombolysis, but rather, the patient exited the model when they received thrombolysis and the event that led to receipt of thrombolysis (be it minor or major stroke) was not counted. This will have resulted in an over-estimate of the apparent effect of thrombolysis, since it is the equivalent of assuming that it is 100% effective.

Other Cause Death

The probability of "other cause" death within one year of entry to the model is given by age group as follows. This is based on data from the government actuary's department. (Government Actuary's Department, 2006). The values here are for England and Wales, and have been adjusted for stroke deaths. This was done by determining the proportion of deaths classed as cerebrovascular diseases (ICD-10 codes I60-I69) among total deaths registered in England and Wales in 2006. (Health Statistics Quarterly, 2007).

**Table 3.27: Probability of other cause death**

| Age group | Males | Females |
|---|---|---|
| 20-25 | 0.000770 | 0.000268 |
| 25-30 | 0.000751 | 0.000319 |
| 30-35 | 0.001018 | 0.000459 |
| 35-40 | 0.001256 | 0.000662 |
| 40-45 | 0.001757 | 0.001090 |
| 45-50 | 0.002834 | 0.001880 |
| 50-55 | 0.004450 | 0.002760 |
| 55-60 | 0.006986 | 0.004319 |
| 60-65 | 0.011902 | 0.007055 |
| 65-70 | 0.018369 | 0.011078 |
| 70-75 | 0.030947 | 0.019340 |
| 75-80 | 0.050886 | 0.032233 |
| 80-85 | 0.082922 | 0.056332 |
| 85-90 | 0.131553 | 0.096706 |
| 90-95 | 0.195029 | 0.160009 |
| 95-100 | 0.275590 | 0.237942 |

Applying the general population mortality to the population entering the model with genuine TIA gives a one-year mortality risk of 0.057. The observed mortality in the OXVASC data set was 0.059, so it is likely that excess mortality is sufficiently accounted for by the mortality associated with strokes following TIA.

# 4: Methods for the discrete event simulation model

## *4.1 Aim of the model*

The aim is to compare the outcomes in terms of strokes prevented and cost of different patterns of service provision for people presenting with a transient ischaemic attack or minor stroke.

## *4.2 Development of the Model*

The structure of the model was developed over a series of meetings involving the core Birmingham team. The face validity of the model was tested against the clinical experts (GF & PR), and modifications made as a result. The face validity was also explored with the Patient Advisory Group (PAG), who did not come up with different patterns of service delivery than were being proposed by the model.

### 4.2.1 Study population represented by the model

The study population is people who contact the health service with symptoms suggestive of a transient ischaemic attack (TIA) or minor stroke. Minor stroke for the purposes of this model is pragmatically defined as a stroke that does not lead to significant disability and does not result in hospital admission. The study population therefore comprises three sub-categories: people with a genuine TIA, people with a minor stroke, and people with symptoms that mimic a TIA/ minor stroke where the underlying diagnosis is not related to cerebrovascular disease.

The population size is set at 500,000, with 1,000 people presenting per annum with symptoms suggestive of a TIA or minor stroke. This comprises 35% genuine TIAs, 15% minor strokes and 50% 'TIA mimics', and equates to an annual incidence of TIA of 0.7 per 1,000, an incidence of minor stroke (not admitted to hospital) of 0.3 per 1,000 and an incidence of TIA mimic of 1 per 1,000. *See 3.1.2.1*.

### 4.2.2 Patterns of service provision being tested in the model

The basic comparison is between current practice and the introduction of a rapid access specialist clinic. The assumed benefits of a specialist clinic are that it will lead to more accurate diagnosis; optimal use of secondary prevention medication; and more rapid use of carotid endarterectomy where applicable.

Within this basic comparison, we explore different referral thresholds to the specialist clinic based upon a simple scoring system that predicts risk of subsequent stroke following a TIA – the ABCD2 score. (Johnston, 2007).

We also explore the impact of greater use of emergency ambulance services on the results of our model to reflect the recommendations of the National Stroke Strategy, (Department of Health, 2007) and the consequences of admitting people at high risk of stroke following a TIA to hospital. The assumed benefit of this is that it will enable greater early use of thrombolysis – an effective treatment for acute stroke. (Wardlaw, 2003)

We also explore the impact of the provision of different types of specialist clinic: weekly and twice-weekly clinics with a fixed number of appointments, twice-weekly clinics with extra appointments added to avoid excess waiting, and same day booking.

Finally, we test the conclusions of the model if GP diagnosis was more accurate, and if GP management in terms of secondary prevention reflected optimal rather than current practice.

### 4.2.3 Consequences being evaluated in the model

The principal outcomes are the number of strokes prevented – which are sub-divided into strokes that would have led to a hospital admission and minor strokes that would not have led to a hospital admission, and cost. For the purposes of the model, a major stroke is defined pragmatically as a stroke that leads to a hospital admission. Cost includes the costs of clinics, interventions, and the costs of treating a stroke up until a maximum of 12 months after the event. The incremental cost per major stroke averted is calculated.

### 4.2.4 Model Structure and logic

The model is a discrete event simulation model, programmed in Borland Delphi. Important features of the model are that it tracks individuals who are occasionally competing for resources in a realistic representation of calendar time. In particular, the availability of certain services depends on time of day and day of week.

The model runs using an event-based executive. The core of the model is the events list, each entry of which consists of a patient number and the time and nature of the next event involving that patient. Initially, the events list consists of the first occurrences of each of TIA mimic, genuine TIA, and minor stroke.

When the patient characteristics have been sampled, the patient is set to no management, and the time of onset of symptoms is recorded. For modelling convenience, the patient taking action is modelled as a separate event. Processing entry into the model of a new patient also includes scheduling the entry of the next new patient of the same type (TIA mimic, genuine TIA, or stroke).

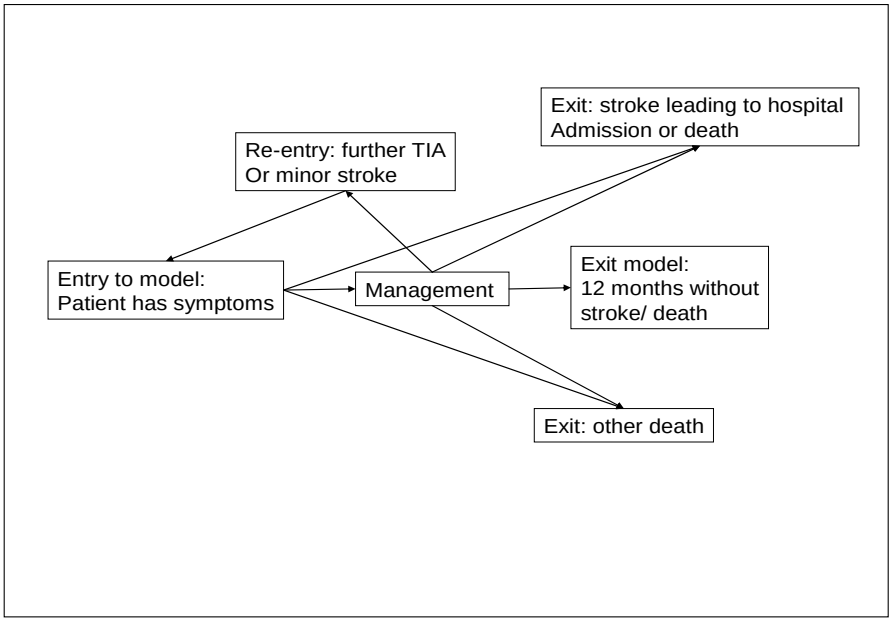
At each step in the running of the model, (simulated) time is advanced to the earliest event on the events list, and the relevant event is processed. If the event is the entry into the model of a new patient, a new event is added to the list for the entry of the next patient of a similar type. (This implies that the events list can never be empty.)

In all cases, the event is processed. The patient's condition is updated, as are any relevant totals of resources used. If the event is the exit of a patient from the model, then no new event is scheduled for that patient. In other cases, the next event for that patient is scheduled. This may be the intended next event, such as attendance at an outpatient clinic. However, the risk of an adverse event (stroke or other cause death) is taken into account. Such an adverse event would prevent the intended next event from taking place. Note that any appointments missed as a result of adverse events are lost.

Patient progression through the model

Patient progress through the model is illustrated in figure 4.1. The patient enters the model when they have an event, which is either a TIA, a minor stroke, or a TIA mimic. They are then managed depending upon which model of service delivery is used, and stay in the model until they die, go on to have a stroke that is either fatal or leads to hospital admission, or survive for 12 months without a further event. If they have a further TIA or stroke that does not lead to hospital admission, then they re-enter the model.

**Figure 4.1: Patient progression through the model**




Patient characteristics on entry

On entry to the model, patients are characterised in terms of:

- Factors that predict risk of subsequent stroke (age; blood pressure; clinical features of event; duration of symptoms and previous diagnosis of diabetes mellitus)
- Additional factors that determine optimum treatment following the event (total cholesterol; atrial fibrillation status; current medications in terms of anti-platelet agents, anticoagulants, and statins; potential to benefit from carotid endarterectomy)
- Life expectancy if death (other than due to stroke) is to occur within 12 months

Three separate groups enter the model. These are TIA mimic, genuine TIA, and minor stroke. Patient characteristics on entry are derived from the OXVASC data set (see OXVASC chapter). On entry, patients are given the following characteristics:

- Actual condition type (TIA mimic, Genuine TIA, minor stroke);
- Age group (see note below);
- Sex;
- Systolic blood pressure (mmHg);
- High or not high blood pressure on onset (see note below);
- Clinical symptoms score (0=neither weakness nor speech disturbance, 1=speech disturbance without weakness, 2=any weakness);
- Duration score (0=0-9 mins; 1=10-59 mins; 2=60 mins or more);
- ABCD score (calculated from above);
- Total cholesterol (in mmol/l);
- AF status (no AF, AF no warfarin, AF warfarin);
- Already on antiplatelet therapy (monotherapy – see note below);
- Already on statin;
- Previous diagnosis of diabetes;

- Suitability for carotid endarterectomy (0=unsuitable for investigation, 1=suitable for investigation but not for CE, 2=suitable for CE: see below);
- Date of "other cause" death;

Age groups are defined in units of 5 years. For ease of interpretation, they are numbered from 4 (20 to 25) to 19 (95 to 100) inclusive.

High blood pressure on onset is selected if the systolic blood pressure is greater than 140mmHg. The OXVASC data set contains a small number of individuals with a systolic blood pressure below 140mmHg but a diastolic blood pressure over 90mmHg, who are regarded as having high blood pressure on onset. For simplicity this model uses SBP only; the distribution used is adjusted to give the correct proportion of patients classified as having high blood pressure.

It is assumed that all patients have the potential to benefit from blood lowering treatment on entering the model, i.e regardless of whether or not they have had a genuine TIA or minor stroke.

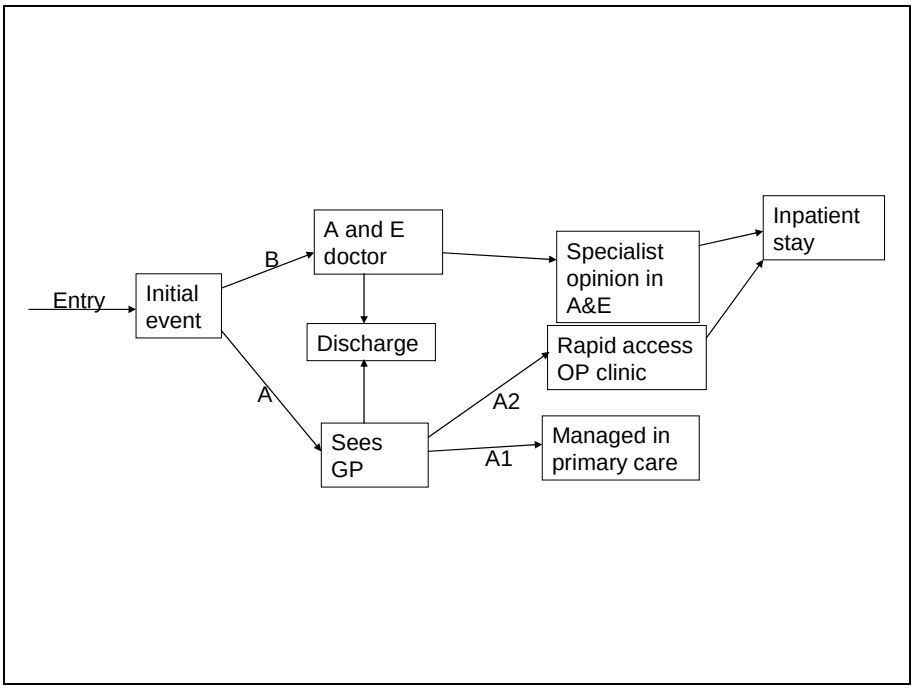
The status of the patient with regard to antiplatelet therapy may be no therapy, monotherapy, or dual therapy (aspirin + dipyridamole). OXVASC data gives the proportion of patients on monotherapy: it is assumed that no patient is on dual therapy on entry to the model. Note that antiplatelet and warfarin are sampled independently, which means that some patients enter the model on both types of treatment.

Suitability for carotid endarterectomy is taken as a two-stage process. First the patient must be suitable for investigation. For this, the territory must be carotid and there must be no contra-indication. Patients who are found to have symptomatic stenosis from 70-99% are deemed suitable for carotid endarterectomy. The proportions in these three categories are based on OXVASC data. It is assumed that the presence of a symptomatic stenosis category corresponds to suitability for investigation.

The date of "other cause" death is sampled by taking account of the appropriate age/sex-related probability of death during the following year. Given the generally low values of this death rate, it is a reasonable approximation that death dates are uniformly distributed through the year.

<u>Modelling of patient management within the model</u>
An outline of the patient pathway options is shown in figure 7.2. The first option is whether the patient goes to Accident & Emergency (A&E) (B in figure 7.2), or whether they contact their general practitioner (A in figure 7.2). The model is concerned with people who contact the health service as a result of symptoms suggestive of a TIA or minor stroke, so people who take no action as a result of their symptoms are not included in the model. The model takes into account both the proportion of people that attend A&E (either under their own resources or through calling an ambulance) or contact their general practitioner (whether to request a home visit or to attend the practice). It also takes into account how long they take to contact health services. *See 3.1.2.2 for explanation of how initial patient actions were incorporated into the model.*.

**Figure 4.2: Patient pathways within the model**




Patients who see GP

The GP may manage the patient in primary care (A1), or refer to a specialist out-patient clinic (A2). The baseline service provision being tested assumes that all patients are managed in primary care (A1). The model tests what would happen if a clinic was available, (A2) and the proportion referred depended on the basis of ABCD2 score and whether or not the GP made a diagnosis of TIA.

The GP will make a diagnosis that the patient has or has not had a TIA/ minor stroke. The sensitivity and specificity of GP diagnosis is set at 80% and 60% respectively. *See section 3.5.1 for supporting literature.*

If the patient is managed in primary care (A1), the GP will treat if they make a diagnosis of TIA/ minor stroke. Two patterns of GP treatment are modelled: standard treatment, which is based upon current practice, and optimal treatment, which is based on current best practice.

*Standard GP treatment*
Standard treatment is based on the results of our analysis of the QRESEARCH database (see section 3.3). There are fixed probabilities of each of the following, sampled independently for each separate category of treatment, but exclusively for alternatives within the same category:
antiplatelet monotherapy if not already taken;

antiplatelet dual therapy;

statin if total cholesterol is greater than 3.5;

immediate assessment for blood pressure and AF;

delayed assessment for blood pressure and AF;

referral if suitable for carotid endarterectomy.

Assessment for blood pressure and AF results in antihypertensive therapy if systolic blood pressure greater than 130mmHg (regardless of what antihypertensive

medications the patient is already on) and warfarin if AF diagnosed. If warfarin treatment is initiated, then antiplatelet is stopped. Based on the literature, delays were built in if the patient was referred for assessment for carotid endarterectomy (see 3.5.3).

If the assessment is delayed, this means a second GP appointment is made. There is a minimum number of days delay, after which the time is sampled from an exponential distributed. The time so generated is then replaced by a random time between 9.30am and 5.30pm on the same day, except that appointments that would occur on Saturday are replaced by the previous day, and appointments that would occur on Sunday are replaced by the following day.

*Optimal GP treatment*
Optimal treatment is based on National guidelines, from the Intercollegiate Stroke Working Party and from NICE – see section 3.5.2.

Patients referred to a specialist clinic
If the patient is referred to a specialist out-patient clinic (A2), then the time it takes them to see the specialist depends upon the outpatient booking system being used.

Four outpatient-booking systems are implemented in the model, as described below. Although there will be some variability in the time taken to see each patient, this variability is not important in the time scales of the model. Appointments are set at fixed intervals of 30 minutes each. If a patient does not attend the appointment, the appointment is lost. Note that the choice of day of the week for these clinics is somewhat arbitrary. The difference between the four service patterns is such that the model should be able to discriminate between them. It is not sensible to expect the model to determine an optimum time of week for outpatient clinics.

It is assumed that patients are booked in sequence into the earliest available appointment. Allowing patients a choice of time within a particular day's clinic would complicate the model to very little advantage.

*Weekly fixed*
Outpatient clinics occur once a week on Tuesday mornings. In each clinic, there are a total of six appointments, which are set at half-hourly intervals from 9.00am onwards. Appointments must be booked no later than 5.00pm on Monday. The next available appointment time is selected, no matter how far in the future that may be.

*Twice weekly fixed*
Outpatient clinics occur on Tuesday and Friday mornings. In each clinic, there are a total of six appointments, which are set at half-hourly intervals from 9.00am onwards. Appointments must be booked no later than 5.00pm on the day before the clinic. The next available appointment time is selected, no matter how far in the future that may be.

*Twice-weekly flexible*
Outpatient clinics occur on Tuesday and Friday mornings. In each clinic, there are a minimum of six appointments, which are set at half-hourly intervals from 9.00am onwards. Appointments must be booked no later than 5.00pm on the day before the clinic. The number of appointments in any clinic is extended if necessary so that no patient waits more than a specified number of days for an appointment. By default this number is set to 7, but it can be changed to any higher number if desired.

*Same Day*
Appointments are available daily (Monday to Friday) at half-hourly intervals from 4.00pm onwards up to a limited number. They must be booked by 4.00pm on that day. For simplicity, the issue of travelling time between booking and arrival at appointment is not considered in the model.

Patients who go to A&E

The A&E doctor is assumed to have the same diagnostic accuracy as the general practitioner for TIA/ minor stroke. If the A&E doctor makes a positive diagnosis, then it is assumed that the patient is referred to a specialist. If the A&E doctor makes a negative diagnosis, then the patient is discharged.

Patients who see a specialist in A&E or attend a rapid access out-patient clinic

These are treated in the model as being the same. The model is predicated on the assumption that specialist diagnosis (supported by brain scanning as appropriate) is 100 per cent accurate. While this assumption is in theory optimistic, there is no better "gold standard", and in any case the treatment effects from trials of management of TIA are estimated on the basis of this assumption. It is assumed that patients are put onto optimal treatment, and will be assessed for carotid endarterectomy and be scheduled for surgery if appropriate

*Carotid endarterectomy*
Where appropriate, this is modelled in parallel to other progression. It is assumed that both assessment and surgery are available only between 9.00am and 5.00pm Monday to Friday.

Referral for assessment takes place as indicated in the pathways above. When modelled, the delay to assessment is sampled from a suitable distribution. If this leads to a time on a Saturday, this is brought forward to the previous Friday, while if it leads to a time on a Sunday, this is moved on to the following Monday. The time is then adjusted to a random time between 9.00am and 5.00pm. Finally, if this leads to a time earlier than the referral time, then the referral is moved on to the same time on the first available working day.

Assessment is assumed to be 100% sensitive and specific. If the patient is suitable for carotid endarterectomy, then the delay to surgery is set in the same way as the delay to assessment.

Patients who are admitted to hospital

The baseline assumption is that no patients are admitted to hospital – indeed the definition of the study population excludes those people with stroke that leads to hospital admission. However, one option is that if people are perceived to be at high risk of subsequent stroke (as reflected in ABCD2 score ≥ 4), then they could be admitted to hospital for a period of observation (set at 3 days) so that if they do have a repeat stroke they would receive immediate thrombolysis. It is assumed that all patients who are admitted because of high risk of stroke who go on to have a stroke while an in-patient are eligible for thrombolysis and receive it.

### 4.2.5 Prediction of outcomes in the model

In this model we have only modelled the effect of treatment on the risk of further TIA/stroke (not on ischaemic heart disease or other vascular events).

The outcomes that need prediction following patient entry to the model are:
-major stroke (fatal or requiring hospital admission)

-new events (further TIA or minor stroke or TIA mimic)
-non-stroke death

The risks of these events occurring are based upon the epidemiology and the evidence of effectiveness of the available interventions. The derivation of the impact of interventions is given in section 3.5.4-3.5.7. The risk of an individual event is taken as the general population risk of that event (taking relevant risk factors into account, with the following exceptions:
-following TIA, there is increased risk of stroke, particularly in the short term, based on the OXVASC data. (Rothwell, 2005) *See section 3.1.1.3*.

-following a minor stroke, there is increased risk of repeat stroke and mortality. The excess mortality following a stroke is treated as stroke-related mortality.

Given that impact of treatment on other vascular disease is not modelled, risk of non-stroke death is defined on patient entry to the model, and need not be modified if the patient changes treatment.

Patients exit the model on stroke-related death or major stroke. A patient who has a TIA mimic or genuine TIA within the model normally re-enters the model at patient first action. The C and D components of the ABCD score are resampled in the case of genuine TIA, and set to zero in the case of TIA mimic; all other parameters are assumed unchanged.

There are two exceptions to this. The first is if either of these events occurs while the patient is already in hospital as an inpatient. In the case of TIA mimic, the patient simply remains in hospital until the appointed discharge time, while in the case of genuine TIA, the hospital stay is extended to the minimum period (set at three days) following the new TIA.

The second exception is if the patient is already on the way to an emergency contact. In that case, the patient continues with the original contact.

In the case of minor stroke occurring within the model, patients normally re-enter the model. One exception is if the patient is in hospital as an inpatient when the minor stroke occurs. In this case thrombolysis is given. Patients exit the model on thrombolysis. Also, all strokes at carotid endarterectomy result in exit from the model.

Days lost in the model due to major strokes are counted as the time from event to scheduled exit or other cause death, whichever is the earlier.

Resource Use

Unit costs are applied to medication and use of services. For A&E and daily OP clinics, only the time actually used is costed. For the weekly OP clinics, the appointments are staffed even if not all of them are used, and so the cost of running the clinics (for the standard three hours in the case of "twice weekly flexible" clinics) is included. The costs of care of a stroke were included up until the time the patient would have left the model if they had not had stroke. All the model outputs listed in table 4.1 (except for the index events) were costed. The cost data used in the model is shown in the appendix.

## *4.3 Running the model*

Since the model began with outpatient queues empty, it was necessary to run the model for a "warm up" period before starting to collect results. The warm up period

was set for one year. The model was then run for an "enrolment" period (ten years), in which all new patients contributed to the outcomes from the model. There was also a "follow up" period, which lasted until all "enrolled" patients had exited the model (one year of simulated time). New patients entered the model during the follow up period, but they were not included in the outcomes collected.

The model was run 10,000 times to minimise the impact of random variation.

### 4.3.1 Model outputs

The process of care and output variables modelled were as shown in the table below:

**Table 4.1 Description of model outputs**

| Item | Description |
|---|---|
| TIA mimics | Number of patients entering the model with a TIA mimic |
| Genuine TIAs | Number of patients entering the model with a genuine TIA |
| Minor strokes | Number of patients entering the model with a minor stroke |
| Ambulances 1 | Number of patients making emergency contact on entry to model |
| Ambulances 2 | Number of patients making emergency contact for a subsequent event (TIA, minor stroke or TIA mimic) |
| GP first surgeries | Number of patients making initial contact through GP (including subsequent events) |
| GP second surgeries | Number of repeat appointments to allow for further assessment of blood pressure and atrial fibrillation status |
| A&E doctors | Number of patients seeing A&E doctor |
| Hospital specialists | Number of patients seeing hospital specialist following referral from A&E doctor or from GP to A&E department |
| Scheduled OP | Number of patients attending outpatient appointments on referral from GP to rapid access clinic. In the case of "twice weekly flexible", only appointments within normal clinic time are counted in this category. |
| Additional OP | Number of outpatient appointments outside normal clinic time for "twice weekly flexible" only |
| Thrombolysis | Number of patients receiving thrombolysis (only applies when inpatient admission is used) |
| Repeat mimic | Number of TIA mimics occurring during follow-up time |
| Repeat TIA | Number of genuine TIAs occurring during follow-up time |
| Repeat minor stroke | Number of minor strokes occurring during follow-up time |
| Repeat major stroke | Number of major strokes occurring during follow-up time |
| Days post maj strk | Days not modelled because patients with major stroke exit the model early |
| CE clinic assess | Assessments for carotid endarterectomy made during specialist clinic (either A&E or rapid access OP) |
| CE appointment ass | Assessments for carotid endarterectomy made during appointments specifically for that purpose |
| CE surgery | Number of patients receiving carotid endarterectomy |
| Stroke at CE | Number of strokes during carotid endarterectomy |
| Stroke related death | Additional deaths following minor stroke due to increased risk of mortality |
| Other cause death | Deaths from other causes during the follow up period – this number would be expected to increase slightly if stroke-related deaths are reduced |

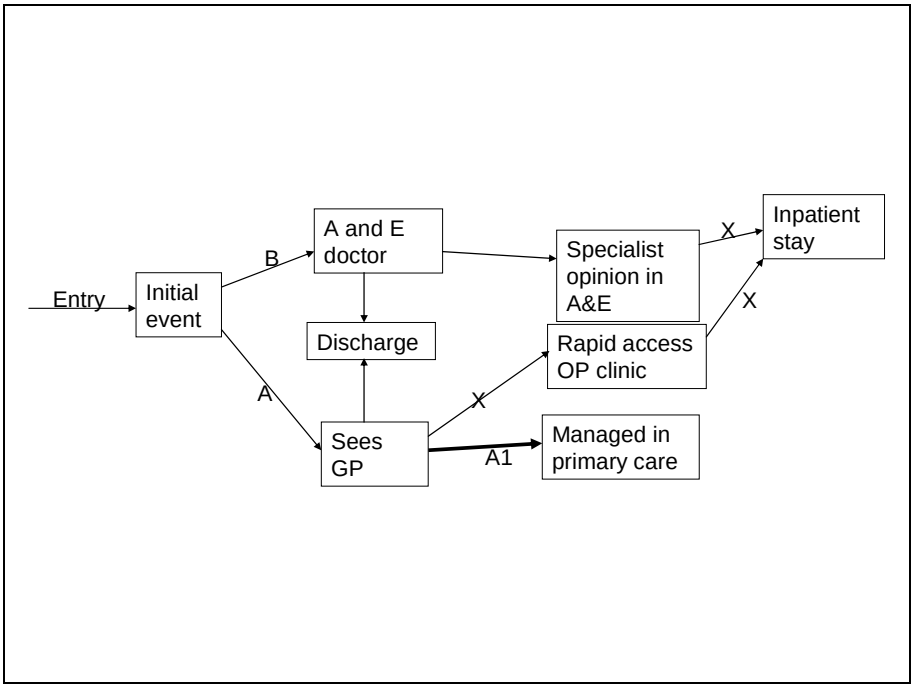
| Item | Description |
|---|---|
| Normal exit | Number of patients exiting the model at 12 months |
| Antiplatelet therapy | |
| Change no to mono | Number of patients switching from no antiplatelet to monotherapy |
| Change no to dual | Number of patients switching from no antiplatelet to dual therapy |
| Chnge mono to dual | Number of patients switching from antiplatelet monotherapy to dual therapy |
| Monotherapy weeks | Number of weeks spent by patients on antiplatelet monotherapy |
| Dual therapy weeks | Number of weeks spent by patients on antiplatelet dual therapy |
| Warfarin started | Number of patients starting warfarin |
| Warfarin weeks | Number of weeks spent by patients on warfarin |
| Statin started | Number of patients starting statin |
| Statin weeks | Number of weeks spent by patients on statin |
| Antihypertensive | |
| Started | Number of patients starting antihypertensive therapy |
| Weeks | Number of weeks spent by patients on antihypertensive therapy |
| IP admissions | Number of patients admitted as inpatients (only applies when inpatient admission is used) |
| Inpatient days | Number of days spent as inpatient (only applies when inpatient admission is used) |

# 5: Results of the Model

## *5.1. Initial analysis*

For the initial analysis, the baseline that is used for comparison is current practice as derived from our analysis of the general practice database QRESEARCH (see chapter 3). We assume that patients make some use of ambulance and A&E services based on the analysis of OXVASC data reported by Giles et al, (Giles, 2006) and that no patients are admitted to hospital for observation. We assume that every patient who presents to A&E in whom the A&E doctor diagnoses a TIA or minor stroke is seen by a specialist while at the A&E department. This baseline pattern of service delivery is illustrated in figure 5.1 below:

**Figure 5.1: Baseline service provision. Xs indicate this option not available. Heavy line denotes major pathway of care.**




This is compared with availability of a daily (Monday-Friday) rapid access specialist clinic. Nine different referral thresholds are modelled, from refer all possible cases of TIA/minor stroke (regardless of whether the GP makes a positive diagnosis), through eight possible referral thresholds for positive diagnoses based upon the ABCD2 score (which can vary form 0 to 7).

The detailed results showing the impact of these ten different patterns of service provision are shown in table 5.14 at the end of this chapter. In general, as one would anticipate, the lower the referral threshold, the lower the number of predicted cerebrovascular events. The model predicts 70 fewer strokes (7 per annum) leading to hospital admission and 65 fewer TIAs and minor strokes if all possible cases are referred to a specialist clinic as compared to current management in general practice. Below a referral threshold of 3 on the ABCD2 score there is no reduction in predicted cerebrovascular events, indeed there is a

small increase. This is because fewer patients with a 'false positive' diagnosis are receiving treatment from the GP, which they would not receive following correct diagnosis by a specialist. The model allows for benefit from such treatment (since lowering blood pressure will lower risk of a subsequent stroke), and hence the small rise in predicted number of strokes at low ABCD2 referral thresholds. Referral of all possible cases leads to the best possible outcome since here the additional benefit of treatment of genuine TIAs by the specialist who had not been diagnosed by the GP outweighs the loss of the 'benefit' through incorrect treatment of 'false positives'.

A referral threshold of ABCD2 score of 4 would generate 2,123 outpatient appointments over the 10 years – about 4 patients per week. If all suspected cases were referred, the workload would rise to 8,337 appointments per week, or 16 patients per week.

A proportion of strokes that lead to hospital admission are fatal. Since the patient exits the model on occurrence of a major stroke, such deaths are not counted. However, there are stroke related deaths that occur following a minor stroke (to reflect the higher mortality of people following a minor stroke than the general population). These are included in the model. There is a small reduction in these (0.7 deaths per year) moving from current practice to refer all cases to a specialist clinic.

The total cost and the number of strokes that lead to hospital admission (labelled 'major stroke') that are predicted to occur in each pattern of care are shown in table 5.1 below:

**Table 5.1: Costs and major strokes under base case assumptions**

| Strategy | Costs (£k) | Major strokes |
|---|---|---|
| Baseline (no referral) | 5004 | 341 |
| Refer at ABCD2 score 7 | 5023 | 339 |
| Refer at ABCD2 score 6 | 5331 | 323 |
| Refer at ABCD2 score 5 | 5723 | 312 |
| Refer at ABCD2 score 4 | 6068 | 302 |
| Refer at ABCD2 score 3 | 6348 | 297 |
| Refer at ABCD2 score 2 | 6563 | 298 |
| Refer at ABCD2 score 1 | 6671 | 298 |
| Refer all diagnoses of TIA/minor stroke | 6688 | 298 |
| Refer all suspected cases | 7616 | 272 |

In general, the more patients are referred by GP to outpatient clinic, the more costly the strategy is overall, but the lower the number of major strokes. However, as noted above, the strategies which retain GP diagnosis, but involve referral at a threshold ABCD$^2$ score of below 3 actually lead to a small increase in the number of major strokes, compared to "refer at 3".

Where a strategy costs more and is less effective (in this case, leads to more major strokes) than another strategy, it is said to be simply dominated. In this case, the strategies "refer at 2", "refer at 1", and "refer all +ve diagnoses" are each dominated by "refer at 3". Where a strategy costs more, but leads to fewer major strokes than, another strategy, an incremental cost-effectiveness ratio (ICER) can be calculated. This represents the additional cost of preventing one major stroke. The ICERs are shown in table 9.2. In each case, the ICER reflects the cost and benefit of a strategy as compared to the strategy on the row above. Thus, to move

from the baseline strategy of current practice to a strategy where patients are referred to a specialist clinic with an ABCD2 score of 7 will cost an additional £19,000, and prevent an additional 3 major strokes, leading to an ICER of £7,000 per stroke averted.

It can be seen that the ICER in moving from refer at ABCD2 score of 3 to refer all suspect (£50,000 per stroke prevented) is lower than the ICER of moving from refer at ABCD2 score of 4 to refer at 3 (£53,000 per stroke prevented). Thus, the option to refer at 3 can never be the preferred option at any cost-effectiveness threshold. This option is said to be excluded by extended dominance. The remaining options are potentially cost effective and are shown in table 5.2.

**Table 5.2: Cost-effectiveness analysis for base case excluding simple dominance only**

| Strategy | Costs (£k) | Major strokes | Incremental cost (£k) | Major strokes | ICER |
|---|---|---|---|---|---|
| Baseline | 5004 | 341 | | averted | |
| Refer at 7 | 5023 | 339 | 19 | 3 | 7 |
| Refer at 6 | 5331 | 323 | 308 | 15 | 20 |
| Refer at 5 | 5741 | 312 | 410 | 12 | 35 |
| Refer at 4 | 6089 | 302 | 348 | 10 | 36 |
| Refer at 3 | 6348 | 297 | 259 | 5 | 53 |
| Refer all suspect | 7616 | 272 | 1268 | 26 | 50 |

ICER = incremental cost-effectiveness ratio (in this case, incremental cost per major stroke averted.) Incremental cost, major strokes averted and ICER are calculated with reference to the strategy shown on the previous line. Model results are averages per 10,000 patients. These are shown to the nearest integer, but full accuracy has been preserved for the calculation of the ICER.

**Table 5.3: Potentially cost-effective options under base case assumptions (counting major strokes averted only)**

| Strategy | Costs (£k) | Major strokes | Incremental cost (£k) | Major strokes | ICER |
|---|---|---|---|---|---|
| Baseline | 5004 | 341 | | averted | |
| Refer at 7 | 5023 | 339 | 19 | 3 | 7 |
| Refer at 6 | 5331 | 323 | 308 | 15 | 20 |
| Refer at 5 | 5741 | 312 | 410 | 12 | 35 |
| Refer at 4 | 6089 | 302 | 348 | 10 | 36 |
| Refer all suspect | 7616 | 272 | 1527 | 30 | 50 |

ICER = incremental cost-effectiveness ratio (in this case, incremental cost per major stroke averted.) Incremental cost, major strokes averted and ICER are calculated with reference to the strategy shown on the previous line. Model results are averages per 10,000 patients. These are shown to the nearest integer, but full accuracy has been preserved for the calculation of the ICER.

This suggests that there are several possible cost effective strategies for implementing rapid access clinics, with the choice of strategy (if purely dependent upon cost-effectiveness) depending upon the value attached to preventing a major stroke. Referring at an ABCD2 score of 7,6,5 and 4 are all potentially cost-effective, with the cost per stroke averted rising as the threshold is lower. Referring at lower

thresholds is not cost effective, except for the option of referring all possible cases, regardless of whether or not the GP has made a diagnosis of TIA.

If a referral threshold was set at an ABCD2 score of 4 or more for this service, then the additional cost per annum would be of the order of £108,500 per annum compared to current practice and result in the prevention of 4 strokes per annum. If all suspect cases were referred, the additional cost as compared to current practice would be £261,200 per annum, and result in the prevention of 7 strokes per annum (at an incremental cost per stroke prevented of £50,000 as compared to refer at threshold score of 4).

We have also considered a composite outcome made up of repeat minor strokes, major strokes, and strokes at carotid endarterectomy, The use of cost per stroke averted is not ideal, as it implicitly weights all strokes equally. However, given that the proportions of the different types of stroke remain much the same, the same strategies remain potentially cost-effective when this outcome is used, as shown in Table 5.4 though the incremental cost per stroke avoided is lower.

**Table 5.4: Potentially cost-effective options under base case assumptions (counting all strokes averted)**

| Strategy | Costs (£k) | All strokes | Inc cost | Strokes | ICER |
|---|---|---|---|---|---|
| Baseline | 5004 | 609 | | averted | |
| Refer at 7 | 5023 | 604 | 19 | 5 | 4 |
| Refer at 6 | 5331 | 579 | 308 | 25 | 12 |
| Refer at 5 | 5723 | 560 | 392 | 19 | 20 |
| Refer at 4 | 6068 | 544 | 346 | 16 | 21 |
| Refer all suspect | 7616 | 495 | 1548 | 49 | 32 |

Figure 5.2 shows the various strategies in terms of incremental cost and major strokes prevented compared to baseline. The scales on these graphs are set to allow comparison with the alternatives considered later.

**Figure 5.2a: Base case result, major strokes only**

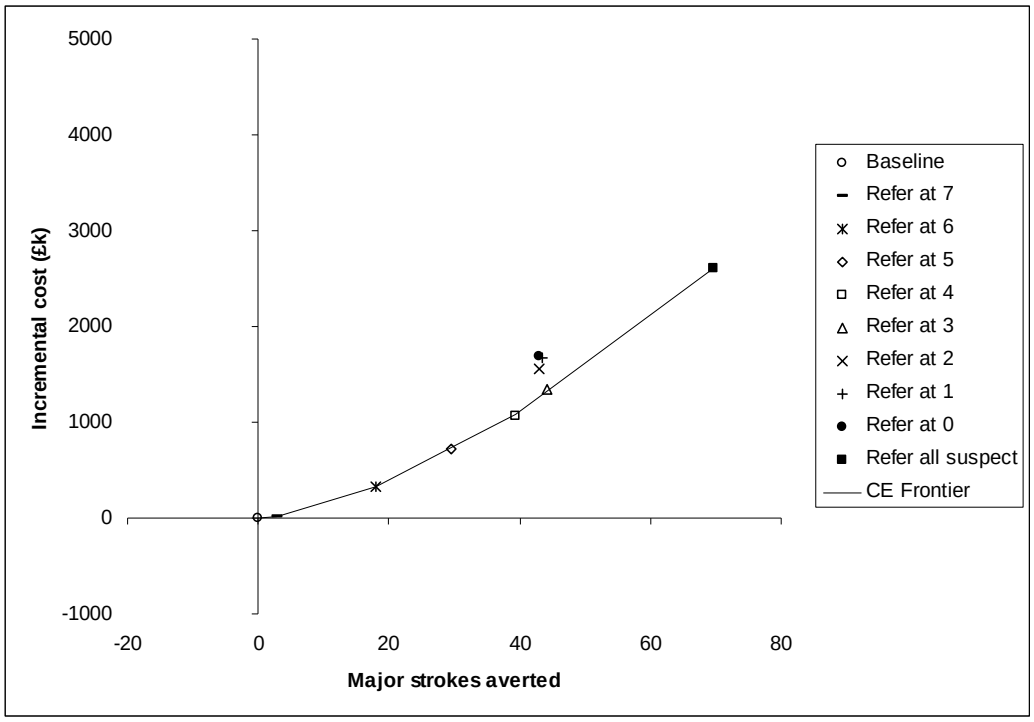
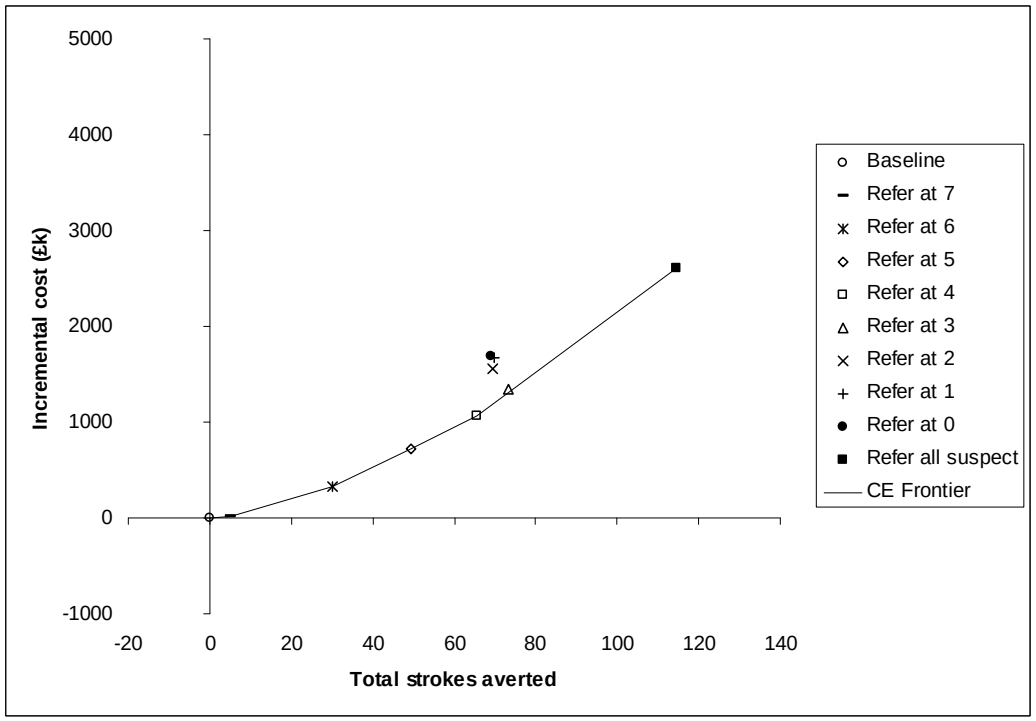



**Figure 5.2b: All strokes**




In each of these graphs, the potentially cost effective options are joined up by a line. The steeper the gradient of the line the higher the ICER. Points that appear above the line represent those strategies that are not cost –effective ("dominated").

## *5.2. Analyses to consider different strategic alternatives*

In this set of analyses, we consider what the optimal referral threshold would be if other strategies were in place. The alternative strategies that we considered were:

- Admission of patients who see a stroke specialist (whether in A&E or in a rapid access out-patient clinic) with an ABCD2 score ≥ 4
- Alternative frequencies of rapid access out-patient clinics (weekly or twice weekly as compared to daily)

In these analyses, the model was run 2,000 times (as opposed to 10,000 times in the initial analyses).

### 5.2.1 Inclusion of inpatient admission

In this analysis, patients with an ABCD2 score ≥ 4 who see a specialist are admitted for 72 hours for observation, and to allow thrombolysis should they have a stroke. The number of admissions varies from 118 per year if in-patient admission is simply added on to current practice, through to 378 admissions per year if the GP refers all suspected cases for specialist opinion (see table 9.13 at end of chapter). This results in between 2 and 4 patients per year receiving thrombolysis.

The impact on total costs and number of major strokes of in-patient admissions is shown in table 5.5. In general, the pattern is similar to the initial analysis, but the costs are higher, and the number of strokes that occur marginally lower.

**Table 5.5: Inclusion of inpatient admission**
(*a*) Costs and outcomes for all options

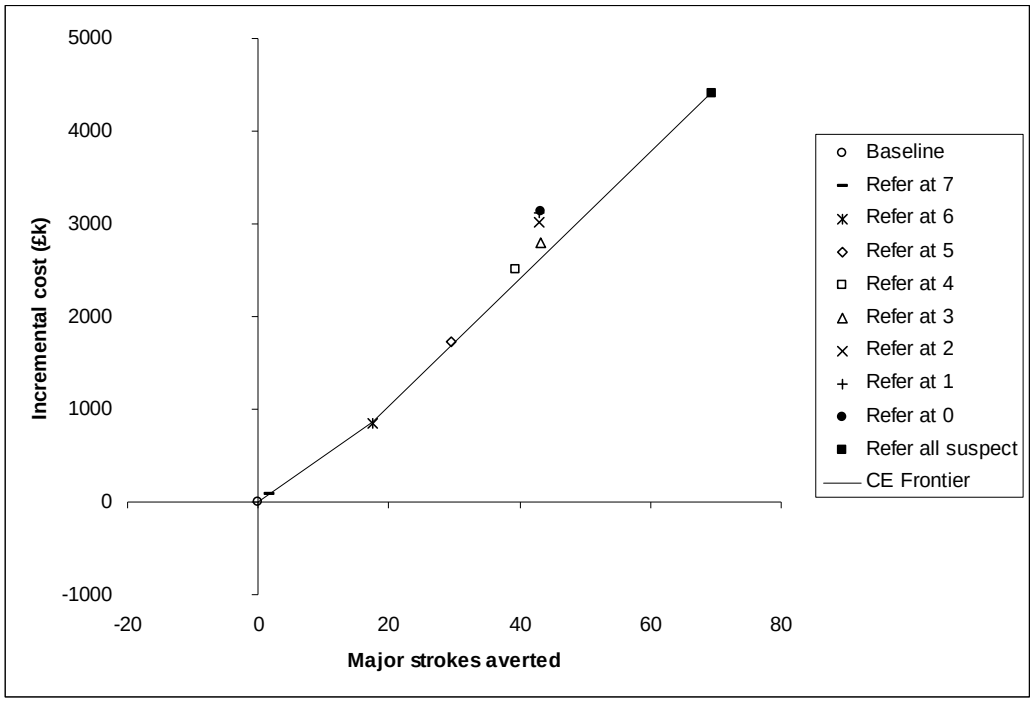
| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5727 | 339 |
| Refer at 7 | 5804 | 337 |
| Refer at 6 | 6567 | 321 |
| Refer at 5 | 7453 | 309 |
| Refer at 4 | 8244 | 299 |
| Refer at 3 | 8526 | 296 |
| Refer at 2 | 8736 | 296 |
| Refer at 1 | 8846 | 296 |
| Refer all +ve diag | 8864 | 296 |
| Refer all suspect | 10129 | 269 |

(*b*) Potentially cost-effective strategies

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5727 | 339 | | averted | maj strk avert |
| Refer at 6 | 6584 | 321 | 856 | 18 | 49 |
| Refer all suspect | 10152 | 269 | 3569 | 52 | 69 |

It can be seen that if in-patient admissions occur, then there are fewer cost effective options, with referral to rapid access outpatient clinic with an ABCD2 score ≥ 6 or refer all suspected cases being the only strategies that are potentially more cost effective than current practice.

**Figure 5.3: Cost-effectiveness plane for inclusion of inpatient admission**




## 5.2.2 Alternative frequencies of rapid access clinics

The initial analyses assessed the impact of introduction of a rapid access clinic that was available daily (Monday to Friday). We also explored the potential impact of different clinic frequencies: weekly fixed; twice weekly fixed; and twice weekly flexible. The fixed clinics are of fixed capacity. The flexible clinics allow for extra appointments if necessary so that no patient needs to wait longer than 7 days.

The predicted impact of these different patterns of service provision on occurrence of major stroke is shown in table 9.6.

**Table 5.6: Predicted numbers of major strokes for all combinations of referral strategy and clinic availability**

| | Daily | Twice weekly flexible | Twice weekly fixed | Once weekly fixed |
|---|---|---|---|---|
| Baseline | 341 | 342 | 342 | 342 |
| Refer at 7 | 339 | 339 | 339 | 340 |
| Refer at 6 | 323 | 325 | 325 | 328 |
| Refer at 5 | 312 | 316 | 316 | 320 |
| Refer at 4 | 302 | 308 | 307 | 312 |
| Refer at 3 | 297 | 305 | 304 | 314 |
| Refer at 2 | 298 | 305 | 305 | *408* |
| Refer at 1 | 298 | 307 | 307 | *415* |
| Refer all +ve diag | 298 | 307 | 307 | *416* |
| Refer all suspect | 272 | 288 | *412* | *416* |

(The difference in baseline between daily and other clinic patterns is a random effect due to the reduced number of replications of the model.)

The italicised numbers in the table reflect that this pattern of clinic provision is inadequate to cope with the number of referrals, and that queues develop, and the rapid access to a specialist can no longer be provided. Thus, a once weekly fixed clinic cannot sustain a policy of referral at ABCD2 score ≥ 2 (or lower) and a twice weekly fixed clinic cannot cope with a policy of referral of all suspect cases. It is not plausible that GPs would refer to a "rapid access" clinic with a long waiting time, so these options are excluded from the cost effectiveness analysis. More strokes occur in the twice weekly options as compared to the daily option, and in the weekly option as compared to the other options. This reflects the longer time delay before a patient sees a specialist.

With regards to costing the clinics, the analyses have been run using two different assumptions. In the first, we have assumed that only clinic spaces that are actually used incur a cost (in other words, the staff would be doing something else if there were no patients to see). In the second, we have assumed that these are fully staffed even if the allocation of six places per day is not used. In the case of twice weekly flexible, there is an additional cost for appointments beyond the minimum of six on any given day. For the daily clinic, where there is no set clinic time, there are no fixed costs, only the costs of each clinic appointment.

Twice weekly flexible clinics

The results for "twice weekly flexible" are shown in Table 5.7 and Figure 5.4. If only clinics used are costed, the pattern is similar to the base case. Costs are similar with a slight increase in the number of major strokes. If unused clinics are costed at full price, the pattern changes considerably. Any referral strategy at a high threshold will incur a large cost for unused clinics, so that only the "refer all" strategy is potentially cost-effective in that case. However, this would require on average 4 additional appointments per week in addition to scheduled appointments to prevent a waiting list developing.

**Table 5.7: Results for twice-weekly flexible clinics**

(*a*) Costs and outcomes costing only clinics used

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 342 |
| Refer at 7 | 5029 | 339 |
| Refer at 6 | 5349 | 325 |
| Refer at 5 | 5751 | 316 |
| Refer at 4 | 6108 | 308 |
| Refer at 3 | 6398 | 305 |
| Refer at 2 | 6613 | 305 |
| Refer at 1 | 6735 | 307 |
| Refer all +ve diag | 6747 | 307 |
| Refer all suspect | 7730 | 288 |

(*b*) Potentially cost-effective strategies costing only clinics used

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk avert |
| Refer at 7 | 5029 | 339 | 25 | 2 | 10 |
| Refer at 6 | 5349 | 325 | 319 | 14 | 23 |
| Refer at 4 | 6108 | 308 | 759 | 17 | 44 |
| Refer all suspect | 7730 | 288 | 1623 | 20 | 83 |

(*c*) Costs and outcomes costing full price for unused clinics

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 342 |
| Refer at 7 | 6307 | 339 |
| Refer at 6 | 6489 | 325 |
| Refer at 5 | 6740 | 316 |
| Refer at 4 | 6964 | 308 |
| Refer at 3 | 7140 | 305 |
| Refer at 2 | 7134 | 305 |
| Refer at 1 | 7067 | 307 |
| Refer all +ve diag | 7060 | 307 |
| Refer all suspect | 7740 | 288 |

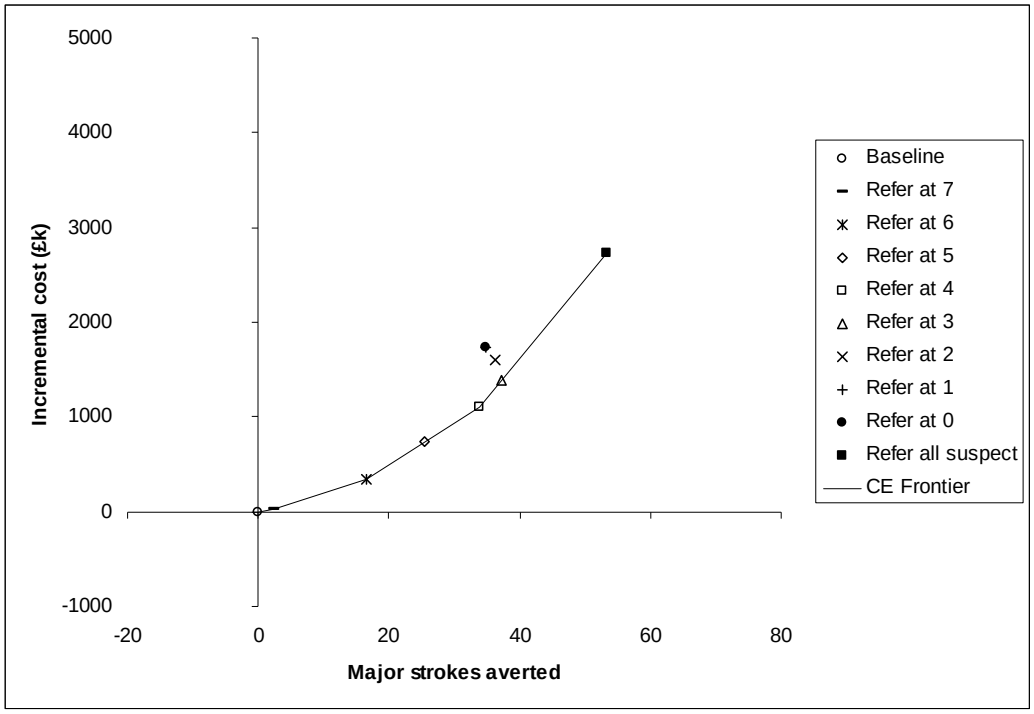
(*d*) Potentially cost-effective strategies costing full price for unused clinics

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk |

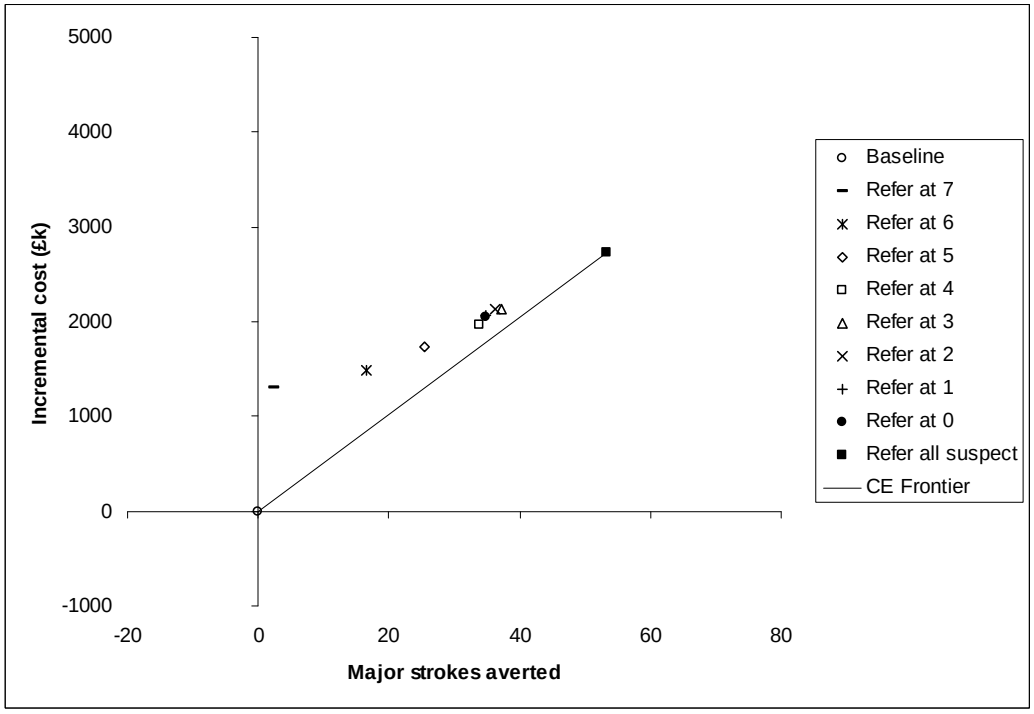
| | | | | | avert |
|---|---|---|---|---|---|
| Refer all suspect | 7740 | 288 | 2735 | 53 | 51 |

**Figure 5.4: Cost-effectiveness plane for twice-weekly clinics**

(*a*) Costing only clinics used




(*b*) Costing full price for unused clinics



Twice weekly fixed clinics

For "twice weekly fixed" see Table 5.8 and Figure 5.5. These are broadly similar to the results for "twice weekly flexible" except for the omission of the strategy "refer all suspect", which is unsustainable with fixed clinics of insufficient capacity. This means that "refer at 3" becomes the most effective feasible strategy in this case, and it replaces "refer all suspect" in the list of potentially cost-effective strategies.

**Table 5.8: Costs and outcomes for twice weekly fixed clinics**

(*a*) Costs and outcomes costing only clinics used

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 342 |
| Refer at 7 | 5029 | 339 |
| Refer at 6 | 5349 | 325 |
| Refer at 5 | 5751 | 316 |
| Refer at 4 | 6105 | 307 |
| Refer at 3 | 6395 | 304 |
| Refer at 2 | 6612 | 305 |
| Refer at 1 | 6730 | 307 |
| Refer all +ve diag | 6749 | 307 |

(*b*) Potentially cost-effective strategies costing only clinics used

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk avert |
| Refer at 7 | 5029 | 339 | 25 | 2 | 10 |
| Refer at 6 | 5349 | 325 | 319 | 14 | 23 |
| Refer at 4 | 6105 | 307 | 757 | 18 | 42 |
| Refer at 3 | 6395 | 304 | 289 | 3 | 87 |

(*c*) Cost and outcomes costing full price for unused clinics

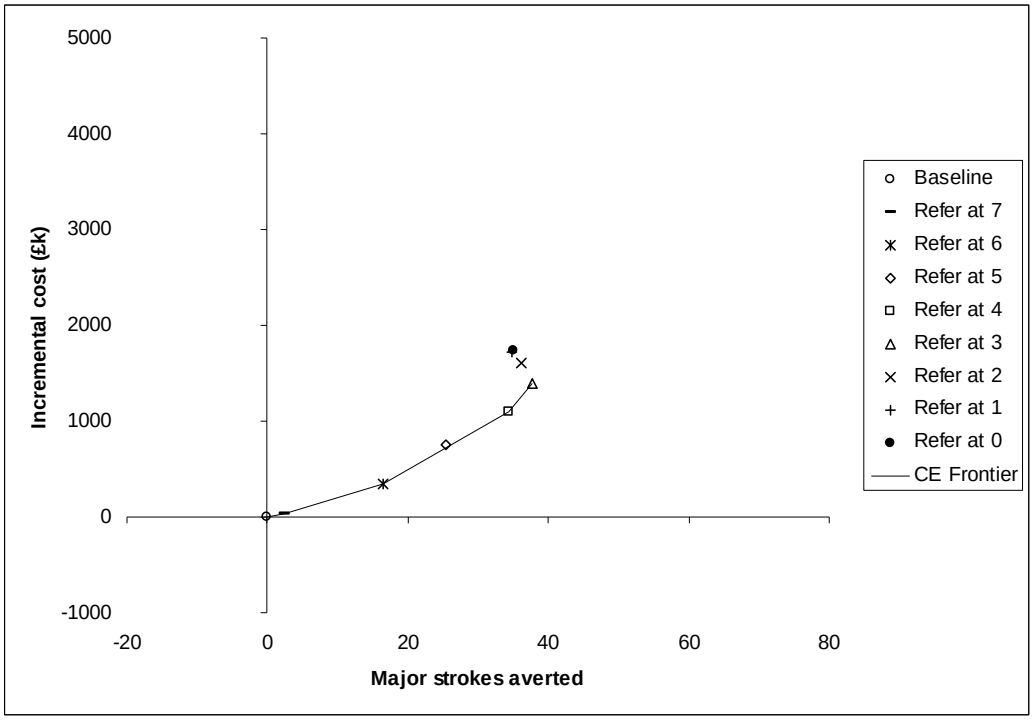
| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 342 |
| Refer at 7 | 6307 | 339 |
| Refer at 6 | 6489 | 325 |
| Refer at 5 | 6740 | 316 |
| Refer at 4 | 6962 | 307 |
| Refer at 3 | 7136 | 304 |
| Refer at 2 | 7133 | 305 |
| Refer at 1 | 7059 | 307 |
| Refer all +ve diag | 7057 | 307 |

(*d*) Potentially cost-effective strategies costing full price for unused clinics

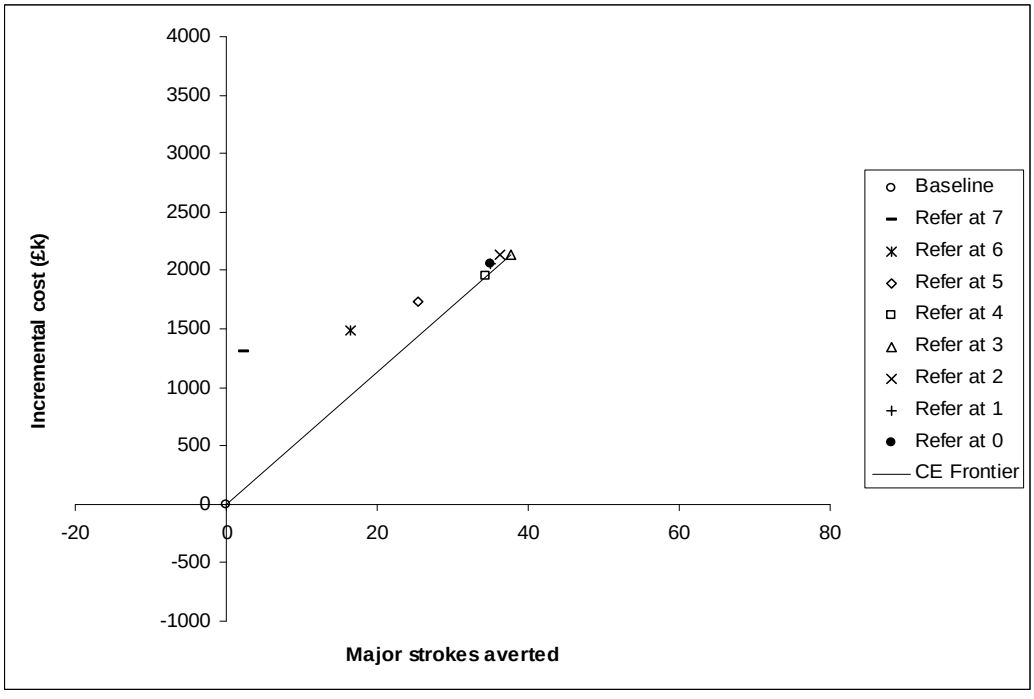
| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk avert |
| Refer at 3 | 7136 | 304 | 2132 | 38 | 57 |

**Figure 5.5: Cost-effectiveness plane for twice weekly fixed clinics**
(*a*) Costing only for clinics used




(*b*) Costing full price for unused clinics




Weekly fixed clinics

Finally in this section the results for weekly fixed clinics are shown in Table 5.9 and Figure 5.6. Compared to twice weekly clinics, a wider range of strategies become infeasible, and "refer at 3" has become appreciably worse. This is a case where the waiting time for clinics does not build up indefinitely but is still appreciable.

For the strategies which are feasible, the pattern when costing only clinics used is again similar to that for twice weekly, with a further small increase in the number of major strokes reflecting the additional waiting time to weekly clinics. When costing full price for clinics unused, the cost of weekly clinics is only half that of twice weekly clinics of the same length.

**Table 5.9: Costs and outcomes for weekly fixed clinics**

(*a*) Costs and outcomes costing only clinics used

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 342 |
| Refer at 7 | 5028 | 340 |
| Refer at 6 | 5365 | 328 |
| Refer at 5 | 5782 | 320 |
| Refer at 4 | 6138 | 312 |
| Refer at 3 | 6461 | 314 |

(*b*) Potentially cost-effective strategies costing only clinics used

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk avert |
| Refer at 7 | 5028 | 340 | 24 | 2 | 13 |
| Refer at 6 | 5365 | 328 | 336 | 12 | 28 |
| Refer at 4 | 6138 | 312 | 773 | 16 | 49 |

(*c*) Costs and outcomes costing full price for clinics not used

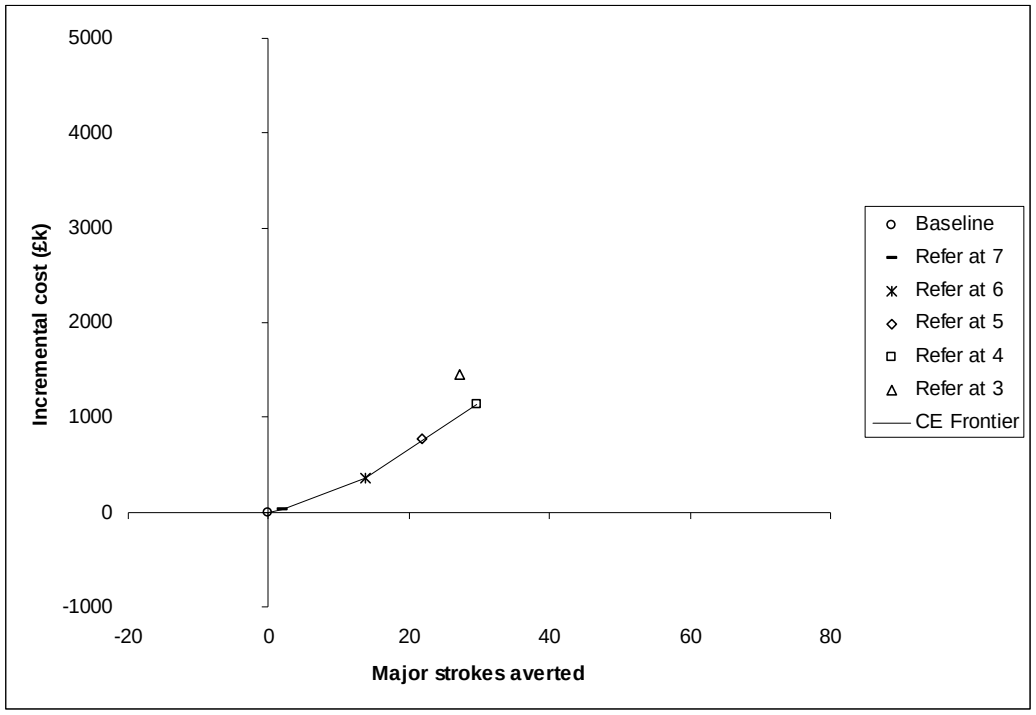
| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5004 | 341.65 |
| Refer at 7 | 5661 | 340 |
| Refer at 6 | 5861 | 328 |
| Refer at 5 | 6127 | 320 |
| Refer at 4 | 6351 | 312 |
| Refer at 3 | 6563 | 314 |

(*d*) Potentially cost-effective strategies costing full price for clinics not used

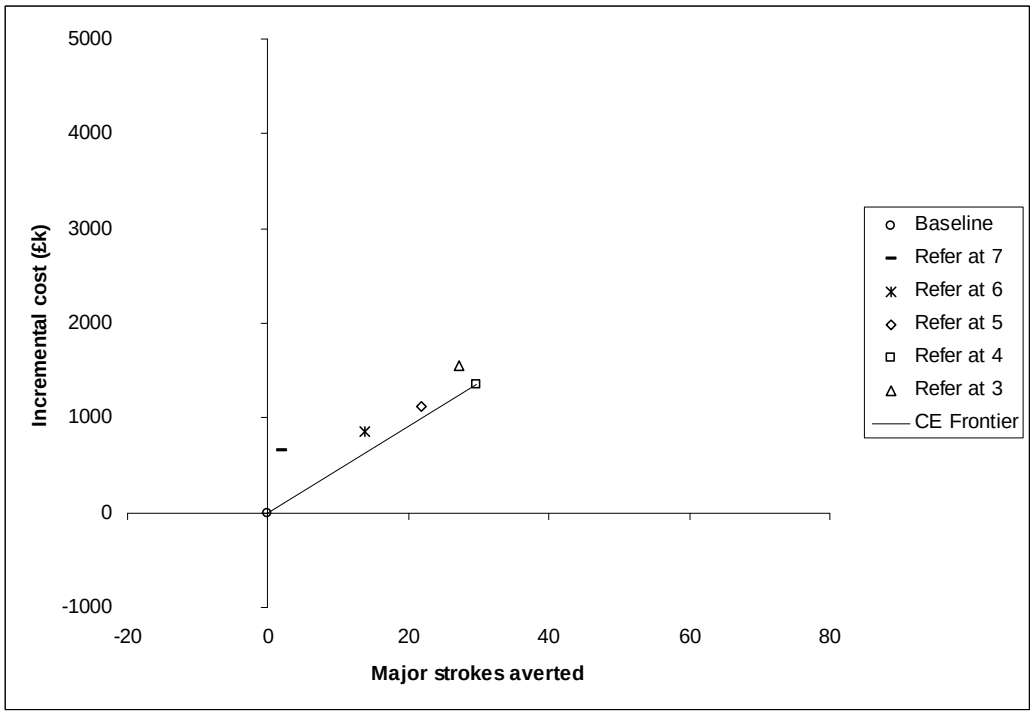
| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5004 | 342 | | averted | maj strk avert |
| Refer at 4 | 6351 | 312 | 1347 | 30 | 46 |

**Figure 5.6: Cost-effectiveness plane for weekly fixed clinics**

(*a*) Costing only clinics used



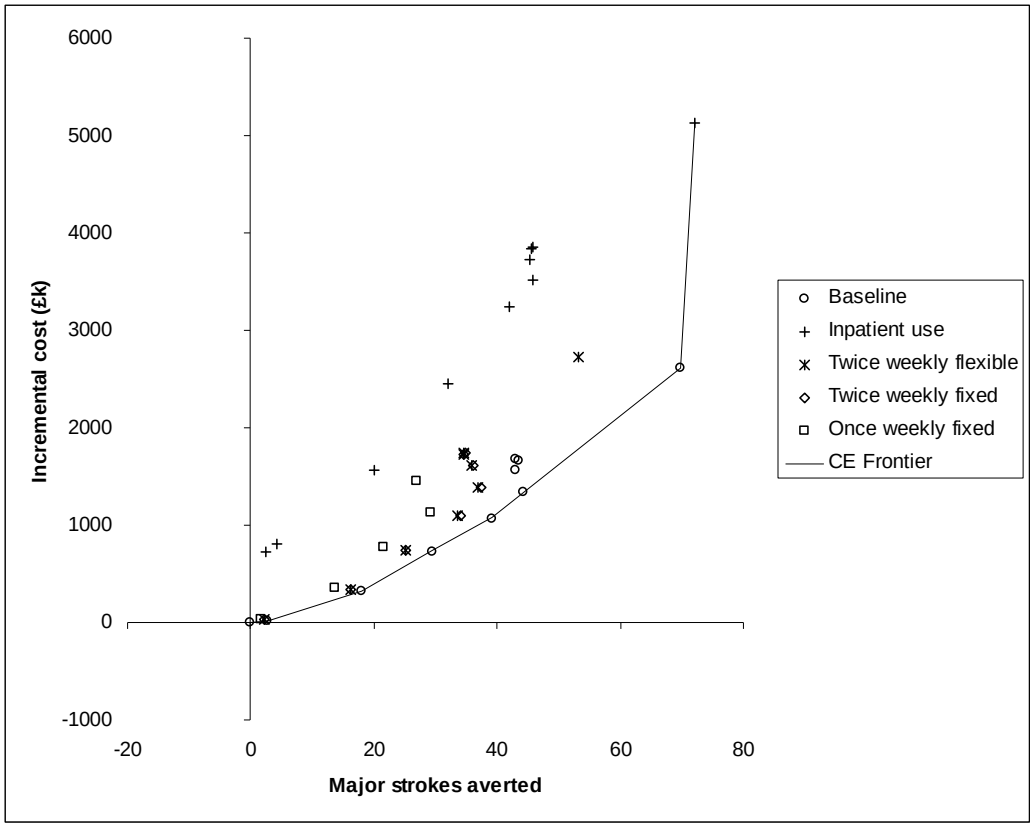

(*b*) Costing full price for clinics not used



### 5.2.3 Direct comparison of different patterns of out-patient provision and in-patient admission

Figure 5.7 shows a combined plot of all the above strategies compared to the initial analysis (with daily clinics). In this analysis, we have costed only the clinics used.

**Figure 5.7: Combined cost-effectiveness plane for five strategy sets**




It can be seen from this graph that the different patterns of outpatient clinic are all dominated by the baseline analysis (daily clinics), since they all fall above the cost effectiveness plane. In patient admission in combination with referral of all suspect TIAs is not dominated, but gives an ICER of over £1,000,000 per major stroke prevented.

## *5.3. Sensitivity analyses*

We also performed sensitivity analyses to test the robustness of our results under different assumptions. The assumptions we tested were:

- Increased use of emergency ambulances
- Optimal management by GPs
- Better diagnosis by GPs

### 5.3.1 Increased use of emergency ambulances

Part of the National Stroke Strategy involves a publicity campaign to alert people to the symptoms and signs of stroke, and to encourage them to seek emergency care if they experience such symptoms. This is to enable prompter access to specialist services so that greater and more effective use can be made of thrombolysis and

other acute medical treatments. A consequence of this, if effective, will be that a higher proportion of people who are experiencing symptoms of a TIA will contact the emergency services, and will go to A&E, bypassing the general practitioner. Therefore, we performed a sensitivity analysis exploring what impact such a change in behaviour would have on the outcomes of our model. We did this by increasing by 20% the baseline probability that the patient would treat the TIA as an emergency.

The impact on costs and outcomes of this assumption is shown in table 5.9. The general pattern is similar to the initial analysis, with costs generally higher and the number of major strokes slightly lower (with the exception of 'refer all suspect').

**Table 5.9: Costs and outcomes with enhanced use of 999 service**

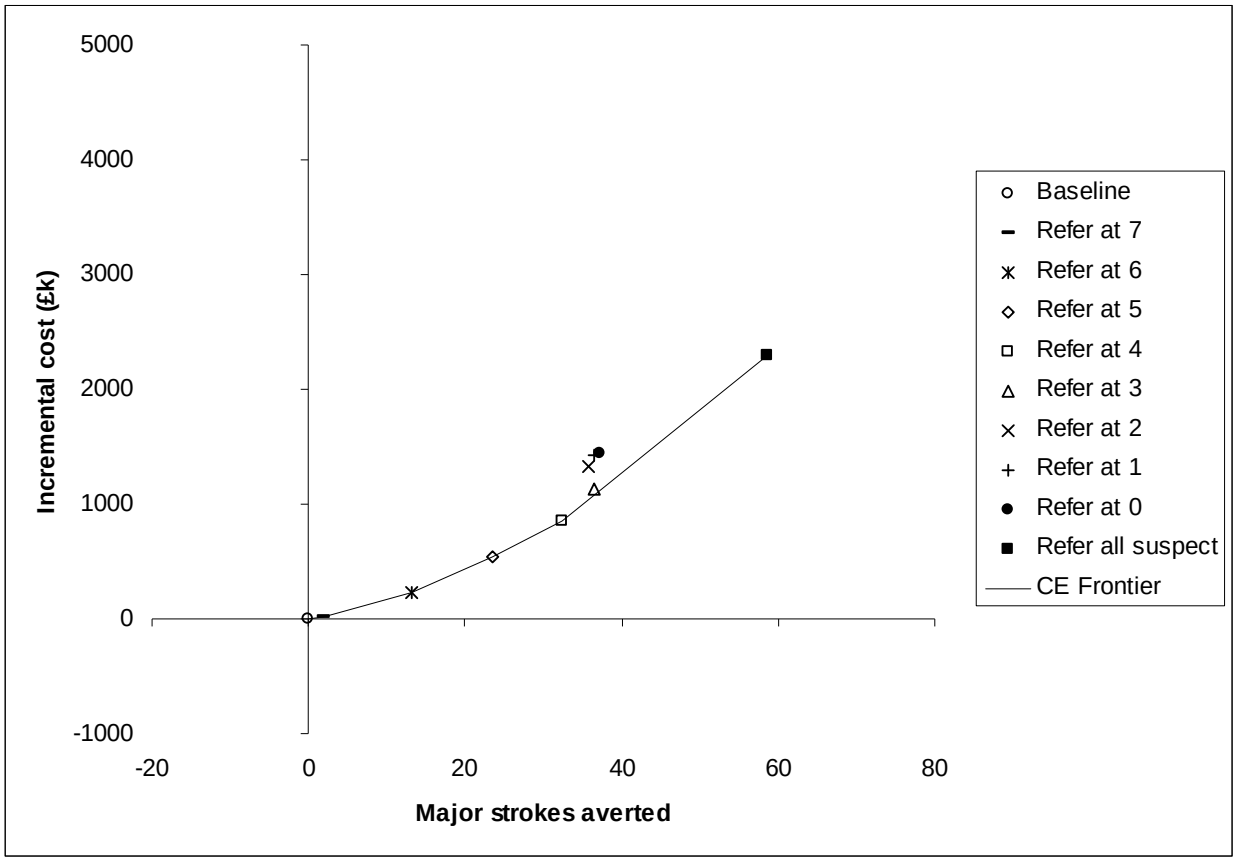
(*a*) Costs and outcomes for all options

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5417 | 331 |
| Refer at 7 | 5432 | 329 |
| Refer at 6 | 5639 | 318 |
| Refer at 5 | 5960 | 307 |
| Refer at 4 | 6277 | 298 |
| Refer at 3 | 6548 | 294 |
| Refer at 2 | 6746 | 295 |
| Refer at 1 | 6849 | 294 |
| Refer all +ve diag | 6855 | 294 |
| Refer all suspect | 7718 | 272 |

(*b*) Potentially cost-effective strategies

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5417 | 331 | | averted | maj strk avert |
| Refer at 7 | 5432 | 329 | 15 | 2 | 8 |
| Refer at 6 | 5639 | 318 | 207 | 11 | 18 |
| Refer at 5 | 5960 | 307 | 321 | 10 | 31 |
| Refer at 4 | 6277 | 298 | 317 | 9 | 35 |
| Refer all suspect | 7718 | 272 | 1441 | 26 | 55 |

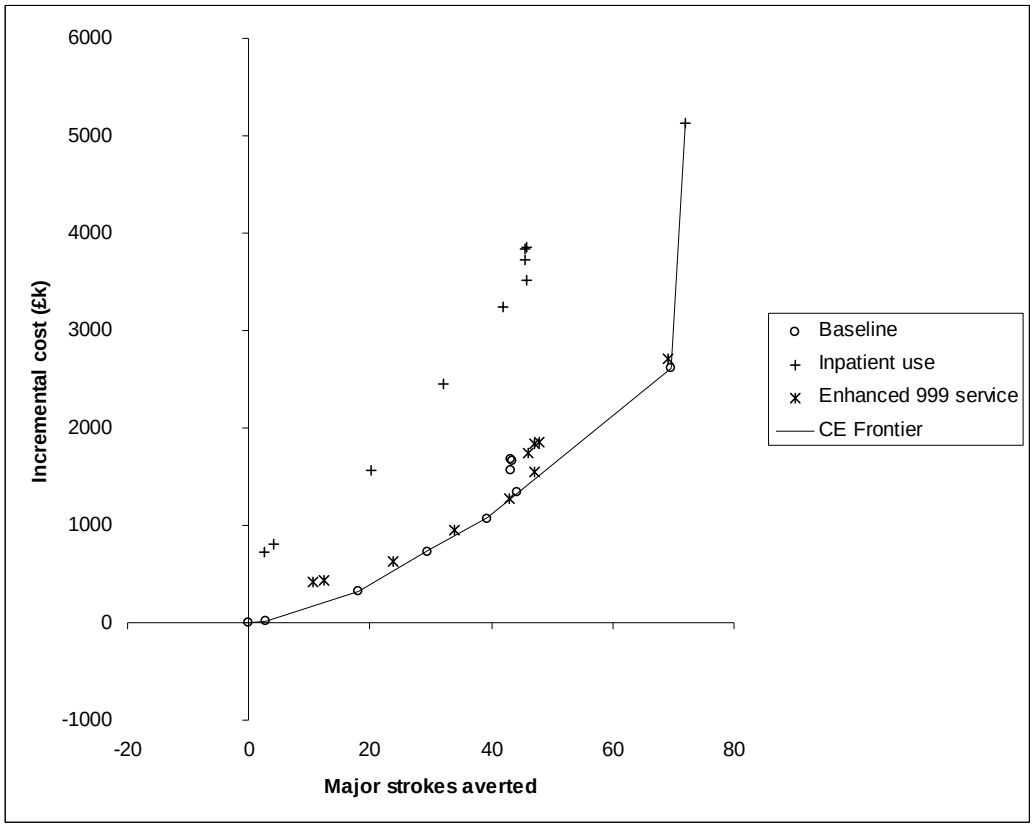
**Figure 5.8: Cost-effectiveness plane for enhanced 999 services**




The cost effective options if greater use of emergency services is made are the same as for the initial analyses, with similar ICERs.

Figure 5.9 shows direct comparison of greater use of emergency services with the other strategies. For clarity, the dominated strategy sets involving once and twice weekly clinics have been omitted. All strategies involving enhanced 999 services are excluded by simple or extended dominance. This suggests that greater use of patients of emergency services will not lead to more cost effective management of TIAs and minor strokes.

**Figure 5.9: Cost-effectiveness plane for strategy sets including greater use of emergency services**




## 5.3.2 Optimal management by GPs

In this sensitivity analysis, we assume that if the GP makes a diagnosis of TIA and minor stroke, then they will initiate optimal medical therapy if they don't make a referral to a specialist clinic.

Costs for most strategies here are higher and number of major strokes that occur considerably lower than the initial analyses, reflecting the greater use of medications. The exception is the 'refer all suspect' strategy, where no patients are managed by the GP, so there is no difference between this and referring all suspect strategy in the initial analysis.

The reduction in costs that occurs when the referral threshold drops below 3 reflects the reduced number of referrals by the GP for assessment for carotid endarterectomy resulting from false positive diagnoses.

If optimal GP management is assumed, then the only possible cost effective use of rapid access clinics would be to refer all positive diagnoses or to refer all suspected cases. Referring all positive diagnoses is potentially cost effective as it reduces unnecessary referrals for carotid endarterectomy assessment (see above); referring all suspected cases is potentially cost-effective as it picks up the GP false negative diagnoses.

In comparison to baseline (i.e optimal GP management with no use of rapid access clinics), referring all positive diagnoses is a less expensive strategy that results in prevention of fewer strokes (i.e. it is in the south west quadrant of the cost effectiveness plane). This means that it would be cost effective to move from the baseline strategy to refer all positive diagnoses at any threshold *below* £49,000 per

major stroke averted. Since it is cost-effective to move from baseline to "refer all suspect" at any threshold above £29,000 per major stroke averted, the baseline strategy itself is excluded by extended dominance between the two potentially cost-effective strategies.

**Table 5.10: Costs and outcomes for optimal GP management**

(*a*) Costs and outcomes for all strategies

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 7098 | 290 |
| Refer at 7 | 7119 | 291 |
| Refer at 6 | 7219 | 291 |
| Refer at 5 | 7319 | 293 |
| Refer at 4 | 7405 | 293 |
| Refer at 3 | 7443 | 294 |
| Refer at 2 | 7103 | 297 |
| Refer at 1 | 6725 | 298 |
| Refer all +ve diag | 6689 | 298 |
| Refer all suspect | 7621 | 272 |

(*b*) Potentially cost-effective strategies

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Refer all +ve diag | 6689 | 298 | | averted | maj strk avert |
| Refer all suspect | 7621 | 272 | 932 | 27 | 35 |

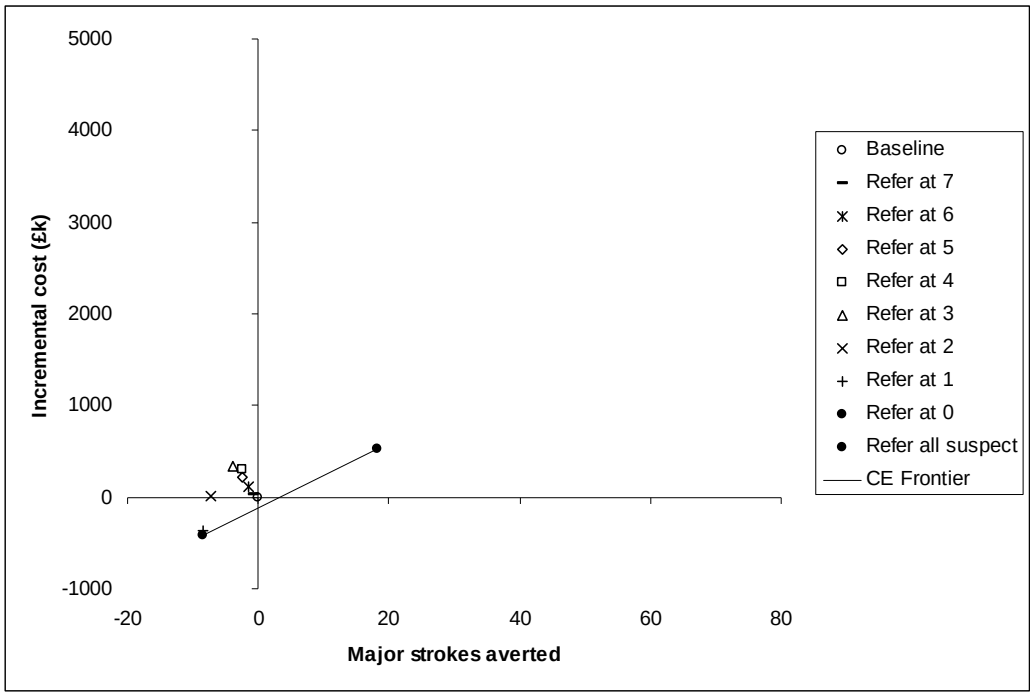
(*c*) Potentially cost-effective strategies shown relative to baseline (current practice)

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| No use of OP clinic | 7098 | 290 | | averted | maj strk avert |
| Refer all +ve diag | 6689 | 298 | -409 | -8 | ***49*** |
| Refer all suspect | 7621 | 272 | 523 | 18 | 29 |

Incremental cost-effectiveness ratios (ICERs) here are relative to the baseline strategy.

** The ICER in *italics* is in the south-west quadrant of the cost-effectiveness plane. This means that it is cost-effective to move from the baseline strategy to "refer all positive diagnosis" at any threshold *below* £49,000 per major stroke averted.

**Figure 5.10: Cost-effectiveness plane for optimal GP management**




## 5.3.3 Better diagnosis by GPs

The initial analyses were based upon an accuracy of GP diagnosis of 80% sensitivity and 60% specificity. In this sensitivity analysis, these parameters are changed to 90% sensitivity 80% specificity respectively. The results are shown in table 5.11 and figure 5.11.

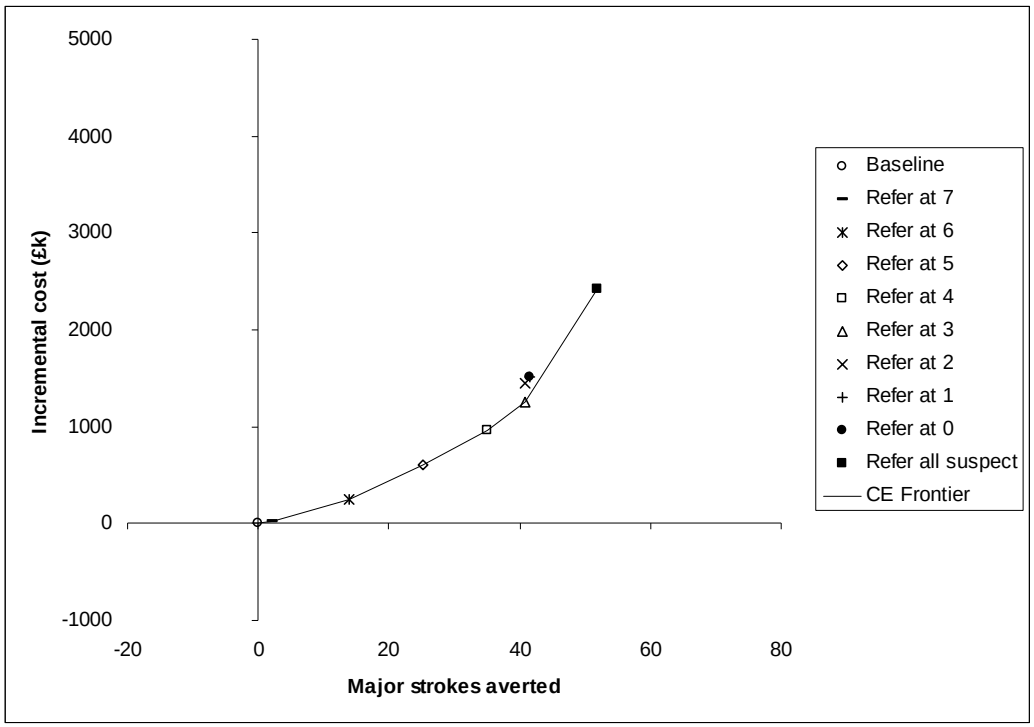
**Table 5.11: Costs and outcomes for improved GP diagnostic ability**
(*a*) Costs and outcomes for all strategies

| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 5356 | 315 |
| Refer at 7 | 5377 | 313 |
| Refer at 6 | 5611 | 301 |
| Refer at 5 | 5967 | 290 |
| Refer at 4 | 6324 | 280 |
| Refer at 3 | 6611 | 274 |
| Refer at 2 | 6799 | 274 |
| Refer at 1 | 6874 | 274 |
| Refer all +ve diag | 6876 | 274 |
| Refer all suspect | 7785 | 263 |

(*b*) Potentially cost-effective strategies

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 5356 | 315 | | averted | maj strk avert |
| Refer at 7 | 5377 | 313 | 21 | 2 | 10 |
| Refer at 6 | 5611 | 301 | 234 | 12 | 20 |
| Refer at 5 | 5967 | 290 | 356 | 11 | 31 |
| Refer at 4 | 6324 | 280 | 358 | 10 | 36 |
| Refer at 3 | 6611 | 274 | 287 | 6 | 51 |
| Refer all suspect | 7785 | 263 | 1174 | 11 | 104 |

**Figure 5.11: Cost-effectiveness plane for improved GP diagnosis**




The impact of improved GP diagnosis in general is to raise costs (as more people are correctly identified and treated) but to reduce the number of major strokes that occur. The advantage of moving from refer at 3 to refer all suspect is comparatively less than in the base case, reflected in the higher ICER, but otherwise improving GP diagnosis makes little difference to the ICERs in the initial analyses.

### 5.3.4 Better diagnosis and optimal management by GP

Finally we considered the joint effect of improved diagnosis with optimal management. The results are in Table 5.12. As was the case when optimal management was combined with baseline diagnostic ability, referring additional patients with positive diagnosis mainly results in delayed treatment. This time the baseline strategy (i.e. no use of out patient services) remains the least costly. The strategy "refer at 7" appears to reduce the number of major of strokes slightly, but

this is within the range of random error within the model. The only possible cost-effective use of rapid access clinics in a scenario where GPs diagnose more accurately and manage optimally is for GPs to refer all suspected cases, with an ICER of £127,000 per major stroke prevented.

**Table 5.12: Costs and outcomes for improved GP diagnosis and management**

(*a*) Costs and outcomes for all strategies

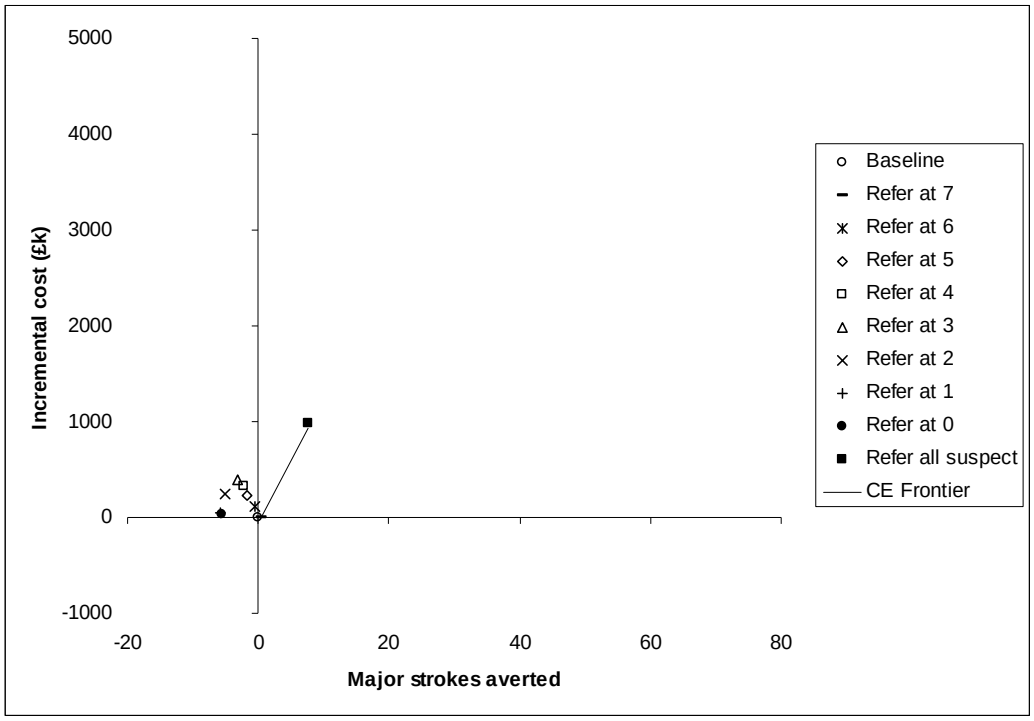
| Strategy | Costs (£k) | Maj strokes |
|---|---|---|
| Baseline | 6670 | 272 |
| Refer at 7 | 6677 | 272 |
| Refer at 6 | 6785 | 273 |
| Refer at 5 | 6902 | 274 |
| Refer at 4 | 6997 | 275 |
| Refer at 3 | 7056 | 276 |
| Refer at 2 | 6910 | 277 |
| Refer at 1 | 6725 | 278 |
| Refer all +ve diag | 6710 | 278 |
| Refer all suspect | 7658 | 265 |

(*b*) Potentially cost-effective strategies

| Strategy | Costs (£k) | Maj strokes | Inc cost | Maj strk | Inc cost per |
|---|---|---|---|---|---|
| Baseline | 9183 | 272 | | averted | maj strk avert |
| Refer at 7 | 9187 | 272 | 4 | 0 | See below |
| Refer all suspect | 10115 | 265 | 928 | 7 | 127 |

Note: the difference in costs and outcomes between "baseline" and "refer at 7" is well within the randomness of the model in this case. It is therefore not meaningful to calculate an incremental cost-effectiveness ratio here.

**Figure 5.12: Cost-effectiveness plane for improved GP diagnosis and management**




## *5.4 Estimation of outcome in terms of QALYS*

**Relevant background information**

1. Median age group of stroke is 75-84 (Rothwell, 2004a)
2. Life expectancy for healthy 75-84 year old is: 6-10 years for a man; 7-12 years for a woman. (Government Actuary's Department, 2006) Assume average life expectancy of 8 years.
3. Most people who have a stroke have underlying cardiovascular disease, so assume that if patient did not have stroke, life expectancy would be less than 8 years – say 6 years.
4. 30 day case fatality following stroke is 17% (Rothwell, 2004a)
5. One year case fatality following stroke is 31%, and commonest cause of death is still stroke. (Dennis, 1993)
6. Two year case fatality following stroke is 43%. (Samsa, 1999)
7. Absolute annual mortality after two years is 7%. (Dennis, 1993)
8. Incidence of stroke by severity is: 0.55 (34%) minor (Rankin score 0-1 at 30 days); 0.47 moderate (29%) (Rankin score 2-3 at 30 days); 0.60 (37%) severe (Rankin score 4-6 at 30 days). (Rothwell, 2004a)
9. Quality Adjusted life year associated with a moderate to severe stroke is 0.39; Quality adjusted life year associated with a mild stroke is 0.75 (O'Brien, 2005)

**Assumptions**

1. The early mortality (i.e up to two years) following stroke is in people who have moderate/severe strokes.
2. The mean survival of people with minor strokes is 6 years (which is the same survival as in people whose stroke was prevented)

**Calculation**

Note that in the model the major outcome is a major stroke. For the purposes of the model, this is defined as one that results in hospital admission.

1. Minor strokes: these comprise 34% of total strokes that lead to hospital admission. No loss of life expectancy, but a QALY loss of 0.25 per year for 6 years – i.e. 1.5 QALYs per minor stroke.
2. Moderate/severe strokes: these comprise 66% of total strokes. Loss of life expectancy is as shown below:

At 1 month: 26% mortality (17/66)
At 1 year: an additional 21% have died (14/66)
At two years: an additional 18% have died (12/66)
At three years: an additional 11% have died (7/66)
At four years: an additional 11% have died (7/66)
At five years: an additional 11% have died (7/66)
The remainder will die during the 6th year (with no loss of life expectancy).

From this, QALY losses for 100 moderate/severe strokes may be estimated as follows:

26: loss of 6 QALYs
21: loss of 5.61 QALYs (loss of 5 years of life, with 1 year with QALY of 0.39)
18: loss of 5.22 QALYs (loss of 4 years of life, with 2 years with QALY of 0.39)
11: loss of 4.83 QALYs (loss of 3 years of life, with 3 years with QALY of 0.39)
11: loss of 4.44 QALYs (loss of 2 years of life, with 4 years with QALY of 0.39)
11: loss of 4.05 QALYs (loss of 1 year of life, with 5 years with QALY of 0.39)
2: loss of 3.66 QALYs (no loss of life, with 6 years with QALY of 0.39)

**Table 5.13: Estimated QALY loss per stroke in the model**

| | Proportion of total | QALY loss | Weighted QALY loss |
|---|---|---|---|
| Minor strokes | 33.33% | 1.5 | 0.5 |
| Mod/ severe strokes | 17.33% | 6 | 1.04 |
| | 14.00% | 5.61 | 0.7854 |
| | 12.00% | 5.22 | 0.6264 |
| | 7.33% | 4.83 | 0.3542 |
| | 7.33% | 4.44 | 0.3256 |
| | 7.33% | 4.05 | 0.297 |
| | 1.33% | 3.66 | 0.0488 |
| | 100.00% | | 3.9774 |

This gives an estimated 4 QALY loss per stroke.

**Table 5.14: Complete results tables for all scenario and sensitivity analysis**

The following tables show the model outputs for the various scenarios considered in Chapter [model results]. Rows consisting entirely of zeroes have been omitted.
For each, a comparison of baseline care is made against different referral thresholds to a daily clinic

***Initial analysis***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4998 | 4997 | 4998 | 4999 | 4998 | 4997 | 4998 | 4998 | 4997 | 4997 |
| Genuine TIAs | 3504 | 3505 | 3504 | 3504 | 3504 | 3505 | 3503 | 3503 | 3504 | 3505 |
| Minor strokes | 1499 | 1498 | 1498 | 1498 | 1498 | 1499 | 1499 | 1499 | 1499 | 1498 |
| Ambulances 1 | 1716 | 1716 | 1716 | 1715 | 1716 | 1716 | 1716 | 1716 | 1716 | 1716 |
| Ambulances 2 | 169 | 168 | 161 | 155 | 151 | 148 | 151 | 150 | 151 | 138 |
| GP first surgeries | 8394 | 8393 | 8387 | 8382 | 8376 | 8374 | 8377 | 8377 | 8377 | 8365 |
| GP second surgeries | 1629 | 1609 | 1397 | 1152 | 935 | 743 | 368 | 36 | 0 | 0 |
| A&E doctors | 1872 | 1871 | 1864 | 1858 | 1854 | 1852 | 1854 | 1854 | 1854 | 1841 |
| Hospital specialists | 1370 | 1369 | 1364 | 1359 | 1356 | 1355 | 1356 | 1356 | 1356 | 1346 |
| Scheduled OP | 0 | 68 | 738 | 1475 | 2123 | 2679 | 3747 | 4682 | 4782 | 8337 |
| Repeat mimic | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 |
| Repeat TIA | 82 | 81 | 78 | 76 | 72 | 72 | 75 | 75 | 75 | 67 |
| Repeat minor stroke | 265 | 263 | 252 | 243 | 236 | 232 | 235 | 235 | 235 | 216 |
| Repeat major stroke | 341 | 339 | 323 | 312 | 302 | 297 | 298 | 298 | 298 | 272 |
| Days post maj strk | 97203 | 96425 | 92359 | 89256 | 86571 | 85204 | 85273 | 85162 | 85246 | 78283 |
| CE clinic assess | 898 | 943 | 1411 | 1937 | 2399 | 2740 | 2898 | 2942 | 2948 | 3439 |
| CE appointment ass | 517 | 510 | 440 | 359 | 289 | 229 | 113 | 11 | 0 | 0 |
| CE surgery | 181 | 185 | 235 | 293 | 344 | 380 | 386 | 378 | 378 | 441 |
| Stroke at CE | 3 | 3 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 7 |
| Stroke related death | 118 | 118 | 116 | 114 | 114 | 113 | 114 | 113 | 114 | 111 |
| Other cause death | 517 | 516 | 517 | 518 | 519 | 518 | 519 | 519 | 518 | 520 |
| Normal exit | 9021 | 9024 | 9040 | 9051 | 9060 | 9065 | 9063 | 9063 | 9063 | 9090 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 723 | 714 | 618 | 507 | 408 | 322 | 163 | 21 | 0 | 0 |
| Change no to dual | 773 | 797 | 1048 | 1345 | 1613 | 1815 | 1880 | 1873 | 1872 | 2188 |
| Chnge mono to dual | 607 | 628 | 839 | 1072 | 1275 | 1417 | 1448 | 1433 | 1433 | 1676 |
| Monotherapy weeks | 204786 | 203395 | 188292 | 170708 | 155084 | 143447 | 136229 | 132251 | 131204 | 117040 |
| Dual therapy weeks | 65836 | 67949 | 90209 | 116476 | 140104 | 157512 | 162510 | 161536 | 161463 | 189328 |
| Warfarin started | 612 | 615 | 639 | 662 | 681 | 688 | 609 | 525 | 522 | 599 |
| Warfarin weeks | 49560 | 49635 | 50953 | 52364 | 53577 | 54075 | 50596 | 46875 | 46712 | 50512 |
| Statin started | 1656 | 1690 | 2039 | 2433 | 2781 | 3024 | 3008 | 2900 | 2890 | 3368 |
| Statin weeks | 197864 | 199464 | 216226 | 235673 | 253059 | 265372 | 264401 | 259033 | 258477 | 282457 |
| Antihypertensive | | | | | | | | | | |
| Started | 4152 | 4158 | 4204 | 4240 | 4271 | 4216 | 3496 | 3222 | 3200 | 3714 |
| Weeks | 185556 | 186098 | 191004 | 195303 | 199160 | 198313 | 166462 | 154236 | 153226 | 178674 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Inpatient admission***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 5000 | 4997 | 5000 | 4998 | 4998 | 4996 | 4997 | 4997 | 4996 | 4998 |
| Genuine TIAs | 3502 | 3503 | 3502 | 3504 | 3504 | 3505 | 3504 | 3505 | 3506 | 3504 |
| Minor strokes | 1498 | 1499 | 1497 | 1498 | 1498 | 1499 | 1499 | 1498 | 1498 | 1497 |
| Ambulances 1 | 1717 | 1717 | 1715 | 1717 | 1715 | 1716 | 1716 | 1715 | 1716 | 1716 |
| Ambulances 2 | 164 | 162 | 153 | 146 | 141 | 139 | 140 | 140 | 141 | 127 |
| GP first surgeries | 8390 | 8388 | 8383 | 8374 | 8370 | 8367 | 8371 | 8371 | 8371 | 8357 |
| GP second surgeries | 1628 | 1608 | 1396 | 1154 | 934 | 744 | 368 | 36 | 0 | 0 |
| A&E doctors | 1868 | 1866 | 1856 | 1851 | 1844 | 1842 | 1844 | 1843 | 1844 | 1831 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Hospital specialists | 1367 | 1366 | 1358 | 1353 | 1348 | 1347 | 1348 | 1347 | 1349 | 1338 |
| Scheduled OP | 0 | 68 | 735 | 1470 | 2118 | 2674 | 3743 | 4677 | 4777 | 8329 |
| Thrombolysis | 19 | 20 | 27 | 32 | 37 | 37 | 37 | 37 | 37 | 40 |
| Repeat mimic | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 |
| Repeat TIA | 81 | 81 | 78 | 75 | 72 | 71 | 74 | 74 | 75 | 67 |
| Repeat minor stroke | 263 | 261 | 250 | 240 | 234 | 231 | 233 | 233 | 234 | 213 |
| Repeat major stroke | 339 | 337 | 321 | 309 | 299 | 296 | 296 | 296 | 296 | 269 |
| Days post maj strk | 96442 | 96103 | 91803 | 88522 | 85873 | 84771 | 84610 | 84596 | 84479 | 77686 |
| CE clinic assess | 898 | 943 | 1411 | 1936 | 2399 | 2738 | 2900 | 2941 | 2948 | 3436 |
| CE appointment ass | 517 | 511 | 440 | 360 | 289 | 228 | 113 | 11 | 0 | 0 |
| CE surgery | 180 | 184 | 236 | 292 | 343 | 379 | 385 | 377 | 377 | 439 |
| Stroke at CE | 3 | 3 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 7 |
| Stroke related death | 117 | 117 | 115 | 113 | 113 | 112 | 113 | 112 | 112 | 110 |
| Other cause death | 516 | 516 | 516 | 518 | 518 | 518 | 518 | 517 | 518 | 519 |
| Normal exit | 9017 | 9018 | 9033 | 9042 | 9048 | 9053 | 9052 | 9054 | 9053 | 9078 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 723 | 714 | 618 | 508 | 408 | 321 | 163 | 21 | 0 | 0 |
| Change no to dual | 773 | 797 | 1048 | 1343 | 1613 | 1815 | 1881 | 1874 | 1872 | 2187 |
| Chnge mono to dual | 607 | 627 | 839 | 1072 | 1274 | 1418 | 1447 | 1432 | 1433 | 1675 |
| Monotherapy weeks | 204816 | 203332 | 188248 | 170612 | 155068 | 143331 | 136199 | 132263 | 131158 | 117061 |
| Dual therapy weeks | 65706 | 67771 | 90002 | 116143 | 139789 | 157219 | 162180 | 161196 | 161183 | 188963 |
| Warfarin started | 612 | 616 | 639 | 664 | 681 | 688 | 610 | 526 | 523 | 600 |
| Warfarin weeks | 49419 | 49578 | 50782 | 52201 | 53279 | 53763 | 50343 | 46638 | 46470 | 50208 |
| Statin started | 1655 | 1689 | 2038 | 2434 | 2780 | 3025 | 3008 | 2901 | 2892 | 3367 |
| Statin weeks | 197594 | 199073 | 215830 | 235224 | 252508 | 264723 | 263923 | 258437 | 258020 | 281839 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Antihypertensive | | | | | | | | | | |
| Started | 4151 | 4157 | 4203 | 4241 | 4273 | 4219 | 3497 | 3222 | 3202 | 3712 |
| Weeks | 185302 | 185797 | 190603 | 194806 | 198682 | 197849 | 165924 | 153647 | 152756 | 177989 |
| IP admissions | 1184 | 1251 | 1909 | 2640 | 3284 | 3283 | 3284 | 3284 | 3286 | 3788 |
| Inpatient days | 4072 | 4323 | 6817 | 9587 | 12024 | 12016 | 12013 | 12003 | 12010 | 13881 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Twice weekly flexible outpatient appointment system for rapid access outpatient clinic***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4996 | 4998 | 4998 | 4999 | 4997 | 4997 | 5001 | 4997 | 4998 | 4999 |
| Genuine TIAs | 3505 | 3504 | 3504 | 3504 | 3503 | 3504 | 3501 | 3504 | 3503 | 3502 |
| Minor strokes | 1499 | 1498 | 1499 | 1498 | 1500 | 1499 | 1498 | 1499 | 1499 | 1499 |
| Ambulances 1 | 1715 | 1716 | 1717 | 1715 | 1716 | 1716 | 1716 | 1715 | 1715 | 1714 |
| Ambulances 2 | 169 | 168 | 162 | 157 | 153 | 152 | 154 | 154 | 154 | 144 |
| GP first surgeries | 8394 | 8393 | 8387 | 8383 | 8377 | 8375 | 8378 | 8379 | 8379 | 8370 |
| GP second surgeries | 1629 | 1609 | 1396 | 1153 | 935 | 744 | 369 | 36 | 0 | 0 |
| A&E doctors | 1871 | 1871 | 1866 | 1860 | 1856 | 1855 | 1857 | 1857 | 1857 | 1846 |
| Hospital specialists | 1369 | 1369 | 1365 | 1361 | 1358 | 1357 | 1358 | 1358 | 1358 | 1351 |
| Scheduled OP | 0 | 67 | 730 | 1460 | 2104 | 2659 | 3720 | 4638 | 4731 | 6195 |
| Overflow OP | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 18 | 22 | 2082 |
| Repeat mimic | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 59 |
| Repeat TIA | 82 | 81 | 78 | 76 | 72 | 72 | 74 | 75 | 74 | 67 |
| Repeat minor stroke | 265 | 263 | 253 | 246 | 240 | 238 | 240 | 241 | 241 | 226 |
| Repeat major stroke | 342 | 339 | 325 | 316 | 308 | 305 | 305 | 307 | 307 | 288 |
| Days post maj strk | 97231 | 96762 | 93066 | 90738 | 88666 | 87734 | 87861 | 88206 | 88245 | 84276 |
| CE clinic assess | 897 | 942 | 1406 | 1928 | 2387 | 2727 | 2883 | 2927 | 2931 | 3408 |
| CE appointment ass | 518 | 510 | 439 | 359 | 289 | 229 | 113 | 11 | 0 | 0 |
| CE surgery | 181 | 185 | 236 | 292 | 343 | 379 | 385 | 377 | 376 | 438 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Stroke at CE | 3 | 3 | 4 | 5 | 6 | 6 | 7 | 6 | 6 | 7 |
| Stroke related death | 118 | 117 | 116 | 114 | 114 | 114 | 114 | 114 | 114 | 112 |
| Other cause death | 517 | 516 | 518 | 518 | 519 | 518 | 518 | 517 | 517 | 519 |
| Normal exit | 9020 | 9024 | 9037 | 9047 | 9054 | 9057 | 9056 | 9056 | 9056 | 9074 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 723 | 712 | 618 | 507 | 408 | 321 | 164 | 21 | 0 | 0 |
| Change no to dual | 773 | 797 | 1046 | 1342 | 1608 | 1811 | 1873 | 1866 | 1863 | 2172 |
| Chnge mono to dual | 606 | 627 | 838 | 1068 | 1272 | 1412 | 1443 | 1430 | 1429 | 1668 |
| Monotherapy weeks | 204894 | 203428 | 188287 | 170822 | 155358 | 143669 | 136614 | 132648 | 131720 | 117978 |
| Dual therapy weeks | 65788 | 67881 | 89980 | 116027 | 139525 | 156789 | 161572 | 160619 | 160370 | 186979 |
| Warfarin started | 612 | 615 | 637 | 658 | 677 | 683 | 603 | 518 | 515 | 586 |
| Warfarin weeks | 49514 | 49694 | 50976 | 52280 | 53425 | 53911 | 50370 | 46566 | 46469 | 49838 |
| Statin started | 1655 | 1688 | 2036 | 2426 | 2771 | 3015 | 2994 | 2887 | 2874 | 3339 |
| Statin weeks | 197807 | 199364 | 215950 | 235153 | 252415 | 264558 | 263451 | 258021 | 257374 | 279976 |
| Antihypertensive | | | | | | | | | | |
| Started | 4152 | 4158 | 4198 | 4231 | 4260 | 4202 | 3478 | 3204 | 3181 | 3673 |
| Weeks | 185557 | 186115 | 190702 | 194822 | 198569 | 197483 | 165432 | 153124 | 152085 | 175931 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Twice weekly fixed appointment system for rapid access outpatient clinic***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4996 | 4998 | 4998 | 4999 | 4998 | 4998 | 4996 | 4998 | 4998 | 4998 |
| Genuine TIAs | 3505 | 3504 | 3504 | 3504 | 3504 | 3504 | 3506 | 3504 | 3503 | 3504 |
| Minor strokes | 1499 | 1498 | 1499 | 1498 | 1498 | 1498 | 1498 | 1497 | 1499 | 1498 |
| Ambulances 1 | 1715 | 1716 | 1717 | 1715 | 1716 | 1716 | 1717 | 1715 | 1716 | 1716 |
| Ambulances 2 | 169 | 168 | 162 | 157 | 153 | 151 | 153 | 154 | 154 | 203 |
| GP first surgeries | 8394 | 8393 | 8387 | 8383 | 8377 | 8375 | 8377 | 8380 | 8379 | 8426 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| GP second surgeries | 1629 | 1609 | 1396 | 1153 | 935 | 744 | 368 | 36 | 0 | 0 |
| A&E doctors | 1871 | 1871 | 1866 | 1860 | 1856 | 1855 | 1858 | 1856 | 1857 | 1905 |
| Hospital specialists | 1369 | 1369 | 1365 | 1361 | 1358 | 1356 | 1359 | 1357 | 1358 | 1396 |
| Scheduled OP | 0 | 67 | 730 | 1460 | 2104 | 2657 | 3724 | 4654 | 4753 | 1487 |
| Repeat mimic | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 59 | 57 |
| Repeat TIA | 82 | 81 | 78 | 76 | 73 | 71 | 74 | 75 | 75 | 102 |
| Repeat minor stroke | 265 | 263 | 253 | 246 | 239 | 237 | 240 | 240 | 240 | 318 |
| Repeat major stroke | 342 | 339 | 325 | 316 | 307 | 304 | 305 | 307 | 307 | 412 |
| Days post maj strk | 97231 | 96762 | 93066 | 90738 | 88522 | 87580 | 87764 | 88246 | 88195 | 115362 |
| CE clinic assess | 897 | 942 | 1406 | 1928 | 2388 | 2726 | 2886 | 2928 | 2930 | 1482 |
| CE appointment ass | 518 | 510 | 439 | 359 | 289 | 229 | 113 | 11 | 0 | 0 |
| CE surgery | 181 | 185 | 236 | 292 | 343 | 379 | 385 | 376 | 377 | 182 |
| Stroke at CE | 3 | 3 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 3 |
| Stroke related death | 118 | 117 | 116 | 114 | 114 | 114 | 114 | 114 | 114 | 124 |
| Other cause death | 517 | 516 | 518 | 518 | 518 | 518 | 518 | 518 | 518 | 513 |
| Normal exit | 9020 | 9024 | 9037 | 9047 | 9055 | 9058 | 9056 | 9055 | 9054 | 8949 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 723 | 712 | 618 | 507 | 408 | 322 | 163 | 21 | 0 | 0 |
| Change no to dual | 773 | 797 | 1046 | 1342 | 1609 | 1810 | 1876 | 1866 | 1864 | 858 |
| Chnge mono to dual | 606 | 627 | 838 | 1068 | 1272 | 1411 | 1444 | 1429 | 1428 | 657 |
| Monotherapy weeks | 204894 | 203428 | 188287 | 170822 | 155261 | 143719 | 136571 | 132621 | 131734 | 184671 |
| Dual therapy weeks | 65788 | 67881 | 89980 | 116027 | 139569 | 156717 | 161785 | 160543 | 160338 | 56724 |
| Warfarin started | 612 | 615 | 637 | 658 | 677 | 683 | 603 | 519 | 515 | 247 |
| Warfarin weeks | 49514 | 49694 | 50976 | 52280 | 53380 | 53883 | 50354 | 46556 | 46487 | 31892 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Statin started | 1655 | 1688 | 2036 | 2426 | 2770 | 3012 | 2997 | 2886 | 2875 | 1332 |
| Statin weeks | 197807 | 199364 | 215950 | 235153 | 252432 | 264526 | 263645 | 257935 | 257355 | 167685 |
| Antihypertensive | | | | | | | | | | |
| Started | 4152 | 4158 | 4198 | 4231 | 4259 | 4202 | 3480 | 3203 | 3180 | 1508 |
| Weeks | 185557 | 186115 | 190702 | 194822 | 198503 | 197469 | 165574 | 153078 | 151974 | 56543 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Once weekly fixed appointment system for rapid access outpatient clinic***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4996 | 4998 | 4995 | 4996 | 4997 | 4995 | 4996 | 4997 | 4997 | 4997 |
| Genuine TIAs | 3505 | 3505 | 3506 | 3505 | 3504 | 3507 | 3504 | 3504 | 3504 | 3505 |
| Minor strokes | 1499 | 1498 | 1499 | 1499 | 1498 | 1498 | 1500 | 1498 | 1498 | 1498 |
| Ambulances 1 | 1715 | 1716 | 1717 | 1717 | 1716 | 1716 | 1716 | 1717 | 1717 | 1715 |
| Ambulances 2 | 169 | 168 | 162 | 158 | 154 | 155 | 202 | 206 | 206 | 207 |
| GP first surgeries | 8394 | 8392 | 8386 | 8382 | 8378 | 8378 | 8423 | 8427 | 8428 | 8432 |
| GP second surgeries | 1629 | 1609 | 1398 | 1153 | 935 | 743 | 369 | 36 | 0 | 0 |
| A&E doctors | 1871 | 1871 | 1867 | 1863 | 1857 | 1858 | 1905 | 1909 | 1909 | 1908 |
| Hospital specialists | 1369 | 1370 | 1367 | 1363 | 1359 | 1359 | 1396 | 1399 | 1399 | 1398 |
| Scheduled OP | 0 | 66 | 724 | 1451 | 2087 | 2627 | 1253 | 405 | 364 | 0 |
| Repeat mimic | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 |
| Repeat TIA | 82 | 81 | 78 | 76 | 72 | 72 | 100 | 103 | 104 | 104 |
| Repeat minor stroke | 265 | 263 | 255 | 248 | 242 | 244 | 316 | 321 | 321 | 323 |
| Repeat major stroke | 342 | 340 | 328 | 320 | 312 | 314 | 408 | 415 | 416 | 416 |
| Days post maj strk | 97231 | 96734 | 93867 | 92034 | 90153 | 91221 | 114760 | 115738 | 115787 | 115725 |
| CE clinic assess | 897 | 942 | 1404 | 1923 | 2378 | 2707 | 1634 | 1223 | 1205 | 1035 |
| CE appointment ass | 518 | 511 | 439 | 358 | 289 | 229 | 112 | 11 | 0 | 0 |
| CE surgery | 181 | 185 | 235 | 293 | 342 | 376 | 215 | 153 | 150 | 130 |
| Stroke at CE | 3 | 3 | 4 | 5 | 6 | 6 | 4 | 2 | 2 | 2 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Stroke related death | 118 | 117 | 115 | 114 | 114 | 114 | 123 | 124 | 124 | 124 |
| Other cause death | 517 | 517 | 517 | 518 | 518 | 517 | 514 | 513 | 513 | 513 |
| Normal exit | 9020 | 9023 | 9035 | 9043 | 9050 | 9048 | 8952 | 8946 | 8945 | 8945 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 723 | 713 | 617 | 506 | 407 | 322 | 164 | 21 | 0 | 0 |
| Change no to dual | 773 | 797 | 1046 | 1339 | 1604 | 1801 | 1055 | 694 | 673 | 572 |
| Chnge mono to dual | 606 | 628 | 838 | 1069 | 1269 | 1406 | 809 | 527 | 515 | 437 |
| Monotherapy weeks | 204894 | 203314 | 188354 | 170933 | 155605 | 144404 | 184574 | 188622 | 188057 | 189192 |
| Dual therapy weeks | 65788 | 67895 | 89913 | 115688 | 138809 | 155015 | 68161 | 51048 | 50142 | 47861 |
| Warfarin started | 612 | 613 | 635 | 656 | 672 | 676 | 375 | 215 | 208 | 188 |
| Warfarin weeks | 49514 | 49627 | 50821 | 52112 | 53157 | 53511 | 37033 | 31305 | 31063 | 30814 |
| Statin started | 1655 | 1690 | 2033 | 2421 | 2763 | 2997 | 1725 | 1094 | 1056 | 908 |
| Statin weeks | 197807 | 199330 | 215802 | 234878 | 251625 | 262885 | 182354 | 163390 | 162151 | 160231 |
| Antihypertensive | | | | | | | | | | |
| Started | 4152 | 4156 | 4196 | 4225 | 4248 | 4183 | 2082 | 1263 | 1216 | 1059 |
| Weeks | 185557 | 185999 | 190509 | 194366 | 197672 | 195713 | 78190 | 52249 | 50680 | 48678 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Greater use of 999 service***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4998 | 4995 | 4997 | 4999 | 4997 | 4998 | 4997 | 4998 | 4998 | 4996 |
| Genuine TIAs | 3504 | 3506 | 3505 | 3503 | 3505 | 3504 | 3505 | 3504 | 3504 | 3505 |
| Minor strokes | 1498 | 1498 | 1499 | 1499 | 1498 | 1497 | 1498 | 1499 | 1498 | 1499 |
| Ambulances 1 | 2438 | 2441 | 2440 | 2441 | 2441 | 2441 | 2442 | 2441 | 2440 | 2441 |
| Ambulances 2 | 219 | 218 | 211 | 205 | 198 | 196 | 200 | 199 | 199 | 184 |
| GP first surgeries | 7644 | 7640 | 7639 | 7634 | 7631 | 7630 | 7631 | 7632 | 7633 | 7625 |
| GP second | 1456 | 1441 | 1296 | 1092 | 892 | 712 | 353 | 35 | 0 | 0 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| surgeries | | | | | | | | | | |
| A&E doctors | 2640 | 2642 | 2634 | 2629 | 2622 | 2620 | 2624 | 2623 | 2623 | 2608 |
| Hospital specialists | 1902 | 1904 | 1898 | 1894 | 1888 | 1887 | 1890 | 1888 | 1888 | 1877 |
| Scheduled OP | 0 | 45 | 509 | 1124 | 1726 | 2248 | 3271 | 4165 | 4262 | 7592 |
| Repeat mimic | 58 | 58 | 58 | 58 | 59 | 58 | 58 | 58 | 58 | 59 |
| Repeat TIA | 81 | 81 | 78 | 75 | 73 | 72 | 75 | 75 | 75 | 69 |
| Repeat minor stroke | 257 | 256 | 248 | 240 | 233 | 230 | 233 | 233 | 233 | 216 |
| Repeat major stroke | 331 | 329 | 318 | 307 | 298 | 294 | 295 | 294 | 294 | 272 |
| Days post maj strk | 94007 | 93491 | 90490 | 87722 | 85280 | 84226 | 84057 | 83862 | 83577 | 78065 |
| CE clinic assess | 1218 | 1250 | 1573 | 2011 | 2437 | 2755 | 2908 | 2950 | 2955 | 3372 |
| CE appointment ass | 462 | 456 | 408 | 341 | 276 | 219 | 108 | 10 | 0 | 0 |
| CE surgery | 214 | 217 | 252 | 300 | 346 | 382 | 386 | 379 | 378 | 432 |
| Stroke at CE | 4 | 4 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 7 |
| Stroke related death | 116 | 116 | 115 | 114 | 113 | 114 | 114 | 114 | 113 | 112 |
| Other cause death | 518 | 516 | 518 | 518 | 519 | 519 | 519 | 519 | 519 | 521 |
| Normal exit | 9031 | 9035 | 9045 | 9056 | 9063 | 9067 | 9066 | 9066 | 9067 | 9087 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 646 | 640 | 572 | 480 | 389 | 308 | 156 | 20 | 0 | 0 |
| Change no to dual | 949 | 967 | 1140 | 1386 | 1631 | 1820 | 1883 | 1876 | 1875 | 2144 |
| Chnge mono to dual | 744 | 759 | 905 | 1100 | 1287 | 1418 | 1449 | 1435 | 1436 | 1642 |
| Monotherapy weeks | 194365 | 193396 | 182849 | 168136 | 153731 | 142819 | 135879 | 132010 | 131207 | 119010 |
| Dual therapy weeks | 81046 | 82587 | 98032 | 119970 | 141707 | 157890 | 162772 | 161809 | 161826 | 185598 |
| Warfarin started | 624 | 626 | 641 | 661 | 679 | 684 | 609 | 529 | 524 | 591 |
| Warfarin weeks | 50158 | 50288 | 51123 | 52320 | 53433 | 53889 | 50575 | 46978 | 46806 | 50047 |
| Statin started | 1885 | 1910 | 2150 | 2478 | 2798 | 3027 | 3011 | 2907 | 2896 | 3304 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Statin weeks | 208871 | 210068 | 221658 | 237903 | 253986 | 265352 | 264532 | 259437 | 258876 | 279301 |
| Antihypertensive | | | | | | | | | | |
| Started | 4142 | 4147 | 4178 | 4206 | 4236 | 4182 | 3493 | 3229 | 3208 | 3644 |
| Weeks | 186715 | 187147 | 190533 | 194129 | 197754 | 196810 | 166348 | 154522 | 153548 | 175231 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Optimal GP management***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4999 | 4998 | 4999 | 4995 | 4996 | 4998 | 4997 | 4998 | 4996 | 4996 |
| Genuine TIAs | 3504 | 3504 | 3502 | 3506 | 3505 | 3503 | 3504 | 3503 | 3504 | 3506 |
| Minor strokes | 1497 | 1498 | 1498 | 1499 | 1499 | 1499 | 1499 | 1498 | 1499 | 1498 |
| Ambulances 1 | 1715 | 1716 | 1716 | 1716 | 1717 | 1717 | 1716 | 1717 | 1716 | 1717 |
| Ambulances 2 | 144 | 144 | 144 | 145 | 145 | 146 | 150 | 151 | 151 | 138 |
| GP first surgeries | 8371 | 8370 | 8370 | 8370 | 8369 | 8370 | 8377 | 8376 | 8378 | 8364 |
| A&E doctors | 1847 | 1847 | 1848 | 1848 | 1849 | 1850 | 1854 | 1855 | 1854 | 1843 |
| Hospital specialists | 1350 | 1351 | 1351 | 1352 | 1352 | 1353 | 1355 | 1356 | 1356 | 1347 |
| Scheduled OP | 0 | 67 | 731 | 1469 | 2120 | 2674 | 3747 | 4681 | 4783 | 8336 |
| Repeat mimic | 59 | 58 | 59 | 59 | 58 | 58 | 59 | 58 | 59 | 58 |
| Repeat TIA | 69 | 69 | 69 | 69 | 68 | 70 | 74 | 75 | 75 | 67 |
| Repeat minor stroke | 225 | 225 | 226 | 227 | 227 | 229 | 235 | 235 | 236 | 216 |
| Repeat major stroke | 290 | 291 | 291 | 293 | 293 | 294 | 297 | 298 | 298 | 272 |
| Days post maj strk | 82906 | 83169 | 83411 | 83905 | 84080 | 84395 | 84993 | 85344 | 85318 | 78266 |
| CE clinic assess | 868 | 915 | 1381 | 1915 | 2387 | 2730 | 2898 | 2941 | 2948 | 3440 |
| CE appointment ass | 3422 | 3378 | 2920 | 2391 | 1924 | 1522 | 749 | 72 | 0 | 0 |
| CE surgery | 553 | 554 | 556 | 555 | 555 | 549 | 468 | 385 | 377 | 442 |
| Stroke at CE | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 7 | 6 | 7 |
| Stroke related death | 113 | 114 | 114 | 113 | 113 | 114 | 114 | 114 | 114 | 111 |
| Other cause death | 519 | 519 | 518 | 519 | 519 | 518 | 519 | 518 | 518 | 520 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Normal exit | 9069 | 9067 | 9067 | 9066 | 9066 | 9065 | 9062 | 9063 | 9063 | 9090 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to dual | 2811 | 2810 | 2798 | 2789 | 2778 | 2735 | 2352 | 1935 | 1872 | 2188 |
| Chnge mono to dual | 2163 | 2164 | 2153 | 2142 | 2136 | 2097 | 1776 | 1457 | 1432 | 1676 |
| Monotherapy weeks | 89532 | 89564 | 89536 | 89623 | 89620 | 91517 | 110801 | 130000 | 131244 | 117053 |
| Dual therapy weeks | 245343 | 245322 | 244408 | 243477 | 242747 | 238663 | 203117 | 165967 | 161452 | 189330 |
| Warfarin started | 650 | 651 | 667 | 683 | 697 | 700 | 614 | 525 | 522 | 600 |
| Warfarin weeks | 53329 | 53368 | 54103 | 54920 | 55646 | 55746 | 51319 | 46858 | 46705 | 50523 |
| Statin started | 4244 | 4245 | 4240 | 4238 | 4238 | 4178 | 3578 | 2955 | 2890 | 3370 |
| Statin weeks | 326913 | 326899 | 326652 | 326594 | 326532 | 323556 | 293289 | 261903 | 258488 | 282515 |
| Antihypertensive | | | | | | | | | | |
| Started | 4374 | 4377 | 4371 | 4368 | 4366 | 4284 | 3515 | 3223 | 3200 | 3714 |
| Weeks | 212442 | 212547 | 212350 | 212313 | 212260 | 208084 | 169206 | 154425 | 153219 | 178693 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Improved GP diagnosis***

Sensitivity 90% specificity 80%

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4998 | 4998 | 4996 | 4998 | 4997 | 4997 | 4998 | 4998 | 4999 | 4999 |
| Genuine TIAs | 3504 | 3504 | 3504 | 3505 | 3506 | 3506 | 3503 | 3504 | 3503 | 3503 |
| Minor strokes | 1498 | 1498 | 1500 | 1497 | 1498 | 1498 | 1498 | 1498 | 1498 | 1498 |
| Ambulances 1 | 2439 | 2440 | 2441 | 2441 | 2440 | 2439 | 2440 | 2440 | 2440 | 2439 |
| Ambulances 2 | 211 | 210 | 203 | 195 | 189 | 185 | 186 | 186 | 185 | 179 |
| GP first surgeries | 7640 | 7638 | 7635 | 7631 | 7627 | 7628 | 7627 | 7627 | 7627 | 7624 |
| GP second surgeries | 1233 | 1219 | 1056 | 826 | 600 | 415 | 191 | 19 | 0 | 0 |
| A&E doctors | 2633 | 2634 | 2627 | 2619 | 2613 | 2608 | 2609 | 2609 | 2608 | 2602 |
| Hospital specialists | 2007 | 2008 | 2003 | 1995 | 1989 | 1984 | 1986 | 1985 | 1986 | 1980 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Scheduled OP | 0 | 50 | 572 | 1263 | 1937 | 2478 | 3117 | 3601 | 3653 | 7591 |
| Repeat mimic | 59 | 58 | 58 | 59 | 59 | 59 | 59 | 58 | 58 | 59 |
| Repeat TIA | 80 | 79 | 77 | 73 | 70 | 69 | 70 | 70 | 70 | 67 |
| Repeat minor stroke | 247 | 245 | 238 | 228 | 221 | 217 | 217 | 217 | 217 | 209 |
| Repeat major stroke | 315 | 313 | 301 | 290 | 280 | 274 | 274 | 274 | 274 | 263 |
| Days post maj strk | 89691 | 89159 | 85998 | 82863 | 80162 | 78648 | 78479 | 78326 | 78243 | 75624 |
| CE clinic assess | 1362 | 1396 | 1758 | 2247 | 2724 | 3082 | 3251 | 3300 | 3304 | 3511 |
| CE appointment ass | 395 | 390 | 334 | 259 | 186 | 128 | 58 | 6 | 0 | 0 |
| CE surgery | 224 | 228 | 266 | 319 | 371 | 411 | 425 | 424 | 423 | 451 |
| Stroke at CE | 4 | 4 | 4 | 6 | 6 | 7 | 7 | 7 | 7 | 8 |
| Stroke related death | 115 | 114 | 113 | 112 | 111 | 111 | 112 | 111 | 111 | 110 |
| Other cause death | 518 | 517 | 519 | 519 | 520 | 520 | 520 | 521 | 520 | 520 |
| Normal exit | 9049 | 9052 | 9063 | 9073 | 9082 | 9087 | 9087 | 9088 | 9088 | 9099 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to mono | 555 | 548 | 473 | 370 | 268 | 183 | 86 | 11 | 0 | 0 |
| Change no to dual | 1011 | 1031 | 1224 | 1499 | 1773 | 1989 | 2080 | 2095 | 2096 | 2230 |
| Chnge mono to dual | 794 | 809 | 974 | 1191 | 1401 | 1551 | 1604 | 1606 | 1608 | 1709 |
| Monotherapy weeks | 188667 | 187487 | 175779 | 159324 | 143213 | 131045 | 124497 | 121722 | 121119 | 115086 |
| Dual therapy weeks | 86449 | 88065 | 105462 | 129957 | 154343 | 172888 | 180215 | 181249 | 181363 | 193108 |
| Warfarin started | 587 | 589 | 606 | 627 | 648 | 658 | 624 | 584 | 583 | 615 |
| Warfarin weeks | 48474 | 48593 | 49556 | 50855 | 52114 | 52843 | 51366 | 49590 | 49591 | 51184 |
| Statin started | 1928 | 1953 | 2224 | 2589 | 2946 | 3210 | 3272 | 3240 | 3237 | 3439 |
| Statin weeks | 210700 | 211935 | 225071 | 243095 | 261162 | 274424 | 277536 | 275933 | 275750 | 285923 |
| Antihypertensive | | | | | | | | | | |
| Started | 3974 | 3980 | 4014 | 4048 | 4080 | 4062 | 3723 | 3592 | 3582 | 3794 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Weeks | 179421 | 179933 | 183671 | 187752 | 191819 | 192746 | 178135 | 172393 | 171959 | 182512 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

***Improved GP management and diagnosis***

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| TIA mimics | 4996 | 4998 | 4997 | 4999 | 4998 | 5000 | 4995 | 4998 | 4997 | 4998 |
| Genuine TIAs | 3505 | 3504 | 3504 | 3503 | 3505 | 3501 | 3506 | 3504 | 3504 | 3504 |
| Minor strokes | 1499 | 1498 | 1500 | 1498 | 1497 | 1499 | 1498 | 1498 | 1499 | 1498 |
| Ambulances 1 | 1716 | 1716 | 1716 | 1715 | 1716 | 1715 | 1717 | 1717 | 1716 | 1715 |
| Ambulances 2 | 137 | 137 | 137 | 137 | 138 | 138 | 141 | 140 | 141 | 134 |
| GP first surgeries | 8365 | 8365 | 8365 | 8365 | 8365 | 8366 | 8368 | 8367 | 8368 | 8362 |
| GP second surgeries | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| A&E doctors | 1841 | 1841 | 1842 | 1841 | 1841 | 1842 | 1845 | 1845 | 1844 | 1838 |
| Hospital specialists | 1439 | 1437 | 1438 | 1438 | 1439 | 1439 | 1441 | 1441 | 1442 | 1436 |
| Scheduled OP | 0 | 75 | 820 | 1648 | 2379 | 2952 | 3626 | 4128 | 4184 | 8335 |
| Repeat mimic | 59 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 | 58 |
| Repeat TIA | 68 | 68 | 68 | 67 | 67 | 68 | 70 | 70 | 70 | 66 |
| Repeat minor stroke | 214 | 215 | 215 | 215 | 216 | 217 | 220 | 219 | 220 | 210 |
| Repeat major stroke | 272 | 272 | 273 | 274 | 275 | 276 | 277 | 278 | 278 | 265 |
| Days post maj strk | 77907 | 77808 | 78250 | 78701 | 78980 | 79342 | 79721 | 79910 | 79877 | 76385 |
| CE clinic assess | 971 | 1020 | 1543 | 2139 | 2670 | 3058 | 3242 | 3290 | 3296 | 3539 |
| CE appointment ass | 2987 | 2936 | 2425 | 1830 | 1304 | 890 | 406 | 40 | 0 | 0 |
| CE surgery | 510 | 510 | 510 | 511 | 510 | 507 | 467 | 426 | 423 | 453 |
| Stroke at CE | 9 | 9 | 9 | 9 | 9 | 8 | 8 | 7 | 7 | 8 |
| Stroke related death | 112 | 111 | 111 | 111 | 111 | 111 | 111 | 111 | 111 | 110 |

| | | Referral threshold ABCD$^2$ score | | | | | | | | Refer all |
|---|---|---|---|---|---|---|---|---|---|---|
| Per 10000 patients | Baseline | 7 | 6 | 5 | 4 | 3 | 2 | 1 | 0 | Cases* |
| Other cause death | 519 | 519 | 520 | 520 | 519 | 519 | 519 | 519 | 519 | 522 |
| Normal exit | 9088 | 9089 | 9088 | 9086 | 9087 | 9085 | 9084 | 9085 | 9084 | 9096 |
| Antiplatelet therapy | | | | | | | | | | |
| Change no to dual | 2592 | 2589 | 2577 | 2563 | 2554 | 2527 | 2335 | 2124 | 2095 | 2251 |
| Chnge mono to dual | 1993 | 1992 | 1982 | 1970 | 1961 | 1940 | 1779 | 1618 | 1604 | 1725 |
| Monotherapy weeks | 100324 | 100345 | 100381 | 100391 | 100462 | 101429 | 110941 | 120649 | 121262 | 114246 |
| Dual therapy weeks | 225200 | 225054 | 224173 | 223023 | 222231 | 219802 | 202039 | 183275 | 181023 | 194862 |
| Warfarin started | 606 | 607 | 623 | 641 | 656 | 663 | 624 | 580 | 579 | 616 |
| Warfarin weeks | 50911 | 50934 | 51714 | 52641 | 53405 | 53705 | 51684 | 49520 | 49427 | 51324 |
| Statin started | 3914 | 3913 | 3910 | 3906 | 3904 | 3872 | 3576 | 3262 | 3230 | 3466 |
| Statin weeks | 309947 | 309827 | 309758 | 309465 | 309466 | 307882 | 292918 | 277081 | 275408 | 287270 |
| Antihypertensive | | | | | | | | | | |
| Started | 4169 | 4167 | 4164 | 4158 | 4155 | 4114 | 3731 | 3583 | 3571 | 3825 |
| Weeks | 201464 | 201380 | 201296 | 201083 | 201039 | 198881 | 179588 | 172086 | 171467 | 184057 |

* This refers to a strategy where the GP refers all suspect TIAs to outpatient clinic

# 6: Discussion

## *6.1 Summary of findings of model*

In this model, we explored the likely outcome of different patterns of service provision for people presenting with TIA or minor stroke in a population of 500,000. Our initial analysis suggested that it would be cost effective to introduce daily specialist rapid access clinics as compared to current practice. If a referral threshold were set at an ABCD2 score of 4 or more for this service, then the additional cost per annum would be of the order of £108,500 per annum compared to current practice and result in the prevention of 4 major strokes per annum. The strategy that would be most effective would be to refer all suspect cases. This would prevent 7 major strokes per annum. The incremental cost effectiveness ratio of moving from referring patients with an ABCD2 score of 4 or more to referring all suspected cases is £50,000 per major stroke averted. The number of patients seen per week in the rapid access clinic would rise from 4 to 16 per week.

If patients with an ABCD2 score of 4 or more were admitted to hospital, this made referral strategies more expensive, with referral at an ABCD2 of 6 or more or refer all suspect cases the only potentially cost effective options, though the ICER of the latter at £69,000 per stroke prevented is at the borderline of what would be considered value for money. When admission to hospital was compared to a strategy of non-admission, then it became apparent that this strategy was not cost effective, with the ICER rising to over £1,000,000 per stroke prevented.

With regard to different patterns of clinic provision, we found that daily clinics were the most effective and the most cost effective. Twice weekly clinics were effective with an ICER of £44,000 per major stroke prevented at a referral threshold of ABCD2 of 4 or more, but not at lower thresholds. How clinics were costed was crucial to determining cost-effectiveness. If unused clinic slots were costed, then the only cost effective option for twice weekly clinics that are flexible becomes seeing all suspected cases (with an ICER of £51,000 per stroke prevented) to ensure minimal wastage of capacity. However, this would require on average an additional 4 appointments per week above the scheduled appointments to avoid waiting lists developing. If the twice weekly clinics are of fixed capacity and unused slots are costed, then a referral threshold of 3 is the only potentially cost effective option with an ICER of £57,000 per stroke prevented. A weekly clinic is the least effective option, but would be cost effective at an ABCD2 referral threshold of 4 or more.

We explored the impact of greater use of emergency services, and found that our initial conclusions still applied – namely that it would be cost effective to refer patients to a daily rapid access clinic at different referral thresholds down to an ABCD2 score of 4, or to refer all suspected cases. Comparing greater use with current use, we found that current use (for the management of TIA and minor stroke) was the more cost effective.

If GPs treated patients optimally, then the most cost effective option is for all suspected patients to be referred to a rapid access clinic. If GPs are better diagnostically, but do not change their management, then a referral threshold of ABCD2 score of 3 or 4 appears the most effective option that is still cost effective. If GPs treated patients optimally and were better diagnostically, then there would be no need for specialist rapid access clinics.

## 6.2 Interpretation of findings of model

Our analysis suggests that introduction of rapid access specialist clinics for management of patients with TIA and minor stroke will be cost effective. The optimal option would appear to be for all patients with suspected TIA to be referred to such a clinic. However, this conclusion depends upon capacity – with an expected 16 referrals per week for a population of 500,000. If this capacity is impractical, then a strategy that GPs refer patients with an ABCD2 score of 4 or more would require on average only four consultations per week. Daily clinics are more effective than other options, which reflect the high early risk of stroke following TIA and the importance of minimising delay. However, if daily clinics cannot be provided, then twice weekly clinics or weekly clinics are cost effective options, but of inferior effectiveness (and cost-effectiveness) as compared to daily clinics. How the clinics are costed is of crucial importance to the cost effectiveness analysis. Given the random variability of new onset of TIA and minor stroke, fixed capacity clinics (where unused slots cost resource) are less efficient than flexible clinics where it is assumed that the resources can be used for other purposes if not needed to see TIA patients. If fixed capacity clinics are all that can be provided, then it becomes most cost effective to have referral thresholds as low as possible without allowing queues to develop.

Admitting patients at high risk of stroke in order to allow for early use of thrombolysis did not appear a cost effective strategy in this model. This only resulted in the prevention of 2-3 additional major strokes over the 10-year period as compared to if patients were not admitted to hospital, and resulted in higher costs and very high incremental cost effectiveness ratio (over £1,000,000 per stroke prevented). Furthermore, the way the model was constructed (with patients exiting on receipt of thrombolysis) will have resulted in over-estimate of the benefits of the treatment. If we had lowered the length of stay in hospital or raised the admission threshold this would have reduced costs, but the small return in terms of better stroke prevention would have been lower still. However, it should be noted that the risk of full stroke was estimated by fitting a curve to data for the time risk of stroke from the available data from the OXVASC study, so it may be that we underestimated risk in the first three days. Therefore, while these results provide no support for a policy of admitting patients, in places where this does occur, rather than discontinue the practice it would be valuable to audit the results that were being achieved with this policy.

If more patients use emergency services, this makes no major differences to the results of the model, suggesting that our conclusions will be robust to changes in use of services that might result as a result of implementation of the National Stroke Strategy. (Department of Health, 2007). However, our finding that strategies involving greater use of emergency services are not cost-effective suggests that any publicity campaign should focus on the importance of use of emergency services for people suffering a suspected stroke, as opposed to a TIA. A similar conclusion was reached in an analysis of a possible 24 hour admission following TIA performed using US data. (Nguyen-Huynh, 2005)

If GPs initiate immediate optimal medical therapy in all patients in whom they diagnose TIA (namely statins, blood pressure lowering and dual anti-platelet therapy), then the role of the rapid access clinic becomes primarily one of diagnosis rather than treatment – both identifying TIA in cases where the GP did not make the diagnosis, and stopping treatments where the GP diagnosis of TIA was incorrect. This is reflected in that when we modelled optimal medical therapy by the GP, the most cost effective option was for all patients with suspected TIA to be referred to the clinic.

If GPs are better diagnostically, then it is no longer cost effective (ICER of over £100,000 per stroke prevented) for GPs to refer all suspected TIAs, as opposed to a strategy of referring patients with an ABCD2 score of 3 or more. This makes sense, since the value of the refer all suspected cases was gained largely through the errors in diagnosis of the GP that were assumed in the model.

If better GP diagnosis is combined with better GP management, then the specialist rapid access clinic no longer has a cost-effective role, since its only value left that is modelled is in ensuring faster access to carotid endarterectomy. This raises the question: should policy be directed towards training GPs rather than setting up specialist clinics? The model cannot answer this question, since we do not know what the costs or effectiveness of such a programme would be. A cluster randomised trial of implementation of stroke prevention guidelines for people with atrial fibrillation and TIA in primary care found that this did lead to increased uptake of effective medications, and suggested that the development and implementation of the local guidelines was highly cost effective. (Wright 2007). However, it is not clear what interventions would lead to better diagnosis of TIA by GPs. The underlying problem is that TIA is a relatively rare diagnosis for a GP – with an incidence of 0.7 per 1,000 population, a GP with a list size of 2,000 patients would only expect to see 1 or 2 cases per year.

## *6.3 Limitations of model*

Our principal measure of outcome has been occurrence of major stroke, which for the purposes of this model has been defined as a stroke that would have led to hospital admission under current practice. We have not taken into account prevention of minor strokes or TIAs (though these are reported in the model outputs). More importantly, we have not taken into account the impacts of treatment on cardiovascular risk as a whole. The medical treatments for stroke prevention will also reduce risk of other vascular events such as myocardial infarction. Therefore, we will have under-estimated the benefits of specialist referral.

The accuracy of the predictions made by the model depends upon the quality of the data inputs. The key data included:

Data on the epidemiology of TIA and minor stroke, including its incidence and prognosis in terms of risk of further strokes.

- Data on the effectiveness of medical and surgical interventions.
- Data on current practice

The data on epidemiology of TIA and minor stroke was drawn from the OXVASC study, (Rothwell, 2004a) which is a unique data set, which provides accurate data on the epidemiology of TIA through its intensive and multi-faceted approach to identification and verification of possible events.

The data on the effectiveness of medical and surgical interventions was drawn from randomised controlled trials. For some of these interventions, e.g. carotid endartectomy, there are good data on the effectiveness in relation to time after event. For others, e.g. blood pressure and cholesterol lowering, the evidence is lacking, in that our evidence base is not in people who had an event in the preceding couple of days. We have assumed that the relative risk reduction achieved by these therapies in the chronic treatment of an individual post TIA/ stroke also applies to the early phases of treatment. There is now some observational evidence to support this. (Rothwell, 2007; Lavallée, 2007)

The data on current practice was drawn from the QRESEARCH database, which is a large general practice database that reflects typical primary care in the UK. While

there is likely to be some error in diagnostic coding, (Mant, 2003a) the recording of pharmaceutical interventions is complete and accurate, since prescribing is invariably done using the GP computer system. The errors in diagnostic coding are unlikely to have a serious impact on the results of the model, and the treatments observed reflect how GPs manage people with a diagnosis of TIA (even if that diagnosis is inaccurate).

The area where the evidence was weakest concerned the accuracy with which general practitioners diagnose transient ischaemic attack. Several studies (Dennis, 1989; Gibbs, 2001; Martin, 1997; Jempere, 1996) have reported how many patients referred to a specialist clinic have a final diagnosis of TIA or stroke, but we found no studies that had looked at people in whom the GP did not diagnose a TIA or stroke who had actually had one. As a result, it is relatively straightforward to determine predictive value of a GP diagnosis of TIA, but not sensitivity and specificity. We managed to make estimates of these from the literature (80% and 60%) respectively, but these are subject to error. Therefore, we performed a sensitivity analysis to test the results of the model in circumstances where the GPs were able to diagnose TIA more accurately (with 90% sensitivity and 80% specificity). This made some differences to the results of the model, implying that while the most effective strategy would still be to refer all suspected cases, this would probably not be cost effective (with an ICER of over £100,000 per stroke prevented).

We have assumed that the specialist clinic is 100% accurate in diagnosing TIA. TIA is essentially a clinical diagnosis, with no gold standard test, so it is impossible to validate this assumption. However, the clinical trials of therapy on which the model is based are all based upon clinical diagnosis of TIA, so the assumption is unlikely to have had a significant effect on the results of the model.

While we have assumed that the specialist clinic will enable a 'one stop' assessment with carotid ultrasound available on the same day if appropriate, we have still assumed that the delay to surgery will reflect current availability in the NHS – which is a median delay of 67 days following assessment. (Mehta, 2005) Shorter waiting times would result in better results from surgery, (Rothwell, 2004b) and therefore increase the cost effectiveness of the specialist clinic option.

In terms of clinic costs, we have modelled the costs of investigation of carotid disease, but not the use of brain imaging such as CT or MRI. There is evidence that diffusion weighted MRI can provide clinically useful information in the assessment of TIA and minor stroke, (Schulz, 2004) but use of MRI will not have influenced the outcomes in the model, so use of such investigations were not tested.

To enable a decision to be made as to whether a specific strategy is cost effective, it is useful to be able to present the results in terms of quality adjusted life years (QALYs). QALYS were not incorporated into the model, but we have estimated that prevention of a stroke that would have led to a hospital admission is the equivalent of about a gain of 3-4 QALYs. This suggests that a strategy that costs up to around £60-80,000 per stroke prevented is likely to be considered cost effective.

## *6.4 Discussion of implications of studies to collect data for the model*

While the principal purpose of these studies was to obtain data to inform the model, two of the additional pieces of work that were done to support the model development should be considered in their own right. These are the QRESEARCH analysis, and the patient survey.

### 6.4.1 QRESEARCH study

This study has shown that of a cohort of 3405 individuals suffering a TIA between 2004 and 2005 whilst registered with 463 practices, 6.5 % had died one year later. This compares to mortality rates of 3% of all women and 2% of all men aged 72 in the general population of England in the years 2003-5 suggesting that a diagnosis of TIA is associated with significant mortality risk over and above that in the general population. As expected from the OXVASC data, most non fatal strokes following TIA occurred in the first month following the diagnosis. (Rothwell, 2005)

At the time of diagnosis of TIA, most people had had a blood pressure measurement in the last year but for around half of individuals this reading was above 140 mmHg. The majority of those with a last reading above 140mmHg were not receiving antihypertensive medication although above 160 mmHg the number was very small. Current guidelines are to treat people with systolic blood pressure between 140 and 159 mmHg on the basis of cardiovascular risk and so these results may well reflect guideline compliant primary prevention. Furthermore, this analysis does not take into account the need for multiple BP readings to confirm raised pressure or side effects / intolerances that patients may have suffered in the past precluding treatment.

Following TIA, blood pressure dropped by 6/3 mmHg – equivalent to the addition of a low dose antihypertensive to all patients. This was associated with better achievement of the QOF (150/90 mmHg) and NICE (140/90 mmHg) targets of 80% and 60% respectively. One year after TIA half of the cohort were being prescribed an antihypertensive suggesting that the results from PROGRESS were not accepted or perhaps just not implemented in primary care. (Progress Collaborative Group, 2001; Mant, 2006)

The situation for cholesterol was different with less than half having a recorded total cholesterol before suffering a TIA suggesting that routine measurement of cholesterol for primary preventative purposes is less frequent despite being required for risk calculation in those with moderately raised blood pressure. This may be due to the relative difficulty of measuring cholesterol in comparison to blood pressure or may reflect that current practice is for less frequent screening of cholesterol, possibly using the estimations that are built into the EMIS clinical system. Where cholesterol was measured, 80% of those recorded as having a total cholesterol over 5 mmol/l were not prescribed a statin which as with blood pressure probably reflects current guidelines which do not recommend lipid lowering medication in the absence of raised overall risk. Post TIA there was a change in behaviour with the vast majority (83%) with a recorded cholesterol in the year following diagnosis and a more than doubling in the rate of statin prescription. However, even one year after TIA, less than half of individuals were being prescribed a statin.

The evidence for statin use post TIA comes from two sources: firstly studies of primary or secondary cardiovascular risk reduction such as the Heart Protection Study and secondly from specific stroke trials such as the recently reported SPARCL trial. These show benefit for people with stroke or TIA from lowering cholesterol although arguably most convincing in terms of cardiovascular risk reduction as opposed to cerebrovascular risk reduction. (Heart Protection Study Collaborative Group, 2002; SPARCL, 2006). It appears that as with the prescription of antihypertensives, widespread use of statins after TIA has yet to be implemented.

This study has utilised a large database of routinely collected patient data to assemble a cohort of individuals suffering TIA within the same year drawn from the very recent past. As such it provides high quality information concerning the management of individuals in actual practice as opposed to trial conditions. The

dataset has been shown to be representative of the population of England and Wales although it is under represented in Scotland and Northern Ireland.{www.qresearch.org}

The size of the cohort – over 3000 individuals suffering first TIA in a single financial year reduces some possibly biases that occur in database work. In particular by only including recent diagnoses made during the first year of implementation of the Quality and Outcomes Framework of the new GMS GP contract it is likely that the threshold for entering a diagnosis was higher and therefore more likely to be accurate: all presumptive stroke diagnoses need to be accompanied by evidence of objective investigation by neuroradiological scanning. Whilst this is not the case for TIA, the need to provide appropriate secondary preventative treatment in the form of smoking cessation and blood pressure and cholesterol measurement is likely to have ensured a higher standard of coding.

Perhaps the biggest concern with a study such as this is the verification of diagnosis. The design of the QRESEARCH database precludes tracking back to individual records or practices in order to validate data. However, age adjusted prevalence of Stroke or TIA in the database as a whole in 2004 was 14.5 / 1000 which is similar to that previously reported from community surveys. (Hippisley-Cox, 2004; Geddes, 1996; O'Mahony, 1999)

It is likely that a proportion of primary diagnoses of TIA will have been incorrect. Secondary Care Clinics report 50-60% of primary care referrals to have a confirmed TIA diagnosis following specialist review, but other than in research projects rarely see the patient within 24 hours. (Martin, 1997; Murray, 2007). We have no information regarding the validity of individual diagnoses for patients in our cohort. The age and sex distribution were similar to that found in the OXVASC study: age 72 vs 74 (Rothwell, 2004a) and proportion female 56% vs 52%. (Rothwell, 2004a)

It is interesting to note that patients in our cohort had a similar mortality rate to that found in a previous well validated study: The Oxford Community Stroke Project reported an average actuarial risk of death was approximately 6.3%/yr following TIA in the mid 1980's. (Dennis, 1989) This suggests that whilst a GP diagnosis of TIA may not be accurate in terms of a neurovascular deficit, it is still associated with significant risk: A similar pattern has been found for heart failure: the ECHOES study (Hobbs, 2007) showed that 5 year mortality in individuals with a clinical diagnosis of heart failure was similar to those with confirmed heart failure even though only around a third of the former were confirmed on objective testing as falling in the latter group.

The pre TIA risk factor control found in this study was similar to that found in Oxfordshire in OXVASC two years earlier: blood pressure was marginally lower in our cohort (145/80 vs 147/80 mmHg) and cholesterol was also lower (5.3 vs 5.6 mmol/l). (Rothwell, 2004a) There were similar proportions in both studies receiving primary stroke prevention medication in the form of antithrombotics, antihypertensives and lipid lowering agents. Post TIA the data obtained by the National Stroke Audit (which includes both stroke and TIA) are better in terms of anti thrombotic therapy (100% vs 79%) but contraindications to such therapy are not included in our figures. Interestingly, the current data are better than the North American data from Ontario and North Carolina showing better levels of antithrombotic prescribing even one month after TIA.by UK GPs in comparison to their North American equivalents in the ER and primary care. (Gladstone, 2004; Goldstein, 1995)

Twelve months after TIA, the proportions of men and women receiving antihypertensive or statin medication were similar, suggesting (albeit without correcting for age), that there is little evidence that men are more likely to receive secondary preventative treatment compared to women.

Improving the management of people post TIA might be done in several ways. The early risk of stroke observed in both these data and those from community studies with strict validation of diagnoses is such that early intervention is needed. Two broad models tested in the wider study are improving primary care management, perhaps through education or inducements such as Quality and Outcomes Framework points or a fast track secondary care service utilising one stop clinics and / or increased use of the ambulance service. The recently presented EXPRESS study has shown that through the use of tailored protocols in a rapid access clinic, effective intensive early secondary prevention of TIA via can be delivered. (Rothwell, 2007)

In conclusion, this study has shown the current state of management of cardiovascular risk factors for people suffering a TIA in Primary Care in England and Wales. Whilst there are some methodological issues regarding the ascertainment of cases of TIA, the characteristics of the cohort are similar to those from previous studies. Although both clinically and statistically significant improvements in risk factor management are occurring in people with a clinical label of transient ischaemic attack, one year following TIA, sub optimal proportions of individuals are receiving gold standard treatment with antithrombotics, antihypertensives and lipid lowering drugs.

Implications for service delivery

These findings very much reinforce the overall thrust of the National Stroke Strategy – they suggest that management of TIA is sub-optimal both in the short and the medium term following an event. Introduction of rapid access neurovascular clinics is the mechanism that the National Strategy has selected to try and improve the immediate management of a TIA. Improving the longer-term management of people with a TIA is likely to require a multi-faceted response, perhaps including educational initiatives in primary care, more use of GPs with special interest in stroke, and greater efforts to establish links between specialists and primary care practitioners.

### 6.4.2 Patient survey

The results of the pilot questionnaire differ in some areas to those found in the main questionnaire. For example, the findings of the main questionnaire indicate that patients would prefer to have their TIA managed by their GP rather than a specialist. This could be due to the fact that it may be easier for people to attend their local surgery, and appointments are often available with their GP quickly and at a time convenient to the patient. Although the patient preference question gave *urgent* referral to a specialist as a choice, it is possible that patients would still expect a longer delay before they were able to see a specialist than they would get if they went to see their GP; a perceived delay in access to specialists may account for the fact that this is the least favourite option.

This theory is somewhat supported by the results of the pilot questionnaire. These patients favoured rapid access to a specialist, with visiting their GP as a second choice. However, these patients are all part of the OXVASC study and so would have had the opportunity to see a specialist very quickly. GPs participating in this study would refer any patient with a suspected TIA either directly to a specialist working on OXVASC, or to their local A & E Department (as demonstrated in the

pilot questionnaire, all patients visiting their GP with TIA symptoms were referred to A & E, whereas, only 11% of main questionnaire patients were referred there). On attending A & E, OXVASC patients would then be referred directly to the OXVASC team. This is not standard practice for treatment of suspected TIA, but is peculiar to the OXVASC region.

It is possible that OXVASC patients prefer the urgent specialist appointment option because their treatment experience demonstrated that genuine rapid access is possible. It could, therefore, mean that less atypical patients would also choose this option if genuinely rapid access to a specialist was available to them. However, it must also be remembered that the number of patients completing a pilot questionnaire was very small, so the views expressed in their responses may not be representative of all OXVASC participants.

As well as the differences in how a patient presenting with TIA symptoms are treated and differences in service preferences, there were also slight differences in the proportions of patients reporting different symptoms, with weakness/numbness down one side being the most common symptom in pilot patients and problems with speech being the most common symptom in the main questionnaire. Furthermore, there was a difference in the proportion of patients having their TIA at weekends and during the week between the groups. Again, this is probably explained by the small numbers of patients in the pilot study, making it more likely that the results found in the main questionnaire are more representative of the population as a whole than are those found in the pilot questionnaire results, an assumption that is supported by the similarities found between the pilot and the main results.

Patients in both groups behaved in a similar manner when they had their TIA symptoms. Most patients visited their GP or went to hospital. There were similar proportions of people in both the pilot and the main questionnaire who took no immediate action when they had their symptoms (22% and 17% respectively). This implies that there is no more awareness of stroke/TIA symptoms in the OXVASC region than there is elsewhere in the country, and that how people describe what they did when they had their symptoms is likely to be representative of what the general population would also do. It is only after patients have sought advice about their symptoms that differences become evident, as demonstrated by the outcome of their GP appointment. This implies that patient preference may be influenced by the type or standard of service they have received.

Patient Preference and Implications for Service Provision

Patient choice and preference is an important consideration when looking at how a health service is best delivered. It is important that people are satisfied with the service that is available to them. However, the results of this questionnaire survey imply that patient preference is not an important issue when deciding on the most appropriate form of service delivery for people who have a suspected TIA. As demonstrated by the different priorities given in the pilot study to those seen in the main survey, people seem to choose the service they have had experience of as their prime choice.

It is probable that patient preference also relies on what standard of service they received. For example, it is likely that OXVASC patients received a quick, high standard service, which is why they preferred the urgent referral to a specialist option. The main questionnaire results, which are likely to be more representative of the general population, found the complete opposite, and may well reflect the fact that people generally expect there to be long waiting times to see a specialist. If it could be demonstrated that a fast comprehensive service is available and effective, then their preferences may change.

If patient preferences are, in fact, so influenced both by the kind of service they have experience of and by the effectiveness of that service, then it would be unwise to allow patient preference to have a profound influence on what type of service delivery is offered. If a new model of service delivery were successfully introduced it would seem that patients who have experienced the system would cite that as their main preference, regardless of what their choice would have been prior to that service implementation.

## *6.5 Implications for the National Stroke Strategy*

The National Stroke Strategy made the following recommendations with regard to TIA and minor stroke: (Department of Health, 2007)

- Immediate referral for appropriately urgent specialist assessment and investigation should be considered in all patients presenting with a recent TIA or minor stroke.
- All patients with minor stroke and all higher risk patients with TIA and minor stroke (e.g. ABCD2 ≥ 4) need to be assessed by a specialist and treated within 24 hours.
- Lower risk patients are best investigated within seven days of the event. Non-urgent referral for TIA or minor stroke is appropriate only for very low risk patients, such as those presenting with events that occurred several weeks or months previously.
- Patients who are assessed as an emergency in the community should be taken by ambulance to an appropriate acute stroke service if their symptoms have not resolved, or if they are otherwise considered to be at high risk of stroke.
- Patients who attend emergency departments soon after a TIA or minor stroke must be treated and must not be sent home and simply told to see their GP in due course.
- Those at highest risk may justify immediate hospital admission
- Carotid imaging should ideally be performed at initial assessment and should not be delayed for more than 24 hours after first clinical assessment in TIA patients at high risk of stroke (for example ABCD2 score ≥4) or in patients with non-cardioembolic carotid-territory minor stroke
- Carotid endarterectomy for recently symptomatic severe carotid stenosis should be regarded as an emergency procedure in patients who are neurologically stable, and should ideally be performed within 48 hours of a TIA or minor stroke

The results of the model are broadly consistent with these recommendations, and clarify the thresholds at which it is most cost-effective to regard patients as high risk. The model did not differentiate between urgent and non-urgent referrals, with non-urgent referrals being handled in primary care. The model did not find it cost-effective to refer patients with low ABCD2 scores to specialist care, but did find it cost-effective to refer all patients with suspected TIAs. The model did not find it cost effective to admit high risk patients. This is the main area where the model did not support the National Strategy.

# 7: Recommendations

## *7.1 For service delivery*

### 7.1.1 Configuration of rapid access neurovascular clinics

- Where possible, these should allow for same day referrals. Daily clinics are more cost effective than less frequent clinics (e.g. twice weekly or weekly)

  We found that a same day clinic (Monday – Friday) was both more effective and more cost effective than other patterns of clinic provision – see figure 5.7. The same day clinic that we modelled did not incur fixed costs, since we recognised that the expected demand would not sustain a same day fixed clinic pattern. For example, for a clinic even with a catchment population of 500,000, we found that only 4 suspected patients would be referred per week with an ABCD2 score ≥ 4. The assumption was that the appointments would take place on the ward, in A&E, or in out-patients after the regular clinic had finished.

- The referral threshold for these clinics can be varied according to clinic capacity using an ABCD2 score cut off between 4 and 7.

- On grounds of cost-effectiveness the optimal threshold would be to refer patients with suspected TIA with an ABCD2 score of 4 or more if capacity is limited to around 1 patient per day (serving a population of 500,000)

  We found that within the strategy of the same day clinic, it was cost effective to refer at any ABCD2 score between 4 and 7 (see table 5.3 and figure 5.2). The lower the threshold (between 4 and 7) the more major strokes there were prevented, and the higher the incremental cost effectiveness ratio. At a referral threshold of 4, the ICER was £36,000 per major stroke averted, which is well within the bounds by which interventions are generally regarded as cost effective given that we estimate that each stroke prevented in the model equates to 3-4 QALYS (see table 5.13). Therefore, we felt that the key determinant of ABCD2 cut off (if selected above 4) would be on capacity rather than cost effectiveness.

- If capacity is not limited, then it is cost effective to see all possible TIAs

  We found that it was cost effective (ICER of £50,000 per stroke averted moving to this strategy from a strategy of only seeing patients with an ABCD2 score ≥4) for a specialist clinic to see all patients with suspected TIA. The anticipated number of patients for such a clinic in a hospital with a catchment population of 500,000 is of the order of 16 patients per week, and we recognise that this level of demand might stretch the flexibility of the service if additional fixed costs are not to be incurred.

- If daily clinics are not possible, twice or once weekly clinics are cost effective with a referral threshold of ABCD2 of 4 or more.

- Flexible clinics, i.e where staff can do other work when capacity is not required on a given day, are more cost-effective than fixed clinics.

  We found that both twice weekly flexible clinics (table 5.7, figure 5.4), twice weekly fixed clinics (table 5.8, figure 5.5), and weekly fixed clinics (table 5.9, figure 5.6) were all cost effective at an ABCD2 referral threshold of ≥ 4. The ICERs were lower for flexible clinics. This pattern of clinic was tested to provide a direct comparison to the same day clinics, and so we made the same assumption about such clinics – that the consultation would take place in A&E, at the end of out-patients, or on a

ward. The justification is that expected demand is low at the threshold of ABCD2 ≥ 4.

### 7.1.2 In patient admission

- We do not recommend in-patient admission to facilitate thrombolysis for patients at high risk of stroke because of high ABCD2 score

We found the use of in-patient admission to be dominated by other strategies in all cases except for the strategy of refer all suspected TIAs – see figure 5.7. However, the ICER (over £1,000,000 per major stroke averted) suggested that in-patient admission as an addition to the strategy of referring all suspected TIAs was too high to be cost effective.

### 7.1.3 Use of emergency services

- We do not recommend that patients are encouraged to use 999 services where symptoms have resolved

We found that if more patients with TIA come via a 999 service, costs are generally higher – see table 5.9. When we compared a strategy of enhanced use of emergency services with other options, we found that the other optinons dominated enhanced 999 use – see figure 5.9.

## *7.2 For research / audit*

### 7.2.1 In patient admission

- Services that do admit patients with high ABCD2 scores for periods of observation should audit their results to determine what proportion of admitted patients actually receive thrombolysis

We did not find admission for observation to be cost effective. Nevertheless, it is a strategy that is supported by the National Stroke Strategy. Therefore, it may be that some units do adopt this policy, perhaps partly to ensure rapid assessment and treatment for those patients who would benefit from carotid endarterectomy (which we did not model as a benefit of admission). If units do admit such patients, it would be valuable to audit what proportion receive thrombolysis and/ or carotid endarterectomy to make an empirical as opposed to model based judgement as to the cost effectiveness of the strategy.

### 7.2.2 Primary care

- Would initiation of secondary prevention medications acutely by GPs prior to referral to a specialist improve outcome?

We did not find that a GP instituting optimal management without referral was cost-effective (see section 5.3.2). However, in the light of the positive results of EPXRESS and SOS-TIA (Rothwell, 2007; Lavallée, 2007) it may be that an effective way of expediting therapy would be for the GP to give the secondary prevention drugs prior to referral to the specialist, who could then review whether or not the drugs were indicated.

- How accurate is GP diagnosis of TIA?

  We found no studies that could adequately address the likelihood that GPs make false negative diagnoses – see section 3.5.1. This would be valuable data in informing future service development. If GP diagnosis was significantly better than we modelled, it is conceivable that it might be possible to deliver the bulk of early treatment for TIA in primary care without referral to specialist clinics (except where carotid endarterectomy was a possible treatment).

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# Appendices

## 1. Read Codes for TIA used in the QRESEARCH analysis

| Read Code | Description |
|---|---|
| F4236 | Amaurosis fugax |
| G65.. | Transient cerebral ischaemia |
| G65.. | Drop attack |
| G65.. | Transient ischaemic attack |
| G65.. | Vertebro-basilar insufficiency |
| G650. | Basilar artery syndrome |
| G650. | Insufficiency - basilar artery |
| G651. | Vertebral artery syndrome |
| G6510 | Vertebro-basilar artery syndrome |
| G652. | Subclavian steal syndrome |
| G653. | Carotid artery syndrome hemispheric |
| G654. | Multiple and bilateral precerebral artery syndromes |
| G656. | Vertebrobasilar insufficiency |
| G65y. | Other transient cerebral ischaemia |
| G65z. | Transient cerebral ischaemia NOS |
| G65z1 | Intermittent cerebral ischaemia |
| G65zz | Transient cerebral ischaemia NOS |

## 2. QOF Criteria for Stroke / TIA and hypertension during the QRESEARCH study period (2004-5)

| Stroke and Transient Ischaemic Attacks<br>Indicator | Points | Payment Stages |
|---|---|---|
| Records | | |
| STROKE 1. The practice can produce a register of patients with Stroke or TIA | 4 | |
| STROKE 2. The percentage of new patients with presumptive stroke (presenting after 1 April 2003) who have been referred for confirmation of the diagnosis by CT or MRI scan | 2 | 25-80% |
| Ongoing Management | | |
| STROKE 3. The percentage of patients with TIA or stroke who have a record of smoking status in the last 15 months, except those who have never smoked where smoking status need be recorded only once since diagnosis | 3 | 25-90% |
| STROKE 4. The percentage of patients with a history of TIA or stroke who smoke and whose notes contain a record that smoking cessation advice or referral to a specialist service, if available, has been offered in the last 15 months | 2 | 25-70% |
| STROKE 5. The percentage of patients with TIA or stroke who have a record of blood pressure in the notes in the preceding 15 months | 2 | 25-90% |
| STROKE 6. The percentage of patients with a history of TIA or stroke in whom the last blood pressure reading (measured in last 15 months) is 150/90 or less | 5 | 25-70% |
| STROKE 7. The percentage of patients with TIA or stroke who have a record of total cholesterol in the last 15 months | 2 | 25-90% |

| | | |
|---|---|---|
| STROKE 8. The percentage of patients with TIA or stroke whose last measured total cholesterol (measured in last 15 months) is 5 mmol/l or less | 5 | 25-60% |
| STROKE 9. The percentage of patients with a stroke shown to be non-haemorrhagic, or a history of TIA, who have a record that aspirin, an alternative anti-platelet therapy, or an anti-coagulant is being taken (unless a contraindication or side-effects are recorded) | 4 | 25-90% |
| STROKE 10. The percentage of patients with TIA or stroke who have had influenza immunisation in the preceding 1 September to 31 March | 2 | 25-85% |

| Hypertension | | |
|---|---|---|
| Indicator | Points | Payment Stages |
| Records | | |
| BP 1. The practice can produce a register of patients with established hypertension | 9 | |
| Diagnosis and initial management | | |
| BP 2. The percentage of patients with hypertension whose notes record smoking status at least once since diagnosis | 10 | 25-90% |
| BP 3. The percentage of patients with hypertension who smoke, whose notes contain a record that smoking cessation advice or referral to a specialist service, if available, has been offered at least once | 10 | 25-90% |
| Ongoing Management | | |
| BP 4. The percentage of patients with hypertension in whom there is a record of the blood pressure in the past 9 months | 20 | 25-90% |
| BP 5. The percentage of patients with hypertension in whom the last blood pressure (measured in the last 9 months) is 150/90 or less | 56 | 25-70% |

## 3. Additional Tables from QRESEARCH analysis

**Table A3.1: Cross tabulation of last SBP by number of antihypertensive medications prescribed one year after TIA**

| | Number of antihypertensive medications | | | | | | |
|---|---|---|---|---|---|---|---|
| Last SBP mmHg | 0 | 1 | 2 | 3 | 4 | 5 | Total |
| | | | | | | | |
| 1-100 | 28 | 7 | 8 | 4 | 0 | 0 | 47 |
| Row% | 59.57 | 14.89 | 17.02 | 8.51 | 0.00 | 0.00 | 100.00 |
| Column% | 2.03 | 0.89 | 1.62 | 2.15 | 0.00 | 0.00 | 1.63 |
| | | | | | | | |
| 101-120 | 232 | 114 | 53 | 22 | 3 | 0 | 424 |
| Row% | 54.72 | 26.89 | 12.50 | 5.19 | 0.71 | 0.00 | 100.00 |
| Column% | 16.80 | 14.45 | 10.75 | 11.83 | 9.68 | 0.00 | 14.70 |
| | | | | | | | |
| 121-140 | 639 | 351 | 209 | 80 | 11 | 2 | 1,292 |
| Row% | 49.46 | 27.17 | 16.18 | 6.19 | 0.85 | 0.15 | 100.00 |
| Column% | 46.27 | 44.49 | 42.39 | 43.01 | 35.48 | 40.00 | 44.78 |
| | | | | | | | |
| 141-160 | 364 | 254 | 165 | 51 | 13 | 2 | 849 |
| Row% | 42.87 | 29.92 | 19.43 | 6.01 | 1.53 | 0.24 | 100.00 |
| Column% | 26.36 | 32.19 | 33.47 | 27.42 | 41.94 | 40.00 | 29.43 |
| | | | | | | | |
| 161-180 | 78 | 44 | 41 | 19 | 3 | 1 | 186 |
| Row% | 41.94 | 23.66 | 22.04 | 10.22 | 1.61 | 0.54 | 100.00 |
| Column% | 5.65 | 5.58 | 8.32 | 10.22 | 9.68 | 20.00 | 6.45 |
| | | | | | | | |
| 181-200 | 30 | 18 | 13 | 9 | 1 | 0 | 71 |
| Row% | 42.25 | 25.35 | 18.31 | 12.68 | 1.41 | 0.00 | 100.00 |
| Column% | 2.17 | 2.28 | 2.64 | 4.84 | 3.23 | 0.00 | 2.46 |
| | | | | | | | |
| >200 | 10 | 1 | 4 | 1 | 0 | 0 | 16 |
| Row% | 62.50 | 6.25 | 25.00 | 6.25 | 0.00 | 0.00 | 100.00 |
| Column% | 0.72 | 0.13 | 0.81 | 0.54 | 0.00 | 0.00 | 0.55 |
| | | | | | | | |
| Total | 1,381 | 789 | 493 | 186 | 31 | 5 | 2,885 |
| Row% | 47.87 | 27.35 | 17.09 | 6.45 | 1.07 | 0.17 | 100.00 |
| Column% | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |

**Table A3.2: Cross tab of last total cholesterol by treated with Statins one year after TIA**

| totalband | 0 | 1 | Total |
|---|---|---|---|
| | | | |
| 0-3.0 | 29 | 55 | 84 |
| Row% | 34.52 | 65.48 | 100.00 |
| Column% | 2.30 | 4.81 | 3.49 |
| | | | |
| 3.1-4.0 | 223 | 417 | 640 |
| Row% | 34.84 | 65.16 | 100.00 |
| Column% | 17.67 | 36.48 | 26.61 |
| | | | |
| 4.1-5.0 | 463 | 456 | 919 |
| Row% | 50.38 | 49.62 | 100.00 |
| Column% | 36.69 | 39.90 | 38.21 |
| | | | |
| 5.1-6.0 | 319 | 137 | 456 |
| Row% | 69.96 | 30.04 | 100.00 |
| Column% | 25.28 | 11.99 | 18.96 |
| | | | |
| 6.1-7.0 | 172 | 58 | 230 |
| Row% | 74.78 | 25.22 | 100.00 |
| Column% | 13.63 | 5.07 | 9.56 |
| | | | |
| 7.1-8.0 | 46 | 14 | 60 |
| Row% | 76.67 | 23.33 | 100.00 |
| Column% | 3.65 | 1.22 | 2.49 |
| | | | |
| >8.0 | 10 | 6 | 16 |
| Row% | 62.50 | 37.50 | 100.00 |
| Column% | 0.79 | 0.52 | 0.67 |
| | | | |
| Total | 1,262 | 1,143 | 2,405 |
| Row% | 52.47 | 47.53 | 100.00 |
| Column% | 100.00 | 100.00 | 100.00 |

**Table A3.3: Cross tab of last total cholesterol at one year after TIA by prescribed with statins**

| Total Cholesterol Mmol/l | Prescribed at statin (n=2405) |
|---|---|
| | |
| 0-3.0 | 55 (5) |
| | |
| 3.1-4.0 | 417 (36) |
| | |
| 4.1-5.0 | 456 (40) |
| | |
| 5.1-6.0 | 137 (12) |
| | |
| 6.1-7.0 | 58 (5) |
| | |
| 7.1-8.0 | 14 (1) |
| | |
| >8.0 | 6 (0) |
| | |
| Total | 1,143 |
| Row% | 47.53 |
| Column% | 100.00 |

**Table A3.4: Cross tabulation of last SBP by number of antihypertensive medications prescribed one month before TIA**

| Last SBP mmHg | 0 | 1 | 2 | 3 | 4 | 5 | Total |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| **1-100** | 23 | 7 | 7 | 0 | 1 | 0 | 38 |
| **Row%** | 60.53 | 18.42 | 18.42 | 0.00 | 2.63 | 0.00 | 100.00 |
| **Column%** | 1.64 | 1.01 | 1.73 | 0.00 | 3.23 | 0.00 | 1.42 |
| | | | | | | | |
| **101-120** | 185 | 78 | 35 | 10 | 0 | 0 | 308 |
| **Row%** | 60.06 | 25.32 | 11.36 | 3.25 | 0.00 | 0.00 | 100.00 |
| **Column%** | 13.18 | 11.21 | 8.66 | 7.14 | 0.00 | 0.00 | 11.51 |
| | | | | | | | |
| **121-140** | 544 | 259 | 136 | 54 | 8 | 1 | 1,002 |
| **Row%** | 54.29 | 25.85 | 13.57 | 5.39 | 0.80 | 0.10 | 100.00 |
| **Column%** | 38.75 | 37.21 | 33.66 | 38.57 | 25.81 | 50.00 | 37.43 |
| | | | | | | | |
| **141-160** | 443 | 210 | 148 | 39 | 17 | 1 | 858 |
| **Row%** | 51.63 | 24.48 | 17.25 | 4.55 | 1.98 | 0.12 | 100.00 |
| **Column%** | 31.55 | 30.17 | 36.63 | 27.86 | 54.84 | 50.00 | 32.05 |
| | | | | | | | |
| **161-180** | 148 | 99 | 54 | 23 | 3 | 0 | 327 |
| **Row%** | 45.26 | 30.28 | 16.51 | 7.03 | 0.92 | 0.00 | 100.00 |
| **Column%** | 10.54 | 14.22 | 13.37 | 16.43 | 9.68 | 0.00 | 12.22 |
| | | | | | | | |
| **181-200** | 51 | 26 | 19 | 11 | 2 | 0 | 109 |
| **Row%** | 46.79 | 23.85 | 17.43 | 10.09 | 1.83 | 0.00 | 100.00 |
| **Column%** | 3.63 | 3.74 | 4.70 | 7.86 | 6.45 | 0.00 | 4.07 |
| | | | | | | | |
| **>200** | 10 | 17 | 5 | 3 | 0 | 0 | 35 |
| **Row%** | 28.57 | 48.57 | 14.29 | 8.57 | 0.00 | 0.00 | 100.00 |
| **Column%** | 0.71 | 2.44 | 1.24 | 2.14 | 0.00 | 0.00 | 1.31 |
| | | | | | | | |
| **Total** | 1,404 | 696 | 404 | 140 | 31 | 2 | 2,677 |
| **Row%** | 52.45 | 26.00 | 15.09 | 5.23 | 1.16 | 0.07 | 100.00 |
| **Column%** | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |

**Table A3.5: Cross tab of last total cholesterol by treated with Statins one month before TIA**

| | | | |
|---|---|---|---|
| **Last total cholesterol** | **No statin** | **Prescribed statin** | **Total** |
| | | | |
| **0-3.0** | 8 | 14 | 22 |
| **Row%** | 36.36 | 63.64 | 100.00 |
| **Column%** | 0.79 | 2.87 | 1.47 |
| | | | |
| **3.1-4.0** | 95 | 126 | 221 |
| **Row%** | 42.99 | 57.01 | 100.00 |
| **Column%** | 9.41 | 25.87 | 14.76 |
| | | | |
| **4.1-5.0** | 242 | 180 | 422 |
| **Row%** | 57.35 | 42.65 | 100.00 |
| **Column%** | 23.96 | 36.96 | 28.19 |
| | | | |
| **5.1-6.0** | 360 | 94 | 454 |
| **Row%** | 79.30 | 20.70 | 100.00 |
| **Column%** | 35.64 | 19.30 | 30.33 |
| | | | |
| **6.1-7.0** | 209 | 47 | 256 |
| **Row%** | 81.64 | 18.36 | 100.00 |
| **Column%** | 20.69 | 9.65 | 17.10 |
| | | | |
| **7.1-8.0** | 72 | 18 | 90 |
| **Row%** | 80.00 | 20.00 | 100.00 |
| **Column%** | 7.13 | 3.70 | 6.01 |
| | | | |
| **>8.0** | 24 | 8 | 32 |
| **Row%** | 75.0 | 25.0 | 100.00 |
| **Column%** | 2.38 | 1.44 | 2.07 |
| | | | |
| **Total** | 1,010 | 487 | 1,497 |
| **Row%** | 67.47 | 32.53 | 100.00 |
| **Column%** | 100.00 | 100.00 | 100.00 |
| | | | |

## 4. Cost data used in the model

### Final Drug Costs

| **Drug costs** | **(generic unless otherwise stated)** | | BNF, March 2007 | |
|---|---|---|---|---|
| **Monotherapy** | | | | |
| | | **cost** | **cost per week (£)** | Deflate one year |
| **Aspirin** | | | | |
| (75mg od) | 56 | £1.89 | 0.2363 | 0.226 |
| **Dual therapy** | | | | |
| **Dipyridamole** | | | | |
| 84 tablets | 100mg | £5.17 | 0.8617 | 0.824 |
| (200mg bd) | | | | |
| **Simvastatin** | | | | |
| 28 tablets | 40mg | £3.40 | 0.8500 | 0.813 |
| 40mg od | | | | |
| **Antihypertensives** | | | | |
| **Bendrofulmethiazide** | | | | |
| 2.5mg od | 28 tablets | £1.15 | 0.2875 | 0.275 |
| **Anticoagulant for AF** | | | | |
| **Warfarin** | | | | |
| 28 tablets | 5mg | £1.47 | | |

**See final cost data sheet for warfarin clinic visit unit costs**

## Other Final Costs

| | | Cost (£) | Price year | Source | Notes | |
|---|---|---|---|---|---|---|
| **Ambulance** | | | | | | |
| Urban/rural amber incident, stroke/CVA | | 197 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | |
| | | | (Weighted cost using figures for urban and rural ambulance services - amber as almost all stroke/CVA in category) | | | |
| **GP consultation** | | | | | | |
| 10 minute consultation | | 18 | 2005/6 | Curtis & Netten, 06 | excluding qualifications & direct care staff costs | |
| **A&E doctor** | | | | | | |
| Lower cost investigation | | 80 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | |
| **A&E specialist** | O/P clinic 30 mins | | | | | |
| General medicine | 1st attendance | 207 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | Length of clinic unknown |
| **Scheduled OP** | | | | | | |
| Costed as A&E specialist | | | | | | |
| **Major stroke (acute)** | | | | | | |
| Non-transient stroke or cerebrovascular accident (11 days as inpatient) | | 2462 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | Non-elective inpatient >69 or w cc |
| **Major stroke (chronic)** | | per day | | | | |
| Long term care disabled | | 41.78 | 2005/6 | Chambers, 2002 | Inflated to 05/06 using HCHS price index | |
| Long term care not disabled | | 3.23 | 2005/6 | Chambers, 2002 | Inflated to 05/06 using HCHS price index | |
| Cost calculated as 40% disabled, 30% not disabled, 30% dead = 17.68 per day | | | | | | |

**CE clinical assessment (as part of O/P appt or with specialist) - additional cost of ultrasound**

| | | | | | |
|---|---|---|---|---|---|
| Doppler Ultrasound | 87 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | |

**CE appointment assessment (if separate and additional appointment)**

| | | | | | |
|---|---|---|---|---|---|
| General medicine | Follow up attendance | 118 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined |
| plus Doppler Ultrasound as above | | | | | |

**CE surgery**

| | | | | | |
|---|---|---|---|---|---|
| Extracranial or upper limb arterial surgery (3 days as inpatient) | 4352 | 2005/6 | NHS Reference Costs 05/06 | NHS trust & PCT combined | Elective inpatient |

**Inpatient days**

| | | | | |
|---|---|---|---|---|
| Cost per bed day stroke | 182 | 2005/6 | Curtis & Netten, 06 | From NHS reference costs |

**Anticoagulation (A/C) clinic**

| | | | | |
|---|---|---|---|---|
| First outpatient visit day 1 | 27 | 2005/6 | NHS Reference costs 05/06 | 1st attendance A/C clinic, face to face, NHS Trust & PCT combined |
| Follow up visit day 5 | 22 | 2005/6 | NHS Reference costs 05/06 | Follow up attendance A/C clinic, face to face, NHS Trust & PCT combined |
| Follow up visit day 8 | 22 | 2005/6 | NHS Reference costs 05/06 | Follow up attendance A/Con clinic, face to face, NHS Trust & PCT combined |
| Follow up visit day 15 | 7.62 | 2005/6 | SMART study, hospital clinic estimate | (NHS Reference cost non-face to face visit (standard) is £8) |
| Follow up visit day 29 | 7.62 | 2005/6 | SMART study, hospital clinic estimate | |
| Standard monthly visit | 7.62 | 2005/6 | SMART study, hospital clinic estimate | |

Assumptions: Initiation of warfarin in hospital, regular checks in first month then attends hospital clinic monthly
Assume first three visits are face to face when stabilising warfarin dose, remainder are non face to face
Warfarin start up costs made up of three first clinics, monthly costs 7.62 clinic plus 1.47 pack of 28 tablets

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