National Guideline Centre & SSNAP

Sentinel Stroke National Audit Programme

Cost and Cost-effectiveness analysis

Technical report

10 August 2016

Commissioned by NHS England

Contributions
Economic modelling – Xiangming Xu and David Wonderling
SSNAP analysis - Emma Vestesson, Lizz Paley, Alex Hoffman
Clinical advisors – Ben Bray and Tony Rudd
Project lead – Ben Bray
Acknowledgements
SLSR analysis – Anita Desikan
Commissioner – Dimitri Varsamis
Clinical advice – Helen Rodgers
Comments on report – Anita Patel
Technical advice – Alex Haines

Funding
NHS England.

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1 Introduction

1.1 Sentinel Stroke National Audit Programme (SSNAP)

The Sentinel Stroke National Audit Programme (SSNAP) is a programme of work that aims to improve the quality of stroke care by auditing stroke services against evidence-based standards derived from the National Clinical Guideline for Stroke (Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 4th edition. London:Royal College of Physicians, 2012]. It is steered by the Intercollegiate Stroke Working Party, which includes clinicians and patients. SSNAP is the single source of stroke data for the NHS, replacing several previous data collections. For further information go to http://www.rcplondon.ac.uk/ssnap. SSNAP has two complementary elements:

- *SSNAP Clinical*: a continuous audit of the care provided for stroke patients admitted to hospital after they have a stroke; it encompasses details of care for every patient during their inpatient stay as well as outcomes and interventions during the six months following their stroke.

  The audit reports both 'patient centred' and 'team centred' results of processes of care and patient outcomes. In 'patient centred' reporting, results are attributed to every team (service) which treated a patient at any point in their care, demonstrating the quality of care that those patients received across the pathway. 'Team centred' results attribute the results to the team considered the most responsible for a specific outcome. It has full participation of all admitting hospitals in England and Wales since 2013.
- *SSNAP Organisational*: a biennial acute organisational audit provides a snapshot picture of the structure of stroke services in acute hospitals. In 2015 for the first time, a pioneering snapshot of post-acute services took place to ascertain a baseline picture of available services for stroke patient after the acute phase.

1.2 Current practice in stroke care

1.2.1 Acute stroke care

The central aspect of acute stroke care is multidisciplinary care in a specialised stroke unit. A stroke unit consists of a discrete area of a hospital ward that exclusively (or nearly exclusively) takes care of stroke patients and it is staffed by a specialist multidisciplinary team[1]. Most patients should spend the majority of their inpatient stay on either an acute stroke unit or rehabilitation stroke unit, since admission to a stroke unit improves outcomes, reducing the odds of death or death or dependency at one year were by 14% and 18% respectively[1].

Acute care in the stroke unit involves [2]:

- Medical assessment and diagnosis
- Early assessment of nursing and therapy needs
- Monitoring of physiological and neurological status
- Screening and prevention of complications
- Early mobilisation
- Rehabilitation therapy (physiotherapy, occupational therapy, speech and language therapy)

An important early aspect of stroke care is rapid brain imaging. Imaging is essential for diagnosis and in making early important treatment decisions, such as suitability for thrombolysis. Current UK professional guidelines recommend that brain imaging should be carried out within 12 hours of arrival at hospital (Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 4th edition. London: Royal College of Physicians, 2012 update due in 2016.).

Guideline recommendations for stroke unit care

The NICE Quality Standard for Stroke (NICE 2016) recommends:

> *Adults presenting at an accident and emergency (A&E) department with suspected stroke are admitted to a specialist acute stroke unit within 4 hours of arrival*

Current SSNAP data on acute stroke unit care

SSNAP Clinical (SSNAP Jan-Mar 2016) reports that stroke unit care is now ubiquitous, but variations in care remain in the timeliness of access to stroke units:

- 96% of patients are admitted to a stroke unit at some point
- 54% of patients are admitted to a stroke unit within 4 hours of admission
- 77.4% of patients are admitted directly to a stroke unit. Other admission destinations include acute medical units (15.6%), Intensive care units and high dependency units (2%), and other (non-stroke) wards (5%)

1.2.2 Thrombolysis

Thrombolysis refers to the administration of an intravenous "clot busting" drug for patients with acute ischaemic stroke. Alteplase is currently the only drug licensed for this in the UK [3]. Selecting patients suitable for thrombolysis is complex, and only up to 20% of patients with acute ischaemic stroke are eligible. The main decision criteria relate to clinical exclusions and to the time from stroke onset: thrombolysis is only beneficial to most patients presenting within 4.5 hours of stroke onset. Thrombolysis is therefore not indicated in patients who present later than this or if the time from stroke onset cannot be reasonably ascertained.

In suitable patients with ischaemic stroke, thrombolysis significantly reduces the proportion of patients who are dead or dependent (modified Rankin 3 to 6) at three to six months after stroke (odds ratio 0.85, 95% CI 0.78 - 0.93)[4]. The benefit is greater the sooner it can be administered after stroke onset, with most benefit in patients treated within 3 hours of onset. However, thrombolysis also increases patients' risk of intracerebral haemorrhage, which occurs in 4-5% of patients after thrombolysis and which carries a high risk of mortality. The benefits of thrombolysis are therefore offset by early complications; overall, this results in a net benefit but careful patient selection is essential to ensure that potential benefits are likely to be higher than the risks.

Over the past 10 years, there has been a large increase in the proportion of patients with stroke treated with thrombolysis, and it is now received by 11% of stroke patients. There is however wide variation both within the UK and between countries in the uptake of this treatment, with some units achieving thrombolysis rates of 20% (SSNAP Jan-Mar 2016). Thrombolysis rates can be improved by improving public awareness of stroke symptoms, reducing the time from stroke onset to hospital admission and improving inpatient imaging pathways and decision making so that more potentially eligible patients are treated within the therapeutic time window.

Guideline recommendations for thrombolysis

NICE Clinical Guideline 68 [2008] recommends:

Alteplase is recommended for the treatment of acute ischaemic stroke when used by physicians trained and experienced in the management of acute stroke

Measuring thrombolysis in SSNAP

SSNAP uses information provided about patient characteristics to estimate the eligibility of patients for thrombolysis. The eligibility criteria are derived from the Intercollegiate Stroke Working Party Guideline (2012):

Patients with ischaemic stroke, who are one of the following:

- *newly arrived patients aged under 80 with a precise or best estimate onset time and an onset to arrival time of less than 3.5h*
- *newly arrived patients aged 80 or over with a precise or best estimate onset time and an onset to arrival time of less than 2h*
- *patients already in hospital at time of stroke*

Current SSNAP data on thrombolysis eligibility

- SSNAP estimates that 12.9% of patients meet these criteria, of whom 80.7% are treated with thrombolysis
- In patients treated with thrombolysis, the median time between clock start and thrombolysis is 55 minutes, and the median time from onset to clock start is 81 minutes [SSNAP 2016]

1.2.3 Early supported discharge and community rehabilitation

Early supported discharge (ESD) refers to a model of stroke care where medically stable patients receive rehabilitation in their own home at the same intensity they would receive as an inpatient. The ESD team should be stroke specific and delivered by teams with specialist stroke skills [Intercollegiate Stroke Working Party 2012].

There is strong evidence that ESD leads to better patient outcomes: reduced death or disability (OR 0.78 95% CI 0.61 to 1.00), reduced institutionalization, improved patient satisfaction (OR 1.60, 95% CI 1.08 to 2.38), and reduced length of hospital stay[5]. The reduction in length of stay in clinical trials of ESD was approximately seven days[5].

Uptake of ESD in the NHS has however been variable. Although ESD is applicable to up to 40% of stroke patients in the UK, 25% of the regions of England and Wales have not commissioned an ESD service and overall only 20% of patients receive the services of a dedicated team [SSNAP 2015].

In addition to ESD, patients with stroke receive a variety of other models of rehabilitation. These include discharging patients to community rehabilitation at a lower intensity than would be received as an inpatient, or as a follow on after a period of ESD. There is also heterogeneity in the provision of stroke or neurology specific versus generic rehabilitation services after stroke.

There is good evidence of effectiveness from clinical trials of ESD but real world data might differ for a number of reasons. Firstly, inpatient care services are in many ways quite different to the services compared in the now, quite old, trials, with shorter overall lengths of stay. Similarly, although the ideal ESD service provides an equivalent intensity of therapy to inpatient services, in practice services might not deliver as much therapy as would be delivered as an inpatient therapy. For example, in the SSNAP Post-Acute Audit, only 29% of ESD teams reported that they provided a 7-day service to patients. Current SSNAP data therefore reflects the average treatment effects of more heterogeneous care models than were assessed in the ESD clinical trials.

1.2.4. What we know about the cost of stroke

Stroke accounts for between 2% and 4% of the total health care expenditure in developed countries. Moreover, stroke incurs substantial costs outside the health care system, reflecting survivors' high rates of disability and dependence. In 2008, the total direct and indirect costs associated with stroke were approximately £8.9 billion per year in the UK[6]. Most costs are incurred in the initial months and years after the patient has been discharged from hospital[7]. Studies from Italy [8], Denmark [9] and France [10] have produced similar estimates of the costs of stroke in Europe, at Euro 7000-20000 per stroke.

The previous modelling work carried out for the National Audit Office in 2008 was done as part of a wide-ranging review into the state of stroke care in the NHS at that time; it informed the development of national stroke strategy[11]. Stroke care has however changed significantly since this previous work: now almost all (96%; SSNAP Jan-March 2016) of patients are admitted to a stroke unit, all units provide 24/7 brain imaging and the proportion of patients treated with thrombolysis has increased from 1% to 11% (Sentinel 2008; SSNAP 2016). These previous cost estimates are therefore not just relatively old but no longer reflect current stroke care practice in the NHS.

1.3 Aim of this study

To provide data and information to providers, commissioners, policy makers and wider stakeholders on the value and cost of health care, in order to complement the current provision of the regular quality of care data from SSNAP. Aligning cost, quality of care, and outcomes data will be a powerful driver for quality improvement in stroke care. The analysis has two components:

Cost of illness

- Health economic modelling was used to generate estimates of the financial burden of stroke to the NHS and social care services. The estimates of costs attributable to stroke from resulting health and social care provision, were estimated up to five years after the first stroke.

Hypothetical scenarios

- Health economic modelling was used to estimate the benefits (QALYs) and cost savings associated with improving two aspects of the quality of stroke care: increasing use of thrombolysis (clot busting treatment) where appropriate; and increasing the proportion of patients discharged to an Early Supported Discharge team.

2 Methods

2.1 Model overview

2.1.1 Population

We have simulated the pathways of hypothetical people who have had a stroke in England, using data from real patients. We did not include in this model people with symptoms that mimic having a stroke or patients with a TIA.

We used the most recently available two years of data from SSNAP for patients aged 40-100: April 2013 – March 2015. In this period, around 90-95% of all stroke patients in England were captured in the SSNAP dataset. Patients with full NIHSS scores were included in the analysis, which were 111,846 in total.

2.1.2 Time horizon and perspective

Time horizon

The individuals were simulated for five years after the first stroke. One year and five years results after the first stroke were recorded.

Cost perspectives

We included NHS & social care perspectives in our analysis. We describe social care costs attributable to stroke but we were unable to differentiate between care home costs falling on the NHS, those falling on local authorities and those paid for by the individual or their family.

Health perspective

We estimated the Quality-adjusted life-years (QALYs) of patients as our primary health outcome; we did not include the quality of life of carers or family members in our analysis. The analysis follows the standard assumptions of the NICE reference case[12, 13] including incremental analysis. However, costs were not discounted.

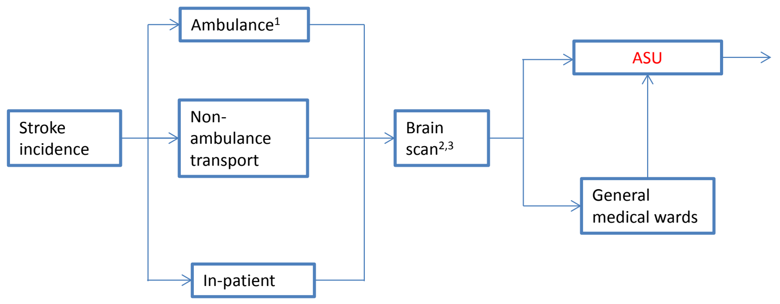
2.2 Model Structure

2.2.1 Approach to modelling

This model is an individual patient sampling model with continuous time (that is to say events can occur at any point in time rather than at fixed time points). The structure is shown in Figure 1. Hypothetical individuals enter the model at stroke onset, and are tracked overtime until they die or the end of the simulation (5 years). In this model, patients go through different 'treatment units' for health care. As patients pass through these treatment units, resources are used and the health status of the patient changes.

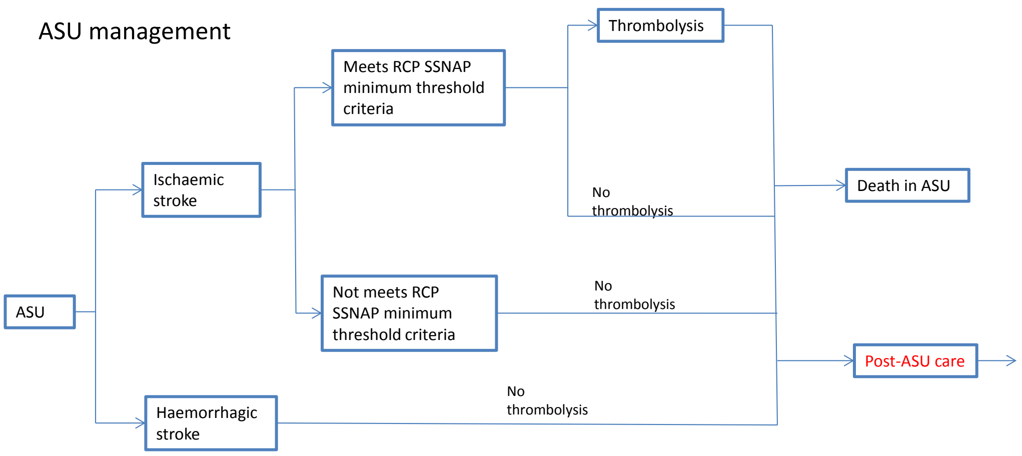
To model a continuous time effect and minimise the time required for the model to run, we built a discrete event simulation model and took the "determine event first then time" approach [14] [15] [16]. At each of the treatment units, the patient's next destination is determined by probabilities and then the time they spend in the current treatment unit is determined by a probability distribution. Length of stay within each unit is used to capture resource use as well as to keep track of the patient's time since onset. Other calculations involved in treatment units in this model are described in more detail in section 2.2.3.

Stroke onset

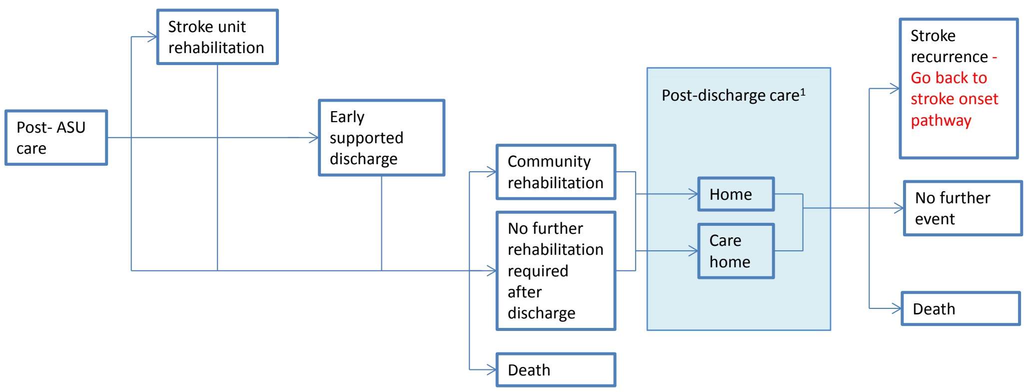


Notes:
1. The reason to separate ambulance from out-patient arrived hospital by other route is to account extra ambulance costs to the analysis
2. Assume 100% accuracy in brain scanning results
3. Patients might get CT or MRI scan

ASU management



Post-ASU management



Notes:
1. Post-discharge care including GP visits and therapies provided to patients after discharged or ESD program completed. Only costs covered by NHS and local authorities will be covered in the analysis

Figure 1: Flow of patients through the model

Other approaches that were considered include:

1) A state transition or Markov model estimates the number of events in a cohort over fixed time intervals rather than simulating individual patients. We wanted to explore thrombolysis and early supported discharge (ESD) in this project. The treatment effect and resources use of thrombolysis and other acute care is highly related to the first few days since stroke onset, and ESD is a more long-term treatment that might take weeks or months. Furthermore, the objective was to measure longer-term effects of these treatments up to 5 years. If days were used as a time-step, then the model would have taken too long to run. If, on the other hand, weeks or months had been used then the model would not capture important differences in acute care. Therefore, a continuous time approach was deemed more appropriate.

2) Discrete event simulation with "separate time to each potential next event" approach [16]is also widely used for models where event timing is an important factor such as transplantation models or cancer screening models. However, the stroke patient's pathway is more likely to be dependent on patient's status and doctor's decision rather than progression of the disease. For example, the patient's discharge destination after acute stroke care does not depend on which option comes to the patient first but rather on stroke severity and patients' level f independence. However we used this approach to estimate patient's survival and stroke recurrence after discharge because the next possible event (recurrence, death or end of simulation) was more likely to be dependent on which event came first to the patient (section 2.3.11).

In the model, patient's next destination is randomly sampled depending on the patient's age and severity, then length of stay is sampled dependent on a number of parameters, which will be explained in later sections.

The model is built in MS Excel Visual Basic Analogue (2010).

2.2.2 Patient specifications

The patient characteristics are randomly drawn before the simulation starts. Patient's sex does not change over time; age progresses with time in the model and health status will change due to the treatments the patient receives. Stroke type would not change during the treatment of the stroke but it might change at a stroke recurrence. Patient characteristics are taken from SSNAP.

Age & sex

Patient sex was determined before drawing other characteristics then patient age is drawn from an empirical distribution for men or women – see Appendix 1. Age was restricted to the range 40-100. A single age was simulated in the model for each patient, but most model calculations were based on age groups. Patients' age group might change during the simulation as age increases.

In the calculations, patients are grouped into four age groups for the purposes of:

- estimating treatment effects (severity change, mortality and length of stay)
- reporting results.

Table 1 Age groups

Age group	Min age	Max age
1	40	64
2	65	74
3	75	84
4	85	100

Stroke type

We only included ischaemic stroke and primary intra-cerebral haemorrhage (PICH) stroke in this study. TIA was excluded in our study, as data is not collected in SSNAP. Due to the big difference in the proportion of patients between the two included stroke types, we simulated them separately to ensure enough haemorrhagic strokes were simulated to estimate accurately the cost. Then aggregated results were calculated using the actual proportion of stroke types obtained from SSNAP data.

Health status

Initial stroke severity was measured in NIHSS in SSNAP and in the model. In our model, initial NIHSS was dependent on stroke type and on 5-year age groups – see Appendix 1. Length of stay in ASU and health status (modified Rankin Scale, mRS) when a patient was discharged from acute stroke unit was dependent directly on the patient's initial stroke severity. NIHSS was categorised into five groups as demonstrated in Table 2.

Table 2 Baseline NIHSS groups

Group	Baseline NIHSS
1	No stroke (0)
2	Minor (1-4)
3	moderate (5-15)
4	moderate/severe stroke (16-20)
5	severe stroke (21-42)

When a patient was discharged from each of the units, a new mRS score was sampled dependent on the patient's age and their health status when they entered that unit – see Appendix 1. All mRS data was obtained from SSNAP.

SSNAP did not have any longer term survival data, so we obtained the survival data from the South London Stroke Registry (SLSR). In SLSR, health status was measured in Barthel Index (BI) scores not mRS. We mapped from mRS to BI using a sub-sample of SSNAP patients where mRS and BI score were both recorded, so that we could estimate survival beyond discharge using the SLSR. There was a strong correlation, such that we decided to generalise using the classification in Table 3.

Table 3 Mapping between modified Rankin Scale and Barthel Index

mRS	BI
0 - No symptoms.	20
1 - No significant disability. Able to carry out all usual activities, despite some symptoms.	18-19
2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.	17
3 - Moderate disability. Requires some help, but able to walk unassisted.	12-16
4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.	2-11
5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.	0-1

Utility (health-related quality of life) was calculated by converting patients' mRS to EQ-5D - see 2.3.14.

2.2.3 Calculation in the units

In this model, patients were transferred between different units (Figure 1). The units are listed below (assumptions and model inputs for each of the units are listed in section *2.3*):

- General medical wards (GMW)
- Acute stroke unit (ASU) represents the acute care stroke experience
- Stroke unit (SU) is the unit where patients get in-patient rehabilitation.
- Early supported discharge (ESD): The unit where patients are treated by an ESD team at home.
- Community rehabilitation (CRT): The unit where patients are treated by a community rehabilitation team, it could happen either in their own home or in their care home.
- Home: Patients are discharged and staying at home.
- Care home: Patients are discharged and staying at care home.

Table 4 Treatment subgroups

Group	Age group	mRS
1	1 (40-64)	0
2	1 (40-64)	1
3	1 (40-64)	2
4	1 (40-64)	3
5	1 (40-64)	4
6	1 (40-64)	5
7	2 (65-74)	0
8	2 (65-74)	1
9	2 (65-74)	2
10	2 (65-74)	3
11	2 (65-74)	4
12	2 (65-74)	5
13	3 (75-84)	0
14	3 (75-84)	1
15	3 (75-84)	2
16	3 (75-84)	3
17	3 (75-84)	4
18	3 (75-84)	5
19	4 (85-100)	0
20	4 (85-100)	1
21	4 (85-100)	2
22	4 (85-100)	3
23	4 (85-100)	4
24	4 (85-100)	5

Calculation in each of the units was dependent on age and health status when the patient enters the unit. Patients were stratified in to sub-groups based on four age groups and six mRS scores therefore **24 sub-groups** in total (Table 4).

Health state change

In the model, a patient's health state changes at the end of the treatment unit. The new health state was dependent on the treatment subgroup using distributions from SSNAP – see Appendix 1.

Mortality

There is a probability of death in each unit, dependent on patient's subgroup when entering the unit – see Appendix 1. All causes mortality was used in the model.

Next destination

If a patient survived in the current unit, then this patient was transferred to another unit as shown in the model flow-chart. The specific next destination was dependent on the patient's health state when discharged from the current treatment unit, using SSNAP data – see Appendix 1.

Length of stay

For all units in this model except for ASU, length of stay in the current unit was randomly drawn from a certain distribution, the mean and standard deviation were different in different units, and dependent on the patient's age group, mRS when entering the unit, and their next destination.

Length of stay with CRT fitted better an exponential distribution; otherwise, the lognormal distribution was fitted to the SSNAP data using the R package "rriskdistribution". When fitting the distributions, the patients were stratified by their characteristics mentioned above.

Length of stay in the acute stroke unit was estimated using Generalised Linear Model (GLM) regression. The detailed method is described in section 2.3.6.1.

Length of stay in ASU, SU and ESD in the model was bounded to the 90th percentile of the length of stay in SSNAP to avoid implausible values:

Treatment unit	Maximum length of stay (days)
Acute stroke unit (ASU)	36.0
Stroke unit (SU)	70.8
Early supported discharge (ESD)	63.1

2.3 Model baseline inputs (data sources, data analysis, and assumptions)

The Sentinel Stroke National Audit Programme (SSNAP) was the major data source for this study. However, South London Stroke Registry (SLSR) was used for some of the longer-term data including survival and resource use, where this was not available in SSNAP.

2.3.1 SSNAP

SSNAP data between April 2013 and March 2015 were used to calculate most of the model inputs unless otherwise stated. All patients during this period were included in the analysis. STATA 2013 was used for data analysis unless stated otherwise.

Patients were stratified in to sub-groups based on four age groups and six mRS scores (Table 4 Treatment subgroups) for the following analysis:

- Mortality in each treatment unit

- Next destination (next treatment unit)
- Length of stay in each treatment unit
- Treatment outcomes (mRS score when the patient leaves the treatment unit).

2.3.1.1 South London Stroke Registry (SLSR) data

The SLSR is a population based stroke register. Subjects in this register are followed up after their first stroke. Data was collected prospectively from 12 referral sources cases of stroke in a defined area corresponding to 22 wards of Lambeth, Southwark, and Lewisham Health Commission.

The total population (357,308) is 56% white, 25% black (14% Black African, 7% Black Caribbean, and 4% Black Other), 6% Asian and 12% other ethnic groups. Hospital surveillance of admissions for stroke includes two teaching hospitals within and three outside the study area.

Survival and longer term resources using data including frequency of using GP and social care services was analysed for this study using STATA 2013.

2.3.2 Summary of inputs

An overview of the data inputs is shown in Table 5. Most data inputs are stratified by age and severity (mRS) subgroup – these detailed data inputs can be found in Appendix 1.

Table 5: Data requirements, by treatment unit

Treatment unit	Health state change	Length of stay	Mortality	Next destinations	Resource use	Other inputs
Acute stroke unit (ASU) and thrombolysis	Thrombolysed patients: mRS when leaving ASU was dependent on NIHSS 24 hours after thrombolysis and age group Not thrombolysed patients – mRS when leaving ASU was dependent on NIHSS when admitted to hospital and age group	GLM with family of gamma and log link • Age • Sex • Thrombolysed patients – NIHSS after thrombolysis • Not thrombolysed patients – NIHSS when admitted to hospital • Discharge destination	Mortality probability in ASU was dependent on age group and mRS and was different in thrombolysed and not thrombolysed patients. All causes mortality was used for both groups.	ESD SU CRT Discharge with no need for rehabilitation	Thrombolytic therapy for those patients who were thrombolysed Acute stroke unit stay	Proportion of patient that was eligible for thrombolysis
General medical wards (GMW)	No health state change involved in GMW due to the lack of data and relatively short period of time in GMW	Fixed average length of stay	No mortality in the model. SSNAP only collected data for patients who entered stroke units and period is typically short.	ASU	General medical ward stay	Proportion that were admitted to GMW (rather than ASU) after brain scan
Stroke unit (SU) - inpatient rehabilitation	Health state change was dependent on age group and mRS when entering SU	Length of stay was sampled from a lognormal distribution with the parameters dependent on the next destination (including death), age group and mRS when entering SU	Dependent on age and mRS on arrival at SU	ESD CRT Discharge with no need for rehabilitation	Stroke unit stay	
Early supported discharge (ESD)	Health state change is dependent on age group and mRS when entering ESD	Length of stay was sampled from an exponential distributions with the	Dependent on age and mRS when arrived to ESD	CRT Discharged to own home or nursing home	Mean number of days of Physiotherapy, occupational therapy, speech and language	

Treatment unit	Health state change	Length of stay	Mortality	Next destinations	Resource use	Other inputs
		parameters dependent on age and mRS when entering ESD			therapy per ESD treatment package on an average patient by age and mRS. Mean number of hours of psychological therapy time per ESD treatment package by age and mRS.	
Community rehabilitation team (CRT)	Health state change is dependent on age group and mRS when admitted by a community rehabilitation team (CRT).	Length of stay with CRT is determined by a discrete event algorithm. Details explained in section 2.3.10	Survival curve was fitted dependent on age, sex, mRS at discharge and stroke type (Cox regression).	Discharged to own home or care home	Community rehabilitation treatment cost episode GP visits Usage by age and mRS of: Care home cost (if newly admitted), Home help, Meals on wheels, Social service day centre	Proportion that stayed at own home/care home while doing community rehabilitation treatment
Discharged to own home or care home	No health state change after discharge (unless they have a recurrence)	Length of stay at own home/care home after discharge is determined by a discrete event algorithm. Details explained in section 2.3.11	Survival curve is dependent on age, sex, mRS at discharge and stroke type (Cox regression).	Patients might have stroke recurrence after discharge.	GP visits Usage by age and mRS of: Care home cost (if newly admitted), Home help, Meals on wheels, Social service day centre	Proportion of patients discharged to own home or care home
Stroke recurrence	Recurrence severity is measured in NIHSS, dependent on recurrence type, independent from age and previous severity	Same pathway as first stroke (dependent on age and severity)	Same pathway as first stroke	Same pathway as first stroke	Same pathway as first stroke	Recurrence rate and severity from SLSR

GLM=generalised linear model, mRS=modified Rankin Scale, NIHSS=National Institutes of Health Stroke Scale, SLSR=South London Stroke Registry, SSNAP=Sentinel Stroke National Audit Programme

2.3.3 Demography

For reporting purposes, we used 80 subgroups from the SSNAP dataset, based upon age, sex, stroke type and initial stroke severity (NIHSS). The sample size for each subgroup is shown in Table 6. Results were calculated for each subgroup separately and then the numbers in Table 6 were used to produce weighted averages.

Table 6: Number of patients in each of the sub-groups in the SSNAP dataset

		Ischaemic		Haemorrhagic	
Age group	Initial NIHSS	Male	Female	Male	Female
1 (40-64)	0	989	476	107	62
1 (40-64)	1-4	5127	2951	361	150
1 (40-64)	5-15	2950	1798	400	193
1 (40-64)	16-20	318	235	113	49
1 (40-64)	21-42	233	147	100	61
2 (65-74)	0	926	446	85	47
2 (65-74)	1-4	5749	3089	356	212
2 (65-74)	5-15	3432	2087	371	233
2 (65-74)	16-20	459	321	82	70
2 (65-74)	21-42	386	272	95	89
3 (75-84)	0	1048	785	120	105
3 (75-84)	1-4	7583	5549	548	366
3 (75-84)	5-15	4807	4270	589	476
3 (75-84)	16-20	777	795	170	153
3 (75-84)	21-42	717	778	215	255
4 (85+)	0	843	1046	107	122
4 (85+)	1-4	6815	8631	487	589
4 (85+)	5-15	5797	9692	655	900
4 (85+)	16-20	1116	2472	201	297
4 (85+)	21-42	1285	3025	317	625

2.3.4 Patient transport

The cost of the ambulance service was included for those patients arriving by ambulance – 77.3% from SSNAP.

2.3.5 Brain scan

Two brain scan methods are included in the analysis, MRI and CT scan. According to the National Clinical Guideline for Stroke [3], all patients should be scanned within 1 hour with urgent indications and everyone within 12 hours of admission. We assume all patients will be scanned. After brain scan, patients will be distributed to either acute stroke unit (ASU) or general medical wards (GMW). Time tracking starts in the model from the point that they are admitted to the ASU or GMW.

Assumptions	Explanation
100% of the patients get scanned	SSNAP data shows that more than 99% of all stroke patients get scanned in the hospital
100% accuracy of scan	Expert opinion
98.1% CT, 1.9% MRI	SSNAP

2.3.6 ASU and Thrombolysis

Configuration of services for patients in the first 72 hours is different in different parts of England. In London, hyper-acute stroke units (HASUs) provide the acute stroke care for the first 72 hours and acute stroke units provide on-going care and rehabilitation. However in other places, there is no distinct HASU, and acute stroke unit provides both acute care and rehabilitation care. In our model, we distinguish between the '**acute stroke unit'** that provides acute stroke care and the '**stroke unit'** that provides the inpatient rehabilitation and longer-term care.

In practice, the distinction between acute care and rehabilitation might not be very clear and it was not always clear looking at the SSNAP data. We assumed the first team the patients were treated with provides acute stroke care and all the rest are rehabilitation services.

In our model, if a patient goes straight to ASU after admission, then the patient will have a chance of getting thrombolysis. This probability is dependent on two factors: the probability that the patient meets the SSNAP minimum criteria and the probability that a patient receives thrombolysis given the patient met the minimum criteria (Figure 2 and Figure 3). These baseline probabilities were obtained from SSNAP data; so too were mortality, length of stay, health status change and next destination - see Appendix 1.

Assumptions	Explanation
Thrombolysis treatment affects mRS and mortality in ASU. Patients were not distinguished by their thrombolysis status after they were discharged from ASU.	Treatment effects in this model were represented by severity change during ASU. There is an additional treatment effect of thrombolysis is represented by the mRS score of the patient when discharged from ASU.
Ischaemic stroke and haemorrhage stroke treatment differs in terms of thrombolysis and length of stay.	Patients with haemorrhagic stroke are more likely to have a more severe stroke and therefore a longer length of stay. Patients with haemorrhagic stroke are contraindicated to thrombolysis.
An average per day cost was used. We assumed the same per day cost for patients with different levels of severity but older patients and those with more severe strokes stay in ASU for longer and therefore incur more cost.	We did not have data to differentiate cost per day in ASU. However, resource use in terms of doctors and nurses might not differ greatly between patients with different levels of stroke severity.

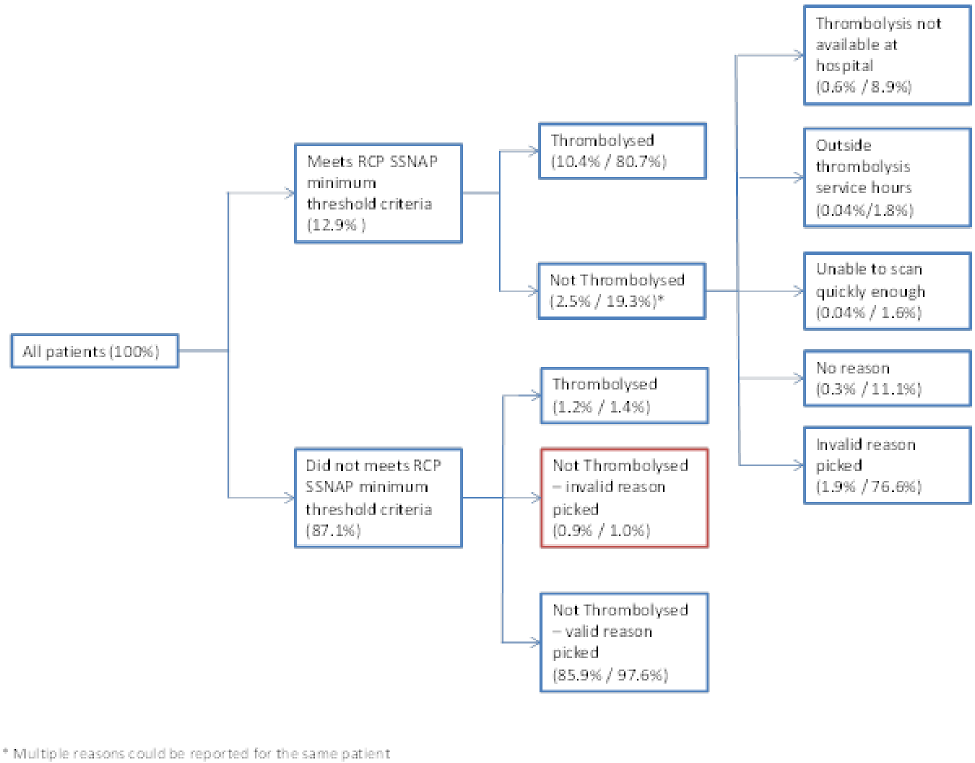
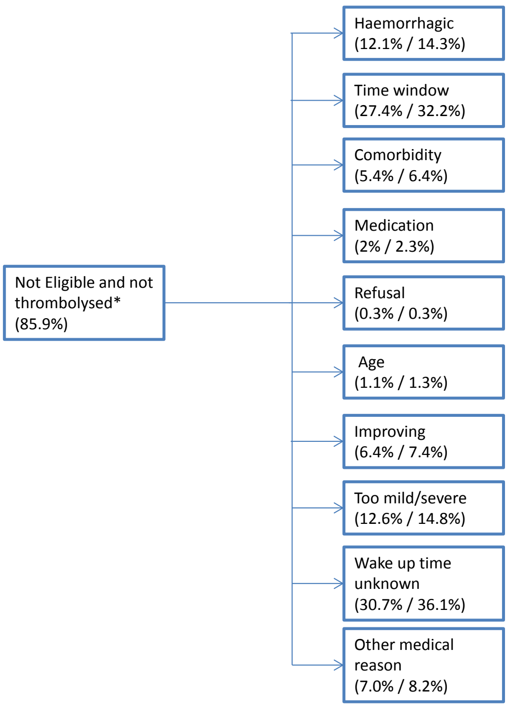


Figure 2 Decision tree of thrombolysis based on RCP SSNAP minimum threshold criteria.
Figures reported are (probability within branch / probability within whole tree).



Notes:
1. More than one reason could be chose for the same patient

Figure 3 Distribution of reasons picked by the doctors why they did not treat patients with thrombolysis.

2.3.6.1 Calculation of length of stay in the Acute Stroke Unit (ASU)

Compared with the other treatment units, length of stay (LOS) in ASU was less clear-cut. In the other treatment units, patients were stratified by their age group, mRS when leaving the unit and their possible discharge destinations to sample their length of stay. However, in ASU, the numbers of possible discharge destinations were greater, and patients needed to be distinguished by their thrombolysis status as well, which made 192 sub-groups in total. Therefore, in ASU we chose to fit a generalised linear model (GLM) for LOS in ASU by patient's age, sex, NIHSS score, discharge destination and thrombolysis status. The model was fitted using Stata14.

The model selection procedure follows the method paper by Grover et al [17], which used the Akaike Information Criterion (AIC) as the criteria to select the best fitted model. We fitted Gaussian, Poisson and gamma GLM models. A gamma distribution with log link had the best fit – see Appendix 1.

In terms of the independent variables to be included in the model, we found that NIHSS score at admission was significant when NIHSS score after thrombolysis was not included in the model. On top of that, when we separated thrombolysed and not thrombolysed patients, then the NIHSS score at admission was a significant variable in the model with not thrombolysed patients, and it was not significant in the model of thrombolysed patients, but NIHSS score after thrombolysed was significant in thrombolysed patients. Therefore, we decided to analyse thrombolysed and not thrombolysed patients separately. For thrombolysed patients, NIHSS score after thrombolysis was used and NIHSS score at admission was used for patients who did not get thrombolysed.

2.3.7 General medical wards admission

A certain proportion of patients are admitted to a general medical ward (GMW) instead of ASU when they first arrive at hospital usually because there are no available beds in the ASU. We included this pathway in our analysis to capture the resource use. For patients who were admitted to GMW when they arrived at hospital, we assume they will not get thrombolysis. We assumed that all of them are transferred to ASU when a bed becomes available.

Assumptions	Explanation
No severity change in GMW	There is not data on how stroke patients health state will be changed in GMW, how patients were treated in GMW could vary from hospital to hospital as well
No thrombolysis available in GMW	[3, 18]
All patients will be transferred to ASU after GMW	95.4% of patients admitted to stroke unit at some point at the first admitting hospital. For simplicity, we assumed that all are, since the pathway for the remaining patients would be varied and difficult to model.
Fixed length of stay on GMW (before transfer to ASU).	Given the small numbers, we could not differentiate length of stay by patients' initial severity and age group, therefore a constant value was used.

2.3.8 Stroke unit (in-patient rehabilitation)

We used the term "stroke unit" to represent the post-acute phase of stroke inpatient care. It was considered as an alternative to ESD. This pathway is called the "conventional discharge" pathway in some studies [18]. Mortality, length of stay, health status change and next destination were estimated by treatment subgroup using SSNAP data - see Appendix 1.

In clinical trials, patients either were discharged to ESD or else get rehabilitation in the hospital as the control intervention. However, SSNAP data also shows that some patients get both inpatient rehabilitations and subsequent discharge to the ESD team. Therefore, in the model, after the stroke units, patients could be discharged to ESD or CRT or they might not need further rehabilitation.

Assumptions	Explanation
We assumed the first team/hospital the patient was treated with provided acute care and classified as ASU when analysed the SSNAP data, and all the rest inpatient treatments were classified as SU rehabilitation (or inpatient rehabilitation)	SSNAP does not contain detailed data on what care a patient gets in each hospital. However, it seems reasonable to assume that for most patients no additional acute care is required for patients who are transferred to the next team or hospital.

2.3.9 Early supported discharge

As mentioned in the earlier sections, ESD is designed to substitute care, replacing rehabilitation procedures performed in hospitals with equivalent ones in the patient's own home. In our model, ESD, as described in the stroke guideline [3], provided rehabilitation services that were similar to inpatient rehabilitation services but in their own home (not in a care home). Calculation in the model for the ESD unit was similar to any other units (as described in 2.2.3). Mortality, length of stay, health status change and next destination were estimated by treatment subgroup using SSNAP data - see Appendix 1.

Teams who identified themselves as an Early supported discharge team were heterogeneous. Not all patients reported as being cared for by the ESD were actually treated to the full ESD standard. In SSNAP data, some community rehabilitation teams do both ESD and CRT treatments and although the teams are advised to separate out the care being delivered within the ESD, this is not always consistently recorded. As there is not complete participation by all ESD teams in SSNAP, there are instances when the acute hospital reported that a patient was discharged to an ESD team but the record was not completed by the team. To avoid dilution of treatment effects, for the purposes of calculating health outcomes, we only included those patients whose discharge info matched their treatment details.

We did not find any source of unit costs for ESD from previous studies; therefore, we used therapists' time to estimate total costs. Average therapists' time per patients by sub-groups was estimated using SSNAP data, and then we used unit costs per visit or per hour of therapist time to estimate total costs of an ESD treatment package (Table 8).

Assumptions	Explanation
Patients will have a maximum of one OT, PT and SLPT visit per day	Unit costs for OT, PT and SPLT are per service based. However SSNAP only has data of days patients see OT, PT and SLPT, therefore we assumed patients will only have one of each per day
All patients in ESD programs are living at home	Patients will only be discharged to ESD if they live with someone at home or are independent enough to live by themselves
23% of staff cost added to cover overhead costs in sensitivity analysis	[19]

2.3.10 Community rehabilitation

Community rehabilitation is a rehabilitation process provided by community teams (CRT). Compared to ESD, it is more likely to be over a longer time but is less intensive. In our model, we assumed CRT patients would be treated in their own home or within a care home.

Since CRT could be a longer-term treatment, and it is less likely to affect mortality of patients, we assumed that survival and recurrence for community rehabilitation patients were the same as for patients who were discharged home without community rehabilitation – see Appendix 1. A discrete event simulation with "separate time to each potential next event" approach [16] was used to determine the length of stay in the CRT programme. A time was sampled for each of the possible events: end of CRT, death, or stroke recurrence, then the earliest event to happen was determined as the next event. If the end of CRT comes first then the next destination will be discharged to own home or care home. The proportion of patients discharged to their own home or care home was obtained from the SSNAP data.

To avoid dilution of treatment effects, for the purposes of calculating health outcomes, we only included those patients whose discharge info matched their treatment details – the same approach as for ESD.

A per episode cost was used and the cost was taken from the PSSRU 2014 report [20].

Assumptions	Explanation
We assume patients did not move location during and after community rehabilitation, i.e. if patient's record shows that patient were at home after CRT then we assume they did not move to a care home during or after the CRT process	Due to the lack of data of patients' location (own home or care home) during community rehabilitation,
We applied an average community rehabilitation programme cost per patient referred	Cost was from the PSSRU's Unit Costs Of Health and Social care 2014 section 1.8

2.3.11 Discharged to own home or care home

Patients were categorised as 'Discharged to own home or care home' once all treatment and rehabilitation procedures were finished. The proportion of patients discharged to own home or care home was obtained from SSNAP. Once the patient has been discharged then a similar discrete event simulation to that used for community rehabilitation (see above) was applied to determine time to recurrence or death.

Assumptions	Explanation
It was assumed that health state (mRS) does not change after the patient is discharged (unless they have a stroke recurrence)	There was a lack of data on patient's health state or severity changes after discharge, and it might be influenced by many things that are not stroke related.
People discharged to their own home or care home will stay at the same place until death or stroke recurrence	We did not have data on the proportion of patients that move between home and care home but again this might be influenced by things that are not stroke related.
if patients were in a care home then they would not use the home help, meals on wheels and social day centre services	These services are generally provided to people who live in their own home.
NHS resource use	
GP visits – 14.1 visits per patient per year.	Frequency of GP visits is from SLSR; the mean number for all stroke patients was used
Social care resource use	

Assumptions	Explanation
Care home – proportion of patient discharged to care home by age group and mRS at discharge – See Appendix 1	From SSNAP. We did not cost care home for those patients who were recoded as independent before their stroke.
Home help – mean number of visits per patient by age groups and mRS.- see Table 9	SLSR survey at 3 months after discharge
Meals on wheels– 3% of patients.	SLSR survey at 3 months after discharge.
Social service day centre visits – 1.5 visits per patient per year	From SLSR, mean for all stroke patients.

2.3.12 Stroke recurrence

Stroke recurrence is more dependent on underlying conditions such as diabetes, hypertension or smoking status [21, 22] but these are not available from SSNAP so we did not model them. Instead, we assumed recurrence was dependent only on the type of the primary stroke.

Recurrence rates were extrapolated from the SLSR dataset – see Appendix 1. SLSR collected recurrence data at 3 months, then yearly for 5 years. Proportions of all stroke patients in SLSR who had recurrence at each of the time points were calculated. The type and severity profile of recurrent stroke was also taken from the SLSR.

Once a patient has a stroke recurrence in the model, they start from the beginning of the clinical pathway, health status and costs will be updated according to the exact path the patient takes. We assume no difference in patient pathway between primary and recurrent stroke. We also assume patients will have a maximum of three recurrences; at the fourth recurrence, it is assumed that the patient will die immediately at stroke onset.

Assumptions	
Patient pathway is assumed to be the same for recurrent and first- stroke	We found no evidence to suggest a different management strategy for patients.
Recurrence rate is not dependent on age or previous stroke severity	Stroke recurrence is more dependent on the underlying risk factors which were not included into the model due to the lack of data
Maximum of 3 non-fatal stroke recurrences per person	Expert opinion [18]

2.3.13 Unit costs

Unit costs(Table 7) were taken from standard sources where possible such as the NHS Reference costs[23] or the Personal Social Services Research Unit's 'Unit costs of health and Social Care'[20]. Early supported discharge costs (Table 8) and social care costs (Table 9) varied by subgroup according to usage of services, as described above.

Table 7 NHS and social care unit costs

Cost Item	Unit cost (£)	Data Sources
Ambulance	233	PSSRU 2014 7.1
MRI	143	NHS reference costs 2013-2014 RA01A
CT scan	91	NHS reference costs 2013-2014 RA08A
Thrombolysis	875	NHS reference costs 2013-2014 YR23A-B (day-case)
Acute stroke unit per day	649	NHS reference costs 2013-2014 – average cost per day of short-stay AA35A-F
General medical ward per day	210	NAO report[18] inflated to 2015 prices
Stroke unit per day	233	NHS reference costs 2013-2014- average per day cost in non-elective long-stay stroke patient AA35A-F
ESD Occupational therapy per visit	74	NHS reference costs 2013-2014 A06A1
ESD Physiotherapy per visit	52	NHS reference costs 2013-2014 WF01B
ESD Speech and language therapy per visit	84	NHS reference costs 2013-2014 A13A1
ESD Psychologist per hour	61	Community therapist are collected from PSSRU 2014, 9.5
Community rehabilitation per patient referred	2808	PSSRU 2014, 1.8
GP visit –23.4 minutes service + 12 minutes travel time	103	PSSRU 2014, 10.8b&B.1
Care home per day	157	PSSRU 2014 1.3 –not including personal expenses
Home help – community care package per week mRS=1	37	PSSRU 2014 8.1 – older person very low cost
Home help – community care package per week mRS=2	148	PSSRU 2014 8.1 – older person low cost
Home help – community care package per week mRS=3-5	370	PSSRU 2014 8.1 – older person medium-high cost
Meals on wheels per week	46	PSSRU 2014 8.1
Social service day centre visit	56	PSSRU 2014 1.6

Table 8 Early supported discharge team resource use and cost

Age group	mRS	Mean number of Occupation-al therapy sessions	Mean number of Physio-therapy sessions	Mean number of Speech and language therapy sessions	Mean number of hours of psycho-therapy	Mean costs without overheads	Mean costs with 23% overheads
40-74	0	6.5	4.9	5.2	3.4	£ 1,381	£ 1,699
40-74	1	6.6	5.3	5.8	2.7	£ 1,410	£ 1,735
40-74	2	7.9	6.4	6.5	2.8	£ 1,633	£ 2,008
40-74	3	10.2	8.2	7.5	2.5	£ 1,969	£ 2,421
40-74	4	15.3	11.3	7.4	2.1	£ 2,478	£ 3,048
40-74	5	12.6	9.9	7.8	1.9	£ 2,217	£ 2,727
75-100	0	6.4	5.1	4.9	2.0	£ 1,269	£ 1,561
75-100	1	6.5	5.1	5.1	2.2	£ 1,307	£ 1,607
75-100	2	7.5	6.1	6.0	1.3	£ 1,452	£ 1,786
75-100	3	8.7	7.6	6.6	1.8	£ 1,704	£ 2,096
75-100	4	10.5	8.0	5.1	1.9	£ 1,744	£ 2,145
75-100	5	9.2	7.4	3.8	1.7	£ 1,495	£ 1,839

Table 9: Social care costs for people living in their own home

Age group	mRS	Home help			Meals on wheels			Social services day centre visits		
		Unit cost (weekly) (£)	Proportion of patients used the service	Yearly cost (£)	Unit cost (per week) (£)	Proportion of patients used the service	Yearly average cost per patient (£)	Unit cost (per visit) (£)	Average frequency using this service(per year)	Yearly average cost per patient(£)
40-74	1	37	10.3%	200	46	3.0%	71.01	56	1.52	85.38
40-74	2	148	14.3%	1,102						
40-74	3	370	20.0%	3,859						
40-74	4	370	44.4%	8,575						
40-74	5	370	0.0%	8,575						
75-100	1	37	25.0%	482						
75-100	2	148	20.0%	1,543						
75-100	3	370	58.3%	11,254						
75-100	4	370	57.1%	11,025						
75-100	5	370	50.0%	9,646						

2.3.14 Utilities

EQ-5D scores were converted from mRS using an equation from a study by Whynes and colleagues [24]. This study used data from 1462 patients from the Efficacy of nitric Oxide in Stroke (ENOS) trial to examine the differential functioning for the EQ-5D instrument between different countries. The trial was a multinational clinical trial that investigated the use of glyceryl trinitrate therapy following acute stroke, it included more than 150 hospitals in 16 different countries. The EQ-5D questionnaire was completed during the trial follow-up with the clinical data collected. The clinical data included mRS, BI, the Short Zung Depression Scale, and other clinical outcomes. Whynes et al conducted their linear regression models and their majority patients were recruited from the UK sites. They predicted EQ-5D scores (UK tariff) using clinical outcomes including mRS scores, BI and Zung scores, they also added other variables including whether the form completed by proxies rather than patients themselves, and the countries of patients.

Due to lack of other data in our data set, we used the results from the equation that used mRS as the only dependent variable to predict EQ-5D. However they reported that the other parameters did not add much to the explanatory power of the model (R^2=0.70 vs R^2=0.66).

An alternative source was the study conducted by Rivero-Arias et al [25]. However, both studies produced very similar regression coefficients and the Whynes study was slightly more recent with a slightly bigger sample size.

Table 10 EQ-5D utilities from modified Rankin Scale

mRS	EQ-5D utilities
0	0.93
1	0.85
2	0.71
3	0.55
4	0.28
5	-0.15

2.4 Model calibration and validation

2.4.1 Internal validity

Model structure, inputs and results were presented to and discussed with clinical experts and the SSNAP technical team to assess face validity and interpret the findings.

The model was systematically checked by the health economists; this included inputting null and extreme values and checking that results were plausible given inputs.

2.4.2 External validity and model calibration

SSNAP would seem to be ideal for estimating the burden of stroke in England. However, there are advantages and disadvantages of using it to estimate treatment effects and cost-effectiveness of treatments.

The advantage is that trials are selective in the patients they use and therefore might not be generalisable. However, the disadvantage with observational studies like SSNAP is that unknown confounders and bias are unavoidable. Organisations that routinely conduct health technology assessment, such as NICE tend to prefer randomised evidence for treatment effects but observational evidence for baseline effects.[13] Therefore, we used relevant Cochrane reviews of randomised controlled trials to calibrate the model input data, for the purposes of conducting the cost-effectiveness analysis of thrombolysis and early supported discharge.

For each parameter that was calibrated, e.g. mortality, it was adjusted by the same factor in all relevant age-severity subgroups.

2.4.2.1 Thrombolysis

To ensure treatment effect of thrombolysis used in this model was as close as possible to the treatment effects observed in the trials, we compared and calibrated our model to the Cochrane review[26] for the following items:

Short-term mortality (7-10 days)

We first compared the mortality rate in the model output with that in the Cochrane review. The Cochrane review reported odds ratio of death at 7-10 days comparing thrombolysed patients with those not thrombolysed. We compared this with the odds of death in the model within ASU (see section 2.3.6 ASU and Thrombolysis) for thrombolysed versus non-thrombolysed ischaemic stroke patients.

Longer-term outcomes (typically 90 days)

The Cochrane review reported mortality, mRS score 3-6, 2-6 and 3-5 for ischaemic stroke patients who were either thrombolysed or not thrombolysed. The most common follow-up period was 90 days so we compared these results with the results from our model at 90 days.

2.4.2.2 ESD

We compared ESD model output with Cochrane review [27] . The three relevant outcomes in the Cochrane review were “Death”,” length of hospital stay”, and “Death or dependency”. There are three different types of ESD in the Cochrane review:

- ESD team co-ordination and delivery

- ESD team co-ordination
- No ESD team

When analysing SSNAP for the model, we defined ESD patients as patients who had record of being discharged to an ESD team and a record of being treated by an ESD team therefore we chose to focus the comparison of the model results to the Cochrane review meta-analysis results under the “ESD team co-ordination and delivery” category only. We excluded patients discharged from ASU directly with no rehabilitation required in the comparison. Most of the studies included in the Cochrane review followed their patients up for around 12 months therefore we took the model results at one year to compare with the Cochrane review data. We defined dependency as mRS 3-5.

2.5 Scenario analysis

2.5.1 Baseline scenarios

Analysis 1. Using SSNAP data directly

To estimate the cost of stroke per patient, we used SSNAP data without modification for the model inputs. Patients were stratified by their age at first stroke onset, sex, initial severity of their first stroke and first stroke type. One year and five years costs are calculated in this analysis.

Analysis 2. Using calibrated treatment effect data

In section 2.4.2, the mRS change and mortality after thrombolysis were calibrated to clinical trial results to ensure the incremental results reflect the treatment effects seen in the randomised trials. Therefore, a different baseline scenario with the calibrated data was used to compare the other scenarios with current practice. This analysis used the calibrated treatment effect data but with the proportion of patients receiving thrombolysis and/or ESD from SSNAP. The results of this analysis were then used for the scenario analysis where additional patients in the model were diverted to receive treatment with thrombolysis (or ESD depending on the scenario being compared).

2.5.2 Thrombolysis scenarios

The input set that was calibrated to systematic review results (section 2.4.2) was used for this analysis to remove potential confounders and bias. We modelled scenarios to estimate differences in costs, outcomes and incremental cost-effectiveness comparing current practice and hypothetical scenarios where more patients were thrombolysed. As can be seen below there are some modifiable characteristics that could increase the rate of thrombolysis if there were changes in practice.

In SSNAP, the reason for a patient not receiving thrombolysis is recorded as shown in Figure 3. It is known from the trials that there is always a proportion of patients that are not suitable for thrombolysis.

In SSNAP data, the reasons patients did not get thrombolysis were recorded and validated. We conducted the following analysis:

Analysis 3. Different percentage of patients who met SSNAP minimum criteria and were not thrombolysed now receive thrombolysis treatment

Analysis 4. 50% of patients who did not get thrombolysis due to the following reasons now meet the criteria by age and initial severity:

a. Not arriving within thrombolysis time window

b. Wake-up time unknown
c. Too mild/severe
d. One or more of criteria above

The new probability of meeting SSNAP minimum thrombolysis criteria for each sub-group was calculated using the equation below:

$$P_{new} = (n_{baseline} + n_{new})/N$$

Where
$n_{baseline}$ = number of people that met the SSNAP minimum criteria in baseline data for this subgroup
N = total number of ischaemic patients in this sub-group in baseline data
$n_{new} = n_{ischaemic\ patients\ who\ had\ not\ met\ criteria\ for\ this\ scenario} * 0.5$
The proportion of ischaemic patients what was thrombolysed is demonstrated in Table 11.

Table 11: Proportion of ischaemic stroke patients being thrombolysed in scenario analyses, by case-mix subgroups

Age group	NIHSS	Baseline	a. Not arriving within thrombolysis time window	b. Too mild/severe	c. Wake-up time unknown	d. One or more of criteria a, b and c
1 (40-64)	0	3%	16%	10%	8%	36%
1 (40-64)	1-4	7%	22%	13%	14%	41%
1 (40-64)	5-15	31%	41%	31%	39%	51%
1 (40-64)	16-20	39%	42%	39%	46%	51%
1 (40-64)	21-42	31%	34%	31%	38%	43%
2 (65-74)	0	3%	16%	11%	9%	36%
2 (65-74)	1-4	7%	20%	13%	15%	41%
2 (65-74)	5-15	28%	37%	28%	37%	49%
2 (65-74)	16-20	38%	42%	38%	46%	52%
2 (65-74)	21-42	34%	38%	35%	42%	47%
3 (75-84)	0	2%	13%	9%	9%	34%
3 (75-84)	1-4	5%	18%	11%	15%	39%
3 (75-84)	5-15	21%	30%	22%	33%	44%
3 (75-84)	16-20	33%	37%	33%	43%	49%
3 (75-84)	21-42	26%	29%	26%	35%	41%
4 (85+)	0	2%	12%	9%	11%	33%
4 (85+)	1-4	4%	15%	9%	15%	37%
4 (85+)	5-15	14%	22%	14%	28%	38%
4 (85+)	16-20	20%	24%	20%	33%	39%
4 (85+)	21-42	19%	22%	20%	30%	38%

2.5.3 ESD scenarios

The purpose of these analyses is to examine the effect of changing the proportion of people receiving ESD. Similar to thrombolysis, not all patients are suitable to be discharged to ESD. In practice, patients will usually be considered suitable to be discharged to ESD if they are:

- Independent or has a carer at home after stroke,
- Not severely disabled before stroke –and
- No language and speech problem

We did not have data on the patients' carer or whether the patient has language or speech problem, therefore the only standard we could use to examine whether a patient is suitable to be discharged to ESD is whether the patient could walk independently or not, which was assumed to be mRS 3 or less.
The following analyses were conducted:

Analysis 5. Increase proportion of patients discharged to ESD regardless of age and severity

- 20% of patients who were not discharged to ESD now discharged to ESD
- 35% of patients who were not discharged to ESD now discharged to ESD
- 50% of patients who were not discharged to ESD now discharged to ESD
- 80% of patients who were not discharged to ESD now discharged to ESD

Analysis 6. Increase proportion of patients discharged to ESD in less severe patients

- 20% of mRS 0-2 patients who were not discharged to ESD now discharged to ESD
- 35% of mRS 0-2 patients who were not discharged to ESD now discharged to ESD
- 50% of mRS 0-2 patients who were not discharged to ESD now discharged to ESD
- 80% of mRS 0-2 patients who were not discharged to ESD now discharged to ESD

For both analyses 5&6, patients were switched as follows:

- ASU->CRT to ASU->ESD,
- ASU->SU to ASU->ESD, and
- ASU->SU->CRT to ASU->SU->ESD.

Patients who were discharged from ASU with no rehabilitation requirement were not switched on the assumption that they did not need rehabilitation.

2.6 Cost effectiveness calculations

The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This is calculated by dividing the difference in costs associated with 2 alternatives by the difference in QALYs. The decision rule then applied is: if the ICER falls below a given cost per QALY threshold the result is considered to be cost effective. If both costs are lower and QALYs are higher, then the intervention is said to dominate the comparator and an ICER is not calculated.

$$ICER = \frac{Costs(B) - Costs(A)}{QALYs(B) - QALYs(A)}$$ Where: Costs(A) = total costs for option A; QALYs(A) = total QALYs for option A	Cost-effective if: • ICER < Threshold

When there are more than 2 comparators, as in this analysis, options must be ranked in order of increasing cost then options ruled out by dominance or extended dominance before calculating ICERs excluding these options. An option is said to be 'dominated' and ruled out if another intervention is less costly and more effective. An option is said to be extendedly dominated if a combination of 2 other options would prove to be less costly and more effective.

It is also possible, for a particular cost-effectiveness threshold, to re-express cost-effectiveness results in term of net monetary benefit (NMB). This is calculated by multiplying the total QALYs for a comparator by the threshold cost per QALY value (for example, 20,000) and then subtracting the total costs (formula below). The decision rule then applied is that the comparator with the highest NMB is the most cost-effective option at the specified threshold. That is, the option that provides the highest number of QALYs at an acceptable cost.

$$Net\ Monetary\ Benefit(X) = \left(QALYs(X) \times \lambda\right) - Costs(X)$$ *Where: λ = threshold (20,000 per QALY gained)*	Cost-effective if: • Highest net benefit

Both methods of determining cost effectiveness will identify exactly the same optimal strategy. The advantage of NMB is it allows the other interventions to be ranked. We calculated both ICERs and NMB.

We use a threshold of 20,000 per QALY gained to assess cost-effectiveness – the lower end of the range considered by NICE.[12, 13]

Where we had multiple strategies we also presented the results graphically where total costs and total QALYs for each strategy are plotted against each other. Comparisons not ruled out by dominance or extended dominance can be joined by a line on the graph where the slope represents the incremental cost-effectiveness ratio.

2.7 Probabilistic Sensitivity analysis

The model was built probabilistically to take account of the uncertainty around input parameter point estimates. A probability distribution was defined for each model input parameter. When we run a probabilistic sensitivity analysis (PSA), simultaneously, for each input, a value was randomly selected from its respective probability distribution; and each set of inputs would generate a new set of results. The model was run repeatedly – 400 times each for the baseline and two key scenarios – and results were summarised. For thrombolysis, we did the PSA around the scenario where 95% of the patients who met the minimum SSNAP criteria get thrombolysed. For ESD we did the PSA for the scenario where 35% patients who were not discharged to ESD now discharged to ESD. Mean results of the 400 sets of key results were calculated, along with the 2.5th and 97.5th centiles. Each of the 3 PSAs took about a week to run on a PC.

The way in which distributions are defined reflects the nature of the data, so for example probabilities were given a beta distribution, which is bounded by 0 and 1, reflecting that the probability will not be outside this range. The distributions used are shown in Table 12 and Appendix 1. Probability distributions in the analysis were parameterised using error estimates from the data sources.

Most of the demographic inputs were not varied in PSA. However, these estimates are the most precise and robust being based upon the full SSNAP data set. Most of the costs that were obtained from reference costs directly were sampled in the PSA but the unit costs that were calculated based on more than one data resources (e.g. social care costs that were estimated based on average frequency of use and unit costs estimated in PSSRU UC) were kept fixed.

Table 12: Description of the type and properties of distributions used in the probabilistic sensitivity analysis

Parameter	Type of distribution	Properties of distribution
a) Distribution of mRS at discharge from each treatment unit b) Distribution of patients to the next treatment unit	Dirichlet	Fitted to multinomial data, it represents a series of conditional distributions, bounded between 0 and 1. The parameters are the number of patients in the sample and the number of patients in a particular subgroup.
Mortality in each treatment unit	Beta	It is bounded between 0 and 1. The parameters alpha and beta values were calculated as follows: Alpha = number of patients that died Beta = number of patients that did not die
Length of stay in each treatment unit	Lognormal	The natural log of the mean was calculated as follows: Alpha = ln(mean α) − (0.5*ln((1+(SE α/mean α)2)) Beta = ln(1+(SE α/mean α)2
a) 1-Utility b) NHS reference costs	Gamma	It is bounded at 0 and positively skewed. The parameters are derived from the mean and its standard error as follows: Alpha = (mean/SE)2 Beta = SE2/Mean

3 Results

The main results of the data analyses that were used as inputs in to the simulation model are reported in Appendix 1.

3.1 Model calibration

3.1.1 Thrombolysis

Some key thrombolysis outcomes are shown in Table 13.

Table 13 Thrombolysis results before calibration

	Number of ischaemic stroke patients that got thrombolysis for their primary stroke in the model	Number of ischaemic stroke patients that did not get thrombolysis for their primary stroke in the model	Odds ratio	Odds ratio in Cochrane review
Total number of patients	4,522	35,478		-
Total number died in ASU	444	3,146	1.12	1.69(1.44,1.98)
Died in 90 days	691	5,341	1.02	1.18(1.06,1.30)
mRS 2-6 in 90 days	2,802	21,492	1.06	0.76(0.70,0.84)
mRS 3-6 in 90 days	2,052	15,709	1.05	0.85(0.78,0.93)
mRS 3-5 in 90 days	1,361	10,368	1.04	0.75(0.69,0.82)

Compared to the Cochrane review results [28], thrombolysis patients were less likely to die but more likely to have higher mRS scores. This might be due to the judgement of clinicians regarding which patients should get thrombolysis and which should not. We adjusted the mortality rate in ASU and mRS score change in thrombolysed patients, so that the odds ratios in the model match those of the Cochrane review as closely as possible. These calibrated results are shown in Table 14. After adjusting the model input, now odds ratios for mortality and mRS scores were all within the confidence interval of the Cochrane review.

Table 14 Thrombolysis results after calibration

	Number of ischaemic stroke patients that got thrombolysis for their primary stroke in the model	Number of ischaemic stroke patients that did not get thrombolysis for their primary stroke in the model	Odds ratio	Odds ratio in Cochrane review
Total number of patients	4,500	35,500		
Total number died in ASU	565	2,683	1.76	1.69(1.44,1.98)
Died in 90 days	768	4,924	1.28	1.18(1.06,1.30)
mRS 2-6 in 90 days	2,475	21,210	0.82	0.76(0.70,0.84)
mRS 3-6 in 90 days	1,810	15,417	0.88	0.85(0.78,0.93)
mRS 3-5 in 90 days	1,042	10,493	0.72	0.75(0.69,0.82)

3.1.2 Early Supported Discharge (ESD)

Some key ESD results are reported in Table 15. The results in the model based on SSNAP were broadly comparable to those of the Cochrane review [29] and within the confidence intervals. For this reason, we decided not to calibrate the model with respect to ESD.

Table 15 Early supported discharge results without calibration

	Non-ESD patients (community or hospital rehabilitation)	ESD patients	Odds ratio	Odds ratio in Cochrane review (co-ordinated and delivered by an ESD team, all ESD patients)	Odds ratio in Cochrane review (all teams, all patients)
Total number of patients	24805	13813			
Number of deaths within 1st year	4685	2414	0.91	0.69 [0.44,1.07]	0.91[0.67, 1.25]
Number of deaths or dependency (mRS 3-6) within 1st year	13105	5932	0.67	0.71 [0.55, 0.91]	0.80 [0.67, 0.97]
	Non-ESD patients (community or hospital rehabilitation)	**ESD patients**	**Mean Difference**	**Mean difference in Cochrane review (co-ordinated and delivered by an ESD team, all ESD patients)**	**Mean difference in Cochrane review (all teams, all patients)**
Mean length of stay	25.11	17.01	-8.10	-6.84 [-11.2, -2.49]	-7.1 [-10.03, -4.17]

3.2 Baseline results – the cost of stroke

The results in this section are based on SSNAP directly, i.e. the inputs were not calibrated to the Cochrane review, as described above. The mean NHS cost for a stroke patient was £13,459 in the first year and £17,931 after five years after their primary stroke from our estimations. The social care cost at 1 year and 5-years was £8,716 and £27,301 respectively. Mean NHS and social care costs by age, primary stroke type, sex, and initial severity of their primary stroke (NIHSS) are shown from Table 16 to Table 21. We also present a breakdown of costs by cost category in Table 22 and Table 23.

Table 16 Mean cost by age group and initial stroke severity for men who had an ischaemic stroke

		1-year costs		5-year costs	
Age group	Initial NIHSS	Mean NHS costs	Mean social care cost	Mean NHS costs	Mean social care cost
1 (40-64)	0	£6,827	£1,350	£13,033	£4,909
1 (40-64)	1-4	£7,967	£1,744	£14,409	£6,915
1 (40-64)	5-15	£12,666	£2,767	£18,755	£15,153
1 (40-64)	16-20	£16,148	£6,089	£21,865	£29,270
1 (40-64)	21-42	£16,942	£5,046	£21,443	£49,864
2 (65-74)	0	£7,838	£2,386	£13,586	£12,173
2 (65-74)	1-4	£9,119	£2,653	£14,654	£12,287
2 (65-74)	5-15	£14,863	£4,536	£20,067	£19,520
2 (65-74)	16-20	£19,713	£7,882	£24,434	£30,100
2 (65-74)	21-42	£15,942	£9,607	£19,576	£57,130
3 (75-84)	0	£9,262	£4,087	£14,130	£20,009
3 (75-84)	1-4	£10,547	£5,718	£15,612	£21,955
3 (75-84)	5-15	£16,681	£9,209	£21,103	£39,118
3 (75-84)	16-20	£19,810	£14,664	£22,955	£58,543
3 (75-84)	21-42	£16,882	£14,623	£18,915	£68,827
4 (85-100)	0	£10,504	£6,526	£14,217	£29,317
4 (85-100)	1-4	£11,275	£10,253	£15,728	£32,955
4 (85-100)	5-15	£17,985	£14,517	£21,619	£43,576
4 (85-100)	16-20	£20,741	£21,561	£23,103	£76,691
4 (85-100)	21-42	£18,096	£18,394	£19,336	£91,762
All	**All**	**£12,728**	**£7,456**	**£17,518**	**£28,554**

Table 17 Mean cost by age group and initial stroke severity for women who had an ischaemic stroke

		1-year costs		5-year costs	
Age group	Initial NIHSS	Mean NHS costs	Mean social care cost	Mean NHS costs	Mean social care cost
1 (40-64)	0	£6,572	£1,642	£12,257	£7,130
1 (40-64)	1-4	£7,633	£1,550	£14,061	£6,377
1 (40-64)	5-15	£12,486	£3,086	£18,916	£12,530
1 (40-64)	16-20	£14,820	£5,218	£21,385	£19,789
1 (40-64)	21-42	£16,288	£5,665	£21,011	£19,065
2 (65-74)	0	£8,017	£2,149	£13,425	£8,788
2 (65-74)	1-4	£9,144	£2,738	£14,538	£10,638
2 (65-74)	5-15	£14,638	£4,350	£20,110	£16,805
2 (65-74)	16-20	£18,808	£9,987	£23,253	£35,575
2 (65-74)	21-42	£15,946	£8,834	£19,269	£29,001
3 (75-84)	0	£9,005	£4,280	£14,050	£16,225
3 (75-84)	1-4	£10,473	£5,508	£15,561	£19,768
3 (75-84)	5-15	£16,267	£9,347	£20,818	£29,757
3 (75-84)	16-20	£20,103	£13,798	£23,075	£44,489
3 (75-84)	21-42	£16,780	£15,013	£18,647	£46,589
4 (85-100)	0	£10,037	£8,312	£14,122	£24,491
4 (85-100)	1-4	£11,391	£9,903	£15,153	£29,191
4 (85-100)	5-15	£18,347	£13,941	£21,560	£40,138
4 (85-100)	16-20	£21,193	£20,086	£23,435	£55,727
4 (85-100)	21-42	£17,827	£18,763	£19,403	£51,279
All	**All**	**£13,985**	**£9,603**	**£18,117**	**£29,140**

Table 18 Mean cost by age group and initial stroke severity for men who had a haemorrhagic stroke

		1-year costs		**5-year costs**	
Age group	Initial NIHSS	Per patient NHS costs	Per patient social care cost	Per patient NHS costs	Per patient social care cost
1 (40-64)	0	£6,544	£993	£13,554	£4,517
1 (40-64)	1-4	£7,962	£2,172	£14,692	£9,685
1 (40-64)	5-15	£13,501	£3,514	£19,998	£14,510
1 (40-64)	16-20	£16,883	£7,224	£22,755	£28,540
1 (40-64)	21-42	£15,108	£8,453	£19,795	£32,743
2 (65-74)	0	£7,927	£2,692	£13,956	£9,316
2 (65-74)	1-4	£9,069	£2,364	£15,155	£10,428
2 (65-74)	5-15	£15,428	£5,230	£20,871	£20,009
2 (65-74)	16-20	£19,020	£10,420	£23,528	£39,635
2 (65-74)	21-42	£15,225	£9,932	£18,247	£37,620
3 (75-84)	0	£8,925	£4,321	£13,943	£15,226
3 (75-84)	1-4	£10,662	£6,152	£16,380	£22,875
3 (75-84)	5-15	£17,157	£10,033	£22,278	£36,585
3 (75-84)	16-20	£20,237	£16,137	£23,659	£52,510
3 (75-84)	21-42	£16,380	£22,200	£18,806	£73,986
4 (85-100)	0	£10,016	£7,057	£14,511	£20,276
4 (85-100)	1-4	£11,621	£9,776	£16,174	£32,634
4 (85-100)	5-15	£18,575	£14,791	£22,383	£47,525
4 (85-100)	16-20	£21,920	£24,879	£25,366	£72,912
4 (85-100)	21-42	£17,296	£22,945	£18,823	£73,149
All	**All**	**£14,198**	**£9,776**	**£19,033**	**£33,366**

Table 19: Mean cost by age group and initial stroke severity for women who had a haemorrhagic stroke

		1-year costs		**5-year costs**	
Age group	Initial NIHSS	Per patient NHS costs	Per patient social care cost	Per patient NHS costs	Per patient social care cost
1 (40-64)	0	£6,412	£1,193	£13,046	£6,029
1 (40-64)	1-4	£7,568	£1,256	£14,201	£5,747
1 (40-64)	5-15	£13,264	£3,647	£19,850	£14,998
1 (40-64)	16-20	£16,480	£6,094	£22,142	£23,542
1 (40-64)	21-42	£14,731	£6,757	£19,297	£27,419
2 (65-74)	0	£7,475	£2,380	£14,383	£8,922
2 (65-74)	1-4	£9,008	£2,544	£15,255	£11,000
2 (65-74)	5-15	£14,708	£4,165	£20,239	£16,538
2 (65-74)	16-20	£18,154	£10,341	£22,524	£42,517
2 (65-74)	21-42	£14,958	£12,305	£18,073	£42,126
3 (75-84)	0	£9,514	£2,841	£14,996	£11,370
3 (75-84)	1-4	£10,402	£5,767	£16,015	£20,332
3 (75-84)	5-15	£16,863	£10,668	£21,589	£35,570
3 (75-84)	16-20	£19,837	£16,033	£23,160	£50,058
3 (75-84)	21-42	£16,134	£21,486	£18,153	£69,658
4 (85-100)	0	£10,672	£6,475	£15,075	£23,254
4 (85-100)	1-4	£11,307	£9,538	£16,014	£31,306
4 (85-100)	5-15	£18,314	£13,952	£22,009	£42,805
4 (85-100)	16-20	£21,165	£21,576	£23,513	£72,748
4 (85-100)	21-42	£17,627	£21,916	£19,144	£59,134
All	**All**	**£15,002**	**£11,794**	**£19,144**	**£37,523**

Table 20 Mean cost (£) by primary stroke type, sex and age group.

			1-year costs		5-year costs	
Type	Sex	Age group	Mean NHS costs	Mean social care cost	Mean NHS costs	Mean social care cost
Ischaemic	Male	1 (40-64)	£9,779	£2,241	£16,017	£8,835
Ischaemic	Male	2 (65-74)	£11,495	£3,684	£16,843	£14,110
Ischaemic	Male	3 (75-84)	£13,217	£7,620	£17,816	£25,148
Ischaemic	Male	4 (85-100)	£14,906	£13,070	£18,613	£38,623
Ischaemic	Female	1 (40-64)	£9,627	£2,312	£15,954	£9,308
Ischaemic	Female	2 (65-74)	£11,705	£3,878	£16,987	£14,668
Ischaemic	Female	3 (75-84)	£13,441	£7,923	£17,995	£26,370
Ischaemic	Female	4 (85-100)	£15,803	£13,500	£18,947	£38,585
Ischaemic	**All**	**All**	**£13,340**	**£8,503**	**£17,810**	**£26,454**
Haemorrhage	Male	1 (40-64)	£11,465	£3,661	£17,857	£15,063
Haemorrhage	Male	2 (65-74)	£12,773	£4,862	£18,188	£18,960
Haemorrhage	Male	3 (75-84)	£14,605	£10,545	£19,389	£36,994
Haemorrhage	Male	4 (85-100)	£16,291	£15,551	£19,896	£49,256
Haemorrhage	Female	1 (40-64)	£11,260	£3,256	£17,538	£13,508
Haemorrhage	Female	2 (65-74)	£12,734	£5,285	£18,143	£20,476
Haemorrhage	Female	3 (75-84)	£14,747	£11,379	£19,103	£37,630
Haemorrhage	Female	4 (85-100)	£16,481	£15,425	£19,750	£46,730
Haemorrhage	**All**	**All**	**£14,584**	**£10,744**	**£19,087**	**£35,361**
All	**All**	**All**	**£13,459**	**£8,716**	**£17,931**	**£27,301**

Table 21 Mean cost (£) by primary stroke type and initial severity (NIHSS).

		1-year costs		5-year costs	
Type	Initial NIHSS	Mean NHS costs	Mean social care cost	Mean NHS costs	Mean social care cost
Ischaemic	0	£8,632	£4,085	£13,702	£14,204
Ischaemic	1-4	£10,035	£5,829	£15,103	£19,244
Ischaemic	5-15	£16,419	£9,741	£20,799	£29,972
Ischaemic	16-20	£20,061	£16,179	£23,180	£47,898
Ischaemic	21-42	£17,382	£16,063	£19,368	£45,809
Haemorrhage	0	£8,697	£3,818	£14,253	£13,372
Haemorrhage	1-4	£10,139	£5,935	£15,709	£21,085
Haemorrhage	5-15	£16,739	£10,022	£21,524	£33,563
Haemorrhage	16-20	£20,011	£17,003	£23,621	£55,905
Haemorrhage	21-42	£16,689	£19,647	£18,840	£60,380
	All	**£13,459**	**£8,716**	**£17,931**	**£27,301**

Table 22: Break down of 5-year costs (£) by stroke type and initial stroke severity – all costs, inpatient care

Type	Initial NIHSS	Ambulance (£)	Scanning (£)	Thrombolysis costs (£)	Other Acute Stroke Unit cost (£)	ED & GMW (£)	Stroke unit rehabilitation (£)
Ischaemic	1	180	92	6	4156	99	1186
Ischaemic	2	181	92	175	15431	108	2694
Ischaemic	3	178	93	131	13936	104	1932
Ischaemic	4	178	92	8	4211	101	1339
Ischaemic	5	181	92	21	5276	103	1589
All Ischaemic		180	92	89	9443	105	2096
Haemorrhage	1	183	92	0	3900	105	901
Haemorrhage	2	181	92	0	4833	108	1243
Haemorrhage	3	180	92	0	10162	105	2511
Haemorrhage	4	179	92	0	13644	111	3218
Haemorrhage	5	177	92	0	11616	104	2467
All Haemorrhage		180	92	0	10887	110	2147
All		180	92	81	9576	106	2101

ED=Emergency department; GMW=general medical ward

Table 23: Break down of 5-year costs (£) by stroke type and initial stroke severity – all costs, longer term costs

Type	Initial NIHSS	Early supported discharge rehabilitation (£)	Community rehabilitation (£)	Social care in own home (£)	Social care in nursing home (£)	Other primary care & community care (£)	Recurrence - hospital & rehab (£)
Ischaemic	1	431	698	3612	6407	3640	3217
Ischaemic	2	202	474	3597	14632	1896	1951
Ischaemic	3	105	331	2191	8815	1207	1273
Ischaemic	4	415	713	3996	7245	3625	3025
Ischaemic	5	475	771	4644	8807	3410	3151
All Ischaemic		370	686	4233	10888	2824	2687
Haemorrhage	1	461	707	3627	3529	3932	3858
Haemorrhage	2	524	783	4768	6422	3984	3752
Haemorrhage	3	480	812	6098	11256	3495	3359
Haemorrhage	4	315	627	5368	15528	2549	2487
Haemorrhage	5	190	430	3705	14013	1740	1634
All Haemorrhage		322	619	4154	12023	2614	2698
All		366	679	4226	10992	2805	2688

3.3 Scenario analysis

Costs (NHS and social care) and quality-adjusted life-years (QALYs) were compared between different scenarios. For costs, aggregated costs and QALY were collected at end of the first and fifth year after primary stroke.

In Appendix 2, NHS costs were stratified as to ASU, inpatient care, and rehabilitation costs.

3.3.1 Proportion of patients meets the RCP SSNAP minimum threshold criteria that get thrombolysis

The means NHS and social care cost and mean QALYs over all stroke patients after 1 and 5 years after primary stroke was shown in Table 24 for different scenarios. These results were also plotted (Figure 4 to Figure 9) and the line of best fit calculated to estimate the cost savings and QALYs gained for each extra person thrombolysed. So after 5 years we would expect NHS savings of £4,100, social care savings of £6,900 and 0.26 QALYs gained in total for each extra patient thrombolysed.

Table 24: Comparison between scenarios with different thrombolysis rate

Percentage received thrombolysis within patients met minimum SSNAP criteria	Percentage received thrombolysis within all ischaemic stroke patients	1-year results			5- years results		
		Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs
82% (Calibrated Baseline)	11%	13220	8702	0.496	17663	27052	1.667
10%	1%	13524	8855	0.487	18008	27624	1.634
20%	3%	13452	8857	0.490	17978	27135	1.649
30%	4%	13427	8899	0.494	17988	28121	1.657
40%	6%	13367	8708	0.494	17903	27080	1.660
50%	7%	13338	8805	0.494	17796	27452	1.658
60%	9%	13315	8539	0.492	17813	26515	1.650
70%	10%	13234	8431	0.495	17640	25982	1.659
95%	13%	13122	8595	0.499	17562	26836	1.677

Figure 4: 1-year mean NHS costs at different proportion of thrombolysis in all ischaemic patients.

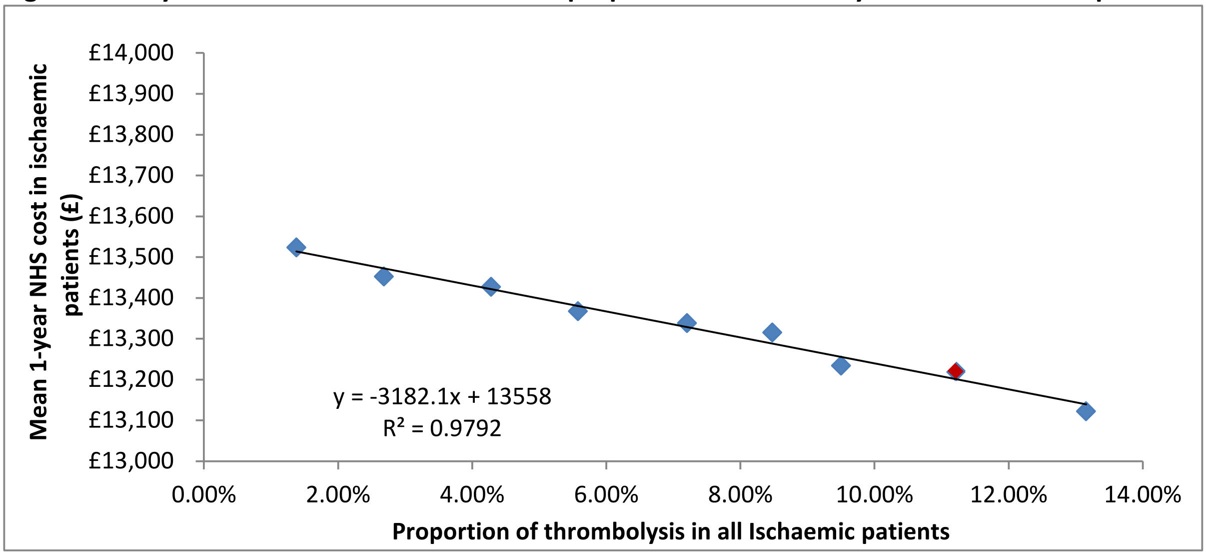


Figure 5 5-years mean NHS cost at different proportions of thrombolysis in all ischaemic patients.

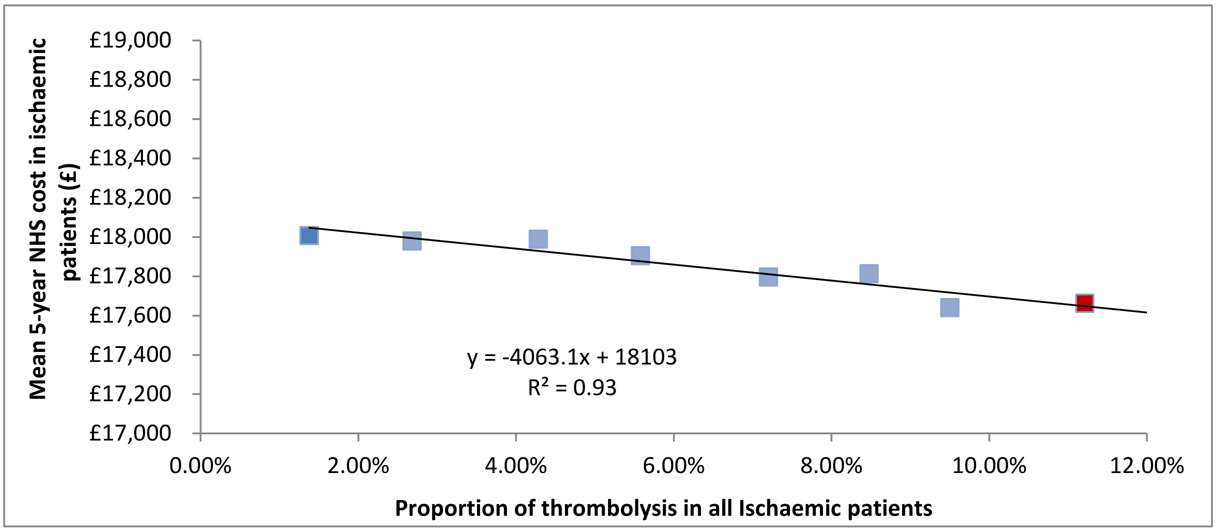


Figure 6: 1-year mean social care cost at different proportions of thrombolysis in all ischaemic patients

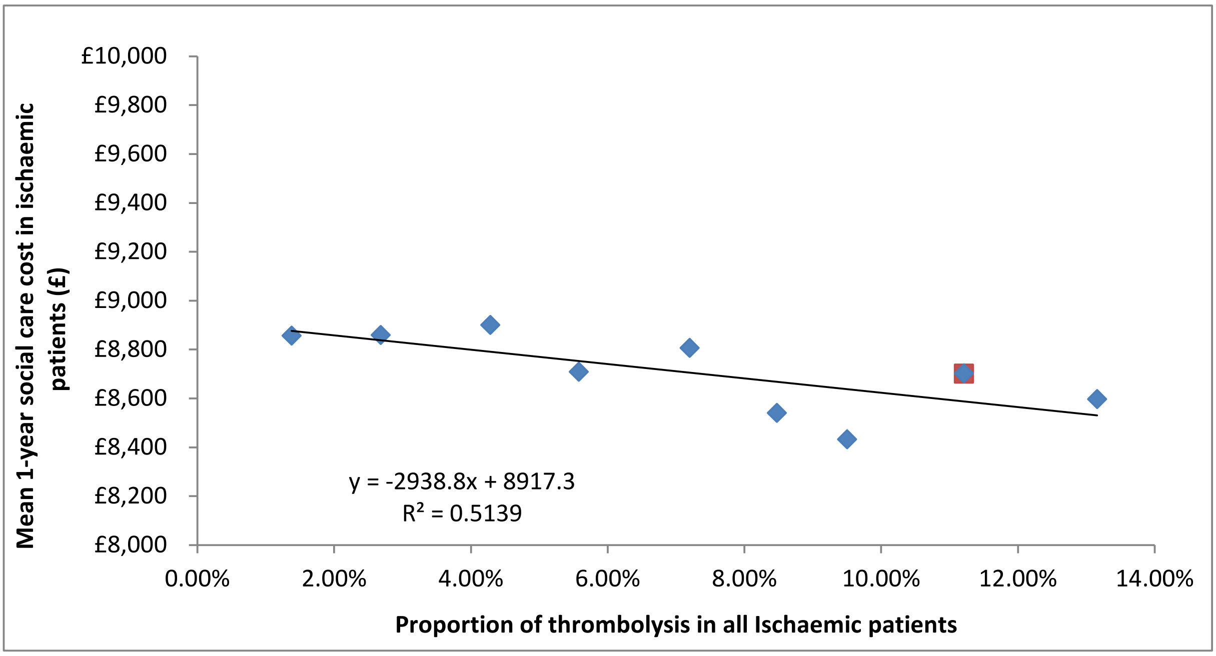


Figure 7 5-years mean social care cost at different proportions of thrombolysis in all ischaemic patients

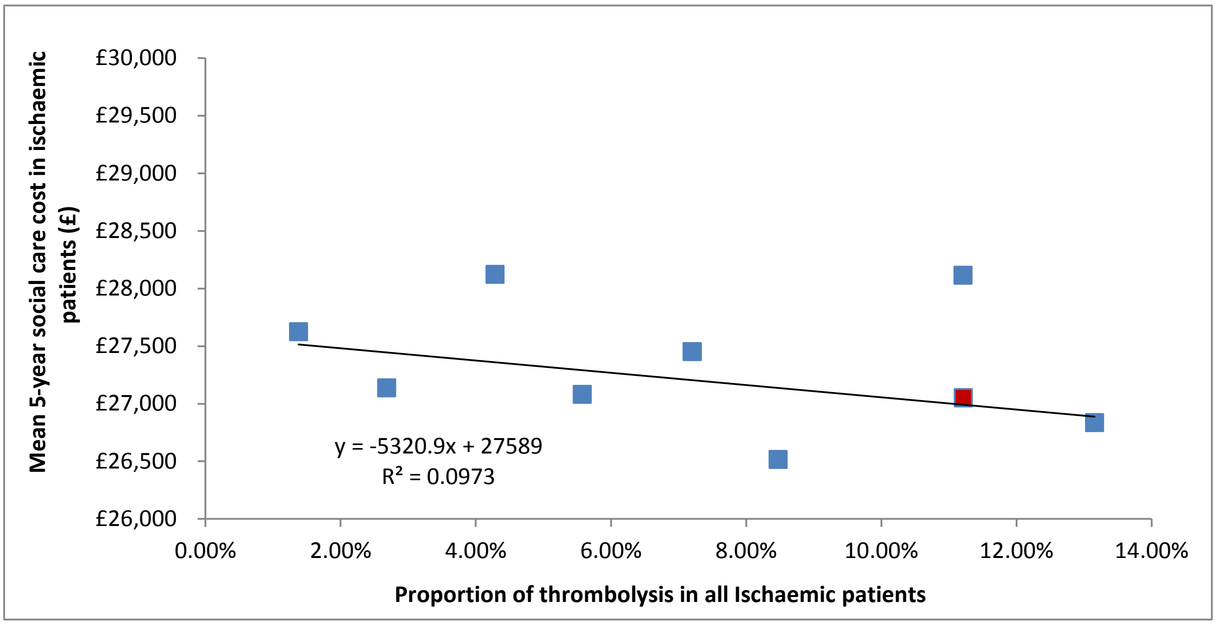


Figure 8: Mean QALY of ischaemic patients with different thrombolysis proportions one year after primary stroke

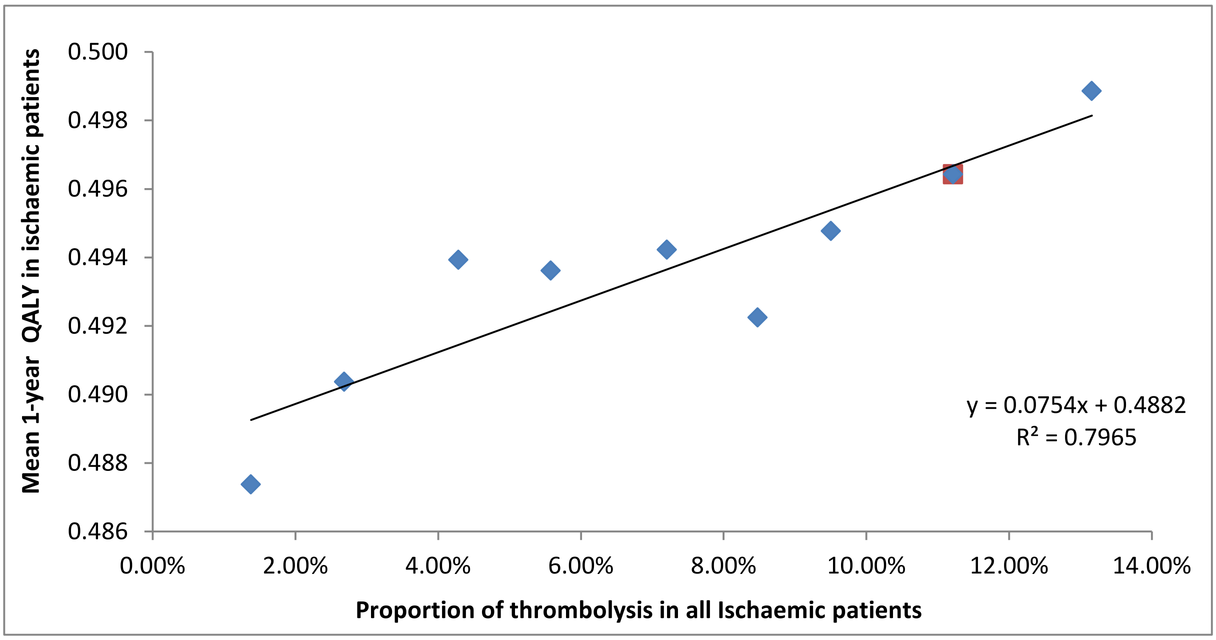
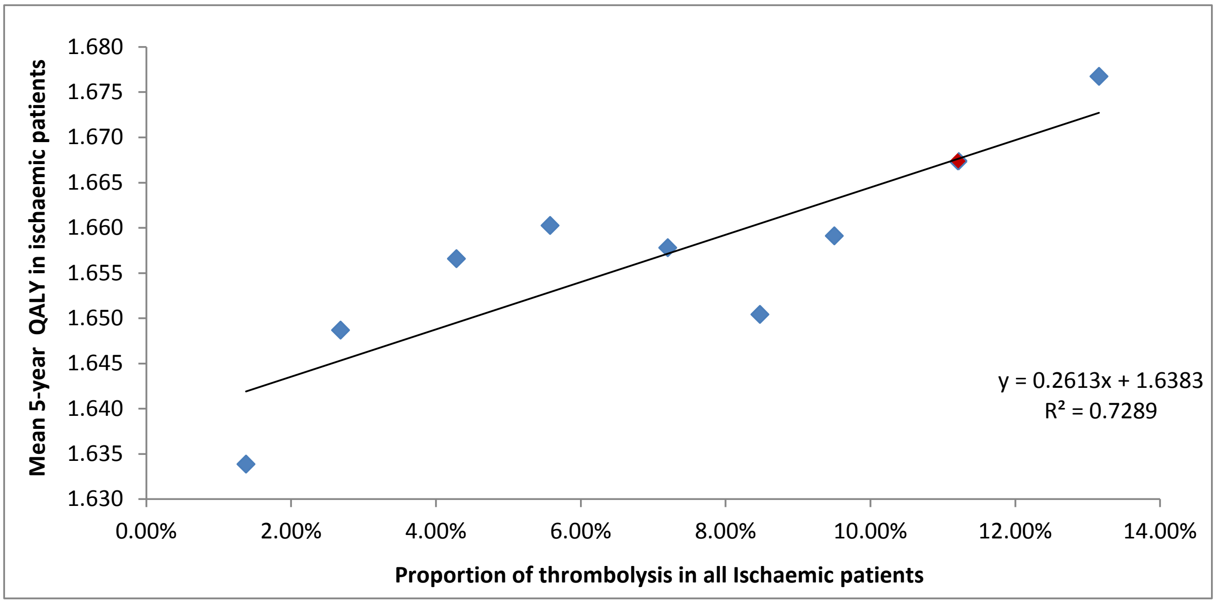


Figure 9: Mean QALY of ischaemic patients with different thrombolysis proportions five years after primary stroke



3.3.2 Patients not thrombolysed due to time window, too mild/severe or wake up time unknown

In the second thrombolysis analysis we explored the effects of redirecting patients in the model to thrombolysis who did not meet the minimum SSNAP criteria in the baseline model for one of the following reasons (a) did not arrive on time, (b) too mild/severe, (c) wake up time unknown, and (d) a combination of (a)(b) and/or (c).

Table 25 shows how these scenarios change the case-mix of thrombolysed patients. Generally, all sensitivity analyses (a-d) are proportionately increasing more the number of less severe strokes that are treated with thrombolysis. Relative to each other, c) is increasing more the most severe strokes receiving thrombolysis compared to (a) and (b); and (a) is increasing more the least severe strokes. Scenario (b) is making little increase to the higher severity groups implying that very few patients in SSNAP were not prescribed thrombolysis because they their stroke was too severe.

Table 25 Ratio of number of patients receiving thrombolysis in scenario compared with baseline, by sub-group

Age group	NIHSS	a. Not arriving within thrombolysis time window	b. Too mild/severe	c. Wake-up time unknown	d. One or more of criteria a, b and c
1 (40-64)	0	**6.37**	3.87	3.15	13.99
1 (40-64)	1-4	3.22	1.88	2.13	6.12
1 (40-64)	5-15	1.33	1.01	1.25	1.66
1 (40-64)	16-20	1.08	1.00	1.19	1.31
1 (40-64)	21-42	1.10	1.01	**1.23**	1.41
2 (65-74)	0	**5.08**	3.55	2.87	11.69
2 (65-74)	1-4	3.01	1.88	2.27	6.04
2 (65-74)	5-15	1.33	1.01	1.34	1.76
2 (65-74)	16-20	1.09	1.01	1.22	1.35
2 (65-74)	21-42	1.10	1.01	**1.21**	1.36
3 (75-84)	0	**5.89**	4.19	3.99	15.16
3 (75-84)	1-4	3.40	2.13	2.82	7.41
3 (75-84)	5-15	1.40	1.01	1.52	2.05
3 (75-84)	16-20	1.11	1.00	1.31	1.48
3 (75-84)	21-42	1.13	1.02	**1.35**	1.59
4 (85+)	0	**5.64**	4.14	4.88	15.16
4 (85+)	1-4	3.98	2.54	3.97	10.00
4 (85+)	5-15	1.54	1.03	1.99	2.72
4 (85+)	16-20	1.21	1.01	1.65	1.97
4 (85+)	21-42	1.18	1.04	**1.62**	2.01

NHS cost perspective

Within 1-year (Table 26), all alternative scenarios were more effective in terms of QALYs compared to baseline. It was cost saving to redirect patients in scenarios (a), (c) and (d) but not (b).

At 5-years (Table 27), only strategy (a) is still cost saving, strategy (c) generated slightly higher NHS cost than the baseline cost, but it is cost-effective, strategy (b) is still neither cost-saving nor cost-effective.

The reason for this pattern is that strategy (b) is treating more low-severity patients with thrombolysis – for such patients the benefit in terms of health status is less but they still incur the mortality risk. It is not treating any more high severity patients with thrombolysis and is not achieving a health gain for these patients. Strategy (c) has the biggest QALY gain because it is redirecting more of the most severe patients. However, this is assuming that, after controlling for severity and age, thrombolysis is as effective in these patients as it is for those patients where the wake-up time was known.

Figure 10 shows the results on the cost-effectiveness plane. Strategies in the South-East quadrant are both cost saving and increase QALYs compared with baseline: (d) is most cost-effective from an NHS perspective as it lies South-East of the other strategies.

Of the three strategies only (a) yields NHS cost savings at one-year. However, this is assuming that, after controlling for severity and age, thrombolysis is as effective in these patients as it is for those patients that did arrive on time. Furthermore, this does not include the cost of any intervention to speed up arrival time.

Social care cost perspective

From a social care perspective, strategy (c) and (d) were cost saving within the 1-year period (Table 28). Strategy (b) was more expensive within the 1-year period but was cost saving at the end of the 5-year period (Table 29). Strategy (a) was more expensive compared to baseline at both 1-year and 5-years.

The reason for this pattern is that strategy (c) is sending relatively more high severity patients to thrombolysis – there are social care savings here, since more high-severity patients will die because of thrombolysis than in the other strategies.

Figure 11 shows the results on the cost-effectiveness plane. Strategies (c) and (d) are most cost-effective from a social care persective as they lie below and to the right of the other strategies (they both have more QALYs and lower cost).

Societal perspective

Taking account of both NHS and social care costs, option (c) is more cost-effective than (a) or (b) since this strategy yields the largest cost savings and the largest QALY gains. This assumes that after controlling for age and initial severity the benefits and risks of thrombolysis for these patients are the same as those who did have thrombolysis in SSNAP, which may not be the case.

Table 26: Cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, 1-year NHS perspective

Scenarios	Total number of patients thrombolysed at primary stroke	Mean cost	Incremental cost compared to baseline	Mean QALYs	Incremental QALYs compared to baseline	Cost per QALY gained compared to baseline	Incremental net monetary benefit compared to baseline (at £20,000 per QALY gained)	Net monetary benefit rank (at £20,000 per QALY gained)
Baseline with calibrated data	4500	£13,272	-	0.490	-	-	-	4
(a) 50% of the patients who had not met the criteria due to time window redirected	7149	£13,143	-£129	0.497	0.0068	dominant	£264	2
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	5259	£13,361	£89	0.491	0.0006	£155,432	-£78	5
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	7209	£13,212	-£60	0.500	0.0094	dominant	£247	3
(d) combination of (a)-(c)	11439	£13,063	-£209	0.502	0.0117	dominant	£443	1

Table 27: Cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, 5-year NHS perspective

Scenarios	Mean cost	Incremental cost compared to baseline	Mean QALYs	Incremental QALYs compared to baseline	Cost per QALY gained compared to baseline	Incremental net monetary benefit compared to baseline (at £20,000 per QALY gained)	Net monetary benefit rank (at £20,000 per QALY gained)
Baseline with calibrated data	£ 17,678	-	1.648	-	-	£ -	4
(a) 50% of the patients who had not met the criteria due to time window redirected	£ 17,635	-£ 43.56	1.670	0.022	dominant	£ 486	3
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	£ 17,840	£ 162.34	1.655	0.007	£ 22,542	-£ 18	5
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	£ 17,683	£ 5.27	1.684	0.036	£ 148	£ 709	2
(d) combination of (a)-(c)	£ 17,466	-£ 211.88	1.687	0.039	dominant	£ 992	1

Figure 10: Cost-effectiveness plane for thrombolysis analysis 2 (NHS perspective, 5-year results)

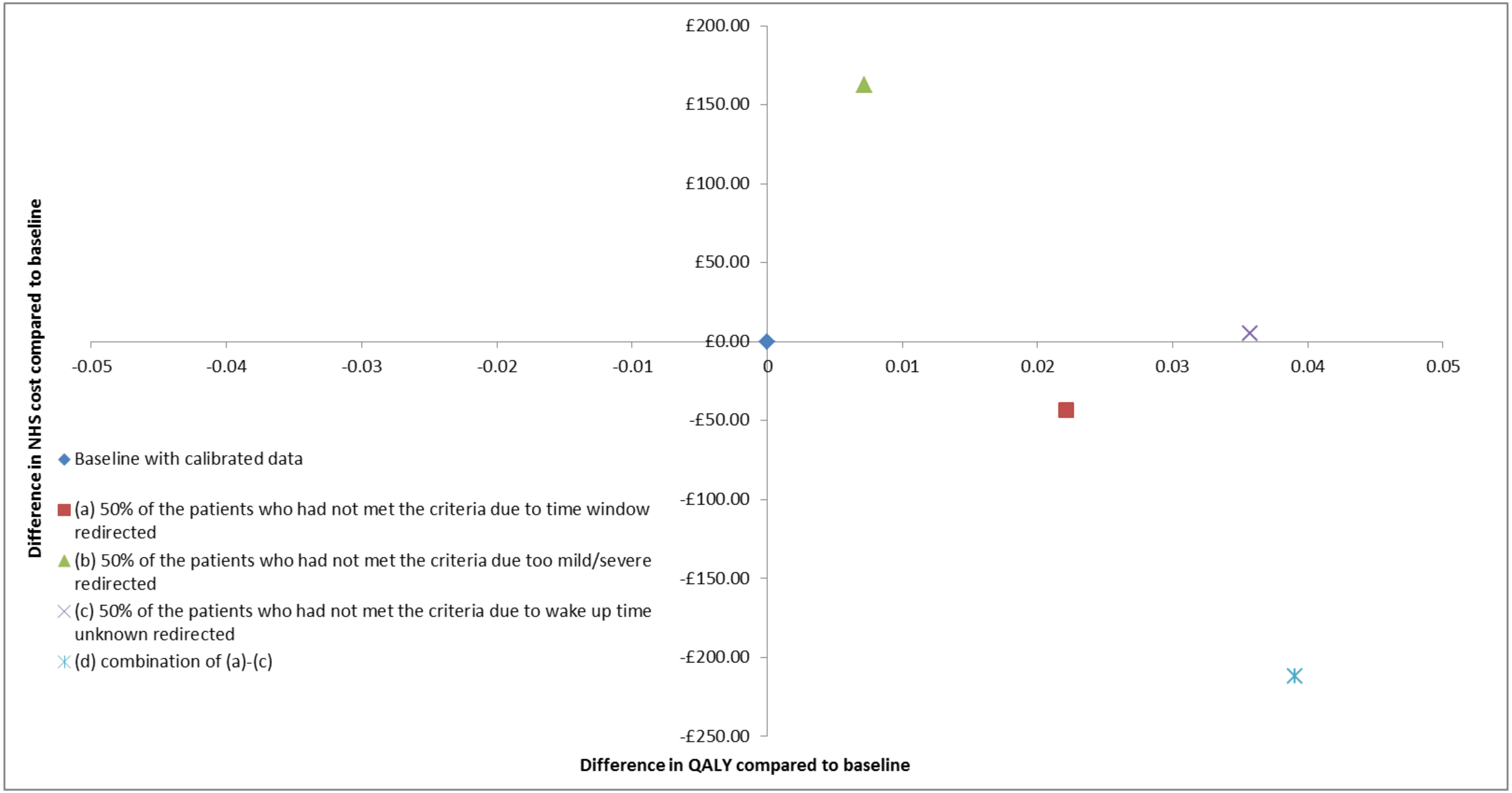


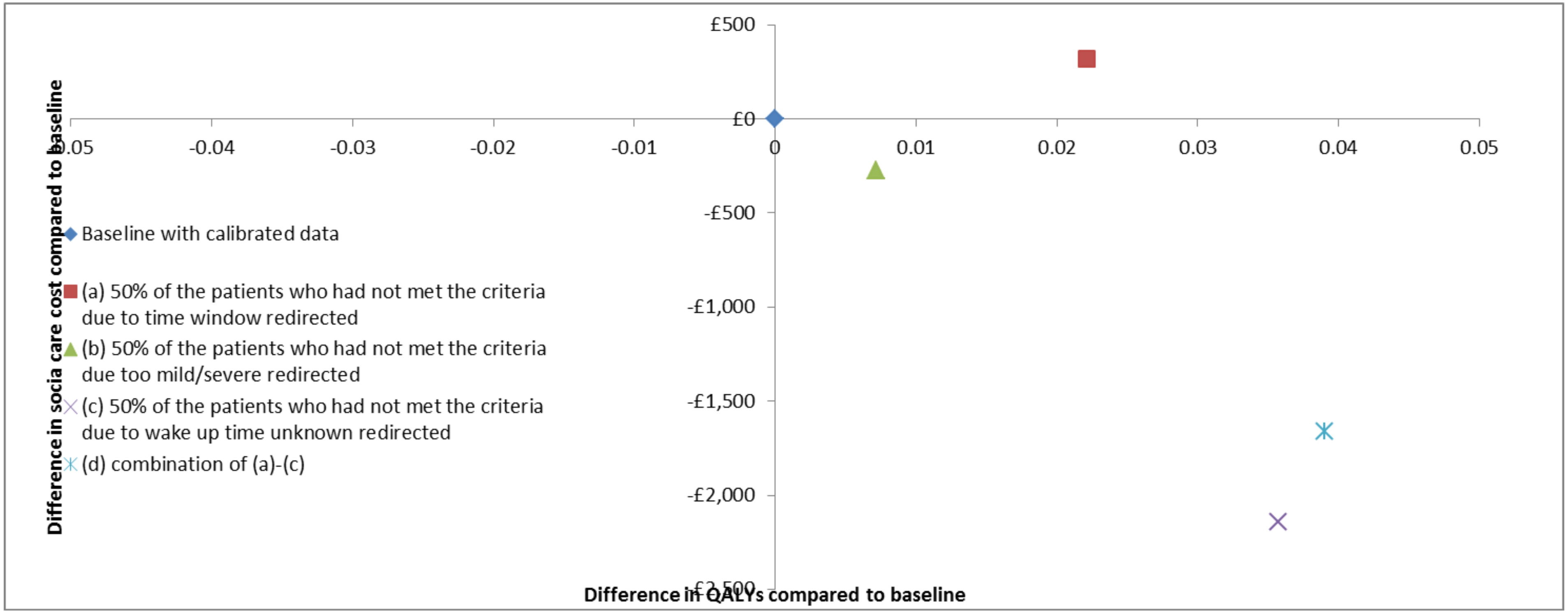
Table 28: Cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, compared to baseline, 1-year social care perspective

Scenarios	Total number of patients thrombolysed at primary stroke	Mean cost	Incremental cost compared to baseline	Mean QALYs	Incremental QALYs compared to baseline	Cost per QALY gained compared to baseline	Incremental net monetary benefit compared to baseline (at £20,000 per QALY gained)	Net monetary benefit rank (at £20,000 per QALY gained)
Baseline								
Baseline with calibrated data	4500	£8,881	-	0.490	-		£ -	4
(a) 50% of the patients who had not met the criteria due to time window redirected	7149	£8,930	48	0.497	0.007	£7,144	£87	3
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	5259	£8,902	21	0.491	0.001	£36,843	-£10	5
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	7209	£8,203	-679	0.500	0.009	dominant	£866	1
(d) combination of (a)-(c)	11439	£8,514	-367	0.502	0.012	dominant	£600	2

Table 29: Cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis compared to baseline, 5-year social care perspective

Scenarios	Total number of patients thrombolysed at primary stroke	Mean Cost	Incremental cost compared to baseline	Mean QALYs	Incremental QALYs compared to baseline	Cost per QALY gained compared to baseline	Incremental net monetary benefit compared to baseline (at £20,000 per QALY gained)	Net monetary benefit rank (at £20,000 per QALY gained)
Baseline with calibrated data	4500	£28,115	£ -	1.648	0		£ -	5
(a) 50% of the patients who had not met the criteria due to time window redirected	7149	£28,431	£316	1.670	0.022	£14,308	£126	4
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	5259	£ 27,841	-£274	1.655	0.007	dominant	£418	3
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	7209	£25,970	-£2,145	1.684	0.036	dominant	£2,859	1
(d) combination of (a)-(c)	11439	£ 26,452	-£1,663	1.687	0.039	dominant	£2,443	2

Figure 11: Cost-effectiveness plane for thrombolysis analysis 2 (Social care perspective - 5-year results)



3.3.3 Early supported discharge

The means NHS and social care cost and mean QALYs over all stroke patients after 1 and 5 years after primary stroke is shown in Table 30 for different scenarios. These results were also plotted (Figure 12 to Figure 17) and the line of best fit calculated to estimate the cost savings and QALYs gained for each extra person thrombolysed. So after 5 years we would expect NHS savings of about £1,700, social care savings of £8,700, and 0.15 QALYs gained in total for each extra patient thrombolysed.

In an additional analysis (not reported in the tables), we extended access to ESD but only for those with a less severe stroke (mRS=0-2). There was a modest cost saving of £200 at one year but by 5 years that had disappeared. There was no impact on social care costs. This implies that most of the benefit of ESD in the model was for more severe patients.

Table 30: Mean costs and QALYs for different levels of ESD use

	1-year results			5-year results			Mean bed days
	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	
Baseline	13,272	8,881	0.490	17,678	28,115	1.648	22.2
ESD scenario 1 - 20% more patients from all groups who did not discharge to ESD now discharge to ESD	12,972	8,506	0.496	17,423	26,683	1.674	20.0
ESD scenario 2 - 35% more patients from all groups who did not discharge to ESD now discharge to ESD	12,783	8,444	0.498	17,220	26,429	1.678	19.0
ESD scenario 3 - 50% more patients from all groups who did not discharge to ESD now discharge to ESD	12,562	8,243	0.500	16,978	25,748	1.685	17.8
ESD scenario 4 - 80% more patients from all groups who did not discharge to ESD now discharge to ESD	12,121	8,191	0.504	16,542	25,754	1.703	15.7

Figure 12: Mean NHS costs at one year after primary stroke with different proportions of patients' discharged to ESD

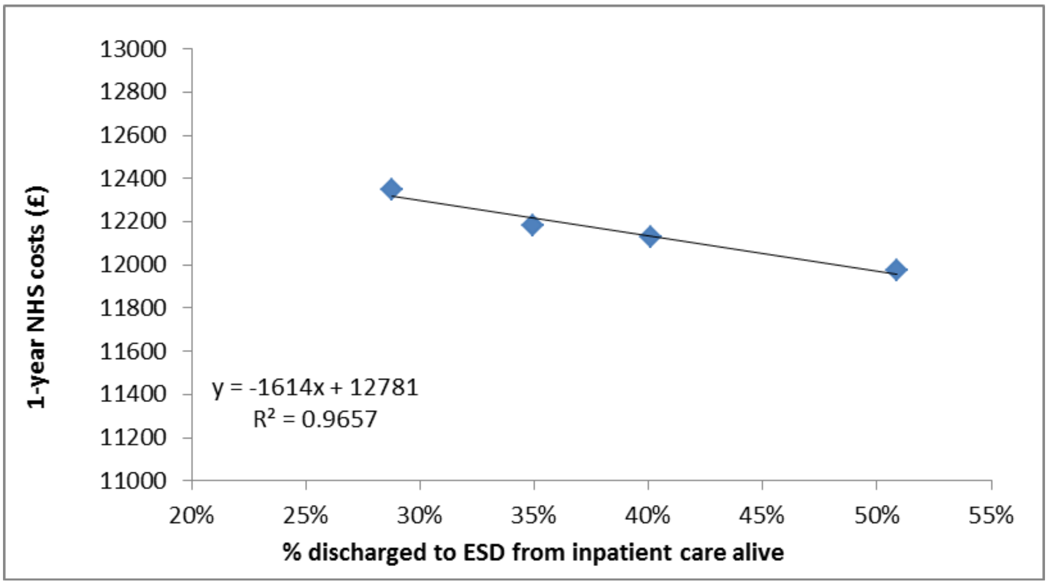


Figure 13: Mean NHS costs within the first 5-years after primary stroke with different proportions of patients discharged to ES

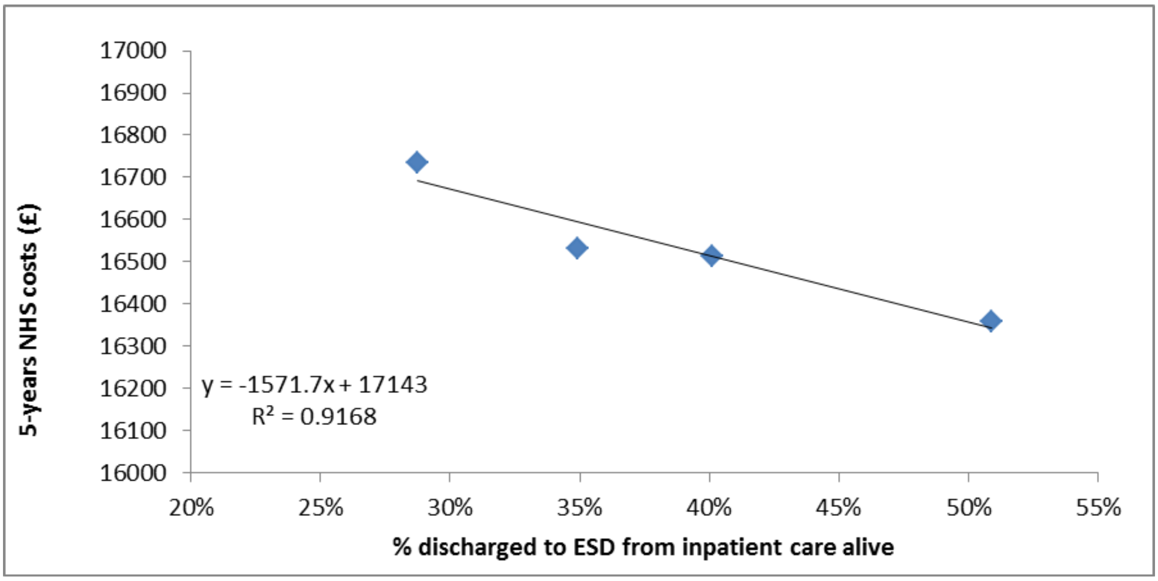


Figure 14: Mean social care cost at one year after a primary stroke with different proportions of patients discharged to ESD

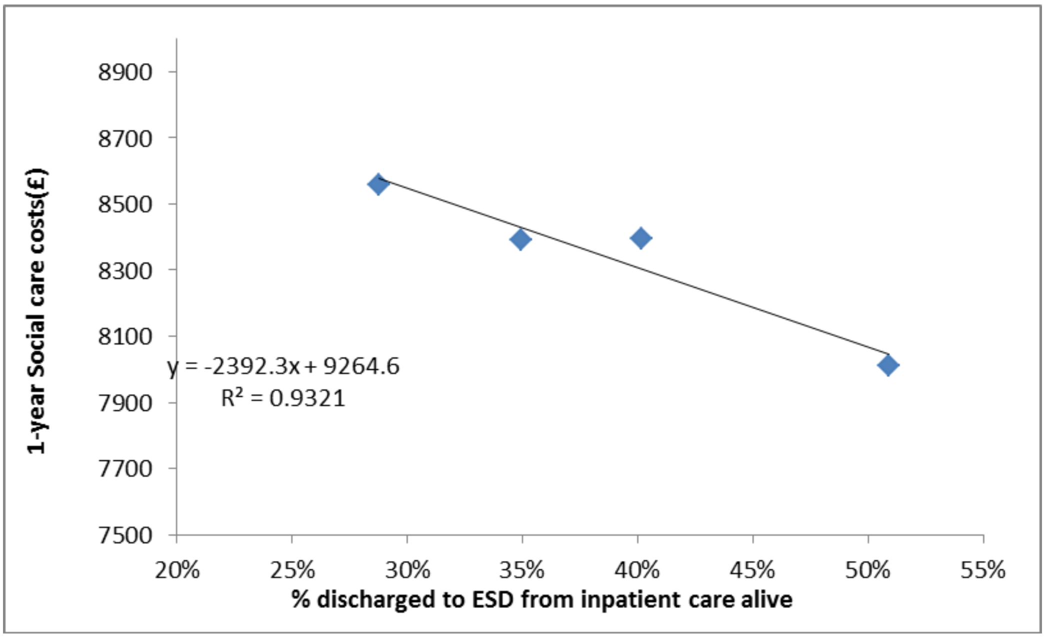


Figure 15: Mean social care cost at one year after a primary stroke with different proportions of patients discharged to ESD

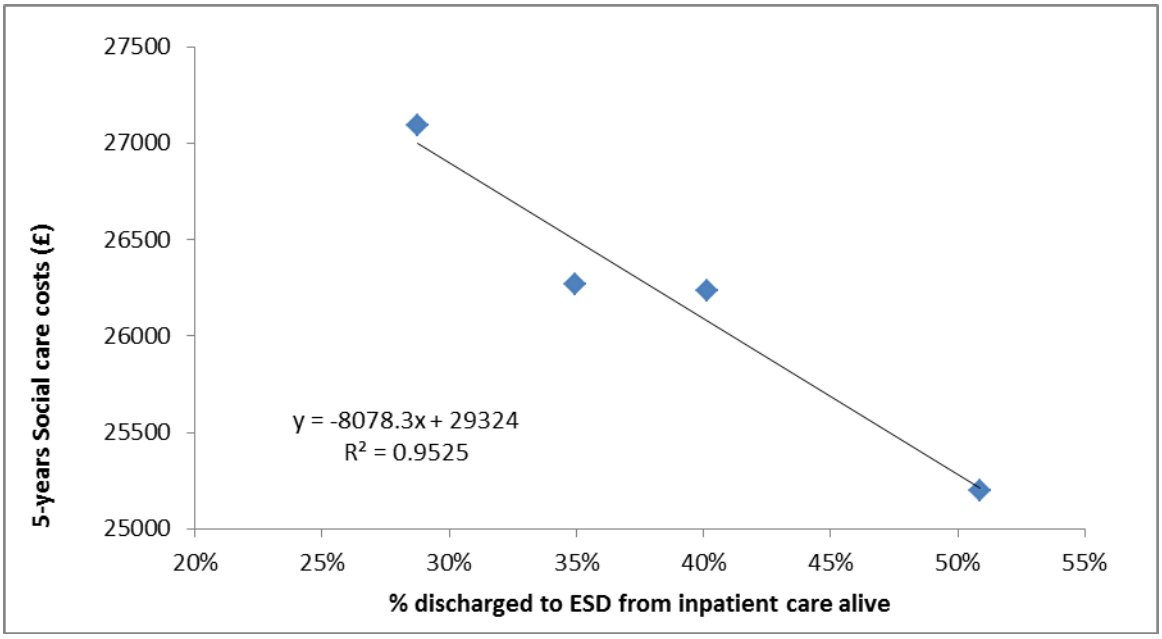


Figure 16: Mean QALYs at 1 year after primary stroke with different proportions of patients discharged to ESD

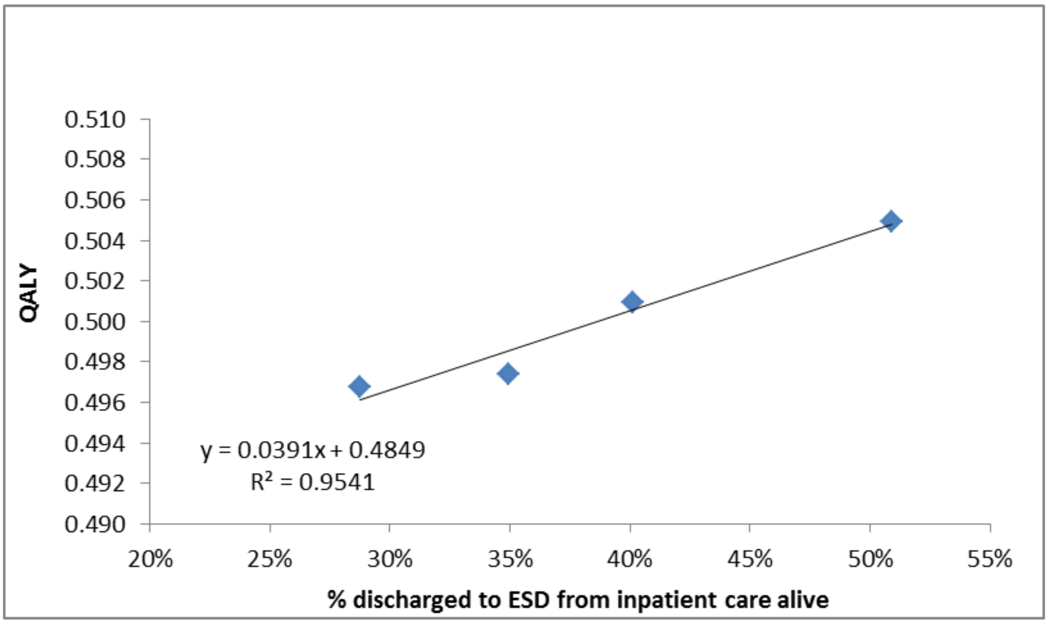
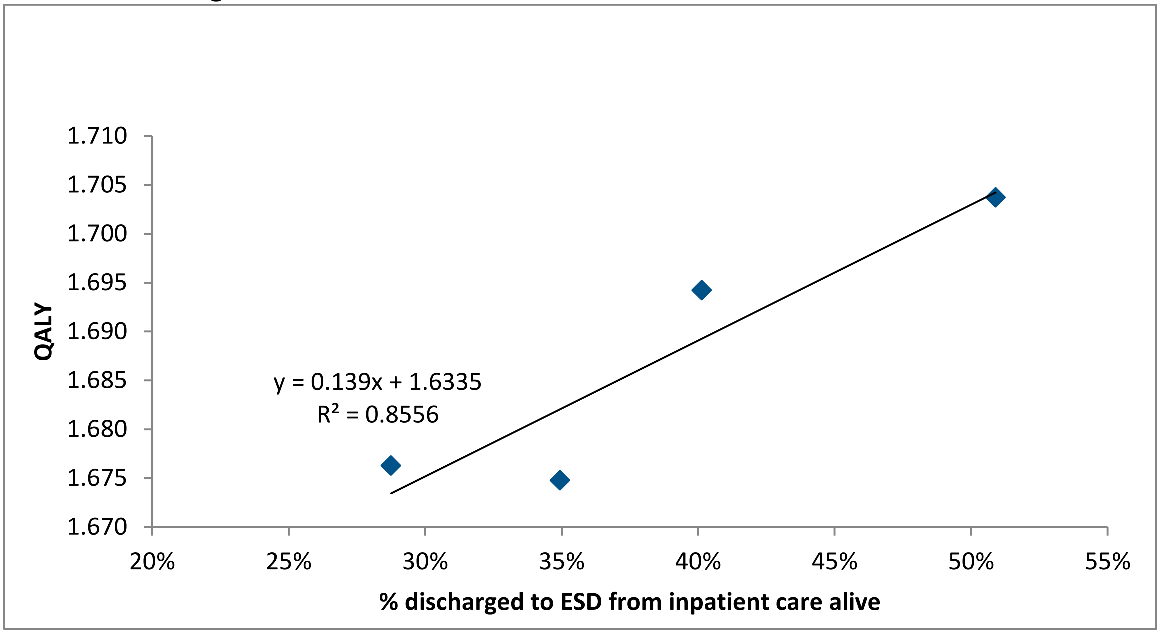


Figure 17: Mean QALY at 5 years after primary stroke with different proportions of patients discharged to ESD



3.4 Probabilistic Sensitivity analysis (PSA)

The results for the probabilistic sensitivity analysis (PSA) for the baseline scenario are shown in Table 31. The PSA for 95% thrombolysis probability in patients who met minimum SSNAP criteria are in Table 32 and the PSA results for 35% or non-ESD patients redirected to ESD are in Table 33.

The 95% confidence intervals (CI) were slightly wider for the two scenarios than for the baseline analysis.

The mean results of the PSA were broadly similar to the mean results from the deterministic analysis, although some of the cost savings were more modest. This could reflect the limited number of patients simulated and the limited number of probabilistic iterations, which had to be curtailed for practical reasons. Hence, the gradients of the lines in the Figures of section 3.3, which are based on far more simulated patients, should be considered the primary source for the average effects.

3.4.1 Baseline PSA

Table 31: The baseline PSA sampled input around original inputs from SSNAP without calibration.

	1-year			5-years		
	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs
Baseline result	£13,452	£8,977	0.483	£17,963	£28,076	1.627
PSA Mean	£13,528	£8,992	0.486	£18,009	£28,283	1.636
SEM	£462	£244	0.007	£538	£871	0.025
Upper 95% CL	£14,434	£9,470	0.500	£19,063	£29,990	1.685
Lower 95% CL	£12,622	£8,514	0.472	£16,955	£26,576	1.587

3.4.2 Thrombolysis PSA

Table 32: Thrombolysis PSA sampled inputs around the scenario which 95% of the patients who met the SSNAP minimum criteria get thrombolysed.

	1 year			5 years		
	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs
Baseline result	£13,278	£8,799	0.493	£17,729	£27,670	1.665
PSA Mean	£13,379	£8,948	0.496	£17,918	£28,300	1.661
SEM	£491	£348	0.011	£742	£2,839	0.108
Upper 95% CL	£14,342	£9,631	0.517	£19,371	£33,864	1.872
Lower 95% CL	£12,416	£8,265	0.475	£16,464	£22,736	1.450

3.4.3 ESD PSA

Table 33: PSA results for the ESD scenario which 35% of patients who were not discharged to ESD redirected to ESD treatment.

	1-year			5-years		
	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs	Mean NHS cost (£)	Mean social cost (£)	Mean QALYs
Baseline result	£12,783	£8,444	0.498	£17,220	£26,429	1.678
Mean	£12,859	£8,656	0.501	£17,346	£27,236	1.682
SEM	£479	£367	0.011	£747	£2,847	0.115
Upper 95% CL	£13,798	£9,375	0.523	£18,810	£32,816	1.907
Lower 95% CL	£11,920	£7,937	0.479	£15,882	£21,656	1.457

4 Discussion

4.1 Summary

We estimated the cost of treating stroke using a bespoke patient simulation model and audit data from SSNAP. The mean NHS cost per stroke patient was £13,500 in the first year and £18,000 over 5 years. Costs were broken down by sex, age group, stroke type and initial stroke severity.

We estimated potential NHS cost savings over 5 years from more intensive intervention

- £4,100 per extra patient thrombolysed,
- £1,600 per extra patient discharged to early supported discharge.

We also estimated better health outcomes (quality-adjusted life-years) over 5 years from more intensive intervention:

- 0.26 QALYs per extra patient thrombolysed,
- 0.14 QALYs per extra patient discharged to early supported discharge.

4.2 Strengths and limitations

4.2.1 Cost burden of stroke

SSNAP collected data from more than 90% of the patients in England, Wales and North Ireland so the inputs used in the model should be representative – SSNAP is an ideal source of data for this work.

We did not seek to estimate productivity losses due to time off work or direct costs to patients. However, we are aware of other research groups that may be carrying out this work in the future.

The average stroke costs that were output by the model are probably slight under-estimates from an NHS perspective because:

- Some costs of stroke were not included because they could not easily be attributed, for example the cost of falls
- It did not include the cost of surgery.
- Only patients with a full NIHSS score in SSNAP were analysed. These represent 76% of patients. However, they are slightly younger on average (median=76 vs. 80) and slightly more independent (median mRS=0 vs 1) than those without full NIHSS scores.

From a local authority perspective, the social care costs are more likely to be an over-estimate, since we could not clearly distinguish between care home costs incurred by social services and those incurred by the NHS or funded by the patient/family.

4.2.2 Cost-effectiveness of interventions

However, there are strengths and weaknesses of using observational evidence, like SSNAP, to estimate treatment effects and the cost-effectiveness of treatments.

The advantage is that trials are selective in the patients they use and therefore might not be generalisable. However, the disadvantage is that with observational studies like SSNAP, unknown confounders and bias are unavoidable. Organisations that routinely conduct health technology assessment, such as NICE tend to prefer randomised evidence for treatment effects but observational evidence for baseline effects.[13] Therefore, we used relevant Cochrane reviews of randomised controlled trials to calibrate the model input data, for the purposes of conducting the cost-effectiveness analysis of thrombolysis and early supported discharge. We also stratified patients by age group and health status (NIHSS or mRS) to reduce confounding.

Reassuringly the average effects of early supportive discharge on mortality and mRS in the model using SSNAP data and the results of meta-analysis in the Cochrane review[5] were similar. The same could not be said for Thrombolysis – no effect was detected after controlling for age and severity - and therefore we calibrated the results using the Cochrane review.

The quality of life benefits of the interventions could possibly be under-estimated, since we only ascribed benefit to those patients whose mRS score changed and no benefit to those who remained the same. As with other economic evaluations, we did not seek to account for the shorter-term benefits, reflected in increased patient satisfaction, as these are not easily captured by the QALY approach.

4.2.3 Heterogeneity

We estimate average costs and cost savings but there is great heterogeneity between services in general and complex interventions such as ESD in particular. For this reason, the use of the results of this study to inform the cost saving potential for local commissioners and providers should be seen as indicative rather than specific to their local situation.

4.3 Thrombolysis

The first analysis was to look at increasing the rate of thrombolysis among patients **who met the minimum SSNAP** criteria. It was found that both NHS and social care cost reduced with increased thrombolysis and QALYs increased. However, this assumes that there are no additional costs associated with increasing thrombolysis such as additional out of hour payments.

The second thrombolysis analysis explored the effects of redirecting patients in the model to thrombolysis **who did <u>not</u> meet the minimum SSNAP criteria** in the baseline model for one of the following reasons:

- (a) did not arrive on time,
- (b) too mild/severe,
- (c) wake up time unknown, and
- (d) a combination of (a)(b) and/or (c).

At 5-years only strategy (a) is still cost saving, (c) generated slightly higher NHS cost than the baseline cost, but it is cost-effective, strategy (b) is neither cost-saving nor cost-effective. The reason for this pattern is that strategy b) is sending more low-severity patients to thrombolysis – for such patients the benefit in terms of health status is less but they still incur the mortality risk. This strategy does not lead to any more high severity patients being treated with thrombolysis and therefore is not realising health gain for these patients. Strategy c) has the biggest QALY gain because it is redirecting more of the most severe patients. However, this is assuming that, after controlling for severity and age, thrombolysis is as effective in these patients as it is for those patients whose wake up time is known.

Of the three strategies, only (a) yielded NHS cost savings at five years. However, this is assuming that, after controlling for severity and age, thrombolysis is as effective in these patients as it is for those patients that did arrive on time. Furthermore, this does not include the cost of any intervention to speed up arrival time.

4.3.1 Comparison with recent studies

With respect to increasing thrombolysis among eligible patients, the findings are consistent with recent modelling studies conducted from a UK perspective which found that increasing the rate of thrombolysis was cost saving and increased health outcome[30] [10]. Another study [31] suggested increased QALYs but higher cost associated with thrombolysis, however that study had an Australian setting and a relatively simpler model structure which might explain the difference in model results. A fourth study[10] demonstrated cost savings from a French health care perspective but they did not evaluate effectiveness.

The NAO report[18] found that increasing thrombolysis from standard care to 24/7 would increase QALYs but also increase the average costs, albeit at a rate that is cost-effective. It is not clear the reason for the apparent disparity between that study and this. This study uses more up to date and more representative estimates of treatment effect and costs and resource use. The NAO report model had restricted capacity for the stroke unit and hence a different structure.

4.4 Early supported discharge

Two analyses related to redirecting patients to ESD were conducted. In the first analysis, we redirected patients to ESD regardless of their mRS when discharged from the hospital (ASU or SU in our model), and in the second analysis only patients with mRS 0-2 were redirected.

In the first analysis, the results demonstrated that with more ESD, both the NHS and social care costs were reduced, and higher QALY were generated by scenarios with higher proportion of ESD. However, this pattern was not observed in results from analysis 2. We did not observe any significant differences in costs or QALYs as ESD use increased, implying that it is patients of moderate to severe disability that gain the most from ESD. Perhaps this is a real effect but it could be that this pattern is caused by confounding.

4.4.1 Comparison with recent studies

A number of studies have looked at the cost impact or cost-effectiveness of early supported discharge

Two quite recent reviews of economic evaluations based on randomised controlled trials[32, 33] have indicated health care cost savings based on the international body of evidence: median cost saving of 20% - range 4% to 30%. The UK studies showed more modest cost savings 4-8%, which are not dis-similar to the 10% reduction found in this study.

Conversely, the NAO report[18] found that increasing ESD would increase costs and improve outcomes. Although, it did find thrombolysis to be cost effective, it is surprising that it did not also find cost savings given that it is also a discrete event simulation mode and takes a UK perspective. Possible explanations for the difference in results between that study and this one are:

a) This study uses more up to date and more representative estimates of treatment effect and costs and resource use
b) NAO report model compared ESD with ‘conventional discharge’. Whereas, in this study ESD was compared with extended stroke unit rehabilitation and/or community rehabilitation; therefore, patients that had less need for rehabilitation were excluded.

4.5 Conclusions

Using data mainly from SSNAP, the South London Stroke Registry and standard sources of unit costs we were able to estimate the cost of stroke by sex, age group, stroke type and initial stroke severity using a patient simulation modelling.

We also investigated the cost-effectiveness of intensifying stroke care. We found both cost savings and health gain associated with increasing thrombolysis or early supported discharge in eligible patients. These results were broadly consistent with the published literature but based on more up to date and representative resource use and cost data. The results will be used to provide bespoke estimates to SSNAP contributing organisations to inform the development of local services and promote clinical practice that is more efficient as well as providing up to date estimates of the burden of stroke at the national level for use in policy-makin and planning.

There are several ways that this work could be usefully extended. Firstly, broadening the perspective to include the full societal costs of stroke would provide a more complete estimate of the financial consequences of stroke on individuals and society. Secondly, we carried out more detailed modelling of the cost effectiveness of two important stroke care interventions, but this modelling could be expanded to include other interventions. In particular, recent evidence of the effectiveness of more centralised models of stroke care and of mechanical thrombectomy (a procedure to remove the blood clot causing stroke in patients with acute ischaemic stroke) mean that practical tools to help commissioners and providers understand the costs and benefits of these interventions would be useful. Finally, the model of embedding this type of health economic modelling within an existing quality register/national audit is novel, and could be extended to other areas of healthcare. Routinely reporting data on health and social care costs alongside information about quality of care and patient outcomes, could give policy makers, commissioners and providers new ways of improving the clinical effectiveness, efficiency and productivity of healthcare services.

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Appendix 1 – Results of SSNAP and SLSR data analyses

See separate Excel file

Appendix 2 – Additional output

Table 34 Break-down 5-year costs (£) by patients stroke type and initial stroke severity –primary stroke costs.

Type	Initial NIHSS	Acute stroke unit (not including thrombolysis)	Inpatient care costs	Rehabilitation costs	Social care costs
Ischaemic	0	£ 4,156	£ 5,440	£ 2,315	£ 10,019
Ischaemic	1-4	£ 5,211	£ 6,751	£ 2,695	£ 12,985
Ischaemic	5-15	£ 10,834	£ 13,365	£ 3,595	£ 16,225
Ischaemic	16-20	£ 14,943	£ 17,856	£ 3,540	£ 18,142
Ischaemic	21-42	£ 13,681	£ 15,803	£ 2,504	£ 10,745
All Ischaemic		£ 8,305	£ 10,301	£ 3,025	£ 14,098
Haemorrhage	0	£ 3,900	£ 4,905	£ 2,069	£ 7,156
Haemorrhage	1-4	£ 4,833	£ 6,184	£ 2,551	£ 11,190
Haemorrhage	5-15	£ 10,162	£ 12,779	£ 3,802	£ 17,355
Haemorrhage	16-20	£ 13,644	£ 16,973	£ 4,160	£ 20,896
Haemorrhage	21-42	£ 11,616	£ 14,187	£ 3,087	£ 17,718
All Haemorrhage		£ 9,600	£ 11,807	£ 3,154	£ 15,853
All		£ 8,428	£ 10,445	£ 3,037	£ 14,265

Inpatient care costs includes costs in ASU, SU and GMW; rehabilitation costs included costs in SU, ESD and community rehabilitation, social care costs included social care costs in own home and care home. Recurrence costs were not included in these calculations.

Figure 18: Change in weighted mean ASU costs with different thrombolysis proportions.

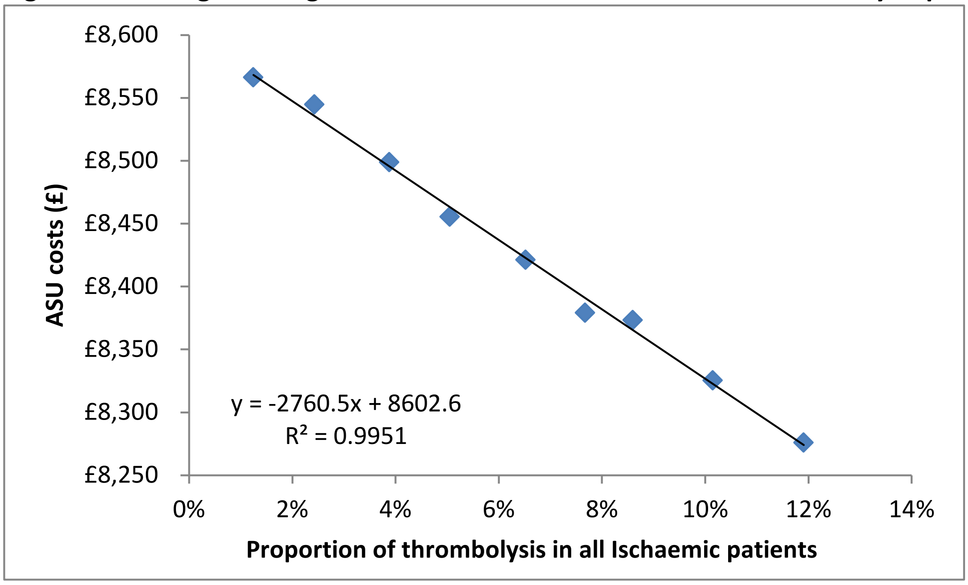


Figure 19: Change in weighted mean inpatient care costs with different thrombolysis proportions

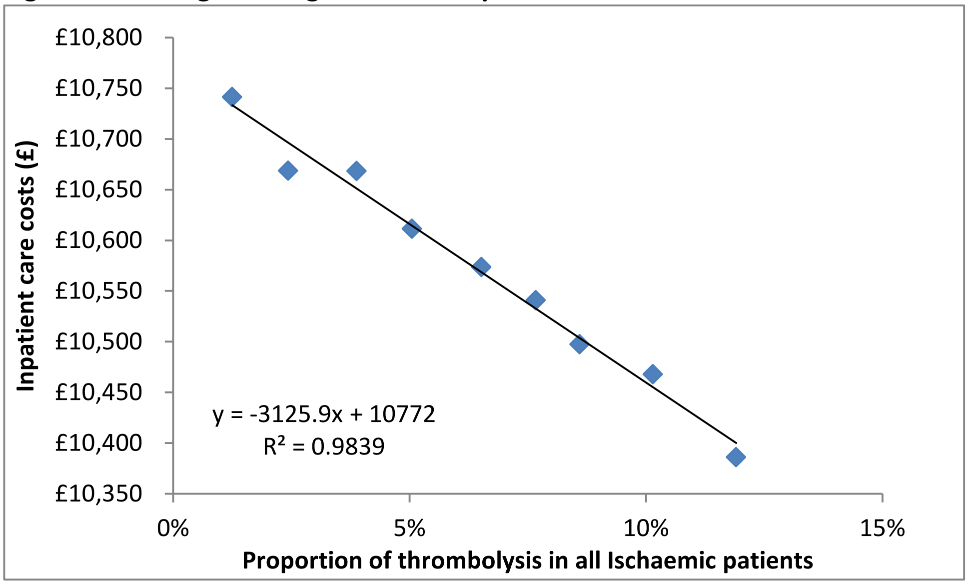


Figure 20: Change in weighted mean rehabilitation costs with different thrombolysis proportions

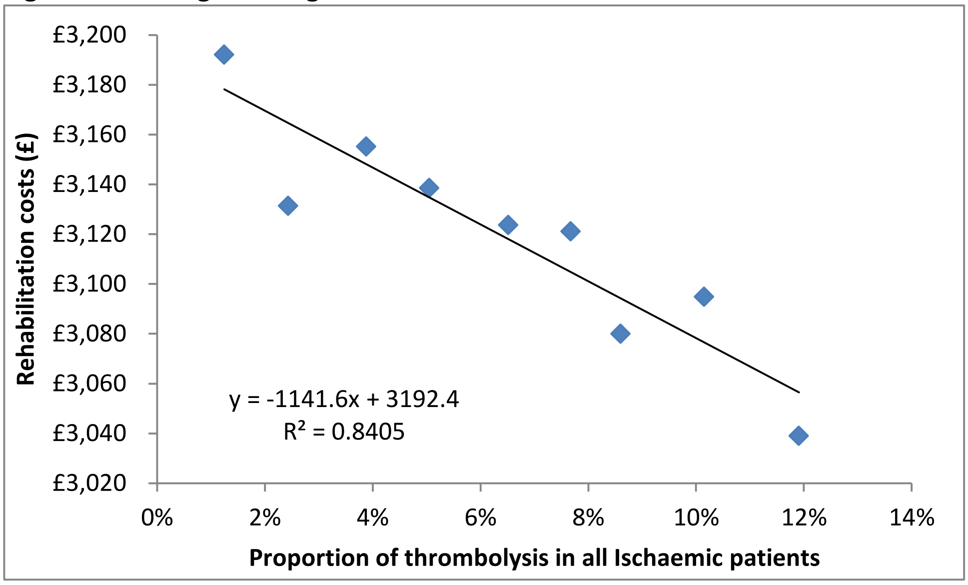


Figure 21: Change in weighted mean social care costs with different thrombolysis proportions

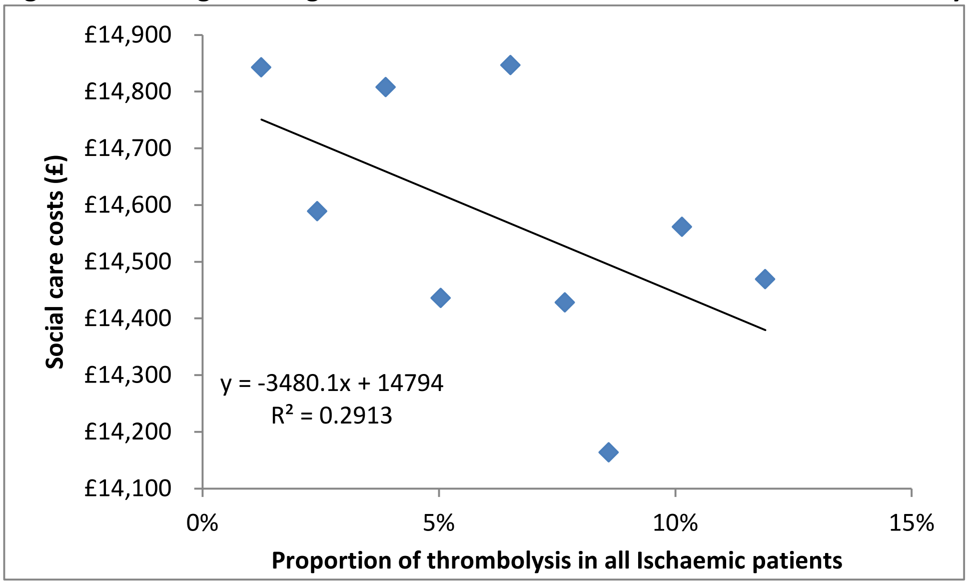


Figure 22: Mean QALYs in the first five years after primary stroke with different proportion of patients discharged to ESD

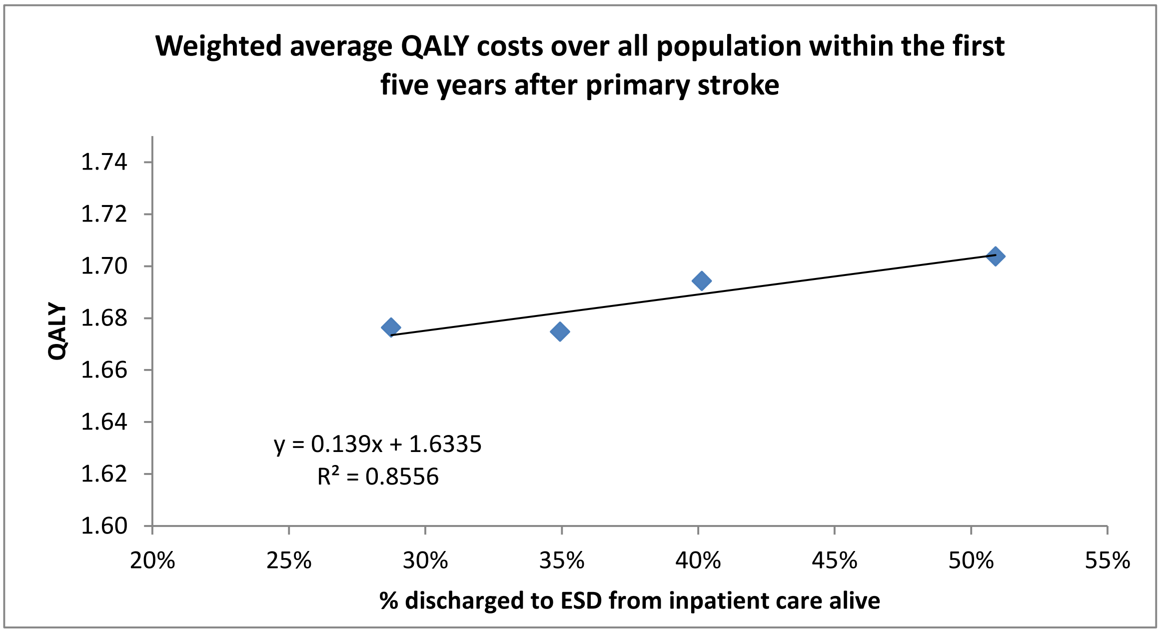


Figure 23: Change in weighted mean ASU costs in the first five years after primary stroke with different proportion of patients discharged to ESD

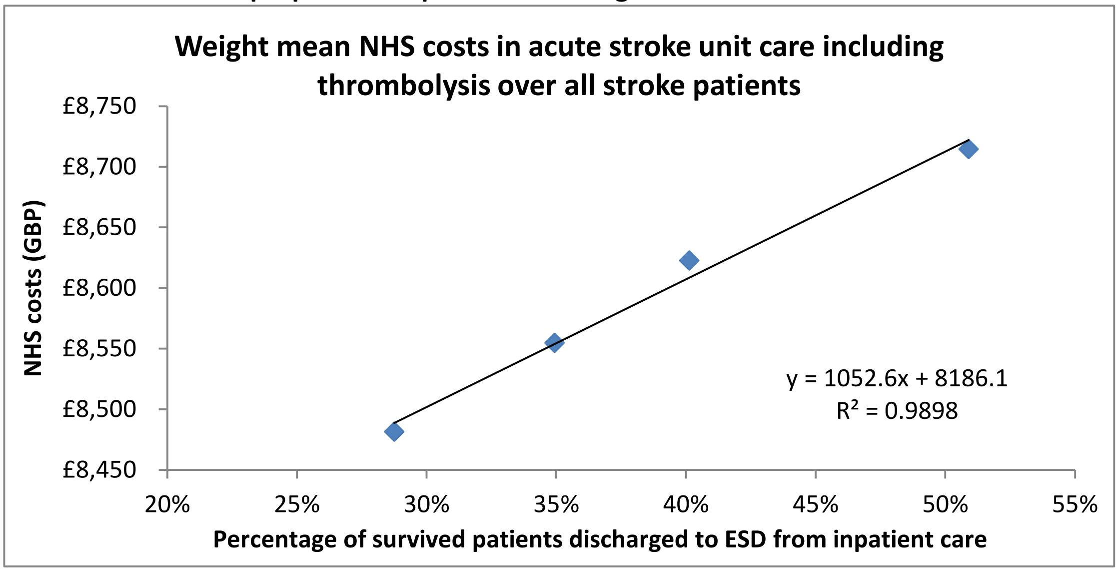


Figure 24: Change in weighted mean inpatient care costs in the first five years after primary stroke with different proportion of patients discharged to ESD

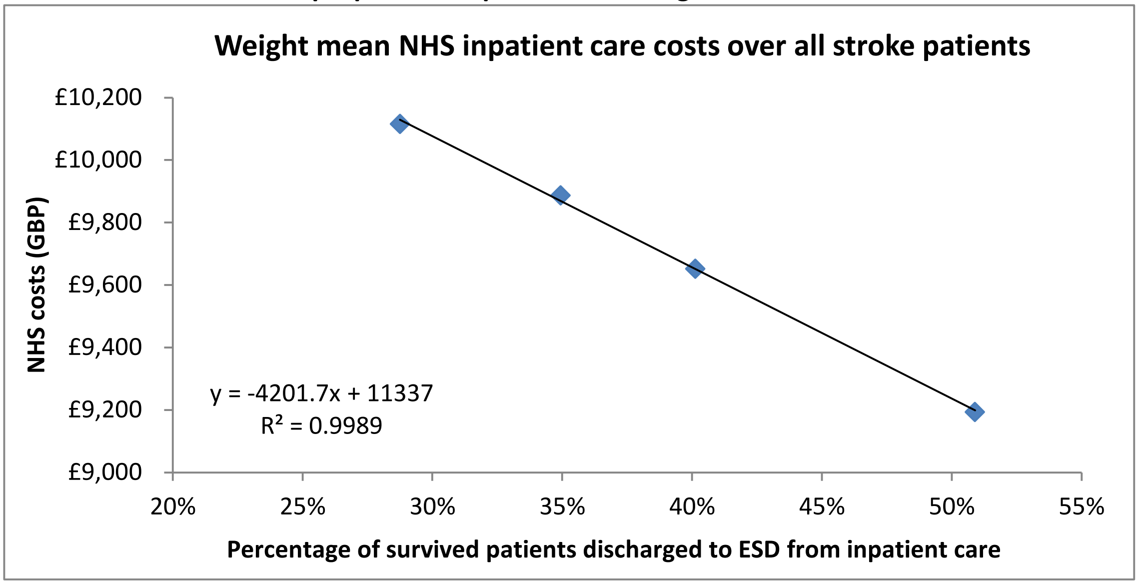


Figure 25: Change in weighted mean rehabilitation costs in the first five years after primary stroke with different proportion of patients discharged to ESD

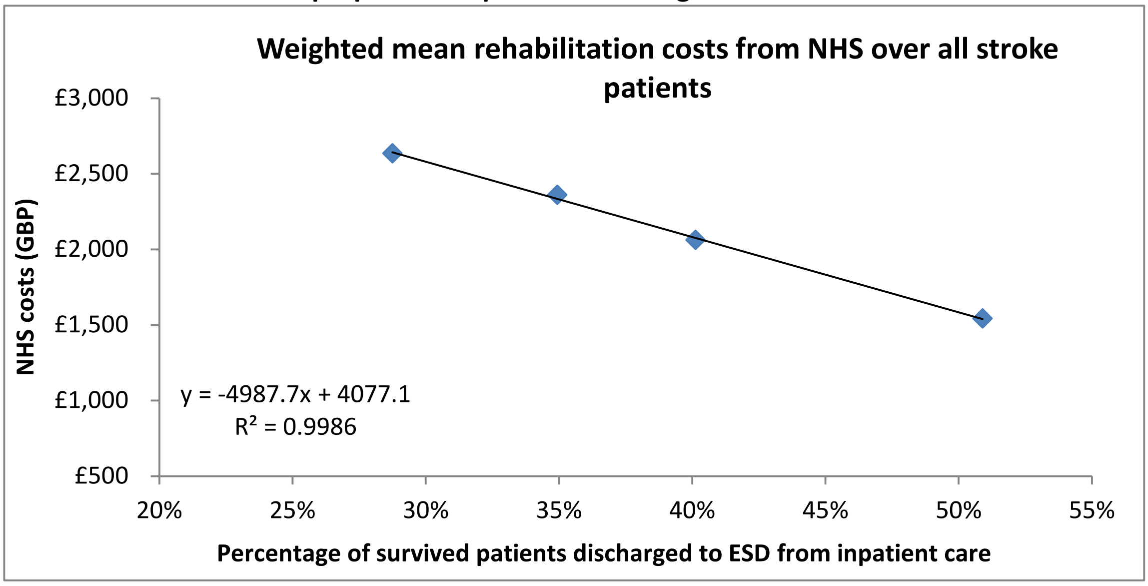
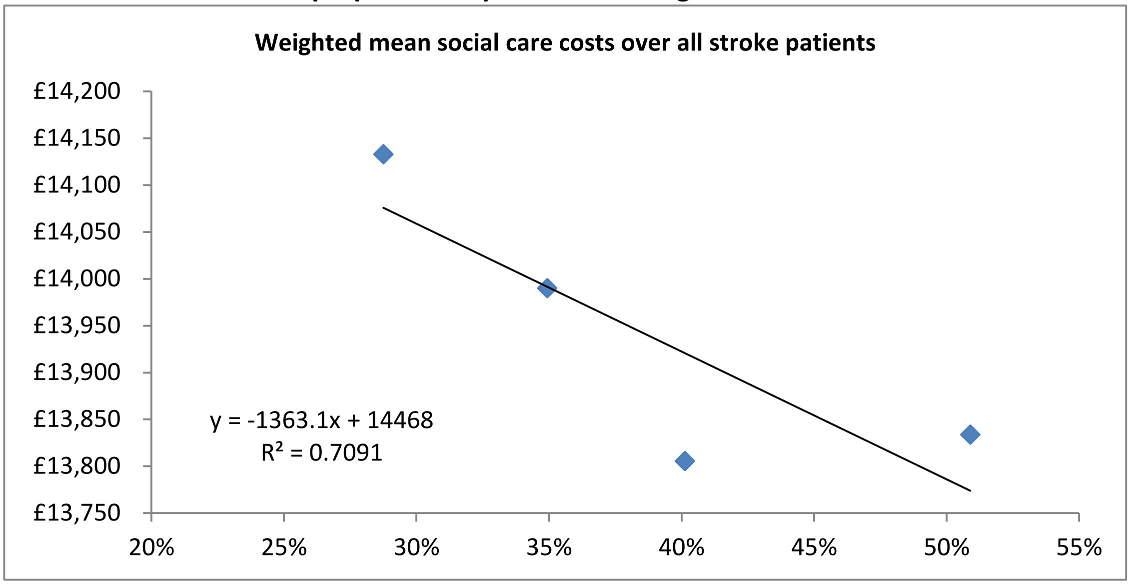


Figure 26: Change in weighted mean social care costs in the first five years after primary stroke with different proportion of patients discharged to ESD



Source: <Insert Source text here>

Table 35 – Incremental cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, one year NHS perspective

Scenarios	Total number of thrombolysis at primary stroke	Mean per-patient costs (£)	Incremental Cost of Scenario	Mean per-patient QALY	Incremental QALY	ICER
Baseline with calibrated data	4500	£13,272	£-	0.490		
(b) 50% of the patients not met the criteria due too mild/severe only redirected	5259	£13,361	£89	0.491	0.00058	£155,432
(a) 50% of the patients not met the criteria due to time window only redirected	7149	£13,143	-£218	0.497	0.00619	dominant
(c) 50% of the patients not met the criteria due to wake up time unknown only redirected	7209	£13,212	£69	0.500	0.00258	£26,744
(d) 50% of the patients not met the criteria due to time window, too mild/severe or wake up time unknow but nothing else redirected	11439	£13,063	-£150	0.502	0.00231	dominant

Table 36: Incremental cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis at 5 years, NHS perspective

Scenarios	Total Cost of Scenario	Incremental Cost of Scenario	Total QALY	Incremental QALY	ICER
Baseline with calibrated data	£ 17,678.09	£ -	1.65		
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	£ 17,840.44	£ 162.34	1.66	0.007	£ 22,542
(a) 50% of the patients who had not met the criteria due to time window redirected	£ 17,634.53	-£ 205.90	1.67	0.015	dominant
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	£ 17,683.37	£ 48.83	1.68	0.014	£ 3,587
(d) combination of (a)-(c)	£ 17,466.21	-£ 217.15	1.69	0.003	dominant

Table 37: Incremental cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, 5 year social care perspective

Scenarios	Total number of thrombolysis at primary stroke	Total NHS Cost	Incremental cost compared with last most effective scenario	Total QALY	Incremental QALY compared with last most effective scenario	Incremental cost-effectiveness ratio
Baseline with calibrated data	4500	£ 8,881		0.490		
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	5259	£ 8,902	21	0.491	0.0006	£ 36,843
(a) 50% of the patients who had not met the criteria due to time window redirected	7149	£ 8,930	27	0.497	0.0062	£ 4,385
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	7209	£ 8,203	-727	0.500	0.0026	dominant
(d) combination of (a)-(c)	11439	£ 8,514	312	0.502	0.0023	£ 135,090

Table 38: Incremental cost-effectiveness analysis results of scenarios redirecting not thrombolysed patients to thrombolysis, 5 year social care perspective

Scenarios	Total number of thrombolysis at primary stroke	Total NHS Cost	Incremental cost compared with last most effective scenario	Total QALY	Incremental QALY compared with last most effective scenario	Incremental cost-effectiveness ratio
Baseline with calibrated data	4500	£ 28,115		1.648		
(b) 50% of the patients who had not met the criteria due too mild/severe redirected	5259	£ 27,841	-274	1.655	0.00720	dominant
(a) 50% of the patients who had not met the criteria due to time window redirected	7149	£ 28,431	590	1.670	0.01490	£ 39,589
(c) 50% of the patients who had not met the criteria due to wake up time unknown redirected	7209	£ 25,970	-2461	1.684	0.01361	dominant
(d) combination of (a)-(c)	11439	£ 26,452	482	1.687	0.00332	£ 145,401