Kent & Medway Public Health Observatory

Kent and Medway Stroke Services

Evidence Review of Hyperacute Stroke Units

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Executive Summary

This literature review was commissioned by Kent and Medway Stroke Review Programme Board and West Kent Clinical Commissioning Group. This review examines the national standards for stroke, clinical and cost effectiveness of acute stroke units and looks at the improvements to stroke care that have resulted from the introduction of hyper-acute stroke units in London since 2010. These are compared with the changes in stroke care in Manchester that began at the same time. There is consideration of whether the London experience could be translated to a more rural context and alternatives to centralised stroke units are considered.

Reducing Burden of Disease from stroke requires systematic interventions at population level across all parts of the care pathway including primary prevention and post stroke rehabilitation.

Clinical and Cost effectiveness of Stroke Units

The National Audit Office 2005 defined a stroke unit as any system of organised inpatient stroke care that is characterised by coordinated multidisciplinary rehabilitation programmes of education and training in stroke and specialisation of medical staff usually housed in a geographically discrete ward. The 2012 National Guideline for Stroke defined a hyper-acute unit as a stroke unit that treats patients in the few days of symptom onset.

The available evidence suggests that stroke units are both clinically and cost effective because of a combination of care provided, of which thrombolysis in the first 4.5 hours is a part. However, these outcomes (reducing death, length of hospital stay and improved quality adjusted life gained) tend to be achievable when appropriate and optimum standards of care are provided through continuous monitoring. The evidence also highlights that the maximum gain to population health is through preventative strategies. According to the National Sentinel Stroke Audit there are inconsistencies and substandard level of care in many of the stroke units in Kent, similar to the rest of the country.

The evidence also highlights that in order to get best clinical outcomes, it is important that along with HASUs there is a supportive infrastructure of sub-acute stroke units and after hospital care for individuals.

Reconfiguration of Stroke Units Elsewhere

The experience from London Stroke Units indicates that when stroke units were centralised (to pool resources together) they were able to improve the standards of care and hence were shown to be both clinical and cost effective. Supported discharge contributed to cost efficiency.

The Manchester experience also suggests that access to quick ambulance transfer to stroke units was an important aspect in improving outcomes as it ensured access to prompt interventions. It further highlighted the importance of stroke recognition by the public in speeding up access to hyper-acute services.

The findings indicate that Greater Manchester achieved a 2-day reduction in hospital stay but years of live saved were not different from other areas in the country. The

differences in mortality was explained by their partial adherence to the centralised model (64% of people were transferred to the appropriate service in Greater

Manchester compared with 98.7% in London) Following its review, Greater Manchester now aims to move closer towards a centralised model, thus supporting the setting up of hyper acute stroke unit.

Telemedicine: Alternative to Hub and Spoke Model

The evidence suggests telemedicine is both safe and effective. In telemedicine, brain scans and delivery of thrombolysis take place locally but expert review of the brain images and treatment decisions takes place in a centralised specialist unit. Different studies in rural settings (Northumbria, Georgia and Arkansas) indicate that in rural areas where travel times may prohibit access to hyper-acute units with access to centralised 24/7 expertise, telemedicine may be beneficial where symptoms can identify which patients are eligible for transfer to a central unit (used in tandem with a stroke code alert system) or alternatively, treatment may take place in local units.

It is pertinent that the introduction of HASU goes in tandem with the improvement in standard of the other stroke units which provide subsequent and after care (such as inpatient rehabilitation, early supported discharge and long term community rehabilitation).

Travel times and other factors affecting door to needle time could to be an issue in more rural areas. The evidence indicates that treatment decreases by 2.5% for every minute of transfer time and suggests that specific transfer time goals are needed.

To make site specific decisions, further modelling work is needed to identify the location of HASUs across Kent and Medway, due to dispersed population in rural locations. However, CCGs will need to be mindful that ambulance times are only one of several factors affecting door to needle times in local hospitals. It is important that decision around HASUs also take into account experience of teams, process for implementation of protocols as these would also affect performance and clinical outcomes.

Acute care should not be the only focus. The National Audit Office highlighted in their 2010 report on “Progress in Improving Stroke Care,” that the best way of improving value for money of stroke care is by preventing strokes from occurring.

Although the prevention of stroke is outside the scope of Kent and Medway Programme Review Board, the literature clearly suggests that at population level, prevention of stroke is the best option. It is recommended that this is considered by the Board and progressed through CCGs at a local level. Therefore, in addition to commissioning of acute care, CCGs will need to ensure that public health interventions are implemented. These include control of high blood pressure, reduced salt consumption, cholesterol, smoking, unhealthy diet, encouraging uptake of exercise and optimal participation in the NHS health checks programme.

1. Methodology of the Evidence Review

A review of stroke services across Kent and Medway was commissioned in December 2014. This literature review was conducted to support this programme review and case for change.

An extensive search was conducted by Library and Knowledge Services between 15 January 2015 and 10 March 2015. A search was conducted in Evidence Search, Cinahl, Medline, the Cochrane, NHS Economic Evaluation Database, the Commissioning Handbook for Librarians, the Learning Environment, NHS England, Google, the Health Service Journal HSJ, the SNAPP audit results of Royal College of Physicians, the National Institute of Health Research, and the University of York Centre for Reviews and Dissemination. Sources were also followed up from a presentation by Greg Fell, a public health consultant in Bradford. HDAS searches were generally limited to 2005 onwards and limited to English language abstracts.

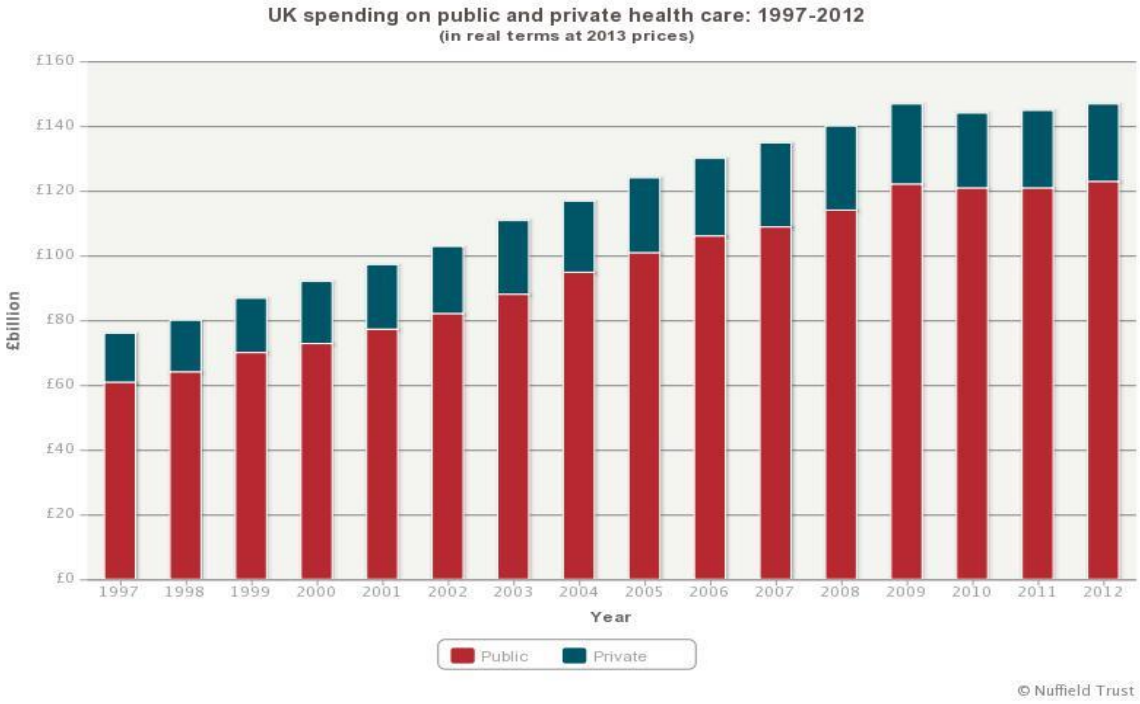
Evidence assessing the clinical effectiveness of acute stroke units was widely available and of good quality, with several systematic reviews since the late 1990s. Evidence of cost effectiveness was less rigorous mainly because the centralisations in London and Greater Manchester were relatively recent and summary analysis is only now beginning to appear. Material on acute stroke units outside the major conurbations in England and Wales was scarce and generally consisted of policy and planning documents, presentations or case studies. International experience of using telemedicine in more rural areas included some higher level research and provided models not yet available on any scale in the UK.

Search terms included: stroke, hyper-acute/hyper-acute stroke unit, thrombolysis, cost effectiveness, quality of health care, treatment outcome, value for money, burden of disease, time factors, transportation/transfer of patients, residence characteristics, rural populations, rural health services, and telemedicine. Searches were also carried out on the names of individual English counties, regions, urban authorities and clinical commissioning groups. References were sometimes followed up, particularly in sources on cost-effectiveness.

2. Background and National Context

Stroke is the third biggest killer in the UK and the leading cause of adult severe disability. Half of all stroke survivors have a disability and 3 in 10 stroke survivors will go on to have a recurrent stroke or TIA. Stroke care accounts for about 5% of total spending on health care (10% when indirect costs such as caregivers are taken into account) (Davie et al 2013). It is therefore important that strokes are either prevented or detected early and treated promptly, especially now that the years of increased NHS public funding from 1997 to 2009 seem to have come to an end (Figure 1).

Figure 1: Real Spending on Public and Private Health Care 1997-2012

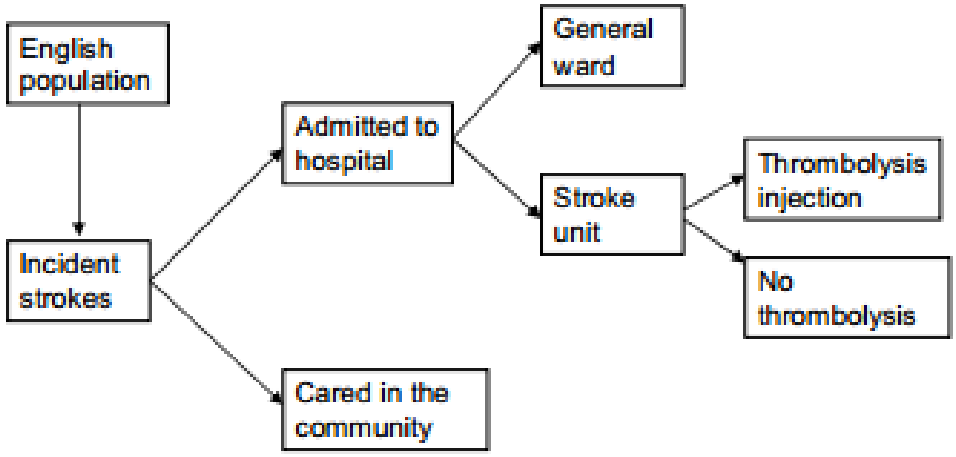


Source: Nuffield Trust

The Department of Health's National Stroke Strategy for England (2007) identified care in a stroke unit as the single biggest factor to improve outcomes after stroke. NHS England's Putting Patients First business plan 2014-15 to 2016-17 aims to "promote the reconfiguration of stroke services across the country, building on the evidence-based model developed in London". This includes developing a specific case for "acute stroke service reconfigurations in two geographical locations by April 2015". The London model is a hub and spoke model of centralised, dedicated hyper-acute stroke units. The alternative looked at is treatment on general wards.

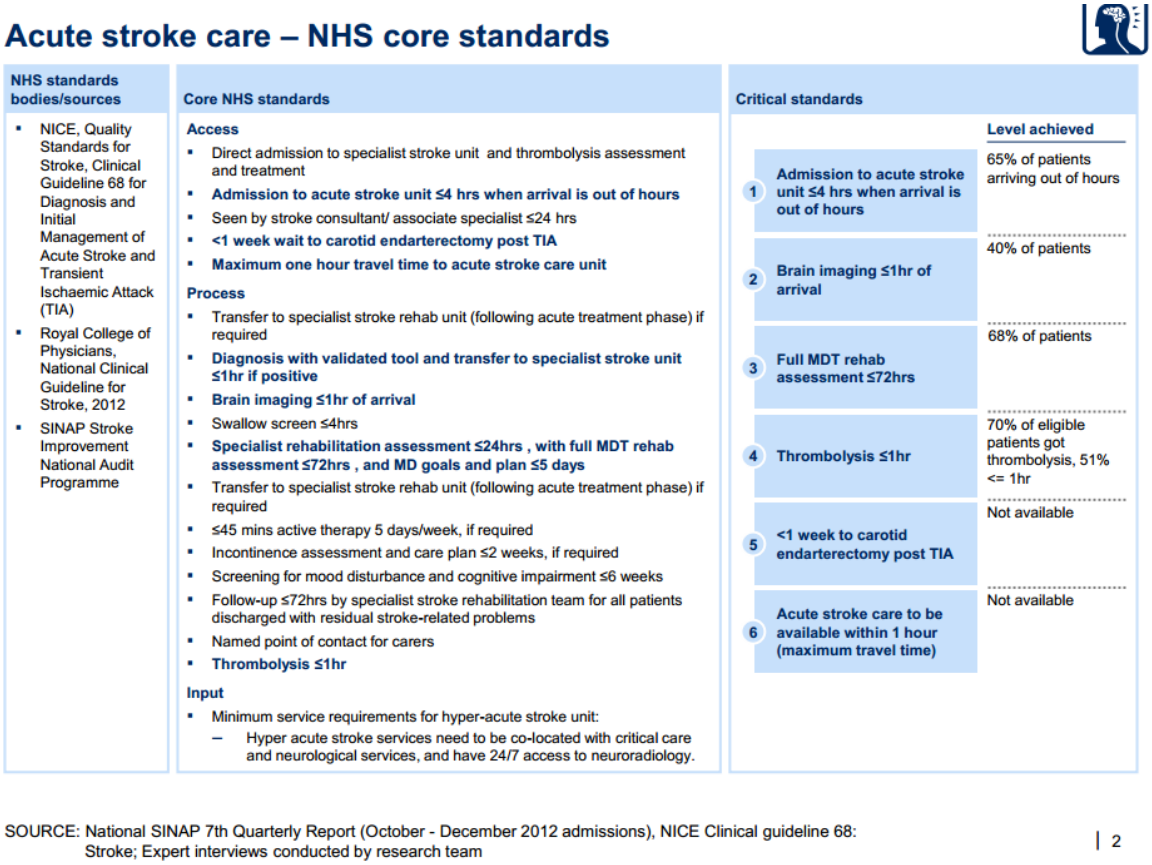
In their study, Airoldi et al (2011) summarised options of treatment available during acute phase of stroke (Figure 2). Individuals who have stroke can expect to receive care within nationally agreed standards (figure3).

Figure 2: Treatment Options



Source: Airoldi et al 2011

Figure 3: Summary of National Standards



Acute stroke care – NHS core standards

NHS standards bodies/sources

- NICE, Quality Standards for Stroke, Clinical Guideline 68 for Diagnosis and Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA)
- Royal College of Physicians, National Clinical Guideline for Stroke, 2012
- SINAP Stroke Improvement National Audit Programme

Core NHS standards

Access

- Direct admission to specialist stroke unit and thrombolysis assessment and treatment
- **Admission to acute stroke unit ≤4 hrs when arrival is out of hours**
- Seen by stroke consultant/ associate specialist ≤24 hrs
- **<1 week wait to carotid endarterectomy post TIA**
- **Maximum one hour travel time to acute stroke care unit**

Process

- Transfer to specialist stroke rehab unit (following acute treatment phase) if required
- **Diagnosis with validated tool and transfer to specialist stroke unit ≤1hr if positive**
- **Brain imaging ≤1hr of arrival**
- Swallow screen ≤4hrs
- **Specialist rehabilitation assessment ≤24hrs , with full MDT rehab assessment ≤72hrs , and MD goals and plan ≤5 days**
- Transfer to specialist stroke rehab unit (following acute treatment phase) if required
- ≤45 mins active therapy 5 days/week, if required
- Incontinence assessment and care plan ≤2 weeks, if required
- Screening for mood disturbance and cognitive impairment ≤6 weeks
- Follow-up ≤72hrs by specialist stroke rehabilitation team for all patients discharged with residual stroke-related problems
- Named point of contact for carers
- **Thrombolysis ≤1hr**

Input

- Minimum service requirements for hyper-acute stroke unit:
  - Hyper acute stroke services need to be co-located with critical care and neurological services, and have 24/7 access to neuroradiology.

Critical standards

		Level achieved
1	Admission to acute stroke unit ≤4 hrs when arrival is out of hours	65% of patients arriving out of hours
2	Brain imaging ≤1hr of arrival	40% of patients
3	Full MDT rehab assessment ≤72hrs	68% of patients
4	Thrombolysis ≤1hr	70% of eligible patients got thrombolysis, 51% <= 1hr
5	<1 week to carotid endarterectomy post TIA	Not available
6	Acute stroke care to be available within 1 hour (maximum travel time)	Not available

SOURCE: National SINAP 7th Quarterly Report (October - December 2012 admissions), NICE Clinical guideline 68: Stroke; Expert interviews conducted by research team

| 2

Source: Monitor Evidence Report 2014.

3. Standards from the National Clinical Guideline for Stroke

- Ambulance services should respond to every possible acute stroke as an emergency.
- Acute services should provide brain scans in the next slot or within 1 hour for those eligible for thrombolysis and always within 12 hours.
- All hospitals should have arrangements to admit patients directly to a specialist acute stroke unit (onsite or at a neighbouring hospital).
- Any patient, regardless of age or stroke severity, where treatment can be started within 3 hours of symptom onset should be considered for treatment using alteplase.
- Between 3 and 4.5 hours of onset, patients under 80 years should be considered for treatment with alteplase.

In its Guidance CG68, the National Institute for Health and Care Excellence is in favour of acute units:

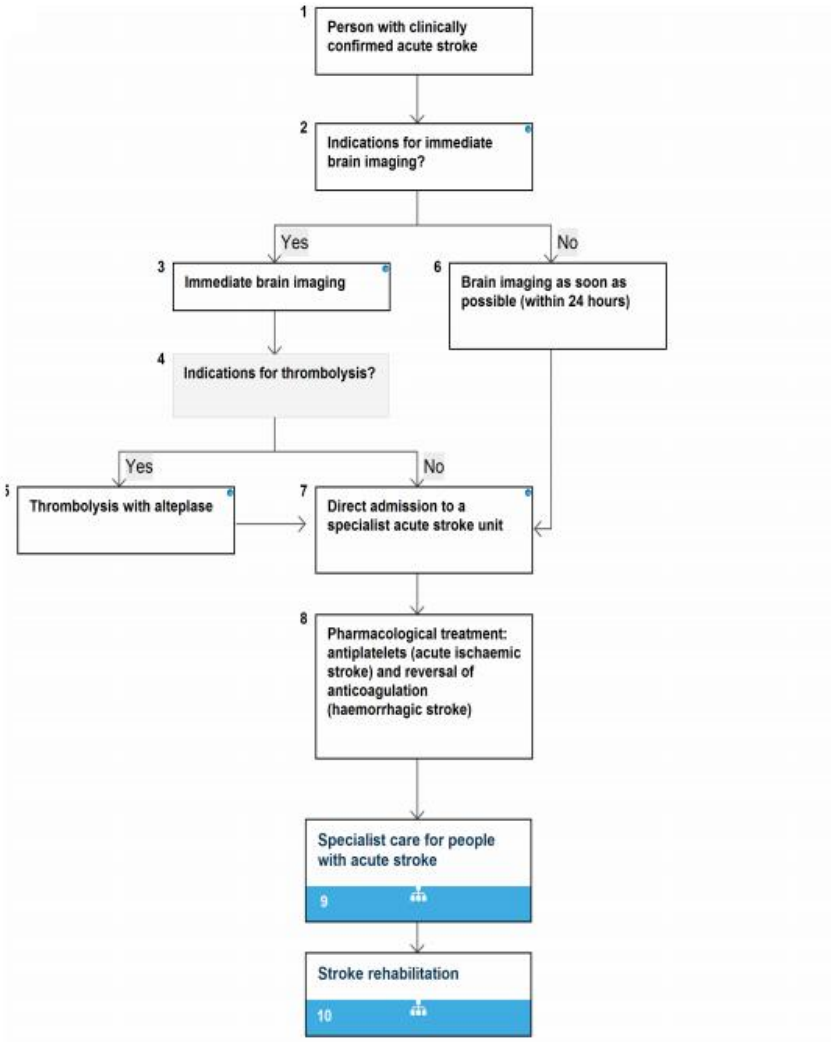
- all people with suspected stroke should be admitted directly to a specialist acute stroke unit following initial assessment from the community or A&E
- brain imaging should be performed immediately if there are indications for thrombolysis or early anticoagulation treatment and as soon as possible for everyone else but wary of the use of thrombolysis outside HASUs. The guidance focuses as much on the use of aspirin and warfarin as the use of thrombolysis.
- Alteplase is recommended for use only when used by physicians trained and experienced in the management of acute stroke within a well-organised stroke service with staff trained in delivering thrombolysis and in monitoring for any complications.

4. Clinical Effectiveness of Stroke Units

During the 1990s, the focus was on prevention, with a pessimistic view of the likely success of treatment after stroke, though the importance of stroke units in improving outcomes was already being recognised. The approval of thrombolytic treatment, the use of “clot-busting” drugs, initially within 3 hours of onset (NINDS 1995), began the focus on care in the first 72 hours.

A Health Technology Appraisal (HTA) conducted by the National Institute for Health and Care Excellence (NICE) found evidence from six randomized controlled trials that alteplase (thrombolysis) reduced the risk of death or dependency, compared with a placebo, if given within 3 hours of the onset of ischaemic stroke. A subsequent NICE HTA found evidence that it reduced the risk if given up to 4.5 hours after onset. The Monitor Evidence Report on international comparisons, (2014) found an international consensus for thrombolysis for eligible patients to be given within a 4.5-hour window from the onset of stroke.

Figure 4: the NICE Pathway



Source: NICE

Figure 4 shows the NICE stroke pathway: where ischaemic stroke is suspected and time of onset is known and recent, immediate brain imaging should be used to confirm the diagnosis; eligible patients should be thrombolysed as soon as possible (and within 4.5 hours of the onset of stroke) and dealt with in a specialist stroke unit.

A Stroke Unit Trialists' Collaboration Cochrane review (2009) was one of several to establish that specialist stroke units were effective. A systematic review by Sun et al (2013) concluded that the resulting high independency rates were particularly important in view of the UK's aging population (figure 5).

Figure 5: Comparison of general medical wards (GMW) with stroke units (SU)

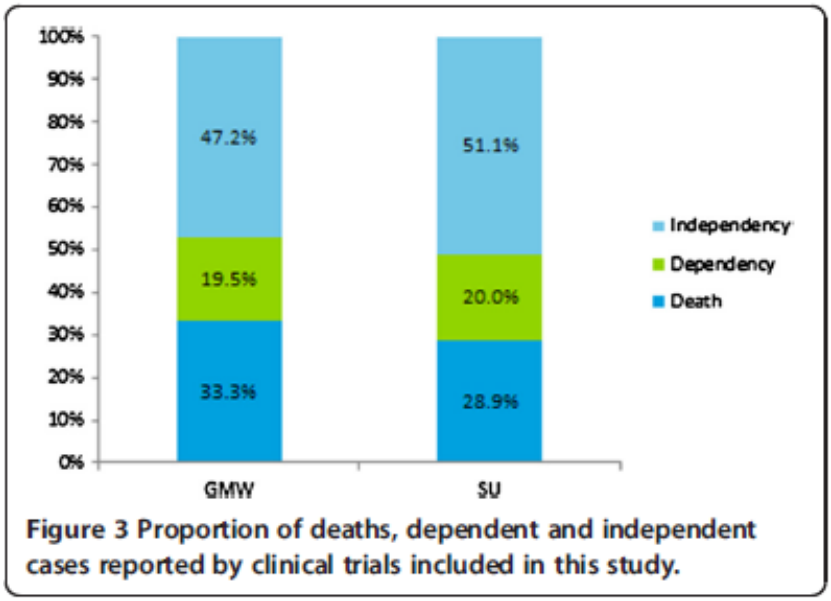
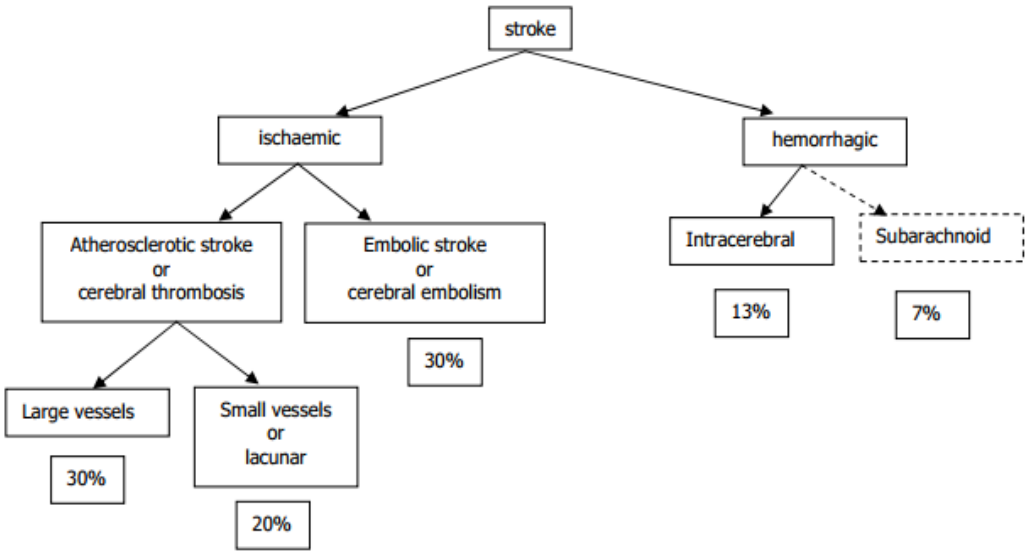


Figure 3 Proportion of deaths, dependent and independent cases reported by clinical trials included in this study.

Source: Sun et al (2013).

Most improvement is seen in ischaemic stroke (Morris et al 2014) which represents approximately 70-80% of the national incidence of first strokes according to the Drug and Therapeutic Bulletin (2009). The estimate of 80% is further supported by Airoldi, citing evidence from Wolfe, Rudd et al (2002) and the first national stroke audit (Clinical Effectiveness and evaluation unit 2005).

Figure 6: Stroke Classification and their Relative Frequency



Source: Airoldi et al 2011

Airoldi et al (2011) argued that it was not clear what had led to the improvement in outcomes for ischaemic stroke noted by Morris et al as it occurred at the same time as an increase in spending on the NHS and at the same time of the introduction of hyper-acute stroke units (HASUs). Airoldi et al (2011) also suggests that studies had shown that causality had been hard to establish and all parts of the stroke pathway have improved. The focus on the use of thrombolysis for ischaemic stroke does not explain the improvements throughout the pathway.

In a research paper published in 2013, Hunter et al (2013), found stroke units were associated with lower risk of death, death and dependency and death and organised care. There were doubts as to the reasons, particularly given that the nature of HASUs, the treatment offered and the extent to which this complied with national guidelines was not at all consistent; but specialist stroke unit care for the first 72 hours produced improvements in all measures. Centralisation led to reduced costs, improved outcomes and earlier discharge. The use of HASUs improved outcomes, concluded Morris (2014) though the process was not clear: "Care in a stroke unit was the single biggest factor that can improve outcome after stroke".

However, Davie (2013) argued that, "though increased thrombolysis is often seen as the primary driver of results, this can only account for a small proportion of the reduced mortality and morbidity: the rest stems from reliable care that is in line with the best evidence and provided across disciplines." This view was further supported through a Cochrane review by Ciccone et al (2013) which concluded that outcomes improved through continuous monitoring. Additionally, Govan, Langhorne and Weir (2007) thought that the prevention and treatment of complications, in particular infections, was important.

A systematic review by Langhorne et al (2013) found that patients with any type of stroke managed in organised inpatient units were more likely to survive and regain independence. Moreover, patients with intracerebral haemorrhage, a group who were not eligible for treatment with thrombolysis, seemed to benefit at least as much as patients with ischemic stroke from organised inpatient (stroke unit) care.

5. Cost Effectiveness of Stroke Units

There is less rigorous evidence on cost effectiveness (systematic reviews are needed in this area) but several studies e.g. Saka et al 2009, have found stroke units to be cost effective. Guzauskas et al (2012) found primary stroke centres were cost effective compared to a less specialist hospital setting. Tan Tanny et al (2013) found the use of thrombolysis to be cost effective in terms of QALYs gained.

Working with the London School of Economics, Airoldi et al (2011) considered the effectiveness of interventions such as thrombolysis, stroke unit provision and the combined intervention of thrombolysis and stroke unit. The study highlights that whilst there is a gain in Quality Adjusted Life Years (QALYs) from thrombolysis intervention alone, for maximum gain this needs to be in

conjunction with the other essential elements of a stroke unit (Figure 7). The study also highlighted that the maximum gain to population health is through preventative strategies.

Figure 7: The Burden of Disease

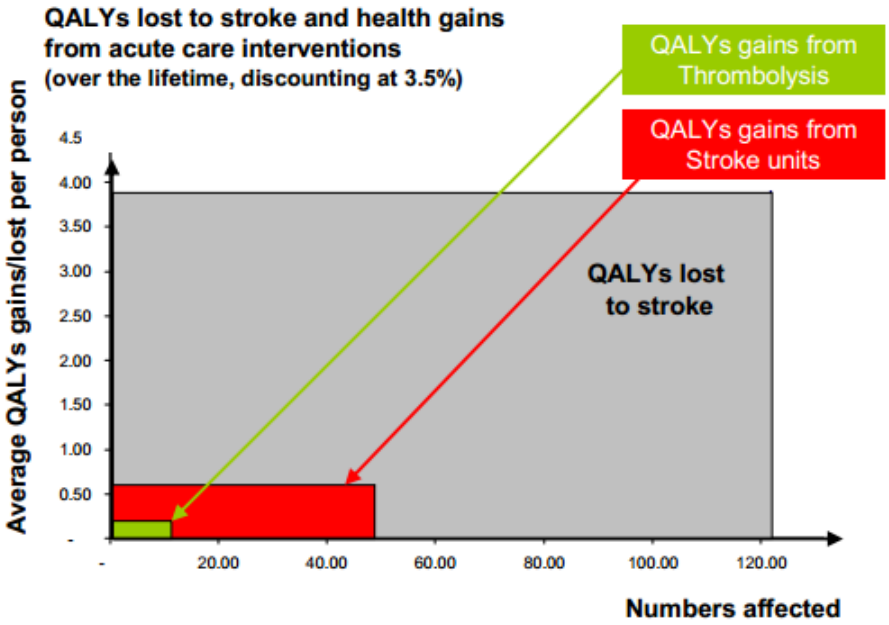


Figure 15 QALY lost to stroke (grey area) and health gains from admitting all hospitalized patients in stroke units (red area) and from giving thrombolysis to 9% of stroke patients (green area).

Source: Airoldi et al (2011)

The study quoted evidence that treatment on a stroke unit, though more costly, was cost effective because of shorter stays. "Stroke units might be up to 16% more expensive than more conventional wards (Epifanov, Dodel et al. 2007), but the length of stay may be up to 30% shorter (Jørgensen, Nakayama et al. 1995)... The improved outcomes are then likely to be associated with savings from ongoing care over the patients' lifetime. For instance, the economic model by the NAO [National Audit Office] indicates that if length of stay were three days shorter, the incremental cost at one-year follow-up would be zero (Saka, McGuire et al. 2005). The Stroke Unit Trialists' Collaboration (2001) suggested six day shorter stays and care savings beyond the first year.

There were mixed reports as to the exact extent to which the use of thrombolysis increased following centralisation in London or the exact increase in life years and fall in hospital days that resulted, but Hunter et al (2013) concluded the gains are positive and statistically significant. "When the model is carried out to ten years, the new model is dominant in every scenario tested" with fewer deaths, improved quality adjusted survival and cost savings of nearly £4,000 per patient.

Does "Stroke Unit" mean Centralised Hyperacute Stroke Units?

Stroke units improve outcomes but there is no clear definition of a stroke unit. The National Audit Office 2005 defined a stroke unit as 'any system of organized inpatient stroke care' that is characterized by 'coordinated multidisciplinary rehabilitation, programmes of education and training in stroke, and specialisation of medical staff usually housed in a geographically discrete ward' (Stroke Unit Trialists' Collaboration 1997). The 2012 National Clinical Guideline for Stroke simply defines a hyper-acute unit as "a stroke unit that treats patients in the first few days of symptom onset".

The Stroke Unit trialists' collaboration of 2007 found the benefits (survival and independence) at one year were "most apparent in units based in a discrete ward". The National Sentinel Audit refers to: "a multidisciplinary team, including specialist nursing staff based in a discrete ward which has been designated for stroke patients" (Clinical Effectiveness & Evaluation Unit 2008). The SNAPP audits look for:

- a consultant physician with responsibility for stroke
- formal links with patient and carer organisations
- multidisciplinary meetings at least weekly to plan patient care
- provision of information to patients about stroke
- continuing education programmes for staff.

Between 2001 and 2006, the number of stroke units in England, Wales and Northern Ireland providing at least four of the five key characteristics increased from 72% to 95% in 2006. By 2008, 73% of units had all five key characteristics (Airoldi et al 2011).

While the improved clinical outcomes associated with organised inpatient stroke care are well documented, it is unknown if centralising acute stroke care to a small number of high volume specialist centres produces better clinical outcomes (Morris et al 2014). In Greater Manchester the External Advisory Group (October 2011) reviewed the first wave of reconfiguration and concluded that, if anything, the system should be further centralised. A systematic review by Price et al 2009 established the superiority of regional collaborations over district hospital units. The Monitor Evidence Report (2014) reported stroke care was moving towards centralisation in Victori (Australia) and the Netherlands. Centralisation was not the preferred model, however, in Arkansas (US) or Sweden. Pickering et al (2014) conducted a systematic review comparing triage and direct transfer to a specialist centre with initial transfer to a local hospital for 3 clinical conditions including stroke. They found the evidence was very limited and did not demonstrate improved outcomes for either pathway; though outcomes were better at a specialist centre if thrombolysis was only available at such a centre.

6. Evidence from other Areas: Hub and Spoke Model

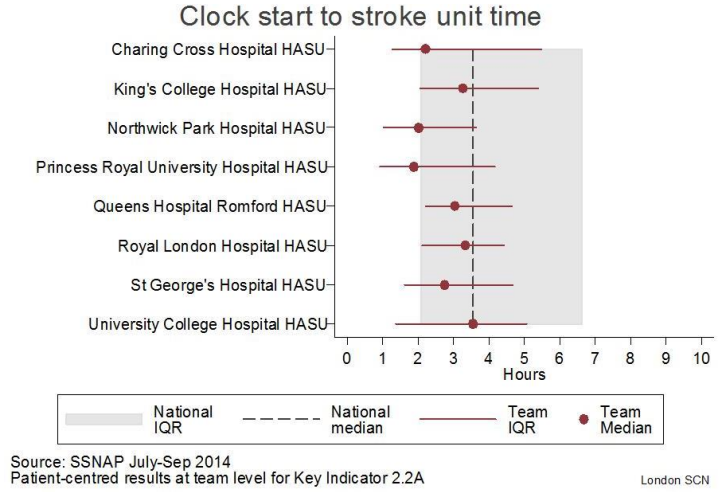
6.1 The reconfiguration in London 2010

In 2010, acute stroke services were centralised in Greater Manchester (population of 2.68 million) and London (8.17 million). Before the changes in London, 30 hospitals provided acute stroke care. After centralisation, specialist care was provided in eight designated hyper-acute stroke units 24 hours a day. Specialised stroke teams, able to offer brain imaging and thrombolysis, assessed all patients. Twenty-four stroke units were designated to provide acute rehabilitation services, and eight of these were attached to a hyper-acute unit. (Morris et al 2014). The remaining hospitals lost some or all of their stroke services.

In 2008-9, before reconfiguration, only 3.5% of stroke patients across London received thrombolysis; by 2012 this was 12% of all patients and by 2014 SNAPP returns suggested it had risen to 17%. Morris et al (2014) concluded that during the first two years after reconfiguration, 96 extra lives per year were saved in London once weighting had been taken into account. Centralisation in Manchester was less than this and Stephen Morris was quoted as telling the Guardian (2014) that if an equivalent service had been introduced in Manchester it would have produced "approximately 50 fewer deaths per year", though the study could not rule out overall that differences are associated with severity of stroke.

In London 98.7% of patients with stroke were transported to a HASU (Morris 2014). Ambulances or self-referrals saw 98% arriving at a HASU within 30 minutes (Davie 2013). Onset to stroke unit times are given below in Figure 8:

Figure 8: Clock Start to Stroke Unit Time



Source: Royal College of Physicians SNAPP

Hunter et al (2013) concluded that the changes were cost effective, certainly within an urban area. They produced cost savings per patient,

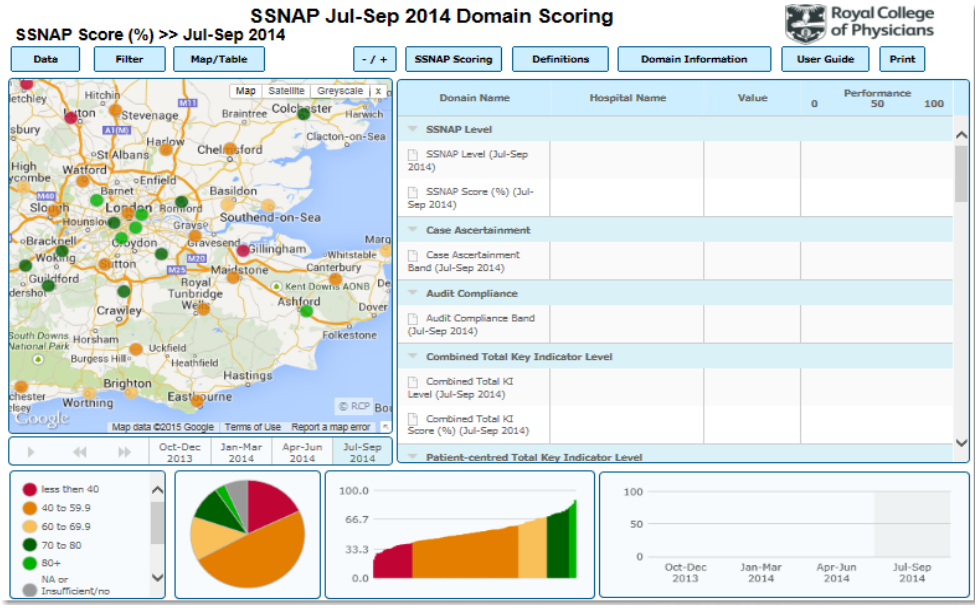
mortality and quality of life gains at 90 days and even more so at 10 years, according to the model. Similar results followed the development of stroke units in US, Canada, Netherlands, Denmark and Australia (Morris et al 2014).

Improvements in mortality in London were higher than the trend in improvement elsewhere, though London had previously lagged behind (Hunter et al 2013). Although the aim to improve thrombolysis rates was an important driver in the development of the new model, it does not fully explain the QALY gains associated with the reconfiguration, given that thrombolysis was still only received by a minority of patients. "It is highly probably that the consolidation of expertise and treating higher volumes of patients leads to improved diagnosis and overall improved processes of care. This is more likely to reduce per-stroke complications and may therefore explain in part the reduced mortality observed." (Hunter et al 2013)

Reduced length of hospital stay was significant in both London (-1.4 days) and Greater Manchester (-2 days) (Morris 2014 and Health Scrutiny Committee report to Manchester City Council 2013,) and contributed to the cost effectiveness (Hunter 2013). Saka et al 2009 modelled cost effectiveness in South London between 2001 and 2006, before the reconfiguration of 2010. They found that supported discharge, which allowed patients to move quickly out of hospital, be it a stroke unit or a general medical ward, was what made the difference to cost efficiency.

London maintained its dominance in the SNAPP results for summer 2014 with scores of over 70 or 80 for most of its eight HASUs (Figure 9):

Figure 9: SNAPP Scores Kent, Surrey and Sussex Compared to London



Source: http://www.strokeaudit.org/results/Clinical-audit/Maps/Domain-Map-Routinely-Admitting.aspx Royal College of Physicians SNAPP

The performance of hospitals can vary significantly between periods (for example, January-March 2014 Ashford scored in the 40-59 D band though by Jul-September 2014 in was in the top band) but higher scores are found more frequently in London that outside.

6.2 Reconfiguration in Manchester 2010 onwards

Reconfiguration in Manchester in 2010 led to shorter hospital stays (2 days on average) but life years saved was no higher than the general trend elsewhere. "The differences in mortality can be explained by the lower levels of adherence in Manchester" to the centralised model and to less compliance with care processes (Morris 2014).

Evidence from London and Manchester suggested it was critical for mortality outcomes that all patients with suspected stroke be admitted to specialist stroke units. In Manchester initially it was only about one third. Outcomes were best if all patients were treated in a HASU, whatever the time frame, whatever the type of stroke. In London 98.7% of patients with stroke were transported to the appropriate service. In Greater Manchester 36% of patients were not taken to a comprehensive stroke centre or primary stroke centre (Morris 2014). Manchester never achieved the 30 minute ambulance transfer times enjoyed in London. The annual review of its services (2013) also highlighted the importance of stroke recognition by the general public in speeding up access to hyper-acute services.

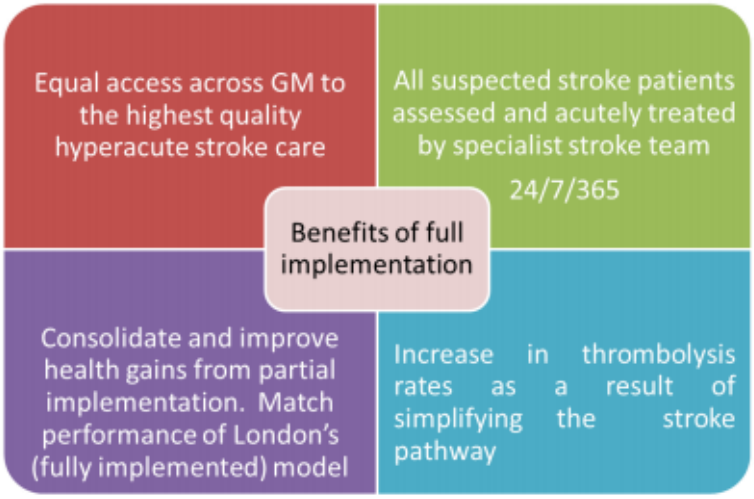
Greater Manchester originally opted for a "thrombolysis-eligible" triage model. One comprehensive stroke centre was available 24/7; two primary stroke centres operated 18 hours a day. All general local units continued to operate. Ambulance crews or A&E staff decided whether patients were eligible for admission to the specialist stroke units. In the twelve month review by Hosker (2013) to the Manchester Health Scrutiny Committee, the Greater Manchester and Cheshire Cardiac and Stroke Network reported a 5% fall in mortality but recognised that services could be further improved. This fall in mortality was not significantly different from that in the rest of the country at the same period. It was therefore proposed that in future "all patients presenting within 24 hours with symptoms suggestive of a new acute stroke will be transferred to a hyper-acute stroke centre" able to deliver the key interventions 24/7 (Manchester City Council report to the Health Scrutiny Committee 2013).

The Monitor Evidence Report (2014) found similarly uneven implementation in Ontario which also operated ambulance triage protocols. A randomised control trial conducted by Berglund et al (2012) looking at the use of triaging and thrombolysis alerts by ambulances in Sweden seemed to show a significant increase in thrombolysis frequency and a shorter time through the acute chain of stroke care; however, a Swedish stroke audit published that same year found

"the alarm was used only in 23% of eligible cases in 2012" (Monitor Evidence Report 2014). Manchester demonstrated lower adherence to protocols and differences in access to hyper-acute care for patients presenting four hours after developing symptoms of stroke.

Following its review, Greater Manchester now aims to move closer towards a centralised model (Figure 10):

Figure 10: The Benefits of All Patients Attending a HASU



Source: Full Implementation of the Greater Manchester Integrated Stroke Service (GMISS)

7. Telemedicine as an Alternative to Hub And Spoke Acute Services

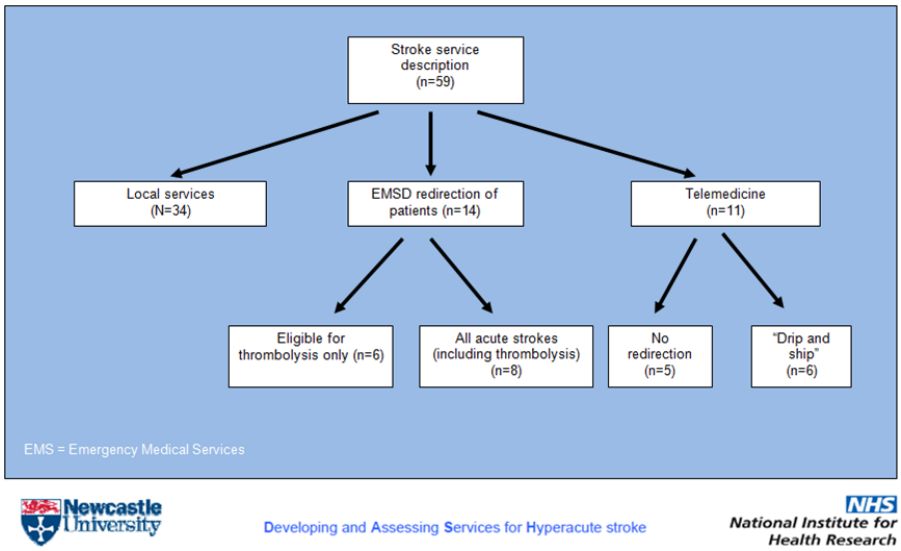
In telemedicine, brain scans and delivery of thrombolysis take place locally but expert review of the brain images and treatment decisions takes place in a centralised specialist unit. Telemedicine, falls into two models: symptoms can identify which patients are eligible for transfer to a central unit (used in tandem with a stroke code alert system); or, alternatively, treatment may take place in local units, in rural areas where travel times may prohibit access to hyper-acute units, with access to centralised 24/7 expertise.

Case studies of stroke service reform in more rural areas of England show examples of both triage (including use of stroke code alerts) and telemedicine. Following triage, Northumbria, for example (Figure 11), offers a combination of:

- local service
- redirection to the HASU for thrombolysis and acute treatment
- telemedicine followed by some redirection to acute units

Northumbria was one of the first more rural areas in England to introduce a HASU.

Figure 11: Example of a Stroke Pathway in Northumbria



Source: Chris Price

The Monitor Emergency Report 2014 reported that telemedicine allowed even small/remote acute hospitals to deliver thrombolysis in Arkansas, USA. Rubin et al 2013 found "telestroke" had a growing literature base though a lack of systematic reviews. Roots, Bhalla and Birns conducted a review in 2011 which concluded that telemedicine was safe and effective and that it increased uptake of thrombolytic treatment and improved geographical equality.

Agarwal et al (2014) looked at the first year of the east of England telestroke project 2010-11. The project covered seven regional hospitals with a population of 5.6 million aimed at enabling out of hours access to thrombolysis where the use of a hub and spoke model was not geographically feasible. They concluded it was safe and effective. A study of a rural stroke network in Georgia (US) 2005 found rapid and safe use of a tissue plasminogen activator was possible through telesystems. Northumbria in north England found telemedicine allowed quicker admission times following stroke onset though final door to needle times were actually slower than for direct admission to the HASU. The Georgia study, however, found that over time the system became more efficient through focus and practice and mean onset to treatment time decreased (Hess et al 2005).

A systematic review of mobile stroke teams found them no more effective than general wards (Langhorne et al 2005).

Discussion

8. How to Implement Change Outside Urban Centres

The Monitor Evidence Report 2014 stressed that the priorities of reconfiguration would depend on the type of commissioning decisions that needed to be made: the challenges might focus on distance to a hyper-acute unit, or on improving processes such as preliminary access to brain scans, or on ensuring sufficient volumes to make units viable.

9. Validity of the Model

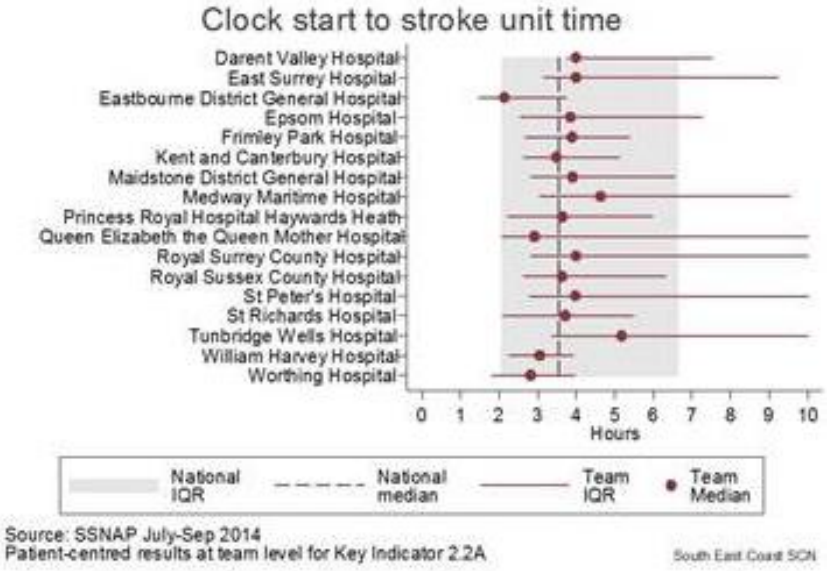
It is not clear that the London model can be transferred to a more rural environment or how effective the centralised model would be outside urban areas (Hunter 2013, Morris 2014) if the populations and stroke types differed. Nor was it clear that the period from 2010-12 in London was typical, though all models seem to have been well tested for the sensitivity of their assumptions. London had made relatively less progress than the rest of England in the period leading up to reconfiguration of its stroke services; so did the gains in London just represent a catching up? When asked to adopt the London model, hospital managers in the Netherlands "reacted by claiming that the reconfiguration in London has only managed to lift low levels of care to match the care quality already present in the Netherlands (Monitor Evidence Report 2014). A meta-analysis by O'Rourke and Walsh concluded that studies of the impact of care delivered in stroke units on mortality were robust but thought that further studies were "very unlikely to alter current knowledge but may have a role in ensuring regional stability of outcome."

10. Travel Times

Travel times and other factors affecting door to needle time were likely to be an issue in more rural areas. Prabhakaran et al 2011 tried to construct a time model for offering intra-arterial therapy (thrombolysis) for acute ischemic stroke. They observed "the odds of treatment decrease by 2.5% for every minute of transfer time" and concluded specific transfer time goals were needed.

Figure 12 highlights Inter Quartile Range (IQR) for various stroke units across South East, with William Harvey with smallest IQR.

Figure 12: Clock Start to Stroke Unit Time in Kent, Surrey and Sussex



Source: Royal College of Physicians SNAPP 2014

The Monitor Evidence Report on international comparisons quoted a 1-hour maximum travel time. However, Monks 2014 stressed that simulations of travel times would need detail and sophistication to allow for peak traffic, busy departments, physician availability etc. There would be trade-offs for patients and the commissioning model needed to encompass probabilities for gain and loss.

11. Motivation

The London HASUs were "chosen based on their commitment to meeting specified staffing and quality standards of care." (Davie et all 2013) The reconfiguration was designed and managed (under London Strategic Health Authority) by the physicians who would operate the units. The 24 acute stroke units ASUs were also designated by a competitive tendering process of hospitals bidding to provide the right staffing at the right price. London was able to move staff round easily.

Tony Rudd, London Stroke Clinical Director, outlined the importance of bringing the stakeholders on board, and how the need for unity was one of the reasons why the initial reconfiguration in Manchester was compromised.

"Set up and ability to meet quality standards was overseen by a pan-London board (Clinical Advisory Group) and the five London teams of the UK cardiac and stroke network who were accountable to the London Health Authority (NHS London). The Health Authority also provided approximately £20million ($30m) funding to implement the development of the units and created an enhanced tariff of payment which was linked to meeting the quality standards." Davie 2013.

This reconfiguration was hugely complex involving many NHS organisations and engagement from public and health professionals. This included publicity campaigns and town-hall meetings to persuade potential patients and relatives of the anticipated benefit of bypassing their local hospital.

The Manchester review (2013) produced a long list of areas, which required further reconfiguration to further improve its system. These included:

- Increased capacity
- increased workforce
- finance impact to both HASUs and the old district stroke centres.
- more rehabilitation and early supported discharge and an improvement programme for the current services to improve quality, duration and consistency
- much more uniform standards and use of assessment tools

The Commissioning for Quality and Innovation (CQUIN) payment framework enables commissioners to reward excellence by linking a proportion of providers' income to the achievement of local quality improvement goals. Specific Stroke CQUINs were developed across the north west of England to drive improvement in stroke services. The Best Practice Tariff enforces some standards by financially rewarding those providers that meet the standards

12. Numbers

Davie (2013 suggests the London HASUs were designed to receive 600-1200 per year (up from 150-450). The Monitor Evidence Report (2014) quoted 1 million as a typical population base, and gave the following international standards:

Figure 13: Minimum Patient Volumes for a HASU

	Victoria	Netherlands	Germany	Arkansas
Volume for specialist acute stroke unit	>100 pts/yr for acute unit >350 pts/yr for Comprehensive Stroke Centre	Not yet – but national insurers want a 50pts/yr minimum	>250[2] pts/yr for acute unit >450 pts/yr for Comprehensive Stroke Centre	≥25 IV tPA patients/yr for Comprehensive Stroke Centre[,5]
[2] *Plans to increase this to 300 patients/year*		[5] *Also ≥20 subarachnoid haemorrhage patients and ≥15 endovascular coiling or surgical clipping procedures for aneurysm*		

Source: Monitor Evidence Report (2014)

The NHS Future Fit report Aldridge and Turner (2014) quoted Glanville J et al (2010): "A safer solution can be a lower-cost solution only where it is possible to bring services together in a larger centre." And Ham et al (2012) cited

evidence supporting the concentration of services in higher volume units and an association with better clinical outcomes for services including stroke.

Manchester in its 2013 review was planning to increase numbers and data from the Royal College of Physicians stroke audit shows that patients are more likely to receive the early processes of care associated with better long-term outcomes in centres with high volumes of activity. This includes those that arrive "in hours".

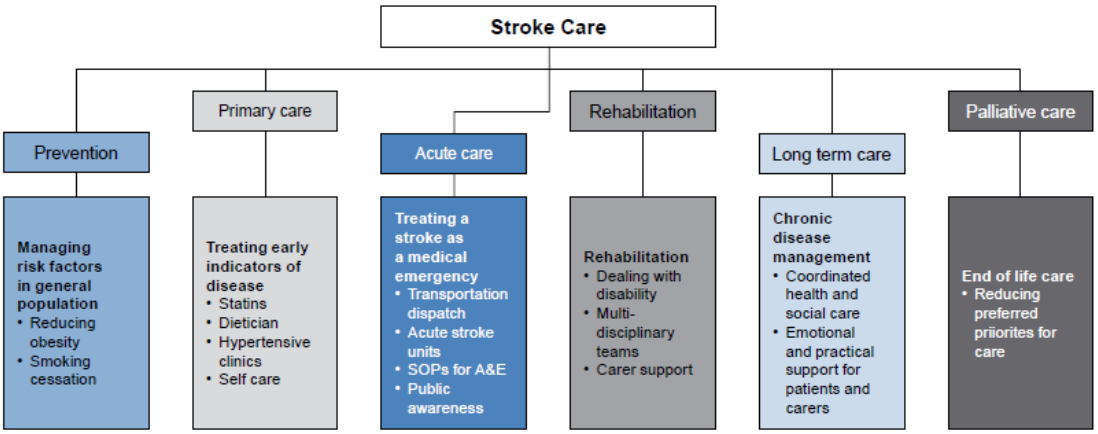
13. Making use of Patient Groups

Formal links with patient organisations are part of the criteria on which the National Sentinel Audit judges successful units. Manchester funded the production of education and training programmes by its patient support groups and detailed patient group involvement throughout the reconfiguration of the Manchester service.

14. Acute Care is Not the Only Focus

As shown by Figure 14 below, acute care is only one part of the stroke care pathway that begins with prevention and ends with palliative care.

Figure 14: The Context of Stroke Care



Source: Leatherman, Sutherland, Airoldi (2008)

Airoldi et al's 2011 working paper considered six interventions to reduce the burden of disease (BoD) from stroke, which are detailed in Figure 15. They found that each produced significant gains in quality-adjusted of life years (QALYs) but concluded that prevention (Figure 16) would cause a greater reduction in the burden of stroke than acute care intervention.

Figure 15: How Alternative Interventions Reduce the Burden of Disease

Table 1 Interventions evaluated

Intervention	Description
SU	Admit all patients that presents to hospital on a stroke unit
T	Provide thrombolysis (intravenous tPA) to 9% of stroke patients
BP_{all}	Prescribe a first line anti-hypertensive drug to all 55-years old or older people
BP_{high}	Prescribe a first line anti-hypertensive drug to all people with blood pressure above 140/90 mmHg who are not currently prescribed any anti-hypertensive
Na_5	Reduce average blood pressure in the population reducing sodium content in diet by 30% (3g salt) through agreement with food industry
Na_2	Reduce average blood pressure in the population reducing sodium content in diet by reducing salt content in bread and cereals through agreement with food industry

Figure 16: Gains in Quality-Adjusted Life Years from Prevention

Table 16 Numbers needed to treat and average QALY per person

	Treated per year (millions)	Stroke avoided in current year ('000s)	NNT ('000s)	Average QALY gains per person treated	Average QALY gains per person avoiding a stroke in the first year
BP_{all}	8.1	16.8	.5	0.01	3.88
Bp_{high}	3.5	8.2	.4	0.01	3.61
Na_5	49.9	18.8	2.7	0.002	4.56
Na_2	49.9	7.9	6.3	0.001	4.60

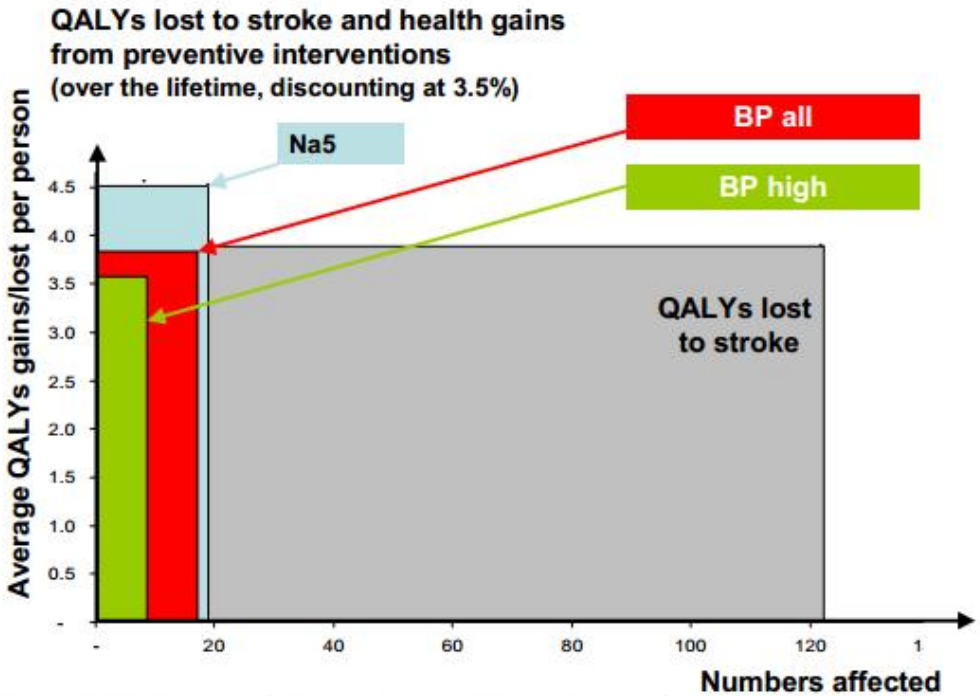


Figure 16 QALY lost to stroke (grey area) and health gains from a selection of preventive interventions. The variation in average QALY gains from preventing a stroke is due to different age mix.

Source: Airoldi et al 2011

"Assuming that all people above the age of 55 were to take a first line anti-hypertensive, the burden can be reduced by about 14%. If the new prescribing were limited to hypertensive people 7% of the burden would be avoided. A public health intervention to reduce the daily intake of salt (sodium) by 30% as proposed by the target set by the Food Standard Agency in England would reduce the burden by 18% (Airoldi 2011 p3).

The National Audit Office's report "Progress in Improving Stroke Care" (2010) agreed: "The best way of improving the value for money of stroke care is by preventing strokes from occurring. Reducing stroke incidence requires managing the risk factors common to all vascular disease including high blood pressure and cholesterol, smoking, unhealthy diet and lack of exercise."

The same report looked at long-term care after stroke and contrasted its poor quality with the improvements being seen in the first 72 hours of acute care. The National Stroke Strategy (2007) states that people who have had a stroke, and their carers, should be offered primary care reviews at six weeks and six months after discharge. Yet at the start of 2014, less than a sixth of patients in England and Wales had received the six months assessment (BMJ 2014 looking at SNAPP audit Jan-March 2014). Arguably, prevention and aftercare are both areas that could benefit from the same reform being seen in acute care.

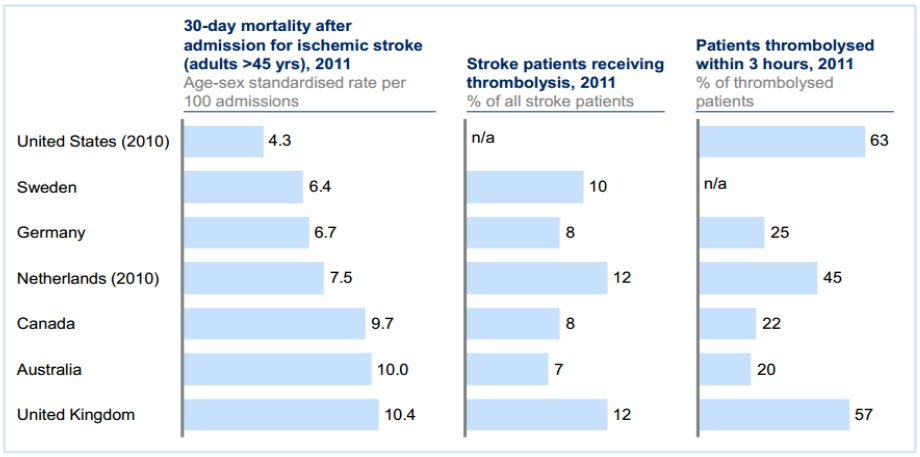
The evidence from Greater Manchester, however, was that reconfiguring the hyper-acute practice itself drove up standards across the entire stroke pathway. This included inpatient rehabilitation, early supported discharge and long-term community rehabilitation. Early stroke discharge (ESD) had to improve in order to move patients through the pathway to free up beds. It was a win/win situation. Manchester's plans for further redesign proposed keeping patients for slightly longer at the hyper-acute centre if this would enable them to be safely discharged home with early support discharge service, though ESD was a complex process.

Clinical Commissioning Groups in Manchester were asked to assess their rehabilitation services (both inpatient and community) against the stroke unit specification to maximise the benefits throughout the pathway. Excellent inpatient rehabilitation was judged to be critical to the gains seen from the reconfiguration of the Greater Manchester Integrated Stroke Service. Whilst the hyper-acute component had been the driving force for change, the other elements of the pathway were found to be of equal importance. On the other hand, Kwan J 2007 quoted a Cochrane systematic review which concluded that it was not rehabilitation that made a difference to outcomes, but the use of acute care pathways.

The following table suggests the United Kingdom needs to look further than hyper-acute stroke units. The UK has some of the highest thrombolysis rates international but performs poorly on international stroke overall (Figure 17: Monitor Evidence Report 2014).

Figure 17:

International comparisons of stroke outcomes and quality of care



SOURCE:
- For stroke mortality: OECD Health Data 2013 (http://www.oecd.org/health/health-systems/oecdhealthdata.htm)
- For thrombolysis: Swedish Stroke Registry ; Canadian Stroke Network (http://www.canadianstrokenetwork.ca/wpcontent/uploads/2011/06/QoSC-EN1.pdf);Hospital Compare (USA); Singer et at, Time trends in systemic thrombolysis in a large hospital-based stroke registry, 2012, Cerebrovasc Dis. 2012;33(4):316-21(Germany, data for 2010 for Hesse state only); Dirks et al, Promoting thrombolysis in acute ischemic stroke, Stroke. 2011 May;42(5):1325-30 (Netherlands);National Stroke Audit Acute Services, Clinical Audit Report, 2011 (Australia); SINAP (NHS England)

| 8 *Source: Monitor Evidence Report 2014*

15. Conclusion

Reducing Burden of Disease from stroke requires systematic interventions at population level across all parts of the care pathway including primary prevention and post stroke rehabilitation.

The available evidence suggests that stroke units are both clinically and cost effective because of a combination of care provided, of which thrombolysis in the first 4.5 hours is a part. However, these outcomes (reducing death, length of hospital stay and improved quality adjusted life gained) tend to be achievable when appropriate and optimum standards of care are provided through continuous monitoring. This includes timely assessment of individuals with strokes who then are able to receive appropriate intervention such as administration of thrombolysis and assessment of their specific needs.

The evidence also highlights that in order to get best clinical outcomes it is important that along with HASUs there is a supportive infrastructure of sub-acute stroke units (such as multidisciplinary team assessment, speech and language therapy, occupational therapy and physiotherapy) and after hospital care for individuals.

Clinical Commissioning Groups as the commissioners of acute care across Kent and Medway need to take urgent action to improve auditable clinical indicators such as timeliness of scans, thrombolysis intervention, multidisciplinary assessment and input, etc. Evidence suggests that these indicators can be improved through Hyper-acute Stroke Units where the

expertise and access to necessary infrastructure such as scanning facility and care be centralised. Although organised (stroke unit) care can increase the chances of stroke patients surviving, returning home and regaining independence, the role of peripatetic mobile stroke teams has been unclear (systematic review, Langhorne et al 2005). Therefore, local priorities of reconfiguration should take into consideration, travel times to a HASU.

However, to decide the location of HASUs across Kent and Medway, due to dispersed population in rural locations, door to needle time will need to be modelled before the site specific decisions can be made. CCGs will need to be mindful that ambulance times were only one of several factors affecting door to needle times in local hospitals. It is important that decision around HASUs also take into account experience of teams, process for implementation of protocols as these would also affect performance and clinical outcomes.

Although the prevention of stroke is outside the scope of Kent and Medway Programme Review Board, the literature clearly suggests that at population level, prevention of stroke is the best option. It is recommended that this should be consider by the Stroke Review Programme Board Members and progressed through CCGs at a local level. Therefore, in addition to commissioning of acute care, CCGs will need to ensure that public health interventions are optimally implemented, these include control of high blood pressure, reduced salt consumption, cholesterol, smoking, unhealthy diet and optimal participation in the NHS health checks programme.

16. References

Agarwal S, Day DJ, Sibson L, Barry PJ, Collas D, Metcalf K, Cotter PE, Guyler P, O'Brien EW, O'Brien A, O'Kane D, Owusu-Agyei P, Phillips P, Shekhar R, Warburton EA (2014) 'Thrombolysis delivery by a regional telestroke network--experience from the U.K. National Health Service'. Journal of the American Heart Association 3/1, 2047-9980

Airoldi M, Bevan G, Morton A, Oliveira M and Smith J (2008) Estimating the Health Gains and Cost Impact of Selected Interventions to Reduce Stroke Mortality and Morbidity in England. http://www.grammatikhilfe.com/management/documents/WP5_-_Estimating_the_health_gains_and_cost_impact_of_selected_interventions_to_reduce_stroke_mo.pdf [Accessed 10/03/2015]

Aldridge S and Turner A (2014) *Future Fit 2014 Rapid evidence review to inform the case for change: Planned care.* Available from https://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&uact=8&ved=0CCwQFjAC&url=http%3A%2F%2Fnhsfuturefit.org%2Fkey-documents%2Fdocuments%2F5-a-rapid-review-of-planned-care-2&ei=Vy7rVJ3HAsLg7QbHioDwAQ&usg=AFQjCNFfZ0uYwaFU7UoJqAKceGl5J9sH8gNHS [Accessed 10/03/2015]

The Association of Greater Manchester Authorities (AGMA) (2013) *Full Implementation of the Greater Manchester Integrated Stroke Service (GMISS).* Available from http://www.agma.gov.uk/cms_media/files/5_1_gm_integrated_stroke_service.pdf?static=1 [Accessed 10/03/2015]

Belgian Stroke Council, Thijs V, Peeters A, Dewindt A, Hemelsoet D, De Klippel N, Laloux P, Redondo P, Cras P, De Deyn PP, Desfontaines P, Brouns R, De Raedt S, Van Landegem W, Vandermeeren Y, Vanhooren G (2009) 'Organisation of inhospital acute stroke care and minimum criteria for stroke care units. Recommendations of the Belgian Stroke Council'. *Acta Neurologica Belgica* 109/4, 247-51

Berglund A, Svensson L, Sjostrand C, von Arbin M, von Euler M, Wahlgren N, HASTA Collaborators, Engerstrom L, Hojeberg B, Kall TB, Mjornheim S, Engqvist A (2012) 'Higher pre-hospital priority level of stroke improves thrombolysis frequency and time to stroke unit: the Hyper-acute Stroke Alarm (HASTA) study'. *Stroke* 43/10, 2666-70.

Ciccone A, Celani MG, Chiaramonte R, Rossi C, Righetti E (2013) 'Continuous versus intermittent physiological monitoring for acute stroke'. *Cochrane Database of Systematic Reviews* 5/ (CD008444), 1361-6137; 1469-493X

Davie C, Hunter RM, Mountford J, Morris S (2013) *London's Hyperacute Stroke Units Improve Outcomes and Lower Costs*. Available from https://hbr.org/2013/11/londons-hyperacute-stroke-units-improve-outcomes-and-lower-costs. [Accessed 10/03/2015]

Department of Health (2007), *National Stroke Strategy for England.* Available from http://clahrc-gm.nihr.ac.uk/cms/wp-content/uploads/DoH-National-Stroke-Strategy-2007.pdf. [Accessed 10/03/2015]

Drug and Therapeutics Bulletin (2009) 'Thrombolytic therapy with alteplase for ischaemic stroke' 47:14-8.

Eissa A, Krass I, Bajorek BV (2012) 'Barriers to the utilization of thrombolysis for acute ischaemic stroke'. *Journal of Clinical Pharmacy & Therapeutics* 37/4, 399-409

Fells G (2014) *Response to Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis*. Available at http://www.bmj.com/content/349/bmj.g4757/rr/762921. [Accessed 10/03/2015]

Govan L, Langhorne P, Weir CJ, Stroke Unit Trialists Collaboration (2007) 'does the prevention of complications explain the survival benefit of organized inpatient (stroke unit) care? further analysis of a systematic review'. *Stroke* 38/9, 2536-40.

The Guardian (2014) *Centralised stroke care saves more lives, says study.* Available from http://www.theguardian.com/society/2014/aug/05/centralised-stroke-care-study-hospitals . [Accessed 10/03/2015]

Guzauskas GF, Boudreau DM, Villa KF, Levine SR, Veenstra DL (2013) 'The Cost-Effectiveness of Primary Stroke Centers for Acute Stroke Care'. *Stroke* 43(6),1617-23

Health and Social Care Information Centre (2015) *Clinical Commissioning Group Outcomes Indicator Set (CCG OIS)*. Available from http://www.hscic.gov.uk/ccgois. [Accessed 10/03/2015]

The Health Foundation (2012) *Learning report: Looking for value in hard times: How a new approach to priority setting can help improve patient care while making savings.* Available from http://www.health.org.uk/public/cms/75/76/313/3725/Looking%20for%20value%20in%20hard%20times.pdf?realName=P8KFa7.pdf. [Accessed 10/03/2015]

The Health Foundation (2010) *Learning report: Commissioning with the community.* Available from http://www.health.org.uk/public/cms/75/76/313/580/Commissioning%20with%20the%20Community.pdf?realName=Qc9n8Y.pdf [Accessed 10/03/2015]

Hess DC, Wang S, Hamilton W, Lee S, Pardue C, Waller JL, Gross H, Nichols F, Hall C, Adams RJ (2005) 'REACH: clinical feasibility of a rural telestroke network'. *Stroke* 36/9, 2018-20)

Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, Mountford J, Schwamm L, Deanfield J, Thompson K, Dewan B, Mistry M, Quoraishi S, Morris S (2013) **'**Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: a comparative effectiveness before and after model'. *PLoS ONE* [Electronic Resource] 8/8(e70420)

Kwan J **(2007) '**Care pathways for acute stroke care and stroke rehabilitation: from theory to evidence'. *Journal of Clinical Neuroscience* 14/3, 189-200

Langhorne P, Dey P, Woodman M, Kalra L, Wood-Dauphinee S, Patel N, Hamrin E (2005) 'Is stroke unit care portable? A systematic review of the clinical trials'. *Age and Ageing* 34, 324–330.

Langhorne P, Fearon P, Ronning OM, Kaste M, Palomaki H, Vemmos K, Kalra L, Indredavik B, Blomstrand C, Rodgers H, Dennis MS, Al-Shahi Salman R, Stroke Unit Trialists' Collaboration (2013) 'Stroke unit care benefits patients with intracerebral hemorrhage: systematic review and meta-analysis'. *Stroke* 44/11, 3044-9

Leatherman S, Sutherland K, Airoldi M (2008) 'Economics QUIPP (Quest for Quality and Improved Performance) Bridging the quality gap: stroke'. *The Health Foundation*. Available at: http://www.wales.nhs.uk/documents/Bridging_the_quality_gap.pdf [Accessed 02/06/2015]

Manchester City Council report to the Health Scrutiny Committee (2013) *Stroke Services.* Available from http://www.manchester.gov.uk/download/meetings/id/16898/5_stroke_services. [Accessed 10/03/2015]

NHS Confederation (2014) *Monitor Evidence Report Appendix 4*. Available from https://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&cad=rja&uact=8&ved=0CC0QFjAC&url=https%3A%2F%2Fwww.gov.uk%2Fgovernment%2Fuploads%2Fsystem%2Fuploads%2Fattachment_data%2Ffile%2F382846%2FAnnex_4_Stroke1.pdf&ei=aBzrVKGePMar7AafsYDAAQ&usg=AFQjCNG4KM5bfvN913b_gWpLvbkSMkq6Qg. [Accessed 10/03/2015]

Monks T, Pitt M, Stein K, James MA (2014) 'Hyper acute stroke care and NHS England's business plan'. *BMJ* 348, g3049

Morris S, Hunter RM, Ramsay AI, Boaden R, McKevitt C, Perry C, Pursani N, Rudd AG, Schwamm LH, Turner SJ, Tyrrell PJ, Wolfe CD1, Fulop NJ (2014) 'Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis'.
BMJ 349, g4757

National Audit Office (2010) *Department of Health: progress in improving stroke care.* Available at http://www.nao.org.uk/report/department-of-health-progress-in-improving-stroke-care/ [Accessed 10/03/2015]

NHS (2013) *Payment by Results Guidance for 2013-14 best practice tariff and CQUIN.* Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214902/PbR-Guidance-2013-14.pdf. [Accessed 10/03/2015]

NHS England (2013) *Putting Patients First business plan 2014-15 to 2016-17*. Available at http://www.england.nhs.uk/pp-1314-1516/. [Accessed 10/03/2015]

NHS South East Coast (2012) *NHS South East Coast Integrated Stroke Care Pathway Service Specification Executive Summary.* Available at http://www.secscn.nhs.uk/files/3014/0930/7398/H-_SEC_Integrated_Stroke_Service_Specification_FINAL_2012.pdf. [Accessed 10/03/2015]

NHS Institute for Innovation and Improvement (2009) *Stroke pathway: delivering through improvement* available at http://arms.evidence.nhs.uk/resources/qipp/29535/attachment. [Accessed 10/03/2015]

The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group (1995) 'Tissue Plasminogen Activator for Acute Ischemic Stroke'. *New England Journal of Medicine* 333,1581-1588

NICE (2012) *Technology appraisal guidance [TA264]*. Available at http://www.nice.org.uk/guidance/ta264. [Accessed 10/03/2015]

National Institute for Health and Care Excellence - NICE (2008) *Guidance Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA) - guidance (CG68) supporting evidence and models.* Available at http://www.nice.org.uk/guidance/cg68/evidence/cg68-stroke-full-guideline-appendices2. [Accessed 10/03/2015]

Northumbria NHS Foundation (2009) *Acute Stroke Imaging Stroke Physician Perspective*. Available at http://www.csnlc.nhs.uk/uploads/files/stroke/imaging_2009/Acute_Stroke_Imaging_-_Physician_Perspective_020609.pdf. [Accessed 10/03/2015]

Nuffield Trust (2014) *NHS in numbers: in detail*. Available from http://www.nuffieldtrust.org.uk/nhs-numbers-detail. [Accessed 10/03/2015]

O'Rourke K, Walsh C (2010) 'Impact of stroke units on mortality: a Bayesian analysis'. *European Journal of Neurology* 17/2, 247-51

Prabhakaran S, Ward E, John S, Lopes DK, Chen M, Temes RE, Mohammad Y, Lee VH, Bleck TP (2011) 'Transfer delay is a major factor limiting the use of intra-arterial treatment in acute ischemic stroke'. *Stroke* 42/6, 1626-30

Price C *Models of hyperacute stroke care.* Available at http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=2&cad=rja&uact=8&ved=0CCsQFjAB&url=http%3A%2F%2Fimprovementsystem.nhsiq.nhs.uk%2FImprovementSystem%2FDocumentArchive%2FViewDocument.aspx%3Fdocumentid%3D3803%26nodeid%3D645%26hideheader%3Dtrue%26email%3Dtrue%26ModuleType%3DForum&ei=luvQVKmsH9Kv7AbhsoGwBA&usg=AFQjCNHGhbAYnkwsH0hU-D_jgC6xH18VCA. [Accessed 10/03/2015]

Price CI, Clement F, Gray J, Donaldson C, Ford GA (2009) 'Systematic review of stroke thrombolysis service configuration'. *Expert Review of Neurotherapeutics* 9/2, 211-33

Roots A, Bhalla A, Birns J (2011) 'Telemedicine for stroke: a systematic review'. *British Journal of Neuroscience Nursing* 7/2, 481-489

Royal College of Physicians (2012) *National clinical guideline for stroke, fourth edition.* Available at https://www.rcplondon.ac.uk/sites/default/files/national-clinical-guidelines-for-stroke-fourth-edition.pdf. [Accessed 10/03/2015]

Royal College of Physicians (2014) *SSNAP Sentinel Stroke National Audit Programme.* Available at https://www.rcplondon.ac.uk/projects/sentinel-stroke-national-audit-programme. [Accessed 10/03/2015]

Rubin MN, Wellik KE, Channer DD, Demaerschalk BM (2013) 'A systematic review of telestroke'. *Postgraduate Medicine* 125/1, 45-50

Rudd T (2012) *London Stroke Care.* Available at http://islondon.files.wordpress.com/2012/07/isl-launch-stroke-presentation.pdf. [Accessed 10/03/2015]

Saka Ö, Serra V, Samyshkin Y, McGuire A, Wolfe C C (2009) 'Cost-effectiveness of stroke unit care followed by early supported discharge'. *Stroke* 40 (1), 24-29.

Sayburn A (2014) 'Stroke care continues to show "unacceptable variation," audit finds'. BMJ 349, g5225

Schwamm LH, Holloway RG, Amarenco P, Audebert HJ, Bakas T, Chumbler NR, Handschu R, Jauch EC, Knight WA 4th, Levine SR, Mayberg M, Meyer BC, Meyers PM, Skalabrin E, Wechsler LR, American Heart Association Stroke Council, Interdisciplinary Council on Peripheral Vascular Disease (2009) 'A review of the evidence for the use of telemedicine within stroke systems of care: a scientific statement from the American Heart Association/American Stroke Association'. *Stroke* 40/7, 2616-34

South London Cardiac and Stroke Network Six-*Month Reviews after Stroke.* Available at **http://www.slcsn.nhs.uk/files/stroke/SLCSN-commissioning-guidance-six-month-reviews-0411.pdf**. [Accessed 10/03/2015]

Stroke Unit Trialists' Collaboration Cochrane review (2007) 'Organised inpatient (stroke unit) care for stroke'. *Cochrane Database of Systematic Reviews* 4(CD000197)

Sun Y, Paulus D, Eyssen M, Maervoet J, Saka O (2013) 'A systematic review and meta-analysis of acute stroke unit care: what's beyond the statistical significance?'. *BMC Medical Research Methodology* 13/ (132)

Tan Tanny SP, Busija L, Liew D, Teo S, Davis SM, Yan B (2013) 'Cost-effectiveness of thrombolysis within 4.5 hours of acute ischemic stroke: experience from Australian stroke centre'. *Stroke* 44(8), 2269-74

Websites searched

http://commissioning.libraryservices.nhs.uk/resources/for-specific-service-sectors
http://community.cochrane.org/editorial-and-publishing-policy-resource/nhs-economic-evaluation-database
http://www.evidence.nhs.uk/
https://www.learnenv.england.nhs.uk/similar
greg.fell@bradford.gov.uk
www.focusonstroke.nihr.ac.uk
www.google.co.uk
http://www.hsj.co.uk/
http://www.library.nhs.uk/hdas
www.lse.ac.uk
https://www.rcplondon.ac.uk/projects/ssnap-clinical-audit
www.york.ac.uk