Oxford Academic Health Science Network

Mechanical thrombectomy for acute ischaemic stroke: an implementation guide for the UK

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A message from the Stroke Association

Juliet Bouverie OBE, Chief Executive, Stroke Association

Mechanical thrombectomy changes the course of recovery from stroke in an instant. Take Gerald, for example, a 65-year-old retired pub landlord and driver. In October 2020, Gerald was having a cup of tea with his wife, Linda, when she noticed his arm had gone rigid and he was beginning to slur his speech. Despite Gerald insisting he was fine, his wife called an ambulance.

Linda could not accompany Gerald to hospital due to the coronavirus pandemic, adding to an already frightening situation. He was taken to Cardiff's University Hospital of Wales, promptly scanned and then prepared for a mechanical thrombectomy.

Gerald said: "*All I remember of the operation was the machine over the top of my head... Without the thrombectomy I would have been in a much worse state. I could have died. I came through and I'm here now. I'd like to add my appreciation to the surgeon and his team, and the nursing staff who attended to me … Their speed and care were exceptional. I think thrombectomy is fantastic. I think it should be made available everywhere. Get it done quickly and get rid of the clot. It's brilliant technology*."

Gerald told me that he was able to return to the things that he loves, and within six weeks he was back out on the golf course. His story shows that thrombectomy can radically change what is possible after a stroke. Not only is it transformational for patients, but for the NHS it should be the catalyst for better care across the whole stroke pathway.

Gerald and his wife did well to call 999 at the first signs of stroke. We know that this wasn't the case for a lot of stroke patients, many of whom delayed seeking medical attention during the height of the COVID-19 pandemic. The effects of the pandemic were felt acutely on thrombectomy services, as **Chapter 12** shows. Commendably, most centres adapted their services to ensure delivery remained, but more than half of thrombectomy centres reported a negative impact.

Over two years on since the first edition of this guidance, the challenges to delivering a 24/7 thrombectomy service in all parts of the UK still remain. Worryingly, what was once slow progress has, in many cases, stalled further.

We still lack a sufficient number of trained specialists, services in many areas are not configured in the most appropriate or efficient way, and equipment availability remains an issue. 24/7 thrombectomy services are more important now than even a few years ago, as delays are preventing progress in other areas of the stroke pathway.

In England, progress is far off the pace needed to realise the NHS Long Term Plan target to increase mechanical thrombectomy 10-fold by 2022. Yet NHS England's new National Stroke Service Model sets an expectation that we must achieve 24/7 thrombectomy services as soon as possible, recognising the substantial evidence base described in **Chapter 1**. Newly established Integrated Stroke Delivery Networks (ISDNs) across England present a real opportunity to prioritise thrombectomy roll-out and give it the attention and investment it deserves.

Each year that thrombectomy isn't fully rolled out across the UK, around 8,400 stroke patients miss out on the enormous benefits. This leads to worse outcomes for stroke survivors, diminished independence post-stroke and an increased reliance on NHS and social care services. The evidence suggests that the cost of fully implementing thrombectomy across the UK would be around £400 million but would save £1.3 billion over five years.[1]

Long-awaited progress across the UK shows us that changes to our current systems are possible. Wales' only native thrombectomy service at Cardiff's University Hospital of Wales, where Gerald was treated, only re-opened around 2018. Dundee's new thrombectomy service has begun to re-establish the procedure in Scotland, after services stopped entirely in 2018. In Northern Ireland, a seven-day service is available, but only 8 am-5 pm. An expansion plan to deliver 24/7 service by 2022 is in development. It's vital we continue to share our experiences, learning from each other and understanding best practice.

We believe that thrombectomy is a life-changing intervention that changes the game for how stroke services should operate across the whole pathway. I hope this how-to guide will give you the evidence and information you need to help make thrombectomy a 24/7 routine option for stroke treatment for the benefit of people affected by stroke across the UK.

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Introduction

Gary Ford, Martin James and Phil White

Stroke remains a major challenge to achieving improvements in global health despite substantial advances in both prevention and treatment in recent years. In Western countries, ischaemic stroke due to large artery occlusion (LAO) predominates as a cause of disability, institutionalisation, and costs to healthcare and society.[2]

Major advances in the treatment of non-communicable diseases are rare. In an era when we have grown accustomed to eking out marginal gains for patients from small advances in existing treatments, mechanical thrombectomy (MT) for acute ischaemic stroke (AIS) represents nothing less than an extraordinary leap forward. Mechanical thrombectomy was developed to address the problem that intravenous thrombolysis (IVT) is effective at reopening the artery in only 10–30% of patients with LAO. Early treatments with intra-arterial thrombolysis and insertion of permanent stents and clot extraction devices have evolved into the stent-retriever devices used in most of the pivotal trials and, more recently, aspiration devices with similar efficacy in achieving recanalisation.

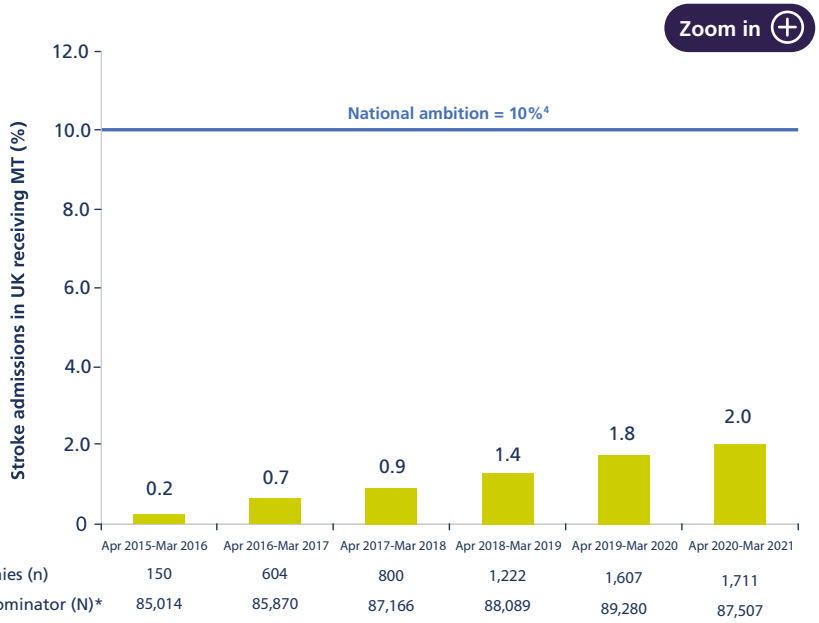
The evidence base behind MT for anterior circulation LAO stroke is clear and unequivocal, with 11 randomised controlled trials published in the past six years demonstrating substantial benefits over best medical therapy. The compelling evidence for MT in patients presenting within 6 hours of onset has been joined by high-quality evidence for benefit in highly selected, late-presenting patients. There is a palpable sense of urgency in the stroke world at these new opportunities to spare many people from major disability, with MT offering a dramatic change in the management of the largest cause of adult disability and the third biggest killer in the UK.[3]

Mechanical thrombectomy is the archetype of a 'disruptive innovation', particularly within the unique circumstances of the NHS, where necessary service development was held back while definitive evidence was awaited. Now it is here, such a step-change in treatment for many people with major disabling stroke requires considerable infrastructure to deliver and presents major challenges to organisations, systems and the workforce – challenges that the NHS has in the past lacked the agility to respond to sufficiently quickly. It can only be through unprecedented system-wide collaboration and innovation that we can achieve the step-change that is urgently needed.

So the challenge is implementation, not more research. The promise of this new era in therapeutics demands the most rapid implementation achievable – 'we must do as much of it as we can as quickly as we can'. We are acutely aware that progress since our first edition two years ago with some of the challenges – in workforce, imaging, redistribution of services or establishing new ones, and how best to serve small remote populations – has been modest at best, and in some cases has stalled. Although overall growth in MT activity in the UK over recent years has been steady[4] (Figure 1), with a few centres achieving rates for MT of 10% or more once transferred patients are included, many areas of the country are far less well served, and progress over this latest pandemic year has been faltering and uneven.

Figure 1. Thrombectomy rate in the UK, April 2015–March 2021.[4]

*Thrombectomy procedures recorded in England, Wales and Northern Ireland each year; no procedures are recorded for Scotland over the same time period.



For England, the 2019 NHS Long Term Plan described the commendable ambition of a 10-fold increase in MT by 2022 – this year.[5] We know now that this ambition, laudable as it is, will not be achieved, and we suspect that an order-of-magnitude change in approach is what is required if the UK is not to be left further behind by our high-income counterparts in the implementation of this dramatically effective and disability-saving innovation. A test of the effectiveness of the recently created Integrated Stroke Delivery Networks (ISDNs) in England will be whether they can drive the system change required to deliver MT to all those who stand to benefit.

The purpose of this implementation guide is therefore unaltered from our first edition in 2019: to accelerate the uptake of this high-value treatment by distilling the best available expertise within the UK into a single definitive volume. We have brought together the most incisive evidence and analysis, practical experience from early adopters, and lessons learned from earlier cardiology and stroke service reorganisations related to delivering primary percutaneous coronary intervention and IVT from more than a decade ago. For this second edition, we have also added a chapter on the response to the coronavirus pandemic, which since our first edition has preoccupied most major health services worldwide and disrupted many hospitals and systems, leading to varying reports regarding the impact on access to reperfusion.[6] As we write this in February 2022, after 2 years of the pandemic, the World Health Organization reports (**https://covid19.who.int/**[7]) over five-and-a-half million confirmed deaths from COVID-19 worldwide – a figure that only now surpasses the five-and-a-half million deaths each and every year from stroke, with a further 80 million survivors often left disabled. If similar vision and effort were focussed on this most damaging of non-communicable diseases, we might at last see big reductions in that recurring annual toll of death and disability from stroke.

Mechanical thrombectomy for AIS represents a once-in-a-generation opportunity to alter the miserable prognosis for the most devastating form of stroke, with substantial and well-proven benefits for individuals and for wider health and social care. As we have previously called for, the NHS's habitual, inertia-laden incremental approach to medical progress won't do this time. Instead we need visionary and concerted effort from all agencies and disciplines involved in stroke care to deliver this treatment, and we trust that this implementation guide continues to make a useful and enduring contribution to that effort.

Note on nomenclature in this guide

We have adopted certain terms and abbreviations consistently throughout this guide because they are both the most commonly used and/or the most descriptive. For instance, we use 'large artery occlusion' (LAO) throughout rather than the term 'large vessel occlusion' favoured by other authorities. We use the term 'mechanical thrombectomy' (MT), as mechanical differentiates the proven technologies for endovascular stroke treatment from other techniques such as intra-arterial thrombolysis. In describing hyperacute stroke units, we have adopted the new nomenclature in England and used the terms 'comprehensive stroke centres' (CSCs, those capable of delivering both thrombolysis and thrombectomy) and 'acute stroke centres' (ASCs, those capable of only thrombolysis, with onward transfer to a CSC for MT). Trial acronyms and abbreviations are defined in a section at the end of the guide, which can be accessed from each page of the guide, along with the references. Interactive links throughout the document also offer access to acronyms and abbreviations, as well as chapter cross-references and webpages.

Acknowledgements

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1 Evidence base for mechanical thrombectomy in acute ischaemic stroke

Phil White and Keith Muir

Key points

- **MT** for anterior circulation stroke due to proven proximal **LAO** within 6 hours of onset is safe and highly effective and sets the new standard of care.
- Overall good functional outcome rate at 90 days is about 20% greater with MT than best medical therapy alone, with about half of patients achieving good outcomes after MT.
- Favourable outcome from MT in most patients is strongly time dependent ('time is brain'); best results are achieved with limited early ischaemic brain injury; if good re-canalisation is achieved within 4.5 hours, the absolute rate of good functional outcome exceeds 60%.
- In carefully selected patients, MT between 6 and 24 hours (using advanced brain imaging techniques and applying trial selection criteria) is also highly effective and safe.
- MT is highly likely to be cost-effective (at conventional willingness-to-pay thresholds) or even cost-dominant over a lifetime analysis (minimum 20 years).
- The cost of implementing MT across the UK would be around £400 million but would give net savings of £1.3 billion over five years.

Clinical safety and efficacy of mechanical thrombectomy

Between December 2014 and February 2018, 11 positive **RCT**s of MT in the anterior circulation were published (Table 1),[8–18] leading to a revolution in the care of patients with **AIS** due to LAO. Of the accompanying raft of meta-analyses and systematic reviews, only the largest meta-analysis using **IPR** data and the latest systematic review incorporating trial sequential analysis will be discussed further.[19, 20] Trials reporting on MT without a non-MT control arm,[21, 22] and trials on early generation devices (such as the **MERCI** device) without imaging-confirmed LAO prior to enrolment[23–25] are not considered further as they do not inform current practice.

Efficacy of MT within 6 hours of stroke onset

For trials after **MR CLEAN**,[8] which predominantly or exclusively enrolled patients within the licensed **IVT** time window (up to 4.5 hours) and used only modern devices (see Figure 2) (**EXTEND-IA**,[14] **SWIFT-PRIME**,[13] **THRACE**,[10] **PISTE**[11] and **EASI**[12]), there is remarkable consistency in the good outcomes for best medical therapy without MT, with rates of functional independence (**mRS** 0–2) between 35% and 42%. MR CLEAN[8] is an outlier at 19% functional independence obtained with best medical therapy, probably due to the higher rate of **ICA** occlusions (more than one-third) compared with other trials and a protocol to potentially wait to see if IVT worked.

Table 1. Effect of MT compared with best medical therapy on good functional outcome (mRS ≤2* at 90 days).

Trial	Patients (%, n/N)		Absolute benefit of MT (%)	Adjusted OR (95% CI) ITT]†
	MT	Best medical therapy		
MR CLEAN[8]	33 (76/233)	19 (51/267)	14	2.2 (1.4–3.4)
EXTEND-IA[14]	71 (25/35)	40 (14/35)	31	3.8 (1.4–10.2)
SWIFT-PRIME[13]	60 (59/98)	35 (33/93)	25	2.8 (1.5–4.9)
ESCAPE[15]	53 (87/164)	29 (43/147)	24	3.1 (2.0–4.7)
REVASCAT[9]	44 (45/103)	28 (29/103)	16	2.1 (1.1–4.0)
THRACE[10]	53 (106/200)	42 (85/202)	11	1.6 (1.1–2.3)
THERAPY[16]‡	38 (19/50)	30 (14/46)	8	1.4 (0.6–3.3)
PISTE[11]	52 (17/33)	38 (12/32)	14	2.1 (0.7–6.9)
EASI[12]	50 (20/40)	38 (14/37)	12	Not available
DAWN[17]	49 (52/107)	13 (13/99)	36	Not available
DEFUSE-3[18]	45 (41/92)	17 (15/90)	28	2.7 (1.6–4.5)

*Corresponds to slight or no residual disability as a result of the stroke.
†Where given, a trial's own calculated OR is presented rather than that derived from a systematic review.
‡A substantial proportion of patients in THERAPY (30/55) were not treated with second-generation (modern) devices.

The range of good functional outcomes in MT arms is wider (33–71%), which most likely reflects the impact of additional advanced brain imaging selection criteria used in some trials that selected patients with a greater volume of salvageable penumbral tissue (such as EXTEND-IA,[14] SWIFT-PRIME,[13] **ESCAPE**,[15] **DAWN**[17] and **DEFUSE**-3[18]).

In the five modern device trials that used vascular imaging to confirm LAO but not advanced brain imaging selection,[8-12] the absolute benefit range for MT is more modest but consistent at 11–16%. Considerable consistency of adjusted **OR**s is seen across trials, most being in the range 2.1–3.1 (see Table 1). The efficacy of MT for an improved functional outcome in a broad range of LAO stroke patients is unmatched by any previous therapy in stroke medicine,[26] with an **NNT** of less than 3 (1-point improvement in 90-day mRS).[19]

There is now overwhelming level 1A evidence that modern-device MT achieves significantly higher re-canalisation rates than alteplase for LAO stroke[10] and better clinical outcomes, with an 11–36% absolute increase in patients recovering from AIS to be independent in activities of daily living. Mechanical thrombectomy is associated with a similar risk of **sICH** to IVT and most trials show no statistical difference in mortality (though generally trend to lower).[19, 20, 27]

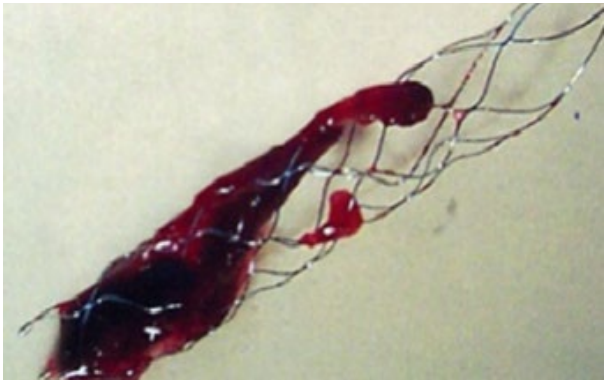
To date, no convincing evidence has shown that one class of MT device is superior to another. Three recent randomised trials and a systematic review have shown no statistically significant difference in functional outcome between **DA**- and **SR**-based MT, and a further ongoing trial is comparing the combination of DA/stent with SR alone.[28–32]

Efficacy of MT beyond 6 hours from onset

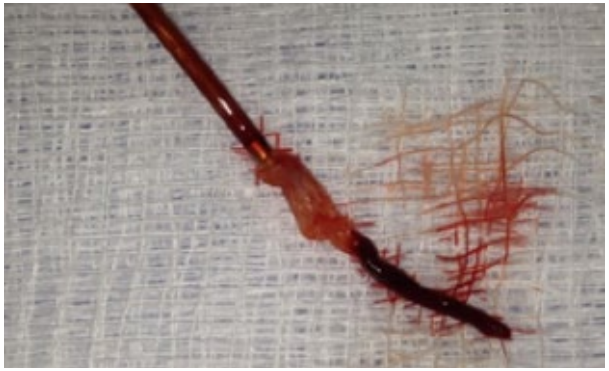
The **REVASCAT** trial used advanced brain imaging in patients recruited 4.5–8 hours after stroke onset,[9] and ESCAPE used **ASPECTS**/collateral score selection up to 12 hours after onset.[15] Both trials found no statistical difference in outcomes following MT between those randomised early or late within the trials. This indicates that patient benefit remains in 6–8- and 6–12-hour windows (when the relevant trial imaging selection techniques are applied to stroke patients meeting their respective eligibility criteria), but the extent of the treatment effect in the late time window using these selection criteria is not clear, as the number recruited after 6 hours in both trials was small.

Figure 2. (a) Stent retriever with extracted clot, and (b) large bore distal aspiration catheter with aspirated clot in acute stroke MT cases using these modern (second-generation) devices.

(a)



(b)



Two RCTs that subsequently focussed on intervention up to 24 hours after stroke onset/patient **LKW** – DAWN (6–24 hours)[17] and DEFUSE-3 (6–16 hours)[18] – confirmed that MT remains very effective and far superior to medical therapy alone in highly selected patients (see Table 1). Both trials used perfusion-based imaging selection based on **RAPID**™ (iSchemaView, California, USA) software processing of **CTP** or **MRI** data. In DAWN, only more proximal occlusions were enrolled (ICA and/or proximal M1 segment), and selection was on the basis of high **NIHSS** relative to small perfusion-defined ischaemic core, as calculated by RAPID,[14] or small **DWI** lesion volume. DEFUSE-3 was slightly less restrictive in its inclusion criteria, allowing moderate-sized core infarcts as long as there was sufficient mismatch, as calculated by RAPID.18 Overall, combining the two trials, no statistically significant difference between MT and control arms was found in mortality (15% *versus* 22%) or sICH (6% *versus* 4%). The Cincinnati group assessed DAWN/DEFUSE-3 eligibility among their population of 2,297 ischaemic strokes over a one-year period: 34 met the DAWN trial eligibility criteria and a further 19 were DEFUSE-3 eligible – giving a total eligibility rate of 1.9%.[29] This extremely low eligibility rate on current evidence does not suggest large numbers of MT referrals will arise from this population (the 12–24-hour subgroup was estimated to comprise just 6% of the LAO stroke patients with NIHSS >6 in the UK) **(see Chapter 2)**.[33, 34]

How generalisable and robust is the evidence?

The benefits of MT have been demonstrated in a wide range of healthcare systems – the trials listed in Table 1 recruited from nine countries across Western Europe (including the UK in PISTE and ESCAPE), USA, Canada, Korea (ESCAPE), Australia and New Zealand (EXTEND-IA).[8–18]

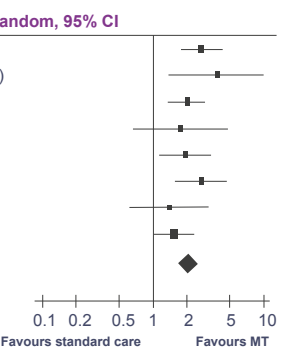
After MR CLEAN first reported in October 2014,[8] most MT trials[9–11, 13–16] stopped early. This effect might introduce bias, including an overestimation of the treatment effect. However, in most cases, these trials stopped early only after accumulating data showed that a predefined efficacy stopping point (favouring MT) had been reached.[9, 10, 13–15] Only two trials were stopped due to evidence removing the clinical equipoise necessary to continue randomising.[11, 16] As regards more delayed MT (>6 hours), individual trials were relatively small and used different selection criteria, so although the evidence for late MT is still classed as level 1, it is not as strong as that for MT up to 6 hours.

In addition to the reproducible consistent treatment effect seen in the early trials of MT, sequential trial analysis shows no change in the odds ratio for treatment benefit with inclusion of later trials (see Table 1 and Figure 3[8–11, 13–16]). In contradistinction to functional independence, an updated meta-analysis (not including DAWN/DEFUSE-3) suggests that MT has no mortality benefit, although there is a non-significant trend to a 20% reduction (see Figure 4). The possible effect of MT on mortality is more striking in the trials that used advanced brain imaging selection and selected for late intervention (beyond 6 hours) – namely ESCAPE, DAWN and DEFUSE-3.[15, 17, 18]

Trial sequential analysis indicates that meta-analyses are substantially underpowered to show differences for sICH. Nevertheless, no increase in sICH has been shown for MT over best medical care alone.[19, 20]

Figure 3. Meta-analyses of first eight trials' data for mRS 0–2 at 90 days.[8–11, 13–16]

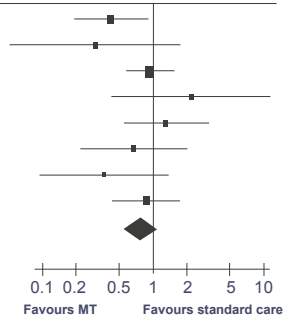
Study	MT Events	MT Total	Standard care Events	Standard care Total	OR, random, 95% CI
ESCAPE	87	164	43	147	2.7 (1.7 to 4.4)
EXTEND-IA	25	35	14	35	3.8 (1.4 to 10.2)
MR CLEAN	76	233	51	267	2.1 (1.4 to 3.1)
PISTE	17	33	12	32	1.8 (0.7 to 4.8)
REVASCAT	45	103	29	103	2.0 (1.1 to 3.5)
SWIFT-PRIME	59	98	33	93	2.8 (1.5 to 4.9)
THERAPY	19	50	14	46	1.4 (0.6 to 3.3)
THRACE	106	200	85	202	1.6 (1.1 to 2.3)
Total (95% CI)		**916**		**925**	**2.1 (1.7 to 2.5)**
Total events	**434**		**281**		



Zoom in

Figure 4. Meta-analyses of first eight trials' data for mortality at 90 days.[8–11, 13–16]

Study	MT Events	MT Total	Standard care Events	Standard care Total	OR, random, 95% CI
ESCAPE	17	164	28	147	0.5 (0.3 to 0.9)
EXTEND-IA	3	35	7	35	0.4 (0.1 to 1.6)
MR CLEAN	49	233	59	267	0.9 (0.6 to 1.4)
PISTE	7	33	4	32	1.9 (0.5 to 7.2)
REVASCAT	19	103	16	103	1.2 (0.6 to 2.6)
SWIFT-PRIME	9	98	12	97	0.7 (0.3 to 1.8)
THERAPY	6	50	11	46	0.4 (0.2 to 1.3)
THRACE	24	202	27	206	0.9 (0.5 to 1.6)
Total (95% CI)		**918**		**933**	**0.8 (0.6 to 1.1)**
Total events	**134**		**164**		



Procedural safety of MT

A comprehensive narrative review by Balami *et al* summarises the whole field succinctly.[27] Mechanical thrombectomy is associated with a number of intraprocedural and postoperative complications (Table 2), which need to be minimised and effectively managed to maximise the benefits. Overall, from the pivotal RCTs, the risk of complications from MT with sequelae for the patient is approximately 15%. Minimising the frequency and impact of complications of MT is important to maximise the benefits of the intervention. Some complications are life threatening, and many lead to increased length of stay in intensive care and stroke units. Others increase costs and delay the start of rehabilitation. Some may be preventable; the impact of others can be minimised with early detection and appropriate management. Both neurointerventionists and stroke specialists need to be aware of the risk factors for, strategies for prevention of, and management of these complications. Nonetheless, procedure-related morbidity and mortality nearly all occur within 30 days and so are incorporated within the net benefit of MT on 90-day clinical outcomes, which strongly favour MT.

Table 2. Complications of MT.

Procedural complications	Other complications
• Access-site problems • Vessel/nerve injury • Access-site haematoma • Groin infection • Device-related complications • Vasospasm • Arterial perforation and dissection • Device detachment/misplacement • Symptomatic intracerebral haemorrhage • Subarachnoid haemorrhage • Embolisation to new or target vessel territory	• Anaesthetic-related complications • Contrast-related complications • Postoperative haemorrhage • Extracranial haemorrhage • Pseudoaneurysm

Areas of uncertainty

Additional publications based on level 1 evidence (such as HERMES IPR meta-analyses) have addressed specific subgroups or additional questions around MT in the anterior circulation.

Occlusion location

Meta-analysis data from the HERMES collaboration indicate that MT is effective in proximal M2 **MCA** occlusions, but there were insufficient data to assess isolated distal M2 occlusions.[35] No robust data exist around anterior cerebral artery thrombectomy, particularly A2.

Posterior circulation

Two RCTs of vertebro-basilar versus MT plus IVT have been completed. The Chinese **BEST** trial of basilar artery occlusion was stopped early due to excess crossovers to the intervention arm. There was no benefit for MT on the intention-to-treat analysis but benefit in the as-treated analysis: adjusted OR 3.02 (1.31–7.00).[36]

A larger (n=300), primarily European RCT of vertebro-basilar thrombectomy versus MT plus IVT, which has been presented (**https://eso-wso-conference.org/eso-wso-may-webinar/**) but not yet published in full, also failed to demonstrate superiority for MT. Non-significant trends to better functional outcome, lower mortality and greater sICH were found in the MT arm. A benefit favouring MT was found in the larger subgroup where NIHSS was ≥10 but in no other predefined subgroup.

At present, therefore, MT in the posterior circulation can be regarded as safe and probably indicated in those with NIHSS ≥10 who meet the **BASICS** trial inclusion criteria (in particular, MT can be achieved within 6 hours of estimated time of onset of basilar artery occlusion). However, IPR-level meta-analysis of these trials is awaited for further clarification.

Direct to MT

To date, six RCTs examining whether taking a patient direct to MT has any advantage or disadvantage over the standard approach of IVT first (where eligible for it[37–40]) have completed. An IPR level meta-analysis of all six trials is planned.

The largest trial is **DIRECT-MT** from China,[37] which has a near identical protocol to MR CLEAN No IV of 539 participants,[38] and the main results of both are similar, namely that direct to MT is non-inferior to combined IVT/MT but with a trend to lower reperfusion rates. 'Direct to EVT' is another smaller (234 patients) Chinese trial,[39] which again found non-inferiority but with a trend to better functional outcome and higher reperfusion for direct

to MT. **SKIP**, a Japanese trial of 204 subjects that used a lower dose of IVT, was non-significant for all key outcomes.[40] SWIFT PRIME,[41] **SWIFT-DIRECT**,[42] and DIRECT SAFE[43, 44] have similar findings. All trials were conducted in experienced MT centres and the interval from thrombolytic drug being started to groin puncture was very short (e.g. 29 minutes in the combined treatment arm of DIRECT-MT[37]), as was the interval from hospital arrival to groin puncture. Generalisability to services with different workflow is uncertain. The non-inferiority margins chosen were wide.

Type of IVT to use

The modified tissue plasminogen activator tenecteplase has greater fibrin specificity and longer circulating half-life than alteplase due to resistance to breakdown by plasminogen activator inhibitor type 1. These properties may enhance fibrinolytic efficacy while also reducing bleeding risk.[41] The main practical advantage over alteplase is administration of the whole dose by single intravenous bolus, which may greatly facilitate transfer of patients from **ASC**s to neurointerventional facilities, avoiding the need for medical or nursing management of an intravenous infusion and avoiding the potential detriment to thrombolytic activity by delayed infusion start or interruption.[45] This has led some non-UK healthcare systems to introduce routine use of tenecteplase rather than alteplase among thrombolysis-eligible patients in general or, more selectively, among potential MT candidates.[46]

Several clinical trials comparing tenecteplase with alteplase for thrombolysis-eligible patients are ongoing. The completed **NOR-TEST** trial left uncertainty regarding general safety and efficacy among patients eligible for IVT on clinical criteria as it used a higher tenecteplase dose (0.4 mg/kg) than the one considered equivalent to alteplase (0.25 mg/kg) and recruited a predominantly minor stroke population and also a very high proportion of stroke mimics.[46] In selected patients with anterior circulation LAO and favourable perfusion imaging profile in the **EXTEND-IA TNK** trial, tenecteplase 0.25 mg/kg achieved significantly greater recanalisation (22%) compared with alteplase (10%), which translated into improved functional outcomes.[47, 48] The higher tenecteplase dose of 0.4 mg/kg did not improve recanalisation rates compared with the 0.25 mg/kg dose in the subsequent EXTEND-IA TNK-2 trial.[48] The total number of patients reported to date in trials that compared tenecteplase 0.25 mg/kg with alteplase is small (209 patients treated at this dose in all completed trials to date), and this is reflected in the low-grade recommendation for tenecteplase as an equivalent thrombolytic agent in current **AHA** and **ESO** guidelines.[49, 50] Ongoing trials will provide robust evidence on the general safety and efficacy of tenecteplase compared with alteplase in the near future.

In the interim, ESO guidelines make a weak recommendation for considering tenecteplase 0.25 mg/kg as a single bolus alternative to alteplase in patients fulfilling the imaging and clinical criteria of EXTEND-IA TNK and in whom MT is planned, in recognition that the evidence derives from a single trial of only 202 participants.[50]

Technical procedural aspects

Certain technical aspects of performing MT other than DA/SR and anaesthesia are also uncertain: including: i) the use of balloon-guide catheter, for which accumulating non-RCT data indicate benefit,[51] but this is yet to be definitively confirmed, ii) use of radial rather than femoral access, and iii) whether a 'first-pass effect' is definitively to be pursued, even if it takes longer to achieve reperfusion. Here again, non-RCT data look promising,[52] but there are biases and confounding factors around such data that only RCTs can resolve.

Patient selection for MT

Uncertainty applies to patients with mild stroke (NIHSS <6) but confirmed LAO, and ongoing trials (**MOSTE**, **ENDO-LOW**) are including this patient population (as well as the TEMPO-2 trial, which randomises to tenecteplase or best medical therapy). Those with LAO AIS and more extensive early ischaemic changes are also the subject of several ongoing RCTs (**TENSION**, **LASTE**, **TESLA**). Some evidence from HERMES meta-analyses indicates that an ASPECTS of 5 based on **CT** should not be an exclusion to MT and that MT has a reasonable trend to benefit in ASPECTS 3–4 (although that combines **MRI** and CT assessments and the total number of trial participants with low ASPECTS was very small).[53] Trials are also ongoing to investigate whether less selective brain imaging can be used to choose patients undergoing MT in the later time window and, conversely, whether there is benefit from wider use of advanced brain imaging in early presenters, in the use of general *versus* local anaesthesia in a pragmatic real-world situation, and in the use of MT in patients with pre-stroke disability (mRS 2–4).[54]

Other uncertainty

It is also critical to note that MT has been overwhelmingly performed in all of the discussed trials by experienced neurointerventionists in centres with high volumes of neurointerventional procedures. Neither the efficacy nor safety profile of MT has been

similarly robustly confirmed for non-expert operators or low-volume units. There is increasing evidence, mainly from North America, linking higher centre volumes, as well as experience, to statistically significantly improved outcomes (adjusted OR 1.1)[55] and reduced mortality;[56] furthermore, the volume outcome effect seems to be linear (rather than sigmoid with an early plateauing of the effect): at least up to 50–100 procedures per year.[57]

Cost-effectiveness of mechanical thrombectomy

A systematic review of economic evaluations on SR MT for AIS published in 2018 found that MT is likely to be cost-effective (all eight studies) at a high probability level (79–100%) at conventional thresholds or even cost-dominant (three of eight studies).[58] The findings of this systematic review are supported by primary studies with substantial heterogeneity of method but consistency.

Several studies that assessed the cost-effectiveness of MT in combination with IVT compared with IVT alone concluded that MT is potentially cost-effective[59–66] and cost-saving.[67–70] Two model-based cost-utility analyses from the perspective of the UK NHS have been published.[62, 69] Based on one meta-analysis of RCTs, MT in combination with IVT compared with IVT alone was associated with an additional £7,061 per **QALY** gained.[31] In the other study, carried out by the same team but based on IPR data from a RCT conducted in the USA and Europe (SWIFT-PRIME), MT in combination with IVT was reported to be associated with cost-savings of £33,190 per patient.[69]

One study has estimated the budget impact of adopting and implementing MT nationally in Eire. A national MT service would lead to incremental costs and benefits of €2,626 and 0.19 QALYs per eligible patient. The **ICER** was €14,016 per QALY at five years, with a probability of being cost-effective of 99% at a threshold of €45,000 per QALY gained[61] and a 9% probability of the intervention being cost-saving relative to standard medical care. Based on treatment being delivered at two centres and treating 268 patients per year, the cost of implementation to provide 24/7 coverage for the 4.8 million population of Eire was estimated to be €7.2 million over five years, comprising €3.3 million in the first year, with estimated annual running costs thereafter of €0.8 million–€1.2 million.[61]

However, when adopting 'surgical' interventions into clinical practice, there are appreciable challenges to implementation, including investment in staff, capital equipment and service reorganisation, which will have an impact on cost-effectiveness calculations that do not consider the costs of service change and implementation.[71] For the UK, the PISTE trial team[11] conducted an economic evaluation based on seven RCTs[8–11, 13–15] to determine the cost-effectiveness of MT but also estimated the monetary cost and value of enhancing implementation of MT using UK clinical and cost data.[51]

In the PISTE analysis, cost-effectiveness was expressed as ICER and incremental **NMB**. The NMB is a measure of the health benefit expressed in monetary terms, which incorporates the cost of the new strategy, the health gain obtained, and societal WTP for those health gains. The economic model found that MT plus IVT had a total cost of £46,684 compared with £39,035 for IVT alone. Over a lifetime horizon, the intervention group gained 7.61 QALYs compared with 5.41 in the control IVT group. This equates to an incremental cost of £7,649 and 2.21 QALYs associated with the addition of MT to standard treatment and an ICER of £3,466 per QALY. The incremental NMB was £36,484 per patient. One-way sensitivity analysis on the key parameters driving the cost-effectiveness estimate of MT in this model found that varying all key parameters had no decisive impact on the ICER, with all estimates remaining below £20,000 per QALY.

The PISTE team also calculated the value of implementation as the value of perfect implementation minus the cost of implementation measured over a five-year time horizon. They estimated the maximum potential value of implementation as the NMB of achieving 100% MT implementation across the UK (51,404 patients treated by MT over five years) and then subtracted from that the cost of expanding services, equipment and staff in 29 **CSC**s to operate 24/7 across the UK. The analysis included costs of staff salaries and set-up costs, such as training and equipment, many of which were not included in the Eire analysis. The value of perfect implementation is the NMB from MT (£36,484 per person) multiplied by the effective population (n=51,404). This implies that the expected value of perfect implementation in the UK would be £1.7 billion, set against an estimated cost of £413 million to implement, which suggests an expected value of implementation of £1.3 billion over five years. The study also estimated the 'break-even' point at which the NMB obtained from the proportion of eligible patients treated is equal to the cost of implementation, which was about 30% – or about 3,000 patients treated by MT per year.

The HERMES Trialists Collaboration has demonstrated the costs of delays to MT in terms of both financial and lifetime outcomes. Within the first 6 hours of symptom onset, every 10 minutes of earlier treatment resulted in an average gain of 39 days (95% prediction interval: 23–53 days) of healthy life per patient and increased the NMB by $10,593 (95% prediction interval: $5,549–14,847) in healthcare costs and $10,915 (95% prediction interval: $5,928–15,356) in societal costs.[72] The amount of healthy lifetime lost associated with each minute of delay was 5.5 days for door-to-puncture and 6 days for door-to-reperfusion delay.[73]

Conclusion

Mechanical thrombectomy for anterior circulation stroke due to proven proximal LAO within 6 hours of stroke onset is safe and highly effective and sets the new standard of care. The overall rate of independent functional outcome (mRS 0–2) at 90 days is about 20% greater with MT than with best medical therapy alone (which in most cases included IVT), and about half of patients achieve very good outcomes after MT. Favourable outcomes from MT in most (but not all) patients are strongly time dependent ('time is brain'), and best results are achieved when early ischaemic brain injury is limited (for example, ASPECTS score ≥5). If good re-canalisation is achieved within 4.5 hours, the absolute rate of good functional outcome exceeds 60%. In carefully selected patients (using advanced brain imaging techniques and applying trial selection criteria), MT between 6 and 24 hours after stroke onset is also highly effective and safe. Furthermore, MT is highly likely to be cost-effective (at conventional WTP thresholds) or even cost-dominant over a lifetime analysis. The cost of fully implementing MT across the UK would be around £400 million but could give net savings of £1.3 billion over five years, offering unprecedented promise both to patients with potentially disabling stroke and to healthcare systems by reducing the long-term costs of care.

2 How many stroke patients in the UK are eligible for mechanical thrombectomy?

Peter McMeekin and Martin James

Key points

- **MT** in the UK is starting from a very low baseline of 0.9% of all strokes receiving MT.
- Based on the available evidence, about 11–12% of stroke patients admitted to hospital are eligible for MT.
- Advanced imaging has little effect on total eligibility, but its use would affect treatment decisions in about 14% of cases, ruling out and ruling in a similar number of patients.

The infrastructure demands for MT create the need for a more centralised model of hyperacute stroke care, and robust activity estimates are required for accurate planning to inform service reconfiguration. In this chapter, we combine results from landmark **RCT**s with data from registries to provide an updated estimate of the number of patients who would be eligible for MT in the UK in one year.[34] We also highlight the effect of advanced imaging techniques used to select late-presenting patients in the most recent RCTs on this estimate.[33]

We updated our original decision tree[74] to estimate the proportion of all stroke patients eligible for MT (Figure 5), independent of geographic or infrastructure constraints. Using national registry data from the prospective **SSNAP** national audit for England, Wales and Northern Ireland[75] and adjusted for Scotland using data from the **SSCA**,[76] we determined that 95,500 patients with stroke are admitted to hospital each year. A decision tree was constructed based on key inclusion and exclusion criteria from published trials: stroke type, severity, presence of anterior or posterior **LAO**, onset time, pre-stroke disability, the extent of ischaemia on **CT** (or **MRI**), re-canalisation before MT and optional advanced imaging. These criteria were applied consistently irrespective of eligibility for **IVT**.

Further data on the distributions for stroke severity and onset time were extracted from two large UK stroke services and national SSNAP data in the case of late presenters. The final decision tree (see Figure 5) includes pathways using advanced imaging within and beyond 4.5 hours after stroke onset. Although basilar artery occlusions were not included in the trials, we have included them in our estimates of eligibility in early-presenting patients because they are treated in practice, but we have not included those after 12 hours, as they represent a small but imprecise number.

Eligibility by stroke type, location and severity

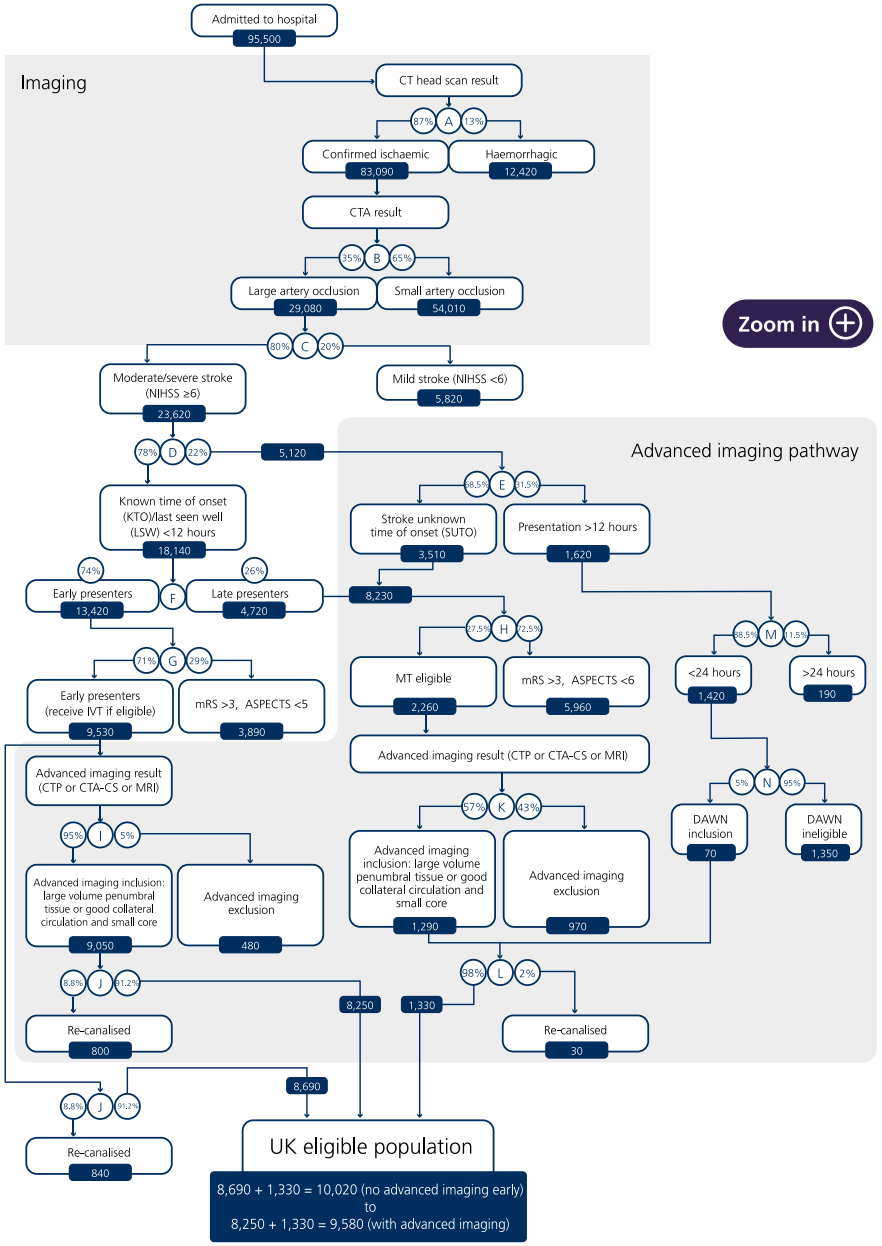
In a recent review into the epidemiology, natural history and clinical presentation of LAO published in 2019, Rennert and colleagues estimated that the hospital incidence ranged between 28% and 40%.[77] The mean incidence of reported LAO, 35%, was therefore used in the decision tree.[17, 78, 79] 'Minor' strokes (**NIHSS** <6) are not conclusively proven to benefit from MT and have not been included pending the outcome of further trials.[17] Of the major RCTs, only **MR CLEAN**[8] specifically enrolled patients with NIHSS <6 and failed to show statistically significant benefit from MT in the subgroup with NIHSS 2–15. We applied an NIHSS cut-off of 6, aligning with the three trials that included the largest numbers of patients in the NIHSS range 6–10. The **STOP-Stroke** study[78] reported that 20% of LAO strokes had NIHSS <6 (Figure 5, node C), an observation reinforced by recent UK data.[79] These proportions give an annual estimate of 23,260 patients with moderate/severe stroke (NIHSS ≥6) and LAO in the UK.

Time of onset and eligibility

Eligible patients were defined by a known onset time of <24 hours or had stroke of unknown onset time with a **LKW** time within 24 hours. Two recent RCTs included patients up to 16 hours (**DEFUSE**-3)[16] and 24 hours (**DAWN**)[15] after LKW. For our estimates, presentation times were derived from two large UK centres (Northumbria and Exeter): 78% of patients with NIHSS ≥6 presented within 12 hours of known onset, with the remainder divided between unknown onset with LKW within 12 hours (68.5%) and known onset time between 12 and 24 hours (28.0%) and beyond 24 hours 3.5% (Figure 5, nodes D/E/M).

FIGURE 5. Eligible population: (A) Total UK hospital-admitted stroke patients, including those deemed to be geographically inaccessible; (B) Patients with confirmed infarction, excluding about 2% of patients whose status is unconfirmed; (C) Includes patients with basilar artery occlusion eligible for treatment if presenting within 12 hours. Others are assumed eligible unless they meet any subsequent exclusion. (F) Early presenters: those patients arriving at hospital within 4 hours of known onset. See chapter text for description of remaining nodes. Between 9,580 and 10,020 stroke patients (10–11% of all stroke admissions) could be eligible for MT per year in the UK.

Note: Patients within the large lower grey shaded box are all managed with advanced imaging (13,210 patients in total); those who are early presenters (9,530 beneath node G on the left side) may bypass that step and be managed without advanced imaging.



Zoom in

Those with known onset within 12 hours divide between 74% within 4 hours and 26% between 4 and 12 hours[75] (Figure 5, node F). After exclusions, two cohorts of patients are potentially eligible for MT: 'early presenters' presenting within 4 hours, mostly eligible for IVT within 4.5 hours, and 'late presenters', ineligible for IVT either because of onset >4 hours ago or because they had stroke of unknown time of onset but LKW within 24 hours. At this point, about 23,870 (25%) admissions are potentially eligible for MT (Figure 5, nodes G, H and N). It is assumed that only early presenters would be able to receive MT treatment within 6 hours of onset.[17] From this point onwards, the three groups are differentially influenced by use of advanced imaging.

Clinical and radiological exclusions among the intravenous thrombolysis-eligible population

Early presenters comprise the largest group eligible for MT: 13,420 patients per year (14% of all stroke admissions). Exclusions within this group were **ASPECTS**[80] <6 or visible infarction of more than one-third of the **MCA** territory (up to 30% of patients[17, 81]). Exclusion by pre-stroke **mRS** was based on trial inclusion criteria. However, we update our estimates of those excluded by pre-stroke dependence to include some patients with a mRS of 3 because SSNAP data indicate MT being performed on this subgroup. We base the percentage on the number of patients in the SSNAP national dataset treated with

IVT who had a pre-stroke mRS of 3 and suffered moderate or severe strokes (NIHSS ≥6). These patients make up 0.3% of all stroke patients, or 270 patients, which represents 3% of patients at node G (early presenters). Pre-stroke mRS therefore excludes about 7% of patients.[17, 78, 82] Allowing for overlap in the two groups, pre-stroke disability and **NCCT** would exclude about 29%. We estimate that among the early-presenting, IVT-eligible population, 71% are eligible for MT before advanced imaging exclusions, equivalent to 9,530 patients per year (Figure 5, node G).

Various modes of advanced imaging (**CTP**, **CTA-CS** combined with ASPECTS, and MRI) have been proposed to identify patients with salvageable brain tissue (penumbra) at any time after onset. Data from **EXTEND-IA**[12] and the **SONIIA** registry[83] suggest that advanced imaging excludes 5% of early presenters with moderate/severe LAO stroke and pre-stroke mRS <3 because of a large core and small penumbra. In the early-presenting group, therefore, 480 patients would be excluded by advanced imaging, leaving a MT-eligible population of 9,050 patients before any re-canalisation with alteplase (Figure 5, node J).

Clinical and radiological exclusions among late presenters

In patients who present with unknown onset but LKW within 12 hours or with known onset time between 4 and 12 hours, information about MT eligibility is significantly less robust. In patients with LAO, we estimate 4,720 moderate-to-severe ischaemic strokes have a known time of onset of 4–12 hours and a further 5,120 would be LKW beyond 12 hours or unknown (3,510 within 12 hours or onset time unknown and 1,610 beyond 12 hours[75]). At this point (Figure 5, node E), the tree splits the 1,610 patients with a known time of onset >12 hours from the 3,510 patients who join the 4,720 patients whose known presentation time makes them ineligible from IVT. This suggests that advanced imaging might identify salvageable brain tissue in up to 8,230 patients, with most having pre-stroke mRS ≤3 (Figure 5, node H). However, a high proportion (up to 73%) of late-presenting patients are excluded by ASPECTS <6 on initial CT.[21,84] Pre-stroke disability would exclude another 5.5%[78,82] (460 patients), leaving only 27.5% (2,260 patients) of those considered for advanced imaging as eligible for MT (Figure 5, node H). Of these, 1,290 would remain eligible for MT after advanced imaging at node K, as they have a core less than 70 ml and a large penumbra.[85]

Of the 1,610 patients excluded at node E because they presented after 12 hours of onset, most present within 24 hours (1,420 patients). Data from DAWN[15] (node M) suggest that as few as 5% (70 patients) would be eligible for MT, giving a total of 1,360 late-presenting patients potentially eligible for MT – just 12% of all those eligible before advanced imaging (node L).

Re-canalisation prior to mechanical thrombectomy

A small proportion of patients will re-canalise spontaneously or in response to IVT before MT is performed. In the **HERMES** meta-analysis, this occurred in 8.7% of those receiving IVT,[86] and spontaneous re-canalisation in patients not receiving IVT is estimated to be as low as 2%[87] (Figure 5, nodes J and L). Re-canalisation prior to MT thus excludes 830 patients, leaving an anticipated total eligible population of between 9,580 (with the use of advanced imaging in all patients) and 10,020 (with advanced imaging limited to late presenters and those with unknown onset). This represents 10–11% of all hospitalised acute stroke, of which just 1.4% are late presenters or of unknown onset.

Discussion

Based on the available evidence, we estimate that 9,580–10,020 patients in the UK with **AIS** are eligible for MT annually – that is, about 10–11% of strokes admitted to hospital – depending on the inclusion or not of late presenters and the use of advanced imaging. Elsewhere, Chia *et al*[88] estimated a range of 7–13% for MT eligibility among patients presenting to two of three Australian hyperacute stroke sites. The lower bound of our estimate is defined by restricting MT to early presenters (those arriving at hospital within 4 hours of known stroke onset – 8,690 patients/year). The upper bound (10,020 patients/year) is defined by the inclusion of all early-presenting patients without the use of advanced imaging (8,690 patients/year) plus those eligible late-presenting patients with a favourable imaging profile (1,330 patients/year). Advanced imaging might exclude about 5% (440/8,690) of early-presenting and otherwise eligible patients but would include about 36% (1,290/2,260) of late-presenting patients. Thus, although the overall requirement (eligibility) for MT is relatively unchanged by advanced imaging, its use would affect decisions about MT treatment in about 14% (2,770/20,040) of otherwise eligible late presenters or ineligible early presenting patients.

The proportion of patients appropriate for MT depends on the frequency of LAO, but previous reports vary. Recent MT trials report a rate of LAO of 48–53%.[12,13] Rai *et al* estimated the incidence of LAO as only 12% in a retrospective sample of nearly 3,000 secondary referrals,[89] whereas Smith *et al* identified a LAO rate of 46% in patients with confirmed stroke referred to two large academic centres in the USA, a proportion of which included the anterior and posterior cerebral arteries and M2 branches.[78] A more recent prospective study in the UK identified a LAO rate of 39%,[79] and Rennert et al recently estimated the proportion to lie between 28 and 40%.[77] However, reported incidence is likely to have been partially determined by selection bias, imaging procedures and the study population.

To identify the proportion of this group excluded by imaging, data from **SWIFT**[21, 84] and **IMS** III[23] trials were used. At baseline, 25% had an ASPECTS below 6. Furthermore, by comparing ASPECTS at baseline to follow-up (mostly at 24 hours), 48% deteriorated from good to poor ASPECTS.[19, 83] It is assumed that this deterioration represented core infarct extension occurring within 12 hours. In total, therefore, 73% of 'late-presenting' patients are excluded by an ASPECTS below 6 on initial CT. Clinical mRS exclusions (as in the early-presenting group) would exclude another 8%.[15, 78]

The selection of patients by advanced imaging has a relatively modest effect on the overall numbers eligible for treatment but alters the eligibility decision in 14% of cases. The impression that a relatively small proportion of early-presenting patients with LAO on **CTA** would be subsequently ruled out by advanced imaging (5% in our model) is corroborated by the EXTEND-IA trial.[14] The results from the DAWN trial, in which advanced imaging was used to select an unknown but small proportion of late-presenting patients for MT, suggest that there is considerable further potential for benefit within this population.[17] The magnitude of the absolute treatment effect (30% difference in an excellent outcome of mRS 0–2 with MT) suggests that the DAWN sample was over-selected – an absolute benefit of 10%, akin to that seen in the MR CLEAN trial,[8] would mean that a far higher proportion of late presenters still stood to benefit from MT, albeit to a lesser extent. Benefit for this group of patients will have to await clarification in further trials, so for the time being we are left applying MT to a highly selected group of late presenters according to the restrictive eligibility criteria for DAWN and DEFUSE-3,[18] but we must anticipate that this proportion will increase as evidence accrues. Until it does, we are left with an estimate that only about 13% of all patients eligible for MT (about one in eight) will come from the group of patients presenting too late for IVT or with an unknown onset time.

Conclusion

Mechanical thrombectomy in the UK started from a very low baseline. In 2018–19, 1,200 MT treatments were recorded in SSNAP in England, Wales and Northern Ireland, equivalent to 1.4% of all strokes, and with very few procedures in Scotland.[90] By 2020–21, over 1,700 treatments were recorded in SSNAP (with still very few procedures in Scotland), equivalent to 2.0% of all strokes.[4] The midpoint of our estimate suitable for MT (10.9% of UK stroke admissions) combined with the absolute benefits estimated in an individual patient data meta-analysis[91] suggest that MT with national coverage could achieve an additional 2,550 patients with independent functional outcomes or as many as 4,520 patients (5% all stroke admissions) with a reduced level of disability compared to IVT alone. Implicit in these estimates is the assumption that outcomes for posterior circulation MT (which are included in our estimate of the early-presenting eligible population) are the same as those for anterior circulation MT. Overall, between 9,580 and 10,020 stroke patients per year in the UK could be eligible for MT based on current level 1 evidence, which approximates to 10–11% of stroke admissions.

3 How many comprehensive and acute stroke centres should the UK have?

Michael Allen, Kerry Pearn, Martin James, Phil White and Ken Stein

Key points

- To maintain the recommended 600 admissions to any acute stroke centre, the number of acutely admitting centres in the UK would need to be reduced. For example, the maximum number of centres in England would be about 80.
- To maintain a minimum of 150 **MT** procedures per unit per year, the maximum number of **CSC**s would be about 40.
- With the current 24 CSCs in England, 94% of patients would have the best chance of a good outcome by being transported directly to a CSC, but this would significantly destabilise the system, with all but 19 **ASC**s depleted of all stroke admissions.
- Implementing a maximum permitted additional travel time to bypass an ASC or using a pre-hospital test for **LAO** both increase net benefit over the current drip-and-ship model, but both similarly destabilise the system.
- Planning for ASCs and CSCs should be performed by maximising the number of CSCs (up to a maximum of 40) and then adding in ASCs (up to a maximum of a further 40) to control admission numbers and stabilise the system.
- Planning for both ASCs and CSCs should be performed with the largest possible footprint; planning at the level of **ICS**s is likely to lead to suboptimal service organisation for patients.

The advent of MT represents a disruptive innovation in the NHS, with substantial implications for the configuration of hyperacute stroke services. These are conventionally divided between CSCs, which are both **IVT**- and MT-capable, and ASCs, which deliver IVT but depend on secondary transfer to a CSC for MT. In the UK, the proportion of patients receiving IVT is consistently about 11%,[92] although higher rates have been achieved as a result of the reconfiguration of urban ASCs, with rates closer to 20%.[93]

Broadly speaking, two main models of hyperacute stroke care have been described.[94, 95] In a 'mothership' model, all patients with suspected stroke are taken directly to a CSC, if necessary bypassing a nearer ASC.[96] This is at the expense of greater onset-to-treatment times for IVT for some patients, but such a system removes the need for any secondary transfers by road ambulance or helicopter. In a so-called 'drip-and-ship' model (sometimes called 'treat-and-transfer'), IVT may be delivered at local ASCs before an eligible subset of patients diagnosed with LAO are transferred to the CSC. The choice between these models can depend on geography and travel times, availability of appropriately skilled staff, urban/rural split and other factors, including the maximum practical size of a CSC under a mothership configuration and the minimum recommended size of an ASC in a drip-and-ship model.

National guidelines recommend a minimum number of admissions to an ASC of 600 patients per year, with a recommendation that travel time should be 30 minutes or less and not more than 60 minutes.[97] There is no guidance on the maximum size of an ASC/CSC, but NHS England reconfiguration guidance recommends a maximum of 1,500 admissions for a single team,[97] and the largest CSC in the UK currently has more than 2,000 admissions.[92] A unit admitting 1,500 patients with strokes each year will also admit and manage, on average, a further 500 mimics, representing about six patients per day.[98]

Multisociety consensus standards for MT centres have been published,[99] with guidance on the minimum number of neurovascular procedures, including MT, to maintain individual operator skills,[100] advising at least 40 procedures/operator/year. Outcomes after MT have been shown to be better as the number of procedures per centre increases.[101, 102] A robust 24/7 MT service realistically requires at least five operators, and all five could not expect to meet minimum activity levels to maintain competence if the centre volume was less than 150 MT procedures/year,[103] equivalent to 1,500 confirmed stroke admissions/year.

Computer modelling allows the advantages and disadvantages of different configurations of hyperacute stroke care to be explored '*in silico*'. Identifying good solutions requires multiple competing parameters to be considered – travel time needs to be minimised, while the number of admissions needs to be controlled. We have previously described detailed methods for this kind of computer modelling based on the population of England.[104–109] Our findings therefore specifically relate to England, but similar principles will relate to the other UK nations, with still greater geographical challenges in some parts of Scotland prompting a greater degree of compromise over travel times and institutional size.

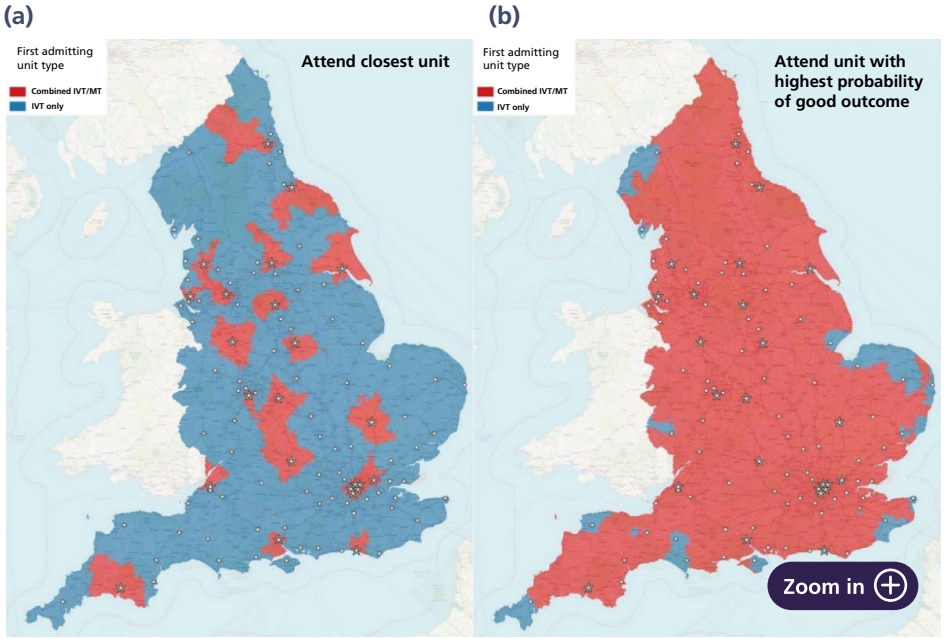
Location of thrombolysis and thrombectomy centres

For our analysis, the location of thrombolysis centres in our base case model was taken as the 107 ASCs in England providing IVT in 2019.[110] Within this number, the location of CSCs was taken as the 24 neuroscience centres in England that are either providing or planning to provide MT.[110]

Mothership versus drip and ship – clinical benefit

Clinical outcome from reperfusion is quantified in terms of a disability-free outcome three months after stroke (**mRS** score of 0–1 describes either no or only minor non-disabling symptoms). We have published the detailed method and code used to estimate outcomes,[108] which is a development of the method of Holodinsky *et al*[111] and incorporates the known decay of effectiveness of IVT[112] and MT[113] over time. For patients with the prospect of treatment, we assume it takes 60 minutes from stroke onset to the ambulance leaving the scene. Time to IVT is therefore 60 minutes + ambulance travel time + door-to-needle time. Door-to-needle time times for IVT in the model are set to a standardised 40 minutes across all hospitals. For patients who attend a CSC as their first admitting hospital, time to MT is given by 60 minutes + ambulance travel time + door-to-puncture time, which is set in the model to a standardised 90 minutes across all hospitals. If a patient first attends a unit that does not provide MT, the time to MT incurs a further net delay and additional inter-hospital travel time. The net delay used may be shorter than the actual **DIDO** time at the first admitting hospital, as some process steps have already been completed on arrival at the CSC. Previously, a large clinical trial showed that patients receiving MT after transfer were treated 110 minutes later than patients admitted directly, 35 minutes of which was attributable to inter-hospital

Figure 6. Catchment areas for either CSCs (stars) or ASCs (circles) if decision on conveyance to first stroke unit is made by either closest unit (a) or the destination that gives the highest probability of a good outcome (without any pre-hospital diagnostic) (b). The model has 24 CSCs at the current neuroscience centres and 83 ASCs at the remaining current acute stroke centres.



travel time, suggesting a net delay of 75 minutes + travel time.[114] In our modelling, we have anticipated some improvement over these historical results and have assumed a 60-minute net delay in addition to the inter-hospital transfer travel time. Applying a drip-and-ship model where the patient attends their closest stroke unit first (and assuming a uniform 20% IVT rate and 10% MT rate), the clinical benefit from IVT and MT is estimated to be 31.1 additional disability-free outcomes/1,000 admissions or 18.9 additional disability-free outcomes/1,000 admissions without MT. Twenty-seven percent of patients would directly attend a CSC in this model of care. If all patients were taken directly to one of 24 CSCs in a mothership model, the estimated clinical benefit is increased to 33.5 additional disability-free outcomes/1,000 admissions. If destination is determined by the estimated probability of a good outcome, 94% of patients would directly attend a CSC,

with only 6% of patients attending a local ASC. Figure 6 shows the catchment areas for the different types of units in drip-and-ship or mothership models. Only patients in remote outlying areas are predicted to benefit from attending a local ASC first. Compared to the drip-and-ship model, the travel time to the first admitting stroke unit is, on average, increased from 19 to 34 minutes, but travel time to a CSC is reduced from 94 to 42 minutes. Overall, the reduction in time to MT outweighs the increased time to IVT.

From the perspective of maximising clinical benefit of reperfusion treatment, most patients would gain most benefit most from bypassing their local ASC and directly attending a CSC. However, with the proportion of patients first attending one of the 24 CSCs increasing from 27% to 94%, there would be significant disruption to admission numbers, with average first admissions to a CSC rising from 918 to 3,187 and the largest centre increasing from 1,964 to 5,578. Average first admissions to ASCs would fall from 572 to 43, with 64 out of 83 ASCs depleted of all their stroke admissions. As this is likely to be unsustainable, we explore options of increasing the number of CSCs and examine the potential use of either a permitted maximum additional travel time in order to directly attend a CSC or the use of prehospital diagnostics to select patients to take directly to the CSC.

How many IVT-providing units in total?

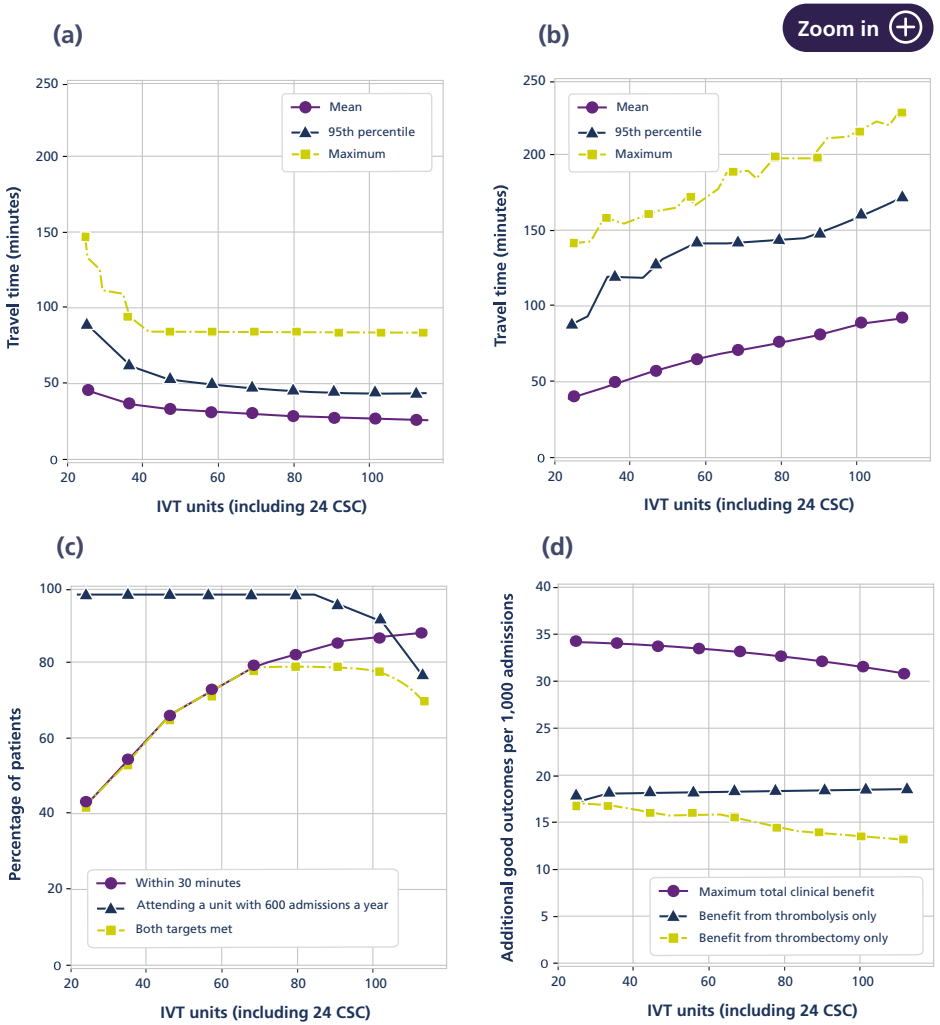
Figure 7 shows the effect of adding ASCs to the 24 CSCs. As the number of ASCs increases, average time to IVT reduces but time to MT increases. This results in a slight overall reduction in clinical benefit, as the loss in benefit from MT slightly outweighs the gain in benefit from IVT. In order to maintain the guideline of 600 admissions per year to an IVT-providing unit, there can be no more than 84 units in total. Above this number, an increasing proportion of patients will attend units with fewer than 600 admissions per year. If the maximum permitted unit size is 2,500 admissions per year, at least 46 units in total would be needed (assuming all patients attend their closest unit). This would increase to a minimum of 60 units if no unit could be larger than 2,000 admissions per year.

How many CSCs?

Figure 8 shows the effect of converting units from ASCs to CSCs, assuming a baseline of 24 CSCs. As more ASCs become CSCs, providing MT in addition to IVT, the time to MT reduces and the clinical benefit of reperfusion increases. The number of MT procedures per unit will reduce. If all new units must perform at least 150 MT procedures per year, assuming 10% of patients receive MT, the maximum total CSCs will be about 40. In such a configuration, just short of 50% of patients would directly attend a CSC.

Figure 7. The effect of adding ASCs to 24 CSCs. (a) Time to a unit providing IVT. (b) Time to a CSC providing MT. (c) Percentage of patients attending an IVT unit meeting size and travel time targets. (d) Predicted benefit of reperfusion treatment.

Zoom in



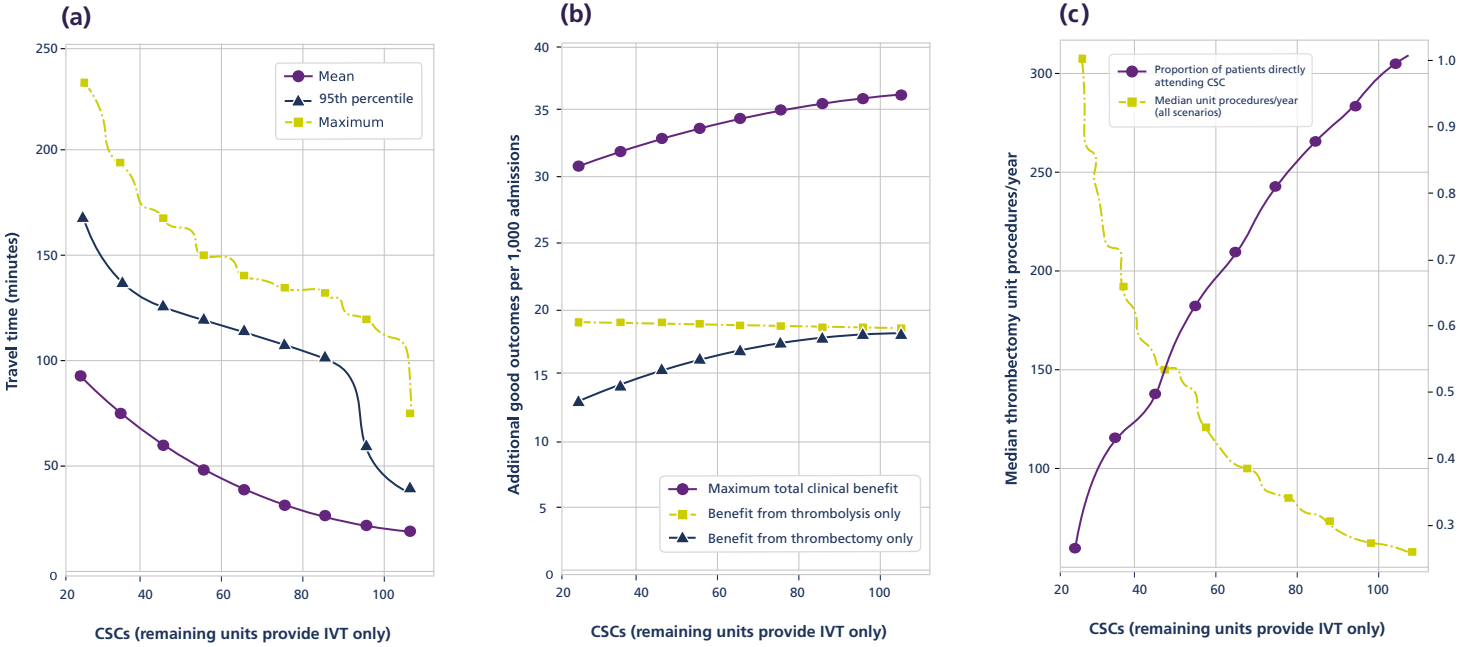
Implementing a maximum permitted additional travel time to a CSC

Figure 9 shows the effect if patients are transported directly to a CSC up to a maximum additional travel time compared with attending their closest unit. We refer to this as 'ambulance bias,' defined as the additional time that an ambulance crew is willing to travel in order to convey a patient directly to a CSC. A number of effects occur as ambulance bias increases: average time to IVT is increased, average time to MT is reduced (panel a), net clinical outcome is improved (panel b), admissions to ASCs fall (panel c), and admissions to CSCs increase (panel d). For example, if ambulance crews are willing to travel 15 minutes further in order to directly attend a CSC, the net benefit of reperfusion treatment increases from 31.1 to 32.3 additional good outcomes per 1,000 admissions. However, the proportion of all stroke patients admitted directly to a CSC would increase from 27% to 52%. The number of units with fewer than 300 first admissions per year increases from three to 18, while the number of units with fewer than 600 first admissions per year increases from 39 to 64 (of 83 ASCs in total). At the same time, the number of units with more than 2,000 first admissions increases from zero to eight, with the largest admitting close to 4,500 stroke patients/year.

Pre-hospital selection for LAO

In recent years, several methods to help ambulance paramedics select patients with LAO as potential candidates for MT have been developed.[115] We have used the performance of one of the most widely studied – the RACE pre-hospital diagnostic for LAO[116] – to assess the potential impact of selection of patients most likely to benefit from bypassing a nearer ASC and being transported directly to a CSC.

Applying the RACE pre-hospital diagnostic test for LAO, with all 'RACE-positive' patients taken directly to a CSC, increases the number of additional disability-free outcomes from 31.1 to 33.4 per 1,000 admissions. However, the proportion of all stroke patients admitted directly to a CSC would increase from 27% to 62%. The number of units with fewer than 300 first admissions per year increases from three to 30, while the number of units with fewer than 600 first admissions per year increases from 39 to 74 (out of 83 ASCs in total). At the same time, the number of units with more than 2,000 admissions increases from zero to 11.

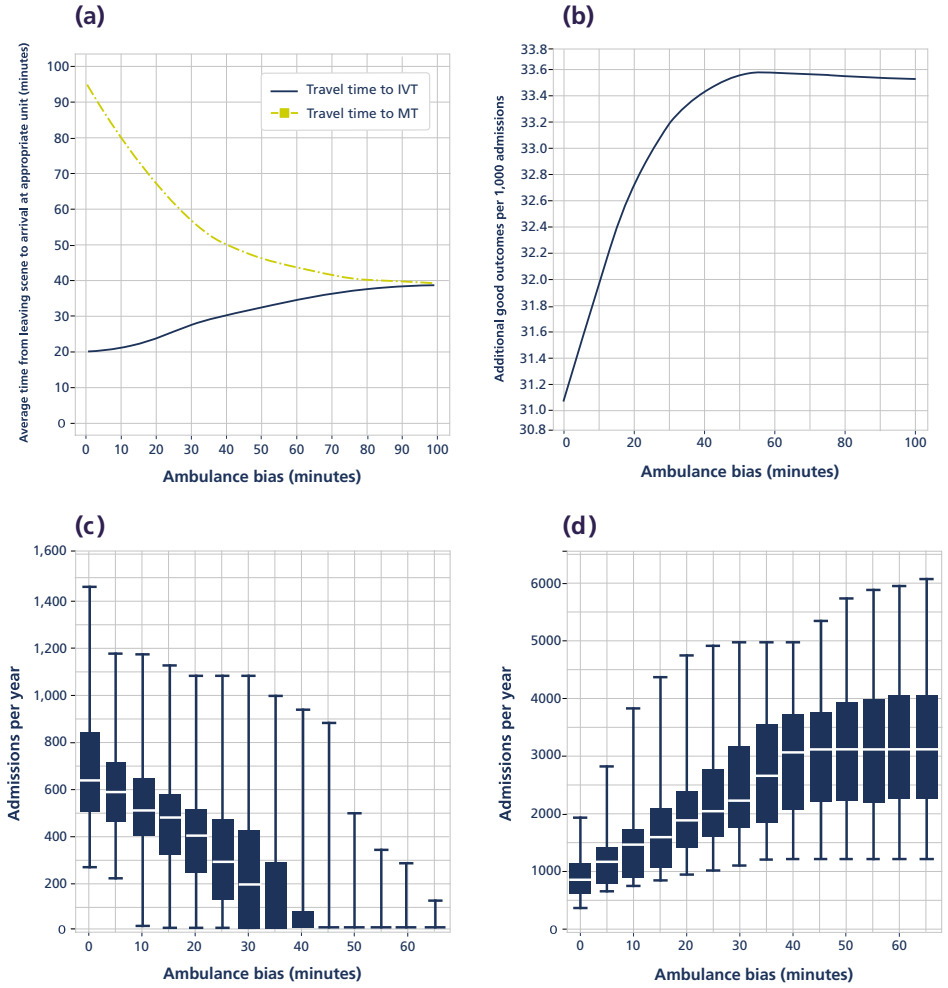


Zoom in

Figure 8. The effect of converting ASCs into CSCs (assuming 24 CSCs as a baseline and assuming there are 107 units in total, all providing at least IVT). (a) Travel time to a CSC. (b) Net clinical benefit. (c) Median MT procedures in a CSC and the proportion of patients directly attending a CSC.

Figure 9. The effect of ambulance bias (the maximum permitted additional travel time to take a patient directly to a CSC). (a) Travel time to IVT and MT. (b) Net clinical benefit. (c) Admission numbers to ASCs. (d) Admission numbers to CSCs. Box plots show median (midway line), interquartile range (box) and range (whiskers) for individual units. If a patient first attends an ASC, time to the CSC will include road transfer time and process-related delays. The model has 24 CSCs at the current neuroscience centres and ASCs at the remaining current acute stroke centres.

Zoom in



Planning footprint

We have also examined the effect of planning footprint size on the ability to meet these travel time and admission targets.[109] In brief, the smaller the planning footprint, the poorer the performance of the system, with planning at individual ICS level leading to significantly reduced capability to meet travel time and admission targets than planning over a larger area, such as NHS regions. Practically, hyperacute stroke care planning should be performed with as large a footprint as realistically can be achieved – in England, the formation of 20 **ISDNs**, typically including one or two ICSs, is based approximately around single CSCs, although in some cases (e.g. East Anglia) a larger planning footprint of several ISDNs is required.

Discussion

Our modelling of national configurations of hyperacute stroke centres, designed to maximise the population benefits from reconfiguration of acute stroke services, has shown the feasibility but also the compromises necessary to deliver these benefits. Maximum patient benefit is achieved by transporting patients directly to CSCs where both IVT and MT are available, but this has the potential to overwhelm CSCs with very large numbers of patients with suspected stroke, including mimics, while depleting ASCs of the large majority of their patients.

Currently, 61% of patients with acute stroke are admitted to a stroke unit with at least 600 admissions per year, and the NHS Long Term Plan (for England) proposes to increase this through centralisation into fewer larger units.[5] These centres would have staffing levels and competencies as specified in national standards[117, 118] and provide intensive (level 2) nursing and medical care for the initial 72 hours after onset (on average) before repatriation of the patient to local stepdown services for ongoing acute care and rehabilitation. In our model, a reduction from the current 107 English acute sites to between 73 and 81 centres (CSCs plus ASCs) would render it possible for all stroke patients to attend a unit of sufficient size, albeit with a reduction in the proportion of patients within 30 minutes' travel from the current 90% to 80–82% and with 95% and 98% of patients within 45 and 60 minutes' travel time, respectively.

Any large-scale reconfiguration of hyperacute stroke services involves striking a compromise between institutional size and travel time, with differential effects from centralisation in urban and rural areas. In seeking to balance these often-competing priorities, an additional issue arises in avoiding any large CSC being overwhelmed by unprecedented numbers of suspected stroke admissions (true strokes plus mimics). In accommodating this constraint, we sought solutions where the largest unit had no more than 2,000 confirmed stroke admissions/year, which is the current largest English CSC at Salford Royal Hospital. In configurations with all centres admitting between 600 and 2,000 admissions/year, fewer than 10% of centres would have more than 1,500 admissions/year. Large-scale reconfigurations raise significant issues around the capacity of a small number of very large CSCs, both in infrastructure and workforce, and the potential disadvantages of such large centres, particularly for frail patients or those without stroke, cannot simply be disregarded. Nonetheless, centralisation to 75–85 centres, with up to 40 centres being CSCs, could be expected to provide a significant benefit to many patients. To yield these benefits, the large majority of patients will travel only moderately further (if at all) to reach a CSC. The 95th percentile travel time would increase from 37 to 42 minutes. Consideration should be given to how the impact on the small proportion of patients most affected by the longer travel times and possible delays in treatment might be mitigated, including how the use of air ambulance services for secondary transfer might prove to be both faster and cost-effective for the most remote 1.5% (only 11–12% of whom might require MT).[119]

In an ideal configuration of hyperacute stroke care, all patients would live close to a CSC offering high-quality acute stroke unit care and both IVT and MT, but our studies suggest that providing all acute stroke care in CSCs in England (that is, a 'pure mothership' model) is not likely to be deliverable. On this basis, a hybrid model of CSCs and ASCs seems inevitable and desirable. Such a model of care reduces time to admission at the first centre (providing IVT) but will delay MT for many eligible patients. The delay comes from additional transport time and from organisational delays in arranging/starting onward travel.[114] Current DIDO times in the UK stand at a median of 2 hours 10 minutes, and this delay could be reduced by having ambulances wait at the first-admitting hospital in case **CT**/**CTA** indicates that MT is required or by otherwise prioritising ambulance provision for transfer to a CSC (as is now done in Eire and Catalonia).[120] It is clear that the substantial impact on ambulance services would need to be considered with any of these strategies.

The optimum balance between CSCs and ASCs will vary across the country. In particular, where populations are dense and differences in travel times between centres are small, such as in major metropolitan areas, there is little to be gained from imposing a further delay to treatment by calling first at a non-MT-capable ASC, and services are ideally delivered entirely through CSCs. In London, this would be in potentially fewer CSCs than the existing eight ASCs. Where populations are less dense in more rural areas, additional ASCs will be required to limit the maximum time from onset to assessment for IVT at the first hospital. However, if there remains an 'oversupply' of more local IVT services, time to MT will be increased significantly for the sake of only marginal improvements in time to IVT. The principal justification for maintaining ASCs in some areas is therefore to mitigate an otherwise unmanageable number of direct admissions to CSCs.

It may be considered clinically justifiable to accept a small delay in IVT for patients to be taken straight to a CSC, as this may significantly reduce overall time to MT at the cost of a smaller effect on time to IVT.[102] Indeed, this clinical justification is anecdotally reported to influence decision-making by ambulance paramedics, who may be willing to travel 15–30 minutes further to deliver the patient to a MT-capable centre; to this can be added the practicality of trying to avoid being called back to the closer ASC a short time later to convey the same patient to a CSC. Our work has shown how this phenomenon of ambulance bias has the potential to improve outcomes but also to destabilise stroke networks by simultaneously overwhelming CSCs and depleting ASCs of admissions, reducing a significant number of the latter below a threshold that might be considered sustainable. This factor must be built in when planning systems of care, as to disregard it risks substantial unintended consequences. Although some might suggest that this effect could be mitigated through the widespread use of pre-hospital selection scales for LAO stroke (such as RACE, for which the preliminary results of a **RCT** have been presented[121]), the low specificity of such tests suggests they would have a disappointingly small impact on the large numbers of patients who would be preferentially transferred directly to a CSC.

A final consideration is the geographic areas used for planning stroke networks. Our previous work has shown that the larger the planning footprint the better the solutions that may be found to maximise performance and sustainability.[107] Planning of both MT and IVT provision would therefore be best performed at the level of NHS regions (of which there are seven in England; plus the devolved nations) rather than the smaller footprints of ISDNs.

Conclusions

The advent of MT as a highly effective intervention for a significant minority of stroke patients is a disruptive innovation, which should stimulate rationalisation of services and urgent development of new capacity to deliver the treatment. Clinical benefit from reperfusion therapies is best achieved by maximising the proportion of patients who directly attend a CSC. Direct admission to an ASC provides clinical benefit only for a relatively small proportion of the population in remote regions of the country. However, a system based solely on CSCs (a mothership model) is unlikely to be sustainable due to the very large numbers of redirections that would occur, including many patients for whom reperfusion is inappropriate. ASCs are likely to be needed to help maintain a sustainable stroke system, and for this a reliable method of pre-hospital selection for cases of LAO (with both high sensitivity and specificity) will be required. Existing pre-hospital instruments do not yet have the required level of accuracy.

The twin objectives of maximising the population benefit from these interventions within a sustainable system are best served by an increase in the number of CSCs offering MT within an overall reduction in the number of centres offering hyperacute care (including IVT) organised in collaborative regional networks. Metropolitan areas will be best served by a small number of large CSCs with a direct-to-mothership policy, but more dispersed populations will require a hybrid arrangement of CSCs and ASCs in order to limit the maximum time to IVT through the use of a drip-and-ship approach.

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4 Organising ambulance services for effective implementation of mechanical thrombectomy

Chris Price and John Black

Key points

- Ambulance services and commissioners must be involved early in the planning of acute stroke **MT** pathways, including repatriation pathways.
- The content of a national emergency pathway for suspected stroke, which includes options for primary and secondary transfer for MT, should be standardised based on directly relevant clinical trial evidence.
- Services must plan to deal with the implications of an increasing number of MT secondary 'drip-and-ship' transfers, including efficient repatriation.
- The content of training and audit to support effective deployment of the emergency stroke pathway needs to be established.
- Services should be prepared for rapid adoption of technology that can improve the accuracy of **LAO** identification.

Current pre-hospital pathways

The centralisation of stroke care already requires ambulance services to provide pathways promoting rapid access to specialist care in line with national clinical guidelines.[122] Regional variations exist, but the current core components are:

- Call handlers should be trained to recognise people with symptoms indicating possible acute stroke, using dedicated clinical prioritisation software such as NHS Pathways/**AMPDS**, and to initiate an emergency response consistent with national ambulance standards. Although this has not changed substantially because of MT, operational staff and standards need to take into account that the emergency care pathway for stroke is becoming more complex, with potential implications for dispatched crews.
- Ambulance clinicians should identify patients with suspected stroke before they arrive at the hospital, using simple and sensitive clinical checklists such as **FAST**. Hypoglycaemia should always be excluded by measurement of capillary blood glucose. As FAST may not identify stroke causing other symptoms such as loss of co-ordination or vision, paramedics are also encouraged to make a provisional diagnosis based on clinical judgement alone. However, even with the use of FAST and blood glucose assessments, around 40% of pre-hospital suspected stroke patients later receive a non-stroke ('mimic') final diagnosis after admission, as many conditions produce similar symptoms. This additional burden of FAST-positive but non-stroke admissions deters unselected pre-hospital redirection to **CSC**s.
- Ambulance on-scene times should be kept to a minimum, and investigations more appropriately undertaken on arrival in hospital (e.g. 12-lead **ECG**) should not be performed on scene if the patient is being conveyed (see below). However, no national target for a maximum on-scene assessment time is set or monitored, and a lengthier assessment to identify patients potentially suitable for MT may prolong on-scene time.
- Ambulance pre-arrival alerts to the **ED** are associated with significant improvements in time to brain imaging and intervention for stroke patients.
- Transfer to the nearest CSC may require bypass of the nearest hospital. Pre-hospital redirection does not generally add significant extra journey time, as transport times to the nearest CSC are within 60 minutes for the majority of the UK population. Some regions avoid ambulance bypass through remote video assessment by a stroke specialist once the patient arrives at the nearest hospital. However, for MT, the much smaller number of regional CSCs in the UK means that it is necessary to balance the efficiency of pre-hospital redirection versus assessment in the nearest **ASC** with or without video, allied to onward transfer.

When interpreting national guidelines, the results of a recent survey of stroke pathways within ambulance services in the UK show considerable variation (Table 3).[123] As MT provision expands, it will be important for regions to consider whether some of these pathway differences may impact on efficient direct transfers for treatment, such as the conscious level (**GCS**) threshold below which patients will be taken to the nearest ASC rather than directly to a CSC.

Table 3. Content of UK ambulance stroke pathways in May 2018. Adapted from McClelland *et al* (2018).[122]

Ambulance service	Stroke identification tool	Time (hours)	GCS exclusion	Capillary glucose (mmol/L) exclusion	Seizures excluded
1	FAST	4	<8	<4.0	Yes
2	FAST	4.5			Yes
3	FAST	5	Conscious	<3.0	Yes
4	FAST + AVVV	4.5			
5	FAST	5.5		<4.0	Yes
6	FAST				
7	FAST	Variable		<4.0	Yes
8	FAST	3			
9	FAST MEND	Variable		<3.5	
10	FAST	4.5		Hypoglycaemia	
11	FAST	5	<11	<3.5	
12	FAST	4.5		<4.0	
13	FAST Leg/visual symptoms	<12	<8		Yes
14	FAST	4			

The impact of MT on regional ambulance services

The main immediate impact of MT provision for ambulance services will reflect the further centralisation of specialist care for a small proportion of patients with major stroke. It is estimated that 10% of emergency stroke admissions are suitable for MT,[34] although there will be some geographical variation. In the current system using FAST alone for identification of possible stroke, five out of 100 suspected stroke patients who present to ambulance services are likely to have the clinical and radiological characteristics appropriate for MT. These patients should be identified early and rapidly transported to a CSC to reduce time to treatment. In addition, as advanced imaging becomes more widely available and treatment decisions for patients with unknown symptom onset (e.g. wake-up presentation) can be based on assessment of potentially salvageable brain tissue, the proportion of cases needing rapid secondary transfer to the CSC will increase further, with an increased demand on ambulance resources.

If the nearest acute hospital provides MT on site, there may be no immediate impact on emergency ambulance cycle times. However, as most sites receiving acute stroke patients do not have MT capability, all ambulance services will be increasingly affected by a 'drip-and-ship' secondary transfer model for patients assessed as potentially suitable for MT at the initial ASC. Currently, there are no clinical or diagnostic processes used by UK ambulance services to identify patients who may be suitable to bypass a nearer ASC and transfer directly to a CSC (see below).

To provide an efficient MT service, services must consider the following:

- *Ambulance resources* – Additional rapid transfer may be required from the initial acute hospital to the CSC, which is likely to increase pressure on emergency frontline ambulance responsiveness for other emergencies. The potential impact needs to be considered by systems, such as the **ISDN**s recently established in England. It is already recommended that this secondary transfer receives the same emergency response as the initial dispatch, as this is a confirmed time-critical emergency.[123] The latest observational evidence from **SSNAP** indicates a median **DIDO** time in the UK of 2 hours 10 minutes, because of initial clinical and radiological assessments, communication between sites, initiation and in many cases completion of **IVT**, and the availability of a second emergency ambulance. As ASC DIDO times improve (ideally to 20 minutes), it may be feasible for the first ambulance to wait while the patient is assessed to reduce the risk of an ambulance transfer delay if an initial rapid screen during handover in the ASC confirms that MT may be appropriate. An Australian study demonstrated that using the initial ambulance crew for secondary transfer was associated with shorter DIDO times,[120] but additional resources may be required to ensure that the crew remain available following the initial patient handover.

- *Skills* – During secondary transfer, an intravenous infusion may be required to continuously administer alteplase or parenteral **BP**-lowering treatment (if agreed by local protocols). Transfer should not be delayed waiting for these treatments to finish. Ambulance clinicians are not currently trained to supervise thrombolytic infusions or provide emergency management of hypertension during acute stroke. An appropriately trained healthcare professional (doctor or nurse) from the ASC is required to accompany a patient receiving an alteplase infusion during ambulance transfer to supervise clinical management. However, increasing clinical trial evidence suggests that a tenecteplase bolus injection may be an equivalent thrombolytic agent,[124] and infusions would not be required if tenecteplase were licensed for this indication. Whether or not additional clinicians are present, ambulance protocols are needed for complications such as angioedema, bleeding and seizures. An anaesthetic transfer may occasionally be needed if the level of consciousness is deteriorating or if the patient's airway is jeopardised – both situations seen more commonly in basilar artery occlusion.
- *Air ambulance* – Secondary transfer by air ambulance may need to be considered in parts of the UK where transfer times to the CSC are likely to exceed 60 minutes, as this may reduce call-to-intervention times in these circumstances.[125] Most CSCs are also tertiary neuroscience and/or major trauma centres with helipad facilities and will be accustomed to receiving patients by helicopter.

Selective pre-hospital redirection of suspected large artery occlusion

Clinical identification scales

Once stroke is suspected using the FAST test and/or clinical judgement, ambulance services in the UK currently have no pre-hospital stratification to identify patients potentially suitable for MT. Identification scales for LAO that use combinations of neurological symptoms to create a score indicating the probability of LAO have been published (Table 4).[126, 127]

Table 4. Examples of published LAO symptom scales.[116,128,129]

RACE[116]	FAST-ED[128]	GFAST[129]
Facial palsy • Absent or mild (0) • Mild (1) • Moderate to severe (2) **Arm motor function** • Normal to mild (0) • Moderate (1) • Severe (2) **Leg motor function** • Normal to mild (0) • Moderate (1) • Severe (2) **Head and gaze deviation** • Absent (0) • Present (1) **Aphasia* (if right hemiparesis)** • Performs both tasks correctly (0) • Performs one task correctly (1) • Performs neither task (2) **Agnosia† (if left hemiparesis)** • Performs both tasks correctly (0) • Performs one task correctly (1) • Performs neither task (2)	**Facial palsy** • Normal or minor paralysis (0) • Partial or complete paralysis (1) **Arm weakness** • No drift (0) • Drift or some effort against gravity (1) • No effort against gravity or no movement (2) **Speech changes** • Absent (0) • Mild to moderate (1) • Severe, global aphasia or mute (2) **Eye deviation** • Absent (0) • Partial (1) • Forced deviation (2) **Denial/neglect** • Absent (0) • Extinction to bilateral simultaneous stimulation in only one sensory modality (1) • Does not recognise own hand or orients only to one side of the body (2)	• Gaze in only one direction (1) • Face/facial drop (1) • Arms/legs weak (1) • Speech slurred, confused (1) • Time lost is brain lost (1)
Total score 0–9 • Score ≥5 indicates possibility of LAO	Risk of LAO stroke • Score 0–1: <15% • Score 2–3: ~30% • Score ≥4: ≥~60%	Total score 0–4 • Score 3–4 considered 'positive' for possible LAO

*Aphasia: Ask the patient to (1) "Close your eyes", and (2) "Make a fist", and evaluate if the patient obeys.
†Agnosia: Ask the patient: (1) "Whose arm is this?" while showing them the paretic arm, and evaluate if they recognise their own arm, and (2) "Can you lift both arms and clap" and evaluate if they recognise their functional impairment.

Most of these scales were developed through retrospective analysis of hospital datasets compared against a radiological diagnosis[130] and, consequently, they do not reflect the typical suspected stroke population presenting to ambulance services. Scores are unlikely to have sufficiently high specificity if used in isolation, because:

- at least 12% of hospitalised strokes are due to haemorrhage
- lacunar stroke can occasionally result in a high symptom severity score due to face/arm/leg weakness (**NIHSS** >10), but LAO will not be present
- 'atypical' mild LAO presentations occur in up to 20% of patients (**see Chapter 2**)
- many mimic conditions will not be excluded
- some symptoms may not yet have developed at the early stage when ambulance personnel assess patients
- in some patients, MT would not be appropriate, even if LAO is present, for other reasons, such as pre-existing severe dementia or disability.

The best-case scenario (in hospital populations with few mimics) is that clinical scores fail to identify 20% of LAOs in exchange for 15% false-positive identification of mimics. Clinical cut-off scores with sensitivity of 90% would label most suspected stroke patients as possible LAO due to the associated low specificity, which would defeat the purpose of pre-hospital stratification and risk overwhelming CSCs.[130]

The only randomised pragmatic trial to select patients for pre-hospital redirection to CSCs combined the RACE scale with specialist telephone review in Catalonia, resulting in a 56-minute reduction in time to MT but with a 35-minute delay in IVT treatment and no overall change in health outcomes.[131] Only 46% of redirected patients had LAO. An observational study from Stockholm has also shown that a combination of symptoms identified by ambulance practitioners (arm + leg weakness) and specialist telephone review resulted in MT being performed 69 minutes faster than the previous drip-and-ship pathway, but with an LAO positive predictive value of only 41%.[132] Therefore, although some patients suitable for MT may receive faster treatment following routine pre-hospital application of a LAO scale, arrangements must remain in place to enable rapid secondary transfer of 'false-negative' patients with LAO who were not identified pre-hospital to ensure that LAO cases with less typical or deteriorating symptoms are still able to receive treatment. It would also be essential to have systems in place for the efficient repatriation of untreated stroke and mimic patients from the CSC, who will arrive in significantly larger volumes than through a drip-and-ship approach.

Overall, the attractiveness of ambulance redirection for patients with LAO symptoms is currently offset by the complexities created in terms of false-positive direct transfers and false-negative LAO patients who still arrive at the local ASC first. Systems to deal with these groups would need to be managed actively across a large geographical area and will involve an additional burden on ambulance services. However, clinical identification scales may be useful in future as a first triage tool to decide whether to activate a remote specialist review or deploy a point-of-care diagnostic for LAO.

Remote stroke specialist review

Remote video review by a stroke specialist is not a new concept but has previously been limited by the lack of technology in ambulances to support implementation and by concerns that it may extend the pre-hospital phase without necessarily changing the patient destination or treatment.[133, 134] Some ambulance services in the UK are investing in this capability, which could enable accurate pre-hospital identification of patients who are more likely to have LAO and be suitable for MT. The use of a LAO identification scale by the ambulance service may help identify patients suitable for review by a remote stroke specialist, who can then use their expertise in history, examination, interpretation and knowledge of mimics to decide between redirection to a CSC or conveyance to the nearest ASC. Although the specialist would not be able to specifically identify LAO among ischaemic and haemorrhagic stroke, and the process might extend the prehospital phase, it is possible that the redirected group would be more likely to receive treatment and that mimic transfers might be reduced, but this approach of remote specialist video review has to date not been formally evaluated.

Mobile stroke units

As technology becomes more affordable or reliable, clinical trials are evaluating the benefits for IVT delivery when combined with ambulances offering portable head **CT** scan capability.[135] Although there is already published evidence that adapted ambulances ('mobile stroke units' with a physician and CT scanner on board) can reduce time from call to initiation of IVT by 15–30 minutes, the resource implications are substantial, and there is currently limited evidence that MT is facilitated, although this seems likely.[136] The mobile stroke unit trials showed benefit for patients living near large urban stroke centres where the vehicle was housed and vascular neurologists were immediately available. The units were not part of regional ambulance service provision, and a standard emergency ambulance was dispatched in parallel because most patients were either stroke cases

that did not receive IVT or mimic presentations that needed transfer to the ED. Although mobile stroke units can reduce treatment times for IVT in specific high-resource settings and have recently been shown to improve outcomes for patients eligible for IVT in the urban US,[137] further evidence is needed to show whether remote or direct specialist review pre-hospital can expedite MT while maintaining cost-effectiveness in the UK healthcare system.

Diagnostics

There is currently no point-of-care diagnostic test for stroke or LAO for use in ambulances.[138] However, because of the obvious benefits in informing appropriate triage destination for suspected stroke patients, this is an expanding research topic, with clinical trials currently evaluating point-of-care blood assays and non-invasive portable technologies such as **EEG** devices to help differentiate ischaemic stroke, haemorrhagic stroke, LAO and stroke mimics. If these technologies are subsequently supported by the clinical evidence, hospital and ambulance services should prepare to adopt them by agreeing on funding, their role in the clinical pathway and training implications.

Training

There is no standardised training module for pre-hospital stroke care, and most training is provided locally to reflect pathway preferences and regional service configurations. This approach has been reasonable for the use of FAST to initiate a linear pathway, but more standardised content or models may be required for workforce training for an additional pre-hospital LAO identification step plus selective redirection response.

Previous observational studies have shown that whole-service system performance for IVT delivery can be changed through a programme of multidisciplinary workshops to implement new clinical protocols,[139] whereas specific aspects of care – such as reducing the time on scene – can be addressed by smaller scale initiatives targeted at paramedics.[140] The cost-effectiveness of acute hospital care was improved when the **PASTA** assessment was used to standardise pre-hospital information collection and handover communication,[141] probably through improvements in the quality of IVT treatment decisions at NHS hospitals lacking continuous stroke specialist availability.[142]

Training content will need to remain under review to enable effective future deployment of a new diagnostic and remote specialist video assessment. As advanced imaging for patient selection becomes more available, it will also be necessary for training to acknowledge that selected patients with an unknown onset time (for example, those waking with symptoms) should have the same MT response as those known to have onset within the previous 6 hours.

Audit

The evidence underpinning MT treatment clearly shows the importance of minimising delays along the whole pathway from symptom onset. Due to the additional brain imaging required and possible secondary transfer to a CSC, efficient early care is particularly important – for example, the time spent on scene and overall call-to-CT time should be as short as possible once stroke is suspected.

For all suspected stroke cases with recent onset, it is necessary to have an audit standard for on-scene time, as well as initial response. This is a potentially complex issue, as introduction of remote assessment or diagnostics may extend on-scene time but reduce the overall time from onset to MT through improved early stratification and pre-notification. As well as services aiming to achieve a maximum on-scene target time for all suspected acute stroke (for example, 20 minutes), this should be reported separately for MT cohorts in the context of overall onset-to-treatment time. It will also be necessary to contextualise the reporting of thrombectomy provision according to national changes in ambulance response criteria. For example, the current plan to extend an emergency response to patients within 10 hours of symptom onset will lead to a relative increase in the proportion requiring advanced imaging to make a treatment decision, thereby prolonging in-hospital delays, and a lower overall proportion of patients will be suitable for treatment.

All English ambulance services regularly audit and report their responsiveness for patients with acute stroke to NHS England, and compliance with a stroke care diagnostic care bundle is published nationally.[143] This is reported for the whole emergency stroke pathway, using data from ambulance and hospital services to establish delays and identify training needs, and should be extended to recognise the whole MT pathway, as well as initial IVT. As well as service-level audit, feedback to individual paramedics about adherence to clinical protocols improves performance.[144]

5 Imaging for stroke thrombectomy and resource implications

Alexander Mortimer

Key points

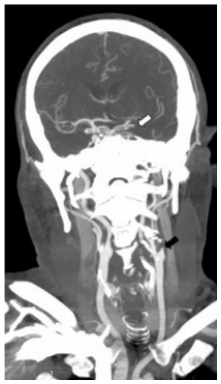
- Stroke **MT** requires additional imaging for patient selection, and a combination of **NCCT** and **CTA** represents the most appropriate combination to allow this.
- Most patients will be imaged in **ASC**s before onward referral to **CSC**s, and standard protocols are required.
- The relatively low levels of MT currently being performed in the UK are, in part, due to lack of routine use of CTA in local stroke imaging protocols.
- A number of solutions exist to aid better implementation of the necessary imaging, but most need increased resourcing and appropriate training in image interpretation.
- The role of multiphase CTA or **CTP** in addition to standard **CT**/CTA remains unclear in early presenting patients. For late presenters, either approach may be used up to 6–12 hours, but current evidence only supports CTP triage thereafter, so, in the longer term, implementation of CTP at ASCs will be required in addition to CT/CTA to select patients.

Emergency vascular imaging of stroke due to **LAO** is a critical step in the selection of appropriate patients for onward referral for MT. As most initial stroke imaging will be performed in ASCs that lack neuroscience centres with neuroradiology expertise, this is where the largest expansion in provision of acute stroke imaging will be needed. With the UK currently significantly below other western European countries in terms of MT rates,[145] increased use of appropriate advanced imaging to identify patients with LAO stroke swiftly is a key step in improving uptake of this highly effective treatment.

Imaging modalities in acute stroke

Broadly, imaging for acute stroke can be performed using CT or **MRI** techniques. In the UK, CT is the basis of most emergency neuroimaging due to speed and ease of access, and this lends itself well to stroke imaging, which is so time critical. Furthermore, use of acute NCCT prior to **IVT** is well established. Much of the information needed for MT triage can be extrapolated from NCCT combined with single-phase CTA, the latter involving a CT scan of the head and neck after intravenous injection of a timed bolus of iodinated contrast medium to image the cervical and intracranial arteries (Figure 10). This imaging strategy formed the sole basis for MT selection in four of the initial published trials.[8,11,12,16] Together, NCCT and CTA allow identification of the site of intracranial occlusion, non-invasive assessment of the cervical vessels and any tandem cervical arterial lesion, estimation of ischaemic core infarct, and, to a degree, collateral flow assessment plus cortical venous opacification, which is increasingly recognised as a marker of effective collateral flow. Combined NCCT/CTA therefore represents the minimum baseline imaging required for effective diagnosis and triage of patients with accute stroke, and universal coverage in all hospitals receiving emergency stroke patients represents the first phase in forming effective acute stroke MT networks across the UK.

Figure 10. CTA showing an atherosclerotic left cervical internal carotid artery occlusion (black arrow) and intracranial left internal carotid artery occlusion (white arrow).

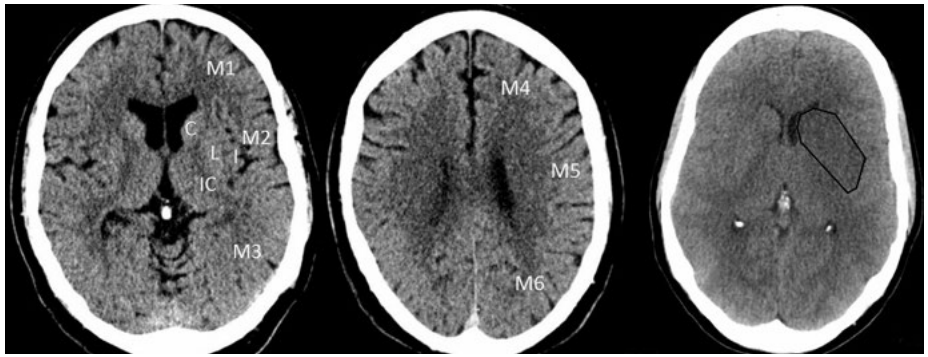


Zoom in

Non-contrast CT allows exclusion of intracerebral haemorrhage and initial estimation of core infarct extent, displayed as regions of low density caused by a shift in brain tissue water content secondary to ischaemia. Core infarct of the **MCA** territory can be estimated using the **ASPECTS** system, which divides the MCA territory into 10 regions, covering the basal ganglionic and supraganglionic levels (Figure 11). A normal scan is designated a score of 10, with one point subtracted for each area with features of infarct. Some MT trials excluded patients with ASPECTS <6, as prior observational evidence suggested re-canalisation could be futile or could be harmful in patients with low ASPECTS. Meta-analysis of trials suggests clear benefit for patients with ASPECTS >5,[19] but data for patients with low ASPECTS (0–5) are currently limited. Criticisms of the ASPECTS system include moderate inter-rater variability,[146] failure to correlate with infarct volume and failure to take into account the functional significance of the infarct location, but it is an established predictor of stroke outcome.

Figure 11. Non-contrast CT ASPECTS. Scoring regions at ganglionic (left) and supra-ganglionic levels (centre). Example case (right) showing low-density infarction in left caudate nucleus, lentiform nucleus and insular cortex outlined in black with an ASPECTS of 7. C, caudate nucleus; I, insular cortex; IC, internal capsule; L, lentiform nucleus; M1–3, cortical regions at the ganglionic level; M4–6, cortical regions at the supraganglionic level.

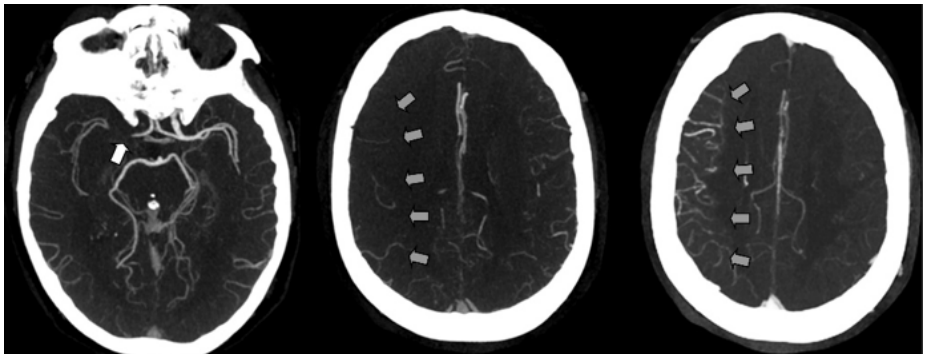
Zoom in



Although most radiology departments routinely provide NCCT, CTA is variably provided but is of great practical use, including in 'grey-area' IVT decision-making. As a result of more routine use of CTA, the number of patients identified as eligible for MT (and possibly IVT) will increase. Multi-phase CTA is an additional tool that involves second and/or third CT acquisition of just the head after initial-phase CTA (aortic arch through head). Use of this technique was established in the North American-led MT trials up to 12 hours after stroke onset.[13,15] It allows dynamic assessment of the collateral flow, may improve outcome prediction over single-phase CTA[147] and also has higher sensitivity for more distal occlusions.[148] This technique is particularly useful in cases where the initial-phase examination is performed relatively early following contrast medium injection or in patients with reduced cardiac output. In both scenarios, there may well be underestimation of collateral flow on a single-phase examination (Figure 12). Multi-phase CTA is an option in radiology departments with an established CTA service. Although it is slightly more complex in image acquisition and interpretation, it becomes a relatively straightforward examination to deliver once there is departmental experience. An alternative option to aid interpretation is remote specialist neuroradiologist assessment of the multi-phase imaging, perhaps if this modality is implemented across a network.

Figure 12. Dual-phase CTA. Axial maximum intensity projection CTA showing right terminal internal carotid artery occlusion (left, arrow). Early arterial phase CTA (centre) showing relatively poor collateral flow to the right hemisphere (arrows). Venous-phase CTA (right) showing delayed collateral filling of the pial network over the right hemisphere (arrows).

Zoom in

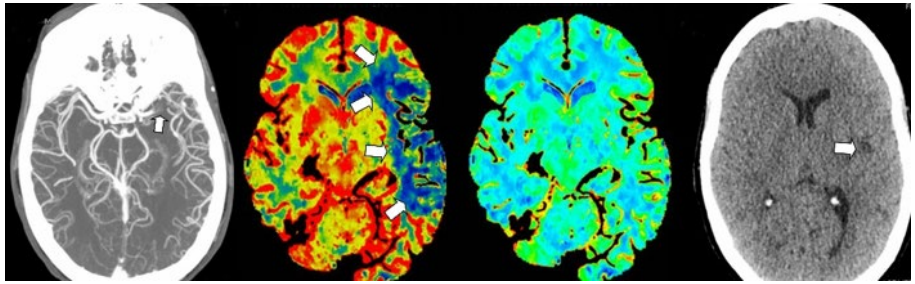


Computed tomography perfusion allows discrimination of the non-salvageable core infarct from salvageable penumbra, with the aim of identifying a 'mismatch' between the extent of each based on dynamic measurement of iodine contrast density as it passes through the brain tissue (Figure 13). Computed tomography perfusion requires additional imaging and contrast injection plus image post-processing using semi-automated or fully automated software and is higher dose than an additional delayed head phase of CTA. Image acquisition for CTP is often relatively simple using modern systems but does require some additional training for radiographers (perhaps through a short elective period in a neuroscience department) plus support from applications specialists from scanner manufacturers to help establish reliable local protocols.

Computed tomography perfusion was used as part of imaging selection in several **RCT**s[9, 14, 15] in which clinical results were superior relative to other trials that treated patients within 6 hours based on CT/CTA alone. However, routine use of CTP imaging in patents presenting early (conventionally that is within 6 hours) is more controversial, and expert opinion remains divided. With more extensive patient selection in the under-6-hour group comes the risk of denying treatment to a group of patients who do not meet strict (RCT-derived) CTP eligibility criteria but would still benefit from MT. Indeed, *post-hoc* analysis of the **MR CLEAN** trial suggests that this would potentially often be the case.[85]

Figure 13. CTP. Axial CTA (left) showing left M1 MCA occlusion (arrow) and good collateral flow. CTP maps of cerebral blood flow (centre left) and cerebral blood volume (centre right) approximating to maps of a large penumbra (arrows) and no clear infarct core, respectively. Post-MT CT (right, arrow) showing small insular infarct only.

Zoom in



It is important to note that CTP formed the basis for imaging selection in the **DEFUSE**-3 and **DAWN** trials, which investigated MT treatment of patients **LKW** beyond 6 hours up to 16 and 24 hours, respectively, and which found evidence of significant benefit for MT in appropriately selected patients (selected by perfusion ± clinical criteria).[17,18] Following the results of these trials, there will be an increasing need to use perfusion imaging in wake-up stroke or late-presenting patients. As CTP will not be available in many hospitals receiving these patients, a decision on transfer to neurointerventional centres will most commonly have to be made on the basis of NCCT and CTA (often with CTP being undertaken in the MT centre on arrival). In cases of favourable collateral flow and limited core infarction, this may be a straightforward decision, but for more borderline cases, CTP performed in ASCs to allow decision-making prior to consideration of transfer would be very useful and may be considered mandatory for patients in the 12–24-hour window. Registry-acquired data suggest that patients may still benefit from MT if selected using NCCT/CTA alone in the 6.5–24-hour window.[149] This needs to be confirmed in ongoing trials.

Computed tomography perfusion is certainly useful in a number of scenarios beyond delayed presentation though: confirming suspicion of very early widespread core infarction, identifying salvageable penumbra despite a large core infarct, and determining the extent of ischaemia in patients with a mild clinical syndrome but proximal occlusion. Computed tomography perfusion can be helpful in clinical practice to aid decision making on the use of either IVT or MT in cases that are uncertain based on clinical or other criteria, including CT/CTA alone. Most neurointerventional centres have CTP capability and variably use this tool depending on local preference, but radiology expertise may be limited in non-neuroscience centres. Use of validated automated software (such as those used in published trials, e.g. **RAPID**®[13,14,17,18] or MIStar®[150]) to provide the local clinical team with a technical report as a basis for discussion with the neurointerventional centre would be a pragmatic way of breaking down barriers to adopting CTP for the proportion of acute stroke patients who do require it. Adoption of CTP in ASCs, particularly to improve selection in late-presenting and wake-up strokes, represents a second phase in the evolution of stroke imaging in the UK.

Magnetic resonance imaging offers another option in acute stroke: **MRA** can be used to identify sites of arterial occlusion, and specific sequences such as **DWI** and **FLAIR** imaging are very sensitive in determining the extent of early core infarction. As for CT, perfusion techniques allow identification of the extent of ischaemic but salvageable brain ('penumbra'). In other countries, particularly France, MRI is used for a much higher proportion of acute stroke imaging. However, access to hyperacute MRI in UK hospitals is limited. Magnetic resonance imaging scanners are commonly not situated close to **ED**s, and MRI departments are most frequently configured as an outpatient imaging facility, with variable access for acute or out-of-hours cases. In our practice, MRI is most useful as an occasional decision-making tool, particularly in cases of basilar artery occlusion that present at later timeframes to assess the extent of core infarction in the posterior circulation. Although it is possible to prognosticate with CTA-based scoring systems,[151] directly imaging the brainstem is not easy using CT, and MRI may be superior in this situation. Yet, in addition to the factors described, the practicalities of routinely scanning acutely unwell patients with MRI (which can be more time consuming and subject to degradation by motion artefact in restless patients), coupled with the difficulties in accessing acute MRI in the UK, will limit widespread adoption of MRI for the foreseeable future.

Implementation of routine computed tomography angiography

Barriers and solutions to more widespread, routine and timely use of CTA at both departmental and individual levels involve image acquisition, image interpretation and image transfer.

Computed tomography angiography requires connection to a contrast-medium pump and acquisition of a second localiser before image acquisition; however, the actual image acquisition takes seconds on modern CT systems, and pre-hospital alerts can minimise delays, allowing contrast-medium pumps to be loaded before patients arrive.

A number of studies have demonstrated no significant delay in delivery of IVT if CTA is acquired routinely,[152,153] as CTA can be acquired even before NCCT can be reconstructed and reviewed. Alternatively, the alteplase bolus can be administered prior to CTA acquisition, although this can still result in delay to the subsequent 90% infusion (future use of bolus-only tenecteplase for IVT would eliminate that issue). If CTA is not performed at to the time of initial NCCT brain, delays in transferring patients from wards or EDs back to radiology departments for CTA will significantly delay stroke onset to re-canalisation times for MT. Local protocols should be established to minimise 'door-to-CTA times', which will, in turn, improve **DIDO** times.[154] This could be aided by rapid front-door assessment and referral for CTA for all patients with a disabling deficit presenting within acute reperfusion time window 4.5/6 or 24 hours depending on the availability of reperfusion treatment and advanced brain imaging (CTP, multi-phase CTA-CS or MRI).

Concerns regarding the risk of contrast-induced nephropathy have been cited as a reason not to incorporate CTA into routine imaging for acute stroke patients but these are probably unfounded. In two retrospective reviews of 175 and 224 patients,[155, 156] the incidence of contrast nephropathy was 2.9% and 3%, respectively. In a subsequent observational cohort study, contrast agents did not seem to cause rates of renal injury above those normally encountered in this population.[157] Another consideration is the increased radiation dose incurred by additional acquisitions. At the population level, the potential for significant benefit, as demonstrated by trial evidence, will invariably outweigh the risk of radiation in a largely elderly patient cohort. The risk to young patients is higher, but the potential for long-term morbidity through failing to identify and re-canalise a proximal intracranial LAO is also high in this population, even in the case of pregnancy. As with all CT imaging decisions, a radiation risk–benefit decision needs to be made, but the balance is strongly in favour of the use of advanced imaging in patients with potentially severely disabling stroke who present within a time window for reperfusion treatment.

Acute radiology services across the UK are stretched and under-resourced in terms of reporting capacity.[158] Anecdotally, there are concerns that routine implementation of CTA for a large number of patients with acute neurological presentations would stretch resources further in terms of scanning and reporting time. The extra activity with implementation of more routine use of CTA should be linked to financial incentives for the receiving hospitals in order to facilitate an enhanced stroke imaging service. A distinction also needs to be made between the need for urgent CTA review in acute stroke for immediate decision-making – perhaps stroke physicians supported by artificial intelligence decision-support tools or regionalisation to CSCs – and the need for a formal radiology report on a CTA. The former is immediate, but the latter need not occur for 48–72 hours or even longer and could therefore be handled as semi-elective work. There are then multiple options available for delayed formal CTA reporting to ASCs – including skill-mix extension of radiographer CT report (e.g. NCCT [head] freeing up radiologist to report CTA), outsourcing, insourcing and contracted arrangements with regional CSCs.

Implementation of advanced brain imaging should involve collaboration with industry to aid standardisation of scan protocols. More widespread radiographer training will be needed, which could be achieved by identifying a local lead(s) to undertake a short elective period at a neuroscience centre to learn and disseminate protocols, pearls and pitfalls. Alternatively, staff from neuroscience centres with established services could visit and aid construction of services in referring hospitals. Indeed, such initiatives are already occurring *ad hoc* at a local level in the UK.

Although NCCT is seen as a general investigation, there is often an assertion that CTA is a specialist investigation, and many radiologists whose subspecialty interest lies in another field may feel they lack competency in reporting these examinations without additional training. Short, intensive CTA training courses can significantly reduce discrepancies among radiology trainees,[159] and it is highly likely that this could be replicated for consultant radiologists who regularly report acute imaging. However, some co-ordination and funding for such training is required. A longer-term solution is the recent inclusion of stroke CTA interpretation in core radiology registrar training, with the potential for the same to be applied to stroke physicians.

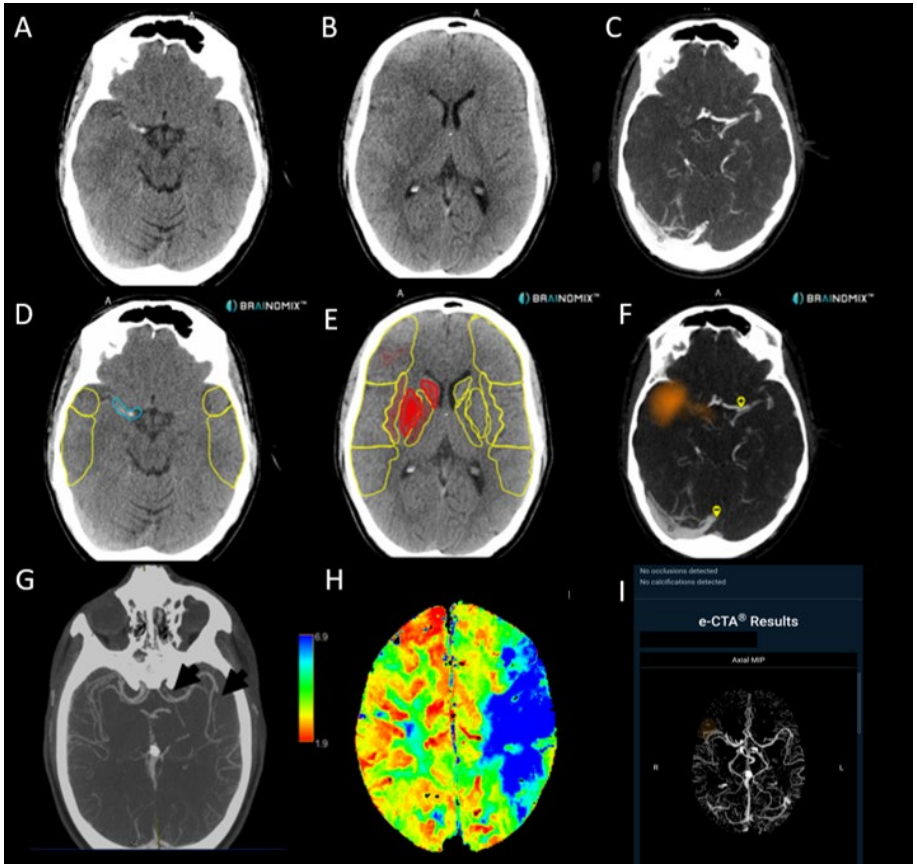
Automated decision aid software to assess NCCT (for core infarct via ASPECTS) and CTA for LAO to aid identification and speed up referral is already commercially available and could be a major aid to MT implementation (Figure 14). More recently, central funding has allowed for more widespread implementation of these systems – perhaps the most widely employed are RAPID and Brainomix® e-Stroke. Independent validation of these tools is starting to be published.[160] Methods of core infarct and LAO detection vary, as do the sensitivity and specificity of artificial intelligence platforms for diagnosis of these features (reviewed in depth by Murray *et al*).[161] It is therefore imperative that clinical decisions based on artificial intelligence interpretation of acute imaging are made by clinicians who are aware of the limitations of artificial intelligence and are able to interpret the imaging independently. However, potential major advantages of these systems are: i) improving workflow with immediate image availability to all who need to see it via cloud-based systems from ASCs to CSCs to facilitate more rapid transfer of patients, and ii) supporting less-experienced clinicians to immediately identify patients very likely to benefit from MT. Implementation of these artificial intelligence platforms in stroke networks has been associated with large reductions in DIDO times.[162]

With more routine use of MT, local networks should be constructed with the aim of strengthening inter-hospital links and governance. Imaging is an important facet of this, and it is vital for local leads for neuroimaging to be involved in stroke networks. On a practical level, fast image transfer to the MT centre is needed to obtain an interventional neuroradiology opinion prior to transfer. This could involve access to web-based **PACS** viewers or a standardised imaging cloud shared by all hospitals within a network, and artificial intelligence platforms essentially deliver this and are increasingly being used in England. Contributing to upkeep of these systems incurs a financial cost that may need to be shared across NHS organisations, but in the case of regional PACS but would have significant clinical advantages that extend far beyond stroke.

As MT provision extends to 24/7 coverage, around-the-clock expert imaging interpretation will be needed to facilitate clinical decision-making. As above, a formal immediate CT/CTA report from a local radiology department is not necessary out of hours; indeed, many hospitals use outsourced emergency radiology reporting with variable CTA expertise, and the number of radiologists with a neuroradiology interest in most hospitals is small.

Figure 14. (A) and (D) Axial NCCT demonstrating dense right terminal ICA and M1 MCA with automated detection using Brainomix®. (B) and (E) Automated ASPECTS analysis using Brainomix. (C) and (F) Automated detection of a right terminal ICA/M1 occlusion on CTA using Brainomix. (G) Axial MIP reconstruction of a CTA in a patient with left ICA and M2 occlusions. (H) Mean transit time map showing extent of ischaemia resulting from the occlusion. (I) Brainomix e-CTA® analysis fails to identify the abnormalities, highlighting the need for independent review of the imaging.

Zoom in



There are a number of solutions for this, which will depend upon local preference and could even be combined:

- Use of automated software to identify LAO stroke to local clinicians (e.g. RAPID or Brainomix mostly) is being widely rolled out across the NHS in England and looks to be the most deliverable solution with some caveats discussed above, but it does incur a recurring new financial cost, and potential barriers include uniform information technology implementation across hospitals.
- Use of an (supraregional) interventional neuroradiology network as a first point of contact for MT decision-making across multiple interventional neuroradiology centres has the advantage of protecting rotas with smaller numbers of **INR**s from being overloaded with out-of-hours calls but the disadvantage of the potential barrier of setting up information technology systems across regions.
- Interpretation of CTA by stroke physicians will require training and networked support similar to that seen for delivery of IVT in some regions.
- Provision of acute CTA reporting by emergency outsourcing companies will require radiology training and audit to ensure quality and carries a cost premium.
- In-house training of radiology registrars to flag LAO stroke to INRs may be preferable in terms of financial cost but will require regular training and retraining. Over time, this has an added long-term benefit of disseminating the skill of CTA interpretation.

In all likelihood, local solutions will differ across the country but could result from a combination of systems (for example, INR network plus a network of stroke physicians with CTA interpretation training supported using decision-aid software to facilitate MT referrals).

The common denominator of most of these solutions is the need for training in NCCT/CTA interpretation and, therefore, efforts should initially be directed at education. The principles of this can be divided into two factors – identification of the site of occlusion and assessment of the viability of the ischaemic territory – which form the basis for a training curriculum.

Image interpretation

Site of occlusion and thrombus load

The hyperdense artery is a well-established sign of hyperacute stroke on NCCT but might not be seen in up to 50% of acute MCA occlusions using standard 3-mm NCCT section thickness (Figure 15).[163,164] More than 10% of patients with LAO show absence of hyperdense thrombus, even using thin-section reconstructions, which are more sensitive for detection.[165] In contrast, CTA accurately demonstrates the site of occlusion (Figure 16).[166,167] With a thick 30-mm **MIP** slab orientated along the plane of the temporal lobes, the entire middle cerebral circulation can often be demonstrated on a single image, and proximal occlusions can clearly be recognised. Similarly, coronal reconstruction can clearly demonstrate basilar artery occlusions (Figure 17).

Figure 15. NCCT (left) showing no clear hyperdensity of occluded left MCA (arrow). CTA (right) showing occluded left terminal ICA and M1 MCA (arrow).

Zoom in

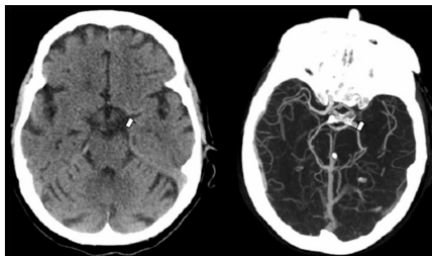


Figure 16. Axial 30-mm MIP CTA showing the MCA anatomy (left): terminal ICA (black arrow), M1 MCA (white arrow), M2 MCA (grey arrows). Example case (right) of a left M1 MCA occlusion.

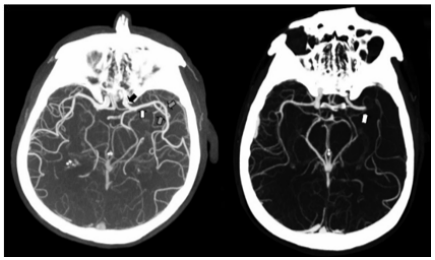
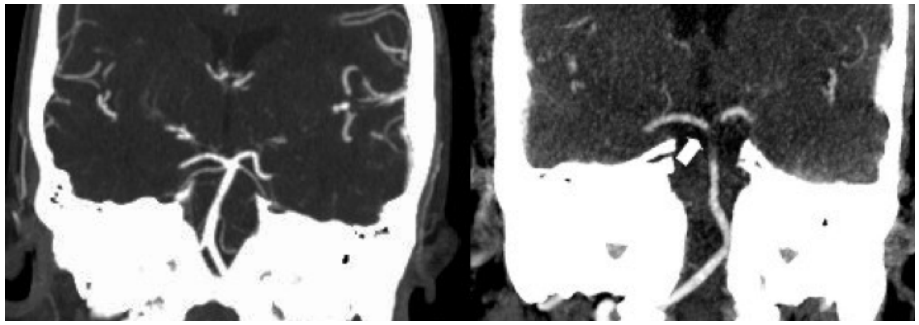


Figure 17. Coronal CTA showing normal terminal basilar artery anatomy (left) and acute occlusion (right, arrow).



Zoom in

The caudal extent of CTA coverage should extend to the aortic arch to ensure that cervical arterial steno-occlusive disease and aortic arch anatomy can be characterised – both important considerations for MT, aiding the INR in decision-making regarding route of access, equipment choices, anaesthetic approach, and the need for adjunctive treatments such as carotid angioplasty or stenting **(see Figure 11)**. In our experience, it is useful to image the distal extent of the thrombus to guide treatment planning, but patients with proximal occlusion should be considered for MT regardless of clot load.

Core infarct estimation and collateral flow

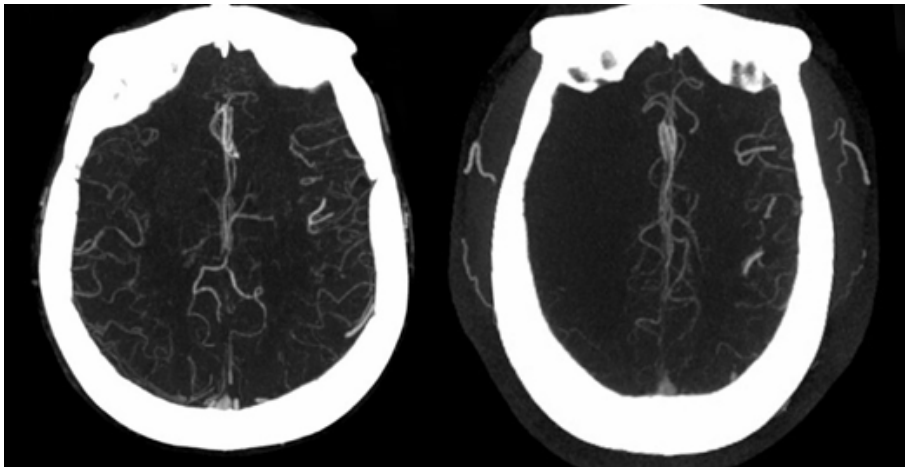
In proximal LAO, collateral vessels preserve viable tissue and can potentially extend the time window for re-canalisation. The extent of core infarct following arterial occlusion is inversely related to collateral status and dependent on collateral flow,[168] so infarct volume at a specified time post-ictus can vary widely between patients.[169] Core infarct volume at presentation can help to predict outcomes: those patients with large core infarct volumes >70 ml often fail to achieve independence at follow-up despite re-canalisation[170] and may be at higher risk of reperfusion haemorrhage.[114] Estimation of core infarct and collateral flow can be gleaned from CTA interpretation.

Hypodensity on **CTA-SI** demonstrates regions of non-enhancement and represents a form of perfusion imaging. As with NCCT, ASPECTS can be estimated from CTA-SI. When read from CTA-SI, ASPECTS shows better inter-reader agreement and is more accurate in the early stages of infarction.[172] Additionally, CTA-SI ASPECTS shows better correlation with baseline stroke severity and infarct expansion.[173] However, care should be taken in interpretation, as very early-phase CTA may overestimate these changes, and this could impact adversely on patient selection.[174] A version of ASPECTS for the posterior circulation using CTA-SI has also been devised but is much less widely used.[175]

Collateral status can be estimated using thick 30-mm axial MIP images from CTA source data. Numerous studies have shown that favourable collateral scores are associated with favourable clinical outcomes, and, conversely, poor collaterals often coincide with poor clinical outcomes.[176] Various grading systems have been devised, but a simple, commonly used system is a scale of 0–3, where 0 is assigned to no collateral filling, 1 to collateral filling <50%, 2 to collateral filling >50% and <100%, and 3 to 100% collateral filling.[176] A relatively simple imaging marker is a malignant collateral profile,[177] where almost no collateral vessels are seen, which correlates well with a large core infarct (Figure 18).

Figure 18. Two patients with right M1 MCA occlusions but very different collateral profiles. Collateral flow approximating to the normal left side (left) and malignant collateral profile in the right hemisphere (right).

Zoom in



It is becoming clearer that baseline CTA collaterals are a robust determinant of final clinical outcome.[178] Patients with poorer collaterals show less benefit from MT, and collateral status has potential to select patients at different intervals after onset; however, its utility is dependent on the phase of imaging. Poor collateral status has been used to exclude patients from clinical trials.[13] Multi-phase CTA improves prognostication.[147]

The ability of collateral vessels to preserve tissue integrity could be guided by the filling of cortical veins. In a recent post-hoc analysis of data from MR CLEAN,[179] patients with acute MCA stroke with absence of cortical vein opacification in the affected hemisphere seemed to have no benefit from MT, whereas patients with venous opacification did benefit. A recent study also identified asymmetrical internal cerebral vein opacification on multi-phase CTA as an independent predictor of poor outcome.[180] Venous opacification, along with collateral scoring, can therefore be used to guide decision-making in MT selection, but evidence for the use of these imaging signs in isolation to select/de-select patients for treatment is thus far limited.

Conclusion

Mechanical thrombectomy for stroke requires additional imaging for patient selection. A combination of NCCT and CTA represents the most appropriate combination to deliver this and is very likely to remain sufficient in early presenters (<6 hours). The relatively low levels of MT in the UK are, in part, due to lack of routine use of CTA in stroke imaging protocols in referring ASCs. A number of solutions exist to aid better implementation of the necessary imaging, but most are underpinned by the need for resourcing and appropriate training in image interpretation so that patient selection for MT can be reliably supported around the clock. Artificial intelligence decision-support software is likely to have an important supporting role here.

The role of multi-phase CTA or CTP in addition to standard NCCT/CTA remains unclear in early-presenting patients and requires further research. For late presenters and wake-up stroke, if we accept that acute MRI is unlikely to provide the necessary imaging capacity in the UK, either CT-based approach may be used up to 6–12 hours. Beyond 12 hours, current evidence only supports CTP-based triage. In the longer term, wider implementation of proven advanced brain imaging methods will be required in addition to NCCT/CTA in many patients.

6 Implementation of mechanical thrombectomy: lessons from implementation of primary percutaneous coronary intervention for ST segment elevation myocardial infarction

Jim McLenachan

Key points

- Continuous data monitoring, of both process and outcome measures, is essential to demonstrate that treatment is benefitting patients and providing cost-effective care.
- All centres offering a new emergency interventional treatment should have a plan that ensures patients will be able to access this treatment on a 24/7/365 basis within a finite time period (e.g. two years).
- Co-ordinated regional networks were critical to the successful implementation of reconfigured services for **PPCI**.
- Regular communications and regular meetings allow newer centres to move quickly up the learning curve and to adopt best practice.

Standard treatment for patients presenting with **STEMI** throughout the late 1980s and early 1990s was **IVT**. Three papers published in a single edition of the *New England Journal of Medicine* in 1993 suggested that immediate percutaneous balloon coronary angioplasty (later renamed 'primary percutaneous coronary intervention') was a more effective treatment than IVT – the standard of care at that time.[181-183] By the mid 1990s, small numbers of patients were being treated with PPCI, but the general assumption was that the inherent delay in transferring patients to PPCI-capable hospitals, followed by the time to perform the procedure, would offset any potential benefit of PPCI for most patients. Logistically, PPCI as the default treatment for STEMI was just too difficult.

In 2003, an updated meta-analysis showed that immediate PPCI, when feasible, was superior to IVT in reducing mortality, reducing stroke, and, importantly, shortening hospital stay.[184] The same year, the UK Prime Minister's Delivery Unit conducted a review of national policy for treatment of heart attack, which recommended that the Department of Health develop a clear policy for expanding PPCI and draw conclusions on the feasibility of national implementation of the service.[185]

Clinical enthusiasm for PPCI, particularly in London, meant that some hospitals had started offering the service in an *ad-hoc* way. Discussions between the Department of Health and the **BCS** resulted in the **NIAP**. This was not a randomised trial but a feasibility study to determine whether PPCI was a practical treatment for STEMI patients in a UK NHS setting. Six major PPCI centres in England enrolled 2,245 patients between April 2005 and April 2006. The study was published in 2008,[185] with many of the study's findings used to inform subsequent implementation of PPCI in the rest of the country.

The Department of Health and professional societies (BCS and **BCIS**) provided strong support for implementation of PPCI as the new standard of care for STEMI.[188] At the time (around 2008), a strong network system comprising 29 cardiac networks in England was under the leadership of NHS Improvement (an entirely separate organisation to the current organisation called NHS Improvement). In general, each cardiac network comprised one or more tertiary cardiac centres and a number of **DGH**s. A national clinical lead and a national improvement lead were appointed to facilitate the implementation over a three-year period.

Implementation by cardiac networks

Regional differences in population density and travel time to the nearest PPCI centre meant that different regions of England needed to evolve different services. Implementation of the PPCI strategy through the cardiac networks allowed for bespoke local solutions to the challenges raised by the implementation of PPCI.

Networks were encouraged to be consistent in their implementation plans in a number of areas (Box 1), but different networks in some areas took different approaches according to their experience, resources and geography.

Who should make the diagnosis?

Some areas of the country had already invested in a system for telemetry of the **ECG** from the ambulance to the receiving hospital to support pre-hospital thrombolysis. Several areas continued with ECG telemetry to support PPCI. In most areas, however, the PPCI centre agreed to accept paramedics' interpretation of the ECG.

Repatriation or not?

A strategy of PPCI reduced the median hospital stay from 5–7 days to 3–4 days. In some hospitals, the patient remained in the PPCI centre for the duration of their inpatient stay. In other centres, the patient was transferred back to their local hospital after the procedure – often at 6 hours. This meant that a link was established between the patient and their local hospital in terms of further investigation, secondary prevention and initiation of cardiac rehabilitation.

Box 1. Areas in which consistent approaches to national implementation of PPCI were recommended.

- Diagnosis should be based on standard and widely accepted ECG criteria together with the clinical presentation.
- Pre-hospital (ambulance) diagnosis with direct admission to the catheterisation laboratory ('cath lab') was the preferred route of access. Travel through an ED at either a DGH or the PPCI centre introduced significant delays that offset the benefit of the PPCI strategy. This had been clearly demonstrated during NIAP, in which transit through ED prolonged the call-to-balloon time by an average of 54 minutes compared with the patient being taken directly to the cath lab by the ambulance service.
- The service had to be 24/7. It was recognised that this was not always possible immediately, but there should be a plan to gear up to 24/7 within a defined period.
- Time standards (call-to-balloon time and door-to-balloon time) were agreed, monitored and reported to the national database (MINAP).

Implementation by geography or by hours of work?

With only one or two exceptions, networks started with a PPCI service that was limited either in time (8 am-5 pm or 8 am-8 pm) or in geography (immediate population first, then implementation to cover surrounding DGHs). Each network was encouraged to have a phased implementation over a finite period of time (usually 1–2 years). For each DGH, setting up the initial service involved extensive consultation and discussion with local cardiologists, cath lab, **CCU**, **ED** and rehabilitation staff and, most importantly, the ambulance service. Each time the catchment area was extended to include the population from another DGH, this series of meetings was repeated. For the PPCI centre, extending the catchment area was fairly straightforward and simply led to an increase in referrals. The major challenge to the PPCI centre was moving from limited hours to a 24/7/365 service, with all of the consequent implications for rotas, shifts and daytime working. For most cath lab staff, including cardiologists, in most PPCI centres, the full 24/7 service meant that they were likely to be working during the night and unavailable for normal work the following morning.

Contentious areas

A number of issues and discussion points occurred during the implementation.

Call-to-balloon time

This is defined as the time, in minutes, from the point at which the patient, or their carer, calls the ambulance service to the time when the occluded artery is identified and first instrumented, usually with a balloon or an aspiration catheter.

For both of the established treatments for STEMI – PPCI and IVT – the benefit of the treatment is reduced by delays to treatment. The relationship between the loss of benefit and time is complex and differs for the two modes of treatment. It also varies according to the site of infarct and the time since onset of symptoms. In practice, it was necessary to establish an expected upper limit for the call-to-balloon time; if it was likely that PPCI could not be performed within that time period, IVT was offered as an alternative treatment. The upper limit of the expected call-to-balloon time was chosen as 150 minutes. Some people felt that this was 'pushing' PPCI, because the **ESC** had set an upper limit of 120 minutes; however, the ESC definition was from the time of 'first medical contact' to balloon time.

As a compromise, an average of 30 minutes between calling the ambulance service and 'first medical contact' was felt to be reasonable, hence the 150-minute standard.

Institutional activity

Prior to implementation, guidance about levels of institutional activity and infrastructure was produced by the BCIS and last updated in 2016.[187] The guidance specified that:

- services must be 24/7
- services must have two adjacent cath labs
- services must perform a minimum of 150 PPCI procedures per annum
- all PCI operators should participate in a PPCI rota
- all operators should perform at least 20 PPCI procedures per annum.

In practice, it was not possible to enforce the BCIS guidance, and some centres continue to perform relatively low numbers of PPCI procedures.

Loss of local services

One of the greatest hurdles in the implementation of a national 24/7 PPCI service was the perception that local services were being removed. Cardiology had seen two decades of decentralisation – diagnostic coronary angiography, pacemaker implantation and coronary angioplasty had all started out as tertiary centre-only procedures but had all moved out to the larger DGHs. The DGHs had invested in staff and equipment, often with local charitable and press support. Primary percutaneous coronary intervention was sometimes then seen as recentralisation of clinical services, with the role of the local CCU being downgraded. It was important to explain that the PPCI strategy would save lives, even if the treatment was delivered later than the time at which local IVT could have been given.

24/7 service

A number of hospitals with a growing PPCI service wished to provide a limited-hours PPCI service (anything from 9 am-5 pm to 8 am-8 pm Monday–Friday) but were unable to provide a 24/7 PPCI service. In general, this was not the preferred operating model; the ambulance services, in particular, were keen that the referral pathway was the same regardless of the time of day or the day of the week. Nevertheless, some networks evolved workable solutions. In the southwest of England, centres in Bath, Swindon and Cheltenham provided daytime PPCI, while Bristol provided 24/7 PPCI to its local population and out-of-hours PPCI to the surrounding areas. In the southeast, Eastbourne and Hastings operated an alternate-week PPCI service.

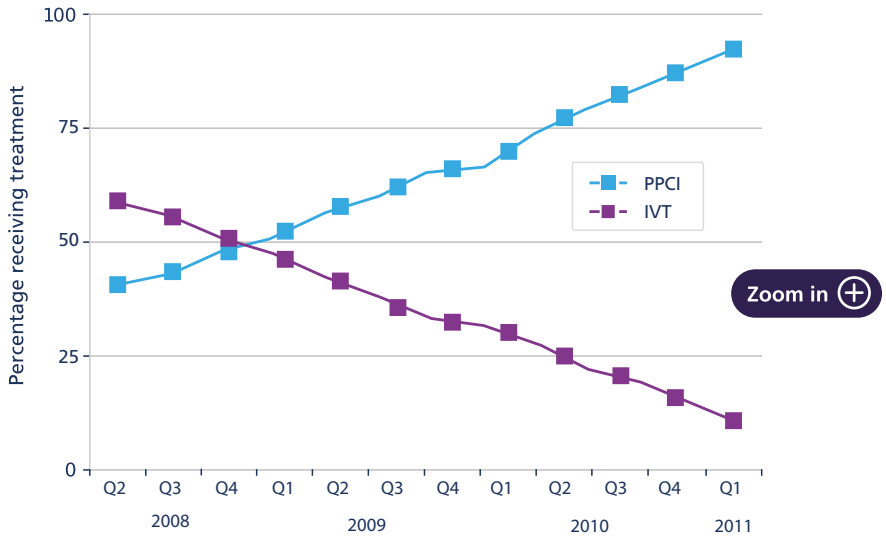
What went well?

Cardiac network support

The cardiac network system, with overarching co-ordination by NHS Improvement and the Department of Health, was critical to the successful implementation of PPCI. It allowed clinicians, managers and commissioners to meet together under one roof to establish patient pathways that focused not only on making the diagnosis and delivering the initial interventional treatment but also on length of stay, repatriation, discharge planning and rehabilitation. The network system also allowed individual networks to reach bespoke solutions that were appropriate for their local geography and their local hospital and ambulance providers. This also ensured that pre-existing local skills and services were recognised and used to best advantage. This included, in different areas, recognition of the ECG interpretation skills of paramedic personnel and the use of ECG telemetry between the ambulance and the hospital. The result was considerable variation in the rate of implementation of PPCI between the cardiac networks.

Figure 19 shows the change from IVT to PPCI as the default treatment for STEMI in England by quarter between 2008 and 2011. Of those patients receiving reperfusion therapy, only 39% received PPCI during the second quarter of 2008. By the first quarter of 2011, this had risen to just over 90% (equivalent to 16,500 patients per annum) (MINAP data, personal communication). The graph gives the impression of a steady and orderly change in treatment; however, this was achieved in different ways in different networks. East Midlands, which had more than one PPCI centre, achieved the change in stepwise fashion as the centres took on larger areas of the population. In contrast, the Kent cardiac network, which had a single PPCI centre at Ashford, effectively switched from IVT to PPCI on 1 April 2010.

Figure 19. Change in treatment for STEMI in England by 2008–11 for those patients receiving reperfusion therapy (3-monthly datapoints) (MINAP data, personal communication).



Continuous data collection

Cardiology was fortunate that there was already a functioning system for national data collection that covered both myocardial infarction (MINAP) and PPCI (BCIS). A number of fields were added to the PPCI database to allow identification of all PPCI procedures and collection of data on time of onset of chest pain, call time, door time and balloon time. These data were then used to report on the performance of PPCI. Hospital episode statistics data for STEMI were unreliable due to coding inaccuracies, obliging commissioners to rely on MINAP and BCIS data.

Communications strategy

A number of papers were published during the implementation phase. The most important of these was the Department of Health's **NIAP** report, *Treatment of heart attack national guidance. Final report of the National Infarct Angioplasty Project (NIAP)*, in 2008.[185] However, three additional smaller reports published by NHS Improvement between 2009 and 2012 all probably helped to galvanise doctors, managers and commissioners into activity:[188–190]

- *A guide to implementing primary angioplasty*
- *National roll-out of primary PCI for patients with ST segment elevation myocardial infarction: an interim report*
- *Growth of primary PCI for the treatment of heart attack patients in England 2008–2011: the role of the cardiac networks.*

During the implementation period from 2008 to 2012, sessions were held each year at the annual national meetings of both the BCS and the BCIS to provide frequent updates of the PPCI implementation in the 29 cardiac networks. These were generally well received and created and sustained a sense of urgency.

What we learned from implementation

Sustainability

Providing a 24/7 service is onerous. National staff shortages mean that the burden may be felt even more by nursing, physiology and radiography staff than by medical staff. Clear guidance is needed about on-call hours and appropriate rest periods if staff are called in during the night. It is likely that there will be consequences for daytime capacity.

Sick patients with alternative diagnoses

Patients are sometimes referred along the PPCI pathway and found to have an alternative diagnosis. This may be cardiac (aortic dissection or pericarditis) or non-cardiac (pneumonia or sepsis). Clear pathways are essential so that these patients are transferred to an appropriate clinical area quickly and safely.

Increasing numbers of referrals

As the PPCI service has evolved, so the threshold for referral has fallen. Perhaps understandably, EDs are less confident about diagnosing pericarditis or 'high take-off' on the ECG without referring the patient for angiography. The number of PPCI procedures has remained fairly constant over the past decade (at around 350–450 per million population), but the number of referrals into the pathway has risen. In some centres, the ratio of referrals to definite STEMI is approaching 2:1.

Unconscious patients

The number of patients who survive an out-of-hospital cardiac arrest is increasing. In the past, such patients, if still unconscious, would be admitted to the **ITU** of their nearest hospital. However, these patients are often now referred along the PPCI pathway and taken to the regional PPCI centre. If they survive but remain unconscious, they will require either admission to the ITU of the PPCI centre or paramedic transfer – still ventilated and with an anaesthetist or intensivist – to their local hospital's ITU. This patient cohort has been an unanticipated consequence of highly successful out-of-hospital resuscitation and the evolution of the PPCI service; it provides an enormous challenge to intensive treatment services, with consequent effects on major surgical specialties that require ITU beds for elective work.

Conclusion

Between 2008 and 2011, the default treatment for patients presenting with STEMI changed from IVT to PPCI. In the second quarter of 2008, just 39% of patients were treated with PPCI, and this had risen to 90% by the first quarter of 2011, this had risen to 90%. This was achieved through the cardiac network structure, supported by substantial centrally funded investment from NHS Improvement and the Department of Health. Some of the issues, such as providing a 24/7 service and the referral criteria, were universally accepted; other aspects of the service, such as whether or not patients were immediately repatriated to their local hospital, were decided locally. Collection of data on numbers of patients treated with PPCI, numbers of patients given IVT, process measures such as call-to-balloon times and door-to-balloon times, and the annual publication of these data have been essential to driving continuous service improvement. Critically, successful implementation of PPCI depended heavily on strong national policy leadership provided by the then National Clinical Director (Sir Roger Boyle) and his deputy (Professor Huon Gray) together with a well-established system of cardiac networks. In recent years, with reduced resources in the networks and reduced direct access of senior doctors to political leaders, the pace of quality improvement has slackened and residual issues in some areas have been left unresolved. It remains to be seen whether, without the same degree of policy direction and central support in a reorganised NHS, a similar level of success can be achieved for stroke service reconfiguration.

7 Establishing a 24/7 interventional neuroradiology service to deliver hyperacute stroke care: core elements of the project and lessons learned

Sanjeev Nayak

Key points

- Setting up a 24/7 **MT** service requires a change of institutional mindset.
- Many perceived barriers and issues with establishing the service can be overcome through collaborative working within a regional network.
- Co-ordination with ambulance services is essential, with agreement of a 'critical code' to expedite transfers from outlying referral centres.
- High-quality, post-MT procedure care is essential to achieve successful patient outcomes.

A 24/7 MT service was established at the University Hospital of North Staffordshire NHS Trust (now called University Hospitals of North Midlands NHS Trust) in January 2010. This chapter describes how this service was established and some lessons that may be of use to other healthcare providers setting up a similar service.

Establish a multi-professional and patient project group

A working group was formed from a range of healthcare professionals across the trust, including interventional neuroradiology, stroke, anaesthesia, intensive care and **ED** teams. The working group developed the case for MT and presented it to the trust's clinical governance committee and the trust board for approval.

The patient inclusion criteria and care pathways for the proposed service were defined and agreed at an early stage, which allowed practical issues such as organising staff, determining referral pathways to be mapped out, and potential problems to be resolved. Integrating opinions and input from all working group participants was complex and required time and negotiation.

Another important feature that contributed to the success of this project was the development of patient partnerships. Patients were contacted by the healthcare teams responsible for their care pathways and also via support groups to recruit them as 'stroke champions', sitting in on project meetings and negotiations with commissioners.

Information from patients and clinicians on their experiences of using the new MT service and patient outcomes was regularly reviewed to ensure that feedback on patient experience was included and that high standards of care were maintained. This regular feedback was a key factor that facilitated early adoption of MT into routine practice.

Identify funding

The local **CCG** provided full funding to the trust for this service in 2010, although the service had started on a case-by-case basis in late 2009. This was due to the positive feedback received from patients and clinicians, coupled with early clinical successes. The CCG agreed to pay per procedure, with an approved coding and costing based on L712 **HRG** tariff for complex percutaneous transluminal embolectomy of an artery: £10,258 at the time. The funding allowed the MT treatment service for severe strokes to be offered on a 24/7 basis to local patients.

Organise staff teams

The interventional neuroradiology service was delivered by a core **MDT** that was available 24/7: **INR**, stroke consultant, radiographer, nurse (interventional vascular radiology), anaesthetist (major trauma rota), and **ODP** (major trauma team).

Agreement for 24/7 service provision from involved teams was achieved through numerous meetings and personal discussion with anaesthetists, interventional radiology nurses and radiographers. The MT service had to be integrated into the vascular interventional radiology service for major trauma to achieve 24/7 anaesthetist and interventional radiology nurse support and into the major trauma service to achieve comprehensive 24/7 funded cover and service, which was initially achieved through the major trauma contract. Incentives such as hourly rate payment for call-outs, additional programmed activity payments and flexible working in job plans were offered and agreed after discussions with teams.

Staff rota

The level of staffing, shown in Box 2, required additional funding from the trust.

Box 2. 24/7 multidisciplinary team care rota

- Eight band 6 nurses trained in initial assessment for thrombolysis as well as recruitment for research studies. Each nurse works on a day shift (7.30 am-8.00 pm) or night shift (8:00 pm-7.30 am)
- 1-in-6 MT local stroke physician rota
  Additional stroke physicians are also available in the region, providing separate 24-hour cover for five regional hospitals on a 1-in-12 rotational basis
- INR available to provide 24/7 MT cover and weekend aneurysm coiling on a 1-in-3 basis
- A consultant neurological anaesthetist is available on call on a 1-in-7 basis (**see Box 3**)
- Two anaesthetic ODPs from the trauma team also assist with MT on a 1:8 rota
- Team of radiographers and nurses from the vascular/general interventional and neurointerventional service provision are available (**see Box 4**)
- 30-bed stroke unit, including 12 hyperacute beds and ITU facilities

Anaesthetic service

A standard operating procedure was agreed for patients who were admitted following a stroke. Based on emergency theatre prioritisation codes, stroke patients were classified as requiring 'immediate transfer to theatre'.

Anaesthetist rota

A rota was set up to ensure that an anaesthetist was available at all times (Box 3).

Anaesthetic procedure pathway

The anaesthetist completes a pre-operative assessment and takes handover from the ED nurse/stroke team – or the paramedic team if the patient is arriving from an out-of-area hospital. Patients are first seen in the ED before transfer to the interventional radiology suite. The choice of anaesthetic depends on the individual case after discussion with the anaesthetist, stroke team and INR, with 60% of patients receiving general anaesthesia and the remainder conscious sedation. General anaesthesia is recommended for patients with agitation, reduced **GCS** (≤12), nausea and vomiting, large dominant hemisphere stroke or posterior circulation stroke. Rapid sequence intubation is used for all non-fasted patients. Standard monitoring procedure includes **ECG**, pulse oximetry, end-tidal **CO_2** and arterial **BP** – measured non-invasively every 3 minutes. The interventionist can provide access for BP measurements via the femoral sheath. Irrespective of the anaesthetic technique, the goal is to minimise any time delay and maintain haemodynamic control, with systolic BP between 140 and 180 mmHg. Patients undergoing MT often also require urinary catheterisation, active warming, and careful fluid balance care to prevent fluid overload.

After MT, patients are observed for a short period in the anaesthetic recovery area before being transferred to the stroke unit. If any clinical instability is observed, the patient is instead transferred to the **ITU**.

Interventional radiographer and nursing services

Box 4 shows the INR and nursing rota set up to ensure service continuity.

Diagnostic imaging

The imaging department at the **CSC** has three **MRI** scanners and four **CT** scanners. Advanced stroke imaging, including **CTP** with core volume/penumbra assessment or magnetic resonance **DWI** core volume assessment, is undertaken in selected patients: those outside the 6-hour symptom-to-presentation window and patients with unknown onset time, low **ASPECTS**, high **NIHSS** scores (>24), low GCS, or poor collaterals on **CTA**. The use of CTP has been routine since 2018 following publication of the **DAWN** and **DEFUSE**-3 trials.[17, 18]

Box 3. Anaesthetic rota

- 8:00 am-7.45 pm Monday to Friday, one consultant neurological anaesthetist on site to ensure care for all neurointerventional/MT patients
- Out-of-hours (7.45 pm-8:00 am on weekdays and all weekend), first port of call is the consultant anaesthetist, who also co-ordinates the anaesthetic team. The consultant anaesthetist is supported by the consultant neurological anaesthetist (1-in-7 rota), who is also responsible for covering neurological theatre emergencies
- Consultant neuro-anaesthetists provide out-of-hours emergency cover in neurosurgery, as well as the interventional neuroradiology/MT service

Box 4. INR and nursing rota

- Theatre suites are staffed 8 am-6 pm, Monday to Friday, with a minimum of two nurses, one healthcare assistant, two radiographers and one INR
- Out-of-hours, the on-call service comprises one nurse, one radiographer and one INR. After completing the daytime shift, staff remain on call from 6 pm until 8 am the next day
- The radiographers and nurses also cover the vascular and neurointerventional radiology units and provide support to the nine-bed day unit
- The interventional vascular and neurointerventional service is supported by 10.8 WTE radiographers and 20.5 WTE nurses (bands 5 and 6). Out-of-hours, radiographers work on a 1:7 rota and nurses on a 1:12 rota
- An additional informal 'back-up' team of nurses and radiographers is available, if necessary, to cover MT cases if the first team is involved in another vascular or neurological emergency. If they are called in after 10 pm Monday–Thursday, they are allocated compensatory rest the following day, when staffing allows

Establish regional care pathways

Networks were set up to link each **ASC** with the CSC in order to provide an emergency specialist review service for local brain imaging via electronic links. Emergency transport networks (including repatriation) were also set up for patients who require treatment. Referral protocols were devised to ensure appropriate care (Box 5).

Box 5. Referral protocols

- Agreed protocols for referring site/ASCs developed through the Heart and Stroke Network
- Clear care pathways for referrals during working hours and out-of-hours
- 'Drip-and-ship' service for patients, with nursing escort
- Out-of-area protocol established – e.g. for referrals from adjacent ASCs

Ambulance service

Early discussions were carried out with the West Midlands Ambulance Service in order to agree protocols for patient transfer and repatriation, including introduction of a 'critical code' for patient transfer.

Establish treatment pathway

To maximise clinical benefits, it is critical to complete MT as soon as possible after the onset of stroke. To achieve this, patients are triaged in the ED and assessed by the stroke team to identify those who meet the clinical criteria for MT eligibility (NIHSS >5 and pre-stroke **mRS** <3) prior to having imaging with **NCCT**/**CTA**.

Organisation of the team and preparation

Once the decision has been made to proceed to MT, the pathway below is followed to ensure rapid organisation and preparation of the team:

- The senior stroke clinician informs the INRs and discusses suitability for MT.
- Next of kin, where available, are asked to remain on site for consent/queries (or telephone contact is established).
- A senior stroke or ED clinician immediately contacts the anaesthetist and ODP via switchboard using pagers.
- The INR informs the radiographer and scrub nurse of the procedure, and the necessary equipment is set up.
- The stroke team informs the stroke unit to arrange a bed for the patient after MT.

Regional thrombectomy protocol

Mechanical thrombectomy should allow reperfusion ideally within 6 hours of stroke onset or as appropriate based on CTP findings. In practice, most eligible patients arrive in the CSC within 6 hours of the stroke. Those arriving late are considered for MT after assessment with CTP. Figure 20 shows the regional thrombectomy protocol for MT.

Exit pathways

Repatriation to referring ASC

Within the first 24 hours after MT intervention, the stroke service co-ordinator identifies the appropriate local ASC. The repatriation paperwork is completed, along with a medical and nursing assessment regarding the patient's suitability for transfer. Patients are repatriated to their local ASC within 24 hours of the decision to transfer – between 9 am and 5 pm, whenever possible, with a 7-day repatriation policy agreed with all regional hospitals in the hub-and-spoke referral pathway. This means that they are expected to have returned to their local ASC within 24 hours of the decision to transfer them – and always within 72 hours.

Patients deemed unsuitable for treatment or whose symptoms have resolved upon arrival for MT at the CSC are transferred back to the local ASC by ambulance without admission. The patient must be medically stable, and a verbal and written handover is completed.

Discharge from CSC to patient's home

When possible, patients are discharged directly from the CSC to their home or to their local **ESD** team. These patients are discharged with a personalised therapy and rehabilitation plan.

Discharge from CSC to hospice/palliative care

Patients requiring palliative care after MT with expected 3–4 weeks' lifespan are discharged to their local hospice or one agreed upon with their carer or family. We have an arrangement with the palliative care team, who assess the patient and makes arrangements for a palliative care bed in their local hospice, as long as a bed is available.

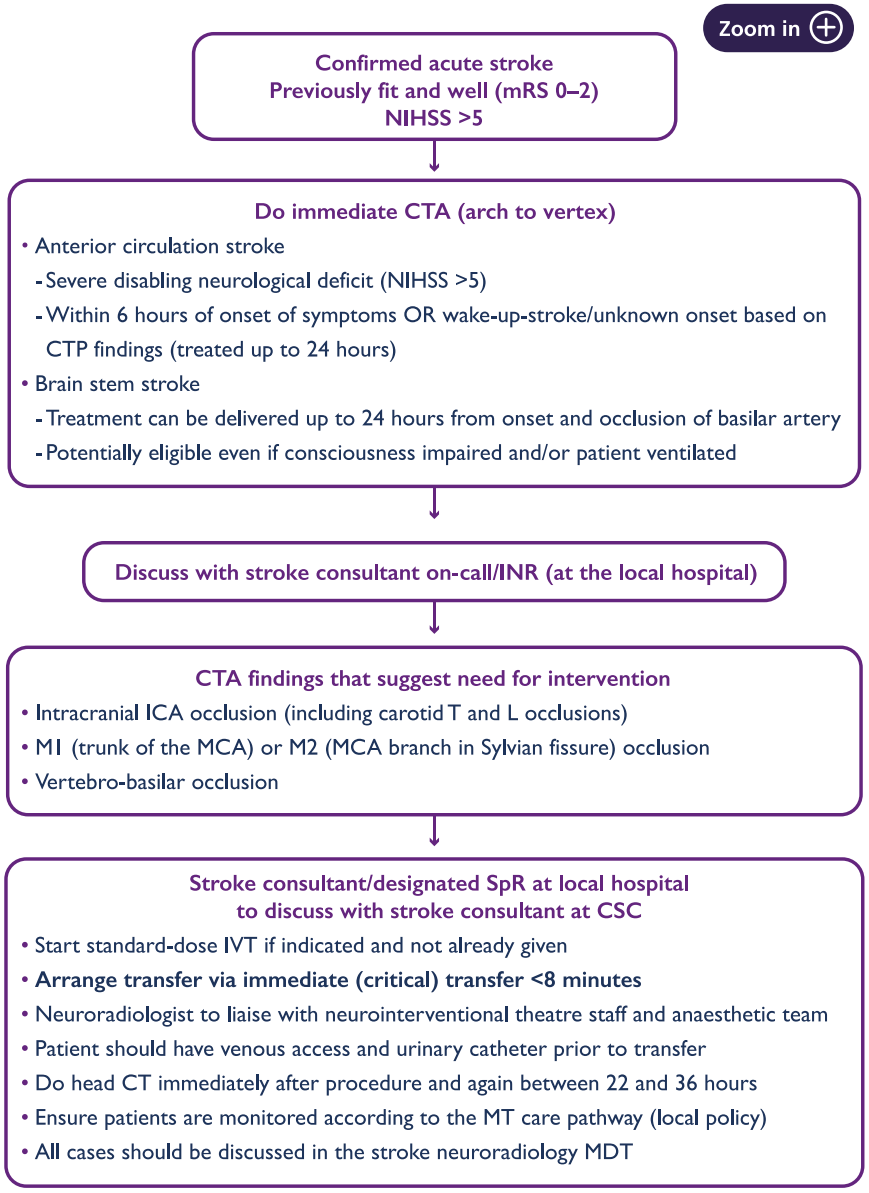


Figure 20. Regional thrombectomy protocol for patients requiring MT.

Follow up

All local stroke patients are followed up as an outpatient at 6 weeks after discharge. For those undergoing MT, a 3-month follow-up clinic is arranged for local patients, while out-of-region patients are followed up in their local ASCs, with mRS/follow-up performed by telephone at 6 months. Box 6 shows current audit outcome measures.

Box 6. Key audit and outcome measures after MT

- Treatment-related mortality
- 30-day post-treatment mortality
- Disability at 6 months (mRS)
- Disease-/procedure-related complications, such as sICH
- Disease-associated complications (e.g. lower respiratory tract infections and urinary infections from SSNAP)
- Time from onset to MT
- Time from onset to arrival at MT centre
- Time from arrival to arterial puncture
- Time from arterial puncture to MT

Promote mechanical thrombectomy service pathways

We used a website to raise awareness of the MT service, promote referral pathways, and share expertise and information with fellow healthcare professionals (**http://new-website.so2s.co.uk/**). We developed innovative digital teaching methods with industry support. These online learning resources provide specialist training to help referring physicians interpret radiological images and identify patients with **LAO**. Since the launch of the MT service, consultant stroke physician training has resulted in a 20–30% increase in the number of patients being referred to us for MT from ASCs within our region. We also run annual regional 'Stroke Alert' courses for stroke doctors, anaesthetists, and ambulance crews to develop the stable infrastructure necessary for the delivery of our regional service. As a result of these initiatives, we have expanded our service from a local population of 666,000 people to a wider regional catchment of 2.5 million.

Evaluate patient outcomes

Monitor and disseminate audit data

A database of stroke patients treated with MT was created to evaluate clinical effectiveness and safety. We have integrated this database into our website, so other partner NHS organisations are able to access this via a secure, password-protected portal. The audit data provided local evidence to confirm the benefits of MT in our patient series. In addition, data about all of the patients who access the MT service are also entered into the **SSNAP** database.

Patient outcomes

Between 2010 and 2018, we treated more than 500 patients with MT. An analysis published in March 2016 by **NICE** based on our data identified that functional independence, mortality rates, median hospital stay (for all patients who undergo MT), and discharge to home were all substantially improved. In a patient cohort of 275 patients from a total catchment of 2.5 million, 23% were discharged home within one week.[191] The analysis also predicted an annual saving of £2.4 million as a result of reduced hospital stays and savings from ongoing social care costs.[191]

The reperfusion rate (**TICI** ≥2b) was 84%, recovery was good (mRS ≤2) in 48% and mortality was 15% at 90 days, which is comparable to published **RCT**s (Table 5).[192] This has been maintained, with near similar outcomes in the latest SSNAP annual review (2019–20).[193]

Table 5. Improvements in patient outcomes following introduction of the MT service.

Outcome	SITS (IVT with NIHSS 14–35) (n=14,145)	UHNM (MT) (n=106)
Median time from onset to thrombolysis	2 hours, 21 minutes	2 hours, 45 minutes
mRS ≤2	4,951 (35%)	51 (48%)
Mortality at 90 days	2,688 (19%)	16 (15%)

The paper also compared our MT outcomes with those reported for patients of similar age and stroke severity in the **SITS** register. Using a similar cut-off date, the age range of 22–76 years, and an NIHSS range of 14–35, we identified a subgroup of 14,145 patients with a mean age of 64 years and a median baseline NIHSS of 18, matching our patient characteristics.[192] The results of our patients treated with MT compared favourably with the SITS population treated with **IVT** alone, with a relative risk for a good outcome of 1.4.[192]

Lessons learned

In our experience, the two main problems with regard to implementation of a 24/7 MT service are the current shortage of INRs and fear that a sudden increase in the number of patients requiring MT will overwhelm the system. We believe that the latter fear is unfounded. There should be buy-in from all involved teams and parties for the project to be successful, and this requires passionate and motivated team members and leaders. Involving physicians and other team members from our surrounding ASCs and ambulance personnel through our regional educational and social meetings helped boost activity, with a significant increase in our MT numbers. However, it is our experience that MT patient numbers take time to grow. It took about three years for our MT service to be fully utilised and for the referral pathways to develop. As referral numbers built up gradually, this allowed more INRs/neuroradiologists to be trained in the specialist skills necessary to deliver MT. The implementation of workflow streamlining improved care delivery times and reduced delays for patients eligible for MT. The application of time-critical measures, including pre-hospital notification, rapid transfer from arrival at the ED to imaging in the CT scanner immediately followed by IVT, and mobilisation of the neurointervention team in parallel with the thrombolysis team, all contributed to reductions in delays. There is a need to develop modern treatment suites where patient assessment, CT scanners and cath lab are located in the same vicinity.

A well-functioning and co-ordinated ambulance service is necessary to ensure that patients are transferred rapidly to CSCs. The agreement of a critical code for inter-hospital transfer significantly reduces transfer time, and it may be necessary to engage air ambulance services to ensure rapid patient transfer from more remote areas.

Ongoing issues to be resolved

The current tariff for MT only funds the procedure itself. At the time of writing, no central funding is available to support additional infrastructure such as new angiographic equipment, to provide more beds in ITU or on the acute stroke unit, or to employ the extra staff required to fully deliver MT services. We recommend that NHS England should take action to provide additional, ring-fenced funding to support these necessary additional transition costs.

The most successful outcome for stroke treatment depends on appropriate care being given promptly after the onset of stroke. Further delays occur in hospital between the time the patient arrives and the start of MT treatment. Some of these delays are related to slow hospital procedures and policies and delays in ambulance transfers. Care systems thus need to be created to facilitate fast and efficient triage of patients with LAO to CSCs capable of providing comprehensive medical, MT, surgical care and post-intervention management. Such care systems can learn from those already used to manage major trauma and **STEMI**.

Conclusion

In 2010, our trust was the first in the UK to implement a commissioned 24/7 MT service and since then we have treated more than 750 patients. This was achieved by redesigning our acute stroke treatment pathways within the trust and across the region. Communication has been key throughout this project, and it could not have worked without the co-operation of many specialties. However, the real challenge for successful implementation of a MT service is to change current thinking and mindset at an institutional level.

National delivery will require a similar change in mindset, together with reorganisation of current stroke services in the UK, substantial investment in staffing and equipment, refinement of care pathways, and extensive co-operation between ambulance services and hospitals.

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8 Lessons from the implementation of intravenous thrombolysis for acute ischaemic stroke

Gary Ford and Martin James

Key points

- Regional clinical networks provided clinical leadership and managerial support and were key to the development of local implementation plans and sharing best practice to deliver **IVT**.
- Working with ambulance services and **ED** teams was critical to improving recognition of stroke and expediting the emergency response.
- Protocol-driven access to urgent brain **CT** imaging was critical to reducing door-to-needle time for IVT.
- Development of teams to deliver around-the-clock IVT services required multiple specialties to support on-call rotas.
- Increasing public awareness and support from patient groups and charities was important in endorsing the service transformation necessary to deliver regional stroke services.In some large metropolitan areas, rates of IVT did not improve until services were centralised.

In 1995, the pivotal North American **NINDS** study reported that IVT with alteplase within 3 hours of onset of ischaemic stroke improved outcomes, with a 12% absolute reduction in disability 90 days following stroke.[194] Although some UK sites had participated in previous trials of streptokinase in **AIS**, NHS services and the Department of Health had no plan or strategy for the implementation of an acute stroke therapy requiring immediate expert clinical review and CT brain scanning. Thrombolysis was a disruptive innovation that was challenging to incorporate into existing care pathways for stroke. Hence it generated a conservative reaction from some quarters on both sides of the Atlantic who were resistant to moving from a pathway where stroke patients admitted to EDs were given a low priority for assessment and the consultant stroke input to many acute hospital stroke services comprised only two or three weekly ward rounds to a 24/7 service capable of delivering IVT. Not until 2012, 17 years after the publication of the NINDS trial, were all hospitals in England that received acute stroke patients delivering IVT and 11% of all ischaemic stroke admissions receiving alteplase. This chapter reviews the lessons from that journey that might be relevant to achieving implementation of **MT** across the NHS more rapidly than was achieved with IVT.

Key factors that influenced intravenous thrombolysis use in the UK

In 2003, the European Medicines Agency gave a provisional licence for alteplase in ischaemic stroke, which was necessary before many physicians would even consider using IVT. The publication in 2004 of the combined individual meta-analysis of trials of alteplase provided a greater understanding of the time-dependent benefits of treatment.[195] A major factor that drove the reorganisation of acute stroke services was the 2005 National Audit Office report *Reducing brain damage: faster access to better stroke care*, which was highly critical of the Department of Health's approach to developing stroke services and its failure to support delivery of IVT in comparison to other countries.[196] The report projected the health gains from a 10% rate of alteplase use, which at the time was regarded as unfeasibly ambitious. This report was followed by publication of the 2006 Department of Health report *Mending hearts and brains*, which set out the case for reorganisation of acute cardiac and stroke services into fewer centres that could deliver 24/7 **PPCI** for acute **MI** **(see Chapter 6)** and IVT for acute stroke.[186] Although IVT rates increased only slightly between 2006 and 2008 (Figure 21), this report led those hospitals and clinicians who were not providing IVT to realise that acute stroke patients might in the future be redirected to other hospitals.

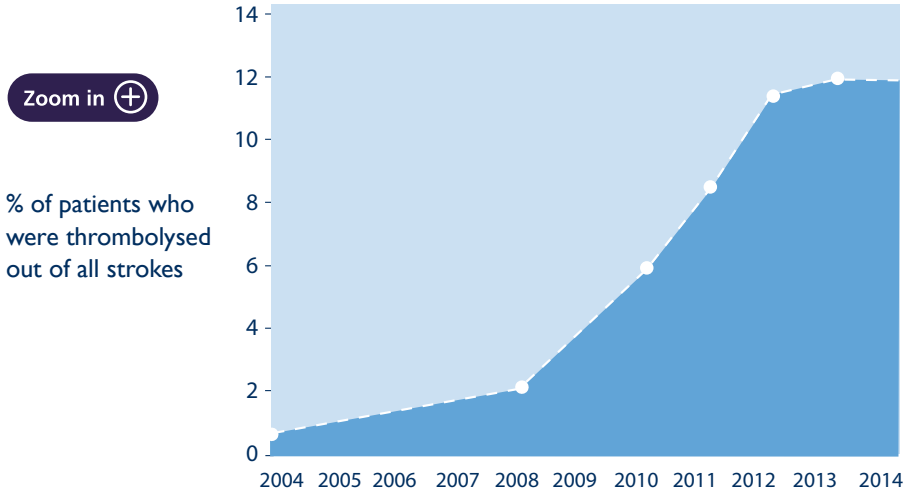
These developments led to the launch and publication of an English stroke strategy in 2007, which set clear objectives and standards to improve care across the stroke pathway, followed by similar policy initiatives in the devolved UK nations.[197] The 2007 strategy was delivered through the creation of clinical stroke networks, using the existing clinical cardiac network footprints. These networks covered populations of approximately 2 million people and funded regional clinical leadership supported by managers, who convened healthcare professionals and developed implementation plans to improve stroke services in their region, with a particular emphasis on the implementation of IVT. The networks benefited from a strong programme of public and patient engagement and the involvement of the voluntary sector, often via the Stroke Association.

The developments between 2005 and 2008 laid the foundations for the future delivery of IVT but saw only modest increases in treatment rates (see Figure 21).[198]

The factors associated with a major change in the trajectory of increase were the favourable **NICE** technology appraisal of alteplase in 2007, the introduction of a tariff for alteplase, the National Stroke Strategy and the **FAST** stroke awareness campaign. Many clinicians used the absence of a NICE recommendation as a reason to defer making plans to introduce alteplase – the phenomenon of 'NICE blight'. The introduction of a stroke tariff helped networks create stronger business cases for providing 24/7 stroke specialist rotas and access to rapid CT imaging. The highly visible FAST campaign, with adverts on primetime TV and radio, increased public awareness of stroke and the importance of calling 999 in response to stroke symptoms and led to increased 999 call ambulance admissions and IVT treatment rates.[199] Consistent with experience of other health awareness campaigns, repeated campaigns were necessary to increase and maintain community awareness. Data on IVT use in individual centres across the country from the National Sentinel Stroke Audit (and the **SSCA** in Scotland) and **SITS** database reports were valuable in incentivising low-performing hospitals to make changes.

Major barriers to hospitals developing 24/7 thrombolysis services were the creation of stroke specialist rotas, which required persuading and training consultants without a major focus on acute stroke to participate in out-of-hours rotas and persuading and supporting radiology departments to provide 24/7 access to urgent **NCCT** brain imaging.

Figure 21. Percentage of all stroke patients who were thrombolysed between 2004 and 2014 (data from National Sentinel Stroke Audit and the Stroke Improvement National Audit Project [SINAP]).[198]



Creating a professional learning community

In 1998, three centres in Glasgow and Newcastle introduced 24/7 IVT protocols and started to treat small numbers of patients (10–20 per year at each centre) within 3 hours, fitting the NINDS trial criteria. These centres contributed cases to the SITS database, which collected real-world data on outcomes from IVT across Europe. In 2004, the UK national SITS leads, with approval from the **BASP**, established 'thrombolysis training days,' which were free-to-access meetings supported by an educational grant from the manufacturer of alteplase, with the content independent of industry. These were well attended by physicians, radiology and nursing staff who wished to develop IVT and shared practical experience of how to deliver an IVT service. In the late 2000s, once IVT was being provided in most hospitals, the meetings evolved into 'thrombolysis masterclasses', during which experience of managing challenging clinical cases was discussed. The stroke clinical networks played a major role in sharing experience across local regions.

Monitoring patient outcomes

Because of opposition to IVT from some groups, and as a condition of the European Medicines Agency's 2003 provisional licence for alteplase, most centres treating patients between 1998 and 2008 recorded patient demographics, processes of care, 3-month clinical outcomes and complications in the European SITS database. This allowed comparison of performance between centres and countries and was key to showing that the results achieved in clinical trials were replicated in real-world practice.[200] The National Sentinel Stroke Audit (covering England, Wales and Northern Ireland) provided more complete data on the number of patients treated but with less information on the processes of care.

Developing ambulance protocols to transport suspected stroke patients to centres able to deliver intravenous thrombolysis

In the 1990s, stroke patients were managed in a large number of hospitals that usually treated small numbers of patients – often fewer than 300 patients per year, with some centres managing fewer than 100 patients per year. At that time, no centre admitted more than 1,000 stroke patients per year. In 1997, Newcastle introduced a rapid ambulance protocol to redirect suspected acute stroke patients who were admitted to three hospitals with acute medical services to a single centre and introduced the FAST assessment to support paramedic identification of suspected stroke patients.[201, 202] This early experience showed paramedic redirection protocols were effective at recognising acute stroke patients and bypassing hospitals without 24/7 organised stroke teams to admit patients early after stroke onset to hospitals capable of delivering IVT. These studies also showed that redirection could be achieved without overwhelming receiving stroke teams with large numbers of stroke mimics. Initial studies reported that 15–20% of suspected stroke patients had a stroke mimic at final diagnosis, although more recent studies and audits suggest a mimic rate of 30–40%.

Centralisation of stroke services

As clinicians and managers considered how to develop sustainable 24/7 hyperacute stroke services, it became clear that, in urban areas, consolidation of acute stroke services to fewer hospitals enabled the creation and funding of 24/7 stroke specialist teams and higher volume units. Evidence also began to emerge of the positive association of institutional size and higher IVT treatment rates with more effective care pathways and rapid delivery of IVT.[203] The most successful example of centralisation of stroke services was the reconfiguration of London stroke services in 2010. **Chapter 9** describes in more detail the impact in London that occurred immediately after centralisation to eight **ASC**s and the impact in Greater Manchester on clinical quality and the large increase in rates of IVT. These and similar service changes demonstrated the importance of establishing high-volume 'expert centres' as a means of increasing IVT treatment rates across large cities.

Outside of major urban centres, centralisation of acute stroke services was not considered practical or feasible, and telemedicine networks were established to create 24/7 cross-organisational teams of stroke physicians able to staff a 24/7 rota, deliver IVT remotely, read NCCT images and assess patients by video link. These networks were successfully able to deliver IVT in hospitals where it was not feasible to provide 24/7 stroke specialist cover out of hours, with acceptable **sICH** complications and mimic treatment rates.[204] However, such networks showed slower door-to-needle times compared with services using direct assessment. Reading of NCCT images supported by remote telephone assessment was also shown to be safe and feasible but, again, with slower door-to-needle times.[206] This indicates the potential role and limitations of remote decision-making support that might be used to help referring hospitals identify and transfer patients with **LAO** for MT.

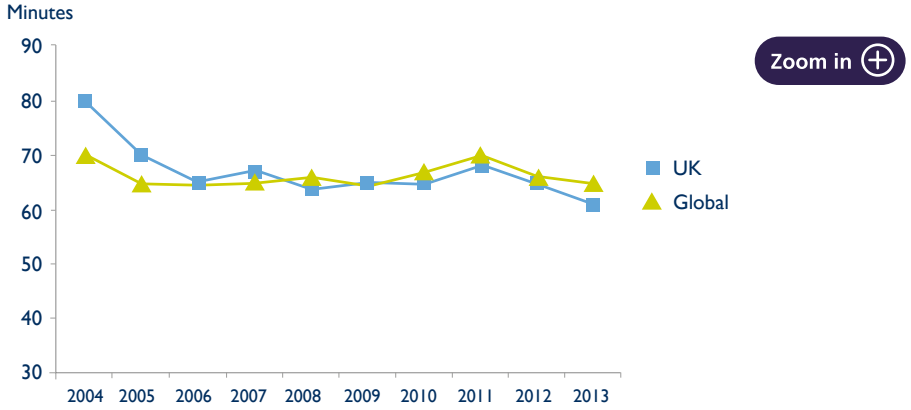
Planning services to manage stroke mimics

Many early clinical service plans modelled bed and staff requirements on the number of confirmed strokes admitted to their hospital and failed to take account of the resources and pathways needed to also manage stroke mimics. As ambulance practice developed and the focus shifted to not missing suspected stroke patients, the proportion of mimics in 999-admitted strokes increased to more than 30%.[206] Suspected stroke diagnoses by ED and non-stroke specialists also had high proportions of mimics,[201] identifying the need to have clear clinical pathways for stroke mimics to minimise unnecessary admission to **ASU** beds. This led to the development of the **ROSIER** scale for use by ED physicians and nursing staff[207] in an attempt to reduce the number of unnecessary assessments in EDs by stroke teams.

The importance of speed and simplifying imaging pathways

When IVT was first introduced, many patients were treated close to the 3-hour time window, with slow access to brain imaging and careful decision-making. Average door-to-needle times in UK centres in the mid-2000s exceeded an hour in most centres. As clinicians became aware of the benefits of treating patients earlier, and became more confident in decision-making, the process of assessment of suspected stroke patients became an area of focus. In the 2000s, protocols for obtaining urgent brain NCCT out of hours frequently mandated discussion with and agreement from the on-call radiologist to perform the scan before a patient was transferred to radiology for a scan, followed by imaging review and reporting by the radiologist. Most efficient IVT pathways now use pre-protocol-driven, nurse-requested imaging, a checklist of eligibility for and contraindications to IVT, and image interpretation by the consultant stroke specialist for decision-making. The adoption of such practices resulted in a steady downward trend in door-to-needle times in the early years after European approval (Figure 22). Initially, delays in accessing immediate NCCT imaging meant UK door-to-needle times were on average 10 minutes slower than other European stroke services but eventually UK services developed quicker door-to-needle times.

Figure 22. Median door-to-needle times in UK and globally.



International experience has shown that with well-organised systems of care, very short door-to-needle times can be achieved without impairing quality of clinical assessment and decision-making. Helsinki is an international exemplar, with door-to-needle times of less than 20 minutes using a 12-step model that has been implemented in other centres in different healthcare systems.[208] The Royal Melbourne Hospital reduced in-hours average door-to-needle times from 43 minutes to 25 minutes after introducing three key components of the Helsinki model: ambulance pre-notification with patient details alerting the stroke team to meet the patient on arrival; transfer of patients directly from triage onto the CT table on the ambulance stretcher; and delivery of alteplase in the CT room immediately after imaging.[209] Pre-notification of suspected stroke admissions by ambulance services to stroke teams has consistently been shown to be associated with more rapid treatment.

Services delivering MT will need to examine similarly the care pathway and use quality improvement approaches to minimise door-to-groin times. A further complexity with the delivery of MT is the need to develop rapid processes for secondary hospital transfers, which is discussed in **Chapter 4**.

One specialty alone could not deliver a national stroke service

In the 1990s, there was much debate about which medical specialty should manage acute stroke. Many neurologists considered that only they possessed the knowledge and skills to diagnose stroke accurately, while geriatricians provided most care to stroke patients who required rehabilitation and were often participating in acute medical rotas, under which most patients with stroke were admitted. The clinicians who had developed acute stroke services and were early adopters of IVT had come from both geriatrics and neurology, with a small number from other specialties such as clinical pharmacology. The creation of stroke medicine as a medical subspecialty, with a defined curriculum including skills from both neurology and geriatrics, was a key development in delivering the necessary workforce and attracting trainees from a range of medical specialties able to deliver high-quality acute stroke care and deliver IVT.

Similar challenges face regional stroke networks and **CSC**s in reporting **CTA** imaging and developing sustainable 24/7 interventionist teams able to perform MT. There are insufficient **INR**s to provide 24/7 services across the 24 English neuroscience centres commissioned to deliver MT and to interpret all CTA imaging undertaken in referring hospitals. As was the case for NCCT imaging and delivery of IVT, stroke specialists in spoke-referring hospitals will need to develop skills to interpret CTA to identify LAO and organise transfer to the CSC. Artificial intelligence developments in CTA analysis may assist physicians in this decision-making process **(see Chapter 5)**.

Training of individuals from other interventional specialties to deliver MT will be necessary to provide sustainable teams of 5–6 operators. NHS England has recently introduced funding to support experienced centres train interventional radiologists to deliver MT.[210]

Conclusion

The implementation of IVT for stroke faced many challenges and was met with opposition by different groups for many years because of the need for radical changes in the way stroke care was provided and the support required from radiology. Although the evidence base for MT is much clearer than was the case after the early trials of IVT, the clinical teams and imaging support required are much more complex, and a number of professional groups oppose implementation of the service changes necessary to deliver MT, albeit less vocally than was the case for IVT. Valuable lessons can be drawn from the experience of implementing IVT to inform the future planning and delivery of MT services across the UK. These include breaking down professional barriers; training stroke specialists to interpret CTA imaging to make treatment and inter-hospital transfer decisions and remove delays in requiring radiologist interpretation; monitoring outcomes and complications over a long period and compared with European centres; working with ambulance and ED teams; increasing public awareness and engaging patients in service transformation plans; and creating multi-professional networks at a regional level.

9 Planning and implementing major system change in acute stroke services: lessons from London and Greater Manchester

Angus Ramsay, Stephen Morris and Naomi Fulop

Key points

- Service models should be designed so that all stroke patients have access to timely evidence-based care.
- Local change leaders should have sufficient authority to ensure all relevant stakeholders engage throughout the planning process.
- Meaningful clinical standards linked to financial incentives, including capital investment and additional transition funding, can help ensure services have sufficient capacity to deliver care.
- Sufficient operational capacity, e.g. from networks, can help facilitate timely implementation of change.
- A clear evaluation plan can help determine whether the planned objectives are achieved.

This chapter describes learning from the implementation of the centralisation of acute stroke services conducted in two large metropolitan areas in England: London (population 8.2 million) and Greater Manchester (2.7 million),[211] drawing out some reflections on how this might inform the approach to delivery of **MT** across England, which will require collaboration across stroke services within a region served by a centre delivering MT (now termed a comprehensive stroke centre; see Box 7).

Although evidence exists on the impact of centralising acute stroke services on delivery of evidence-based care and patient outcomes,[212-220] little is known about how centralisation of stroke services is led and implemented. Exceptions include research on implementing change in Ontario[221] and Denmark[212] and running integrated stroke systems in the USA.[222] We discuss how key factors identified in this other work apply.

Box 7. A note on nomenclature in this chapter

At the time of this analysis of the impact of major system change during 2010–15, centres receiving patients with acute stroke were termed hyperacute stroke units, or HASUs, irrespective of their capability to deliver MT. Updated nomenclature was introduced by NHS England in 2021, referring to comprehensive stroke centres (CSCs, capable of delivering IVT and MT) and acute stroke centres (ASCs, capable of delivering only IVT).

As this chapter describes changes that at the time used the old nomenclature, the Editors have not updated the text to reflect the more recent nomenclature. Similarly, the 'networks' referred to in this chapter have more recently been reconfigured as **ISDN**s.

Background: the drivers for centralisation

The centralisations of stroke services in London and Greater Manchester in 2010 were driven by a potent combination of compelling evidence and policy ambition. The National Sentinel Stroke Audit for 2006 provided evidence of substantial variations in care, with many hospital stroke services performing less well than they had in 2004.[223] There was a lack of 24/7 delivery of care, meaning only people presenting to certain hospitals within certain hours were receiving the right care at the right time – a 'postcode lottery'. There was, in particular, recognition of the need to improve access to **IVT**, which in 2006 was provided to less than 1% of ischaemic stroke patients.[223]

In 2007, the National Stroke Strategy recommended improvements across the whole stroke care pathway – from prevention through to long-term rehabilitation.[197] A key recommendation of the national strategy was that acute stroke care should, where appropriate, be centralised into a reduced number of services.[197] The recommendations noted evidence demonstrating how centralisations could be achieved, including prioritisation of organised stroke care,[186, 196] rapid identification and transfer to stroke units by ambulance,[196, 223] and potential contribution of 'hub-and-spoke' networks of stroke services.[186, 197] However, there was limited evidence on the impact of centralising acute stroke services at scale and on how such major system changes should be implemented.

The changes: centralisation in London and Greater Manchester

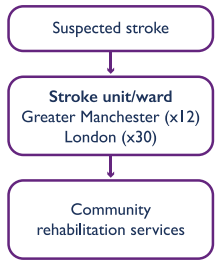
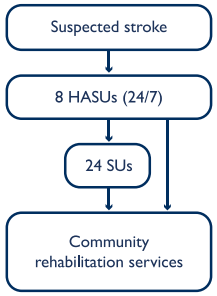
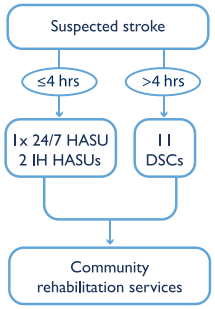
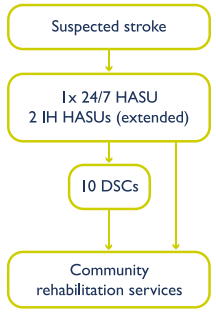
The centralisations are summarised in Table 6. Before reconfiguration, patients with suspected stroke in both areas were taken to the nearest hospital with an **ED** and then admitted to a specialist stroke unit or general medical ward, with significant variation in quality of care (Table 6, 1A). In 2010, both London and Greater Manchester implemented 'hub-and-spoke' models, with a small number of **HASU**s providing acute stroke care over the first hours following stroke, transferring stable patients to units providing ongoing acute and rehabilitation care.[225]

In London (Table 6, 1B), eight 24/7 HASUs were created, offering rapid access to imaging, specialist assessments, and treatment with IVT if appropriate. All suspected stroke patients within 48 hours of onset were eligible for treatment in a HASU, and HASUs were located such that all patients in London were within a 30-minute 'blue-light' ambulance journey. Once stable, patients were discharged to the community or transferred to one of 24 **SU**s providing acute rehabilitation closer to home. Through the changes, five hospital acute stroke services were decommissioned.[225]

In Greater Manchester ('Greater Manchester A'; Table 6, 1C), three HASUs were created (one operating 24/7 and two operating 'in hours', with 'out-of-hours' patients being transferred to the 24/7 HASU). The original plan had been for all patients to be transferred to a HASU, but, following resistance from local providers, a 'partial' centralisation was implemented: only stroke patients arriving at hospital within 4 hours of symptom onset and thereby potential candidates for IVT were eligible for treatment in a HASU. Therefore all services – three HASUs and 11 **DSC**s – still treated acute stroke patients, and no hospitals lost their stroke services.[226]

Following a review that showed this system had not delivered the anticipated benefits, Greater Manchester further centralised acute stroke services in 2015 ('Greater Manchester B'; Table 6, 1D). Through this, all suspected stroke patients were eligible for treatment in a HASU (in line with London), and the in-hours HASUs extended to a 7-day service, receiving patients between 7 am and 11 pm.[226]

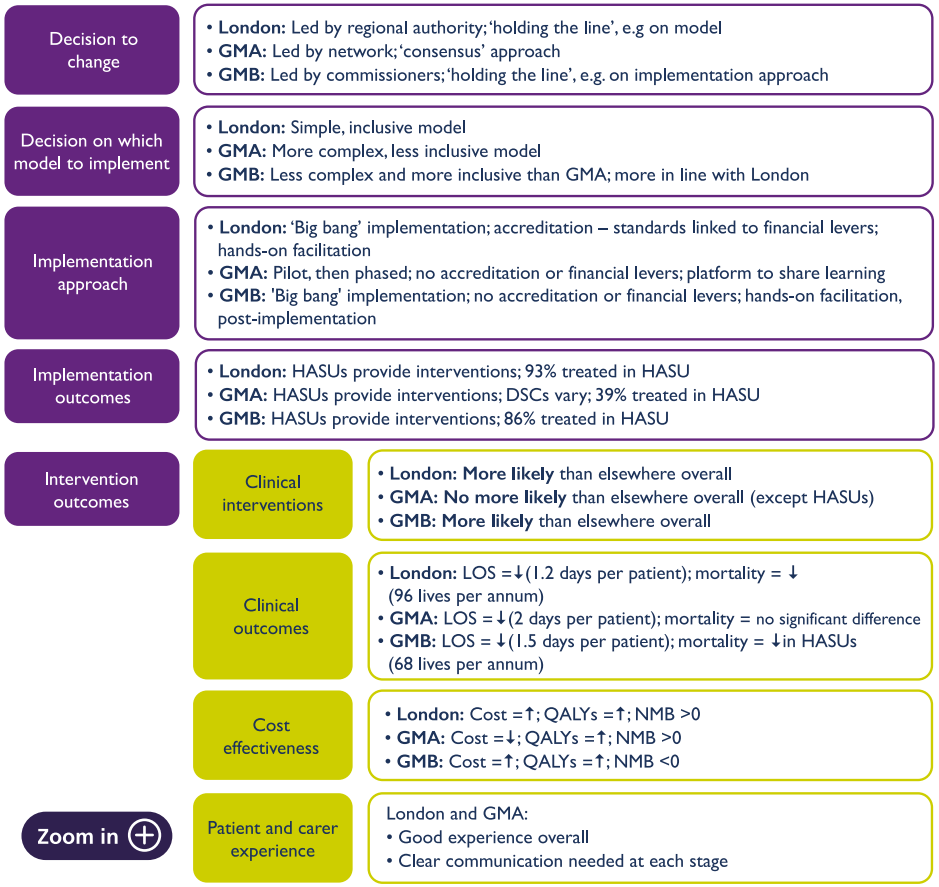
Table 6. Pre- and post-reconfiguration models in London and Greater Manchester. Adapted from Fulop *et al* (2019).[226]

1A. Both areas before – 'local, but variable care' **Services admitting stroke patients:** • Greater Manchester: 12 • London: 30 **Accessing services:** • All patients taken to nearest hospital with SU • Transferred to community once stable • Variable access to evidence-based care • Little/no 24/7 access to thrombolysis	
1B. London (implemented 2010) – 'radical centralisation' • Eight HASUs • 24 SUs (providing acute specialist stroke rehabilitation) • Five services were decommissioned **Accessing services:** • All stroke patients were eligible for treatment in a HASU • All HASUs admitted suspected stroke patients 24/7 • This model remained for the duration of our study	
1C. Greater Manchester 'A' (implemented 2010) – 'partial centralisation' • One 24/7 HASU; two HASUs admitting in-hours (IH) • 11 DSCs provided post-4-hour care and ongoing acute rehabilitation services • No services were decommissioned. **Accessing services:** • Only stroke patients presenting within 4 hours of developing stroke symptoms were transferred to a HASU • In-hours HASUs admitted 7 am–7 pm, Monday–Friday	
1D. Greater Manchester 'B' (implemented 2015) – 'further centralisation': • All stroke patients eligible for treatment in HASU (in line with the London model) • In-hours HASUs extended hours to 7 am–11 pm, 7 days per week • These changes brought Greater Manchester's service model closer in line with the London model Zoom in	

The impact of the changes

Figure 23 summarises the impacts of the service models implemented in London and Greater Manchester. The London centralisation resulted in significant reductions in patient mortality and length of hospital stay over and above those seen in the rest of England (with an estimated 96 additional deaths prevented per year)[219] and significantly higher likelihood of delivering evidence-based clinical interventions than elsewhere;[218] the changes were cost-effective through their impact on outcomes.[227] Follow-up analysis demonstrated that London's greater impact on care and outcomes compared to the rest of England was sustained through to 2016.[219, 226]

Figure 23. Summary of findings in relation to framework for major system change. Figure adapted from Fulop et al (2019).[226]



Greater Manchester A had significantly reduced length of stay but no significant effect on patient mortality over and above the changes seen in the rest of England.[219] Although HASUs were more likely to deliver clinical interventions, only 39% of patients were treated in a HASU, resulting in Greater Manchester patients being no more likely to receive interventions than elsewhere.[218] The changes were cost-effective, mainly due to reduced costs through reduced length of stay.[227]

Following further centralisation, Greater Manchester B had significant reductions in length of stay, a borderline significant reduction in mortality overall, and a significant reduction in mortality over and above the changes seen in the rest of England for the 86% of Greater Manchester patients treated in HASUs; patients were also significantly more likely to receive clinical interventions than elsewhere.[220]

In terms of patient experience, qualitative research suggested that patients and carers had positive experiences of centralised stroke care: although patients had concerns about not going to their nearest hospital, they prioritised high-quality care over shorter travel times. Patients indicated the importance of having clear information at every stage of care.[228]

Planning the changes

At the time, the evidence on how to centralise acute stroke services was not strong, and both areas saw much debate on how best to design a new system. There was resistance from local services, clinicians and the public, raising concerns about loss of services and risks to patient safety through increased travel times.[229]

The London changes were part of a wider programme to reorganise health services led by the Strategic Health Authority (a body with formal authority over local payer organisations and in setting regionwide healthcare objectives which was dissolved in 2012). Programme leaders thus had 'top-down' regional authority and infrastructure to support high 'bottom-up' engagement by local clinical leaders in planning the changes.[229, 230] A wide range of stakeholders – including hospital and ambulance providers, payers, politicians, and patient and public representatives – contributed to development of the service model. They were involved in programme oversight, designing new service standards and pathways, and developing financial arrangements. Such arrangements included an uplifted stroke tariff to cover delivery of the new system, particularly acute and ambulance services (representing about £20 million additional funding annually);

in addition, £9 million capital costs were borne by local hospital services. Local hospitals applied to provide the new HASU and SU services and were selected based on their ability to deliver on service standards and geographic location (to ensure that patients were within 30 minutes of a HASU by 'blue-light' ambulance).[229] Two waves of formal consultation contributed to the London changes. The first of these established substantial public support for the creation of 'about seven' HASUs to serve the London area. The second consultation focused on the shape of the service model and which hospitals would host the new services. Each consultation was led by local commissioners and scrutinised by a committee representing all local authorities across London, helping to achieve pan-London engagement from both payers and politicians.[229] By combining 'top-down' regionwide authority with 'bottom-up' clinical leadership, system leaders of the changes were able to 'hold the line' when significant local resistance to change arose, e.g. in relation to the number, function and location of HASUs.

In Greater Manchester, the changes implemented in 2010 were led by the local stroke clinical network with endorsement from local commissioners, without involving the Strategic Health Authority. This network's approach was mainly 'bottom up', dependent on ongoing support from local stakeholders. Many stakeholders contributed, with local clinicians leading the design of new services and commissioners leading development of financial arrangements. Instead of conducting formal consultation on the changes, planners engaged regularly with local clinicians and held consensus events. The new service model was approved by local commissioners and an advisory group combining external experts and local representatives.[229] As implementation began, some local services became concerned about risks to patients and loss of activity. Because the network's approach had been reliant on consensus, this threat to unanimity led to a revised service model, introducing the '4-hour window'.[229] A 12-month review in October 2011 recommended that further centralisation should be considered. While this prompted new stakeholder consensus events in summer 2012, major obstacles to change emerged at this time, including the impending reform of the English NHS: this led to uncertainty and delays in agreeing further change.[226] A new implementation board was convened in 2014: this regained a degree of systemwide leadership by drawing on local commissioner leadership, increasing engagement of local clinicians, and using evidence from national audit and independent evaluation to make the case for further change. An independent evaluation estimated that further centralisation would save 50 additional lives per year.[220, 226] These changes were then implemented in 2015.[226]

Implementing the changes

How change was implemented also played an important role. Key factors included the models themselves, launch date, use of standards linked to financial incentives, and degree of hands-on facilitation.[231]

The London model was seen as clear and inclusive: it was more likely to be understood and followed by hospital and ambulance staff, maximising the proportion of patients who were treated in a HASU. The London HASU/SU services had to accredit against clear clinical standards in order to launch, and delivery of standards was linked to an uplifted tariff for stroke services. Clinicians and managers indicated that the financial incentive and regular service reviews were an important lever to ensure ongoing prioritisation of stroke by local senior management.[231] While HASU/SU services developed over several months, change leaders agreed (in line with feedback from ambulance services) that there should be a single official launch date after which the referral pathway was applied to all suspected stroke admissions. This single launch date increased people's clarity about the system and thus increased the likelihood of all patients being transferred appropriately.[231] Services had much to do to meet the new service standards (e.g. recruiting staff and developing new care protocols) by the launch date. The local stroke networks took a hands-on approach to facilitate change, providing service development advice, project management support, and central oversight that prioritised timely implementation. This combination of service model and implementation approaches probably increased the likelihood of patients receiving evidence-based care.[231] In addition, many key aspects of implementation – including standards linked to financial incentives, regular service reviews and clinical leadership – were identified as important to the ongoing sustainability of the system;[226] another factor was independent evidence of the impact of the London changes (e.g. national audit data and independent evaluation), which increased clinical and managerial support for the centralised system.[227]

Greater Manchester's more complex referral pathway resulted in reduced adherence.[231] Although service standards were developed in Greater Manchester, services were not accredited against them in order to launch. There was no linkage to financial incentives, which may have led to greater variation across services.[231] Compared to London's launch on a single date, implementation in Greater Manchester was phased, with the system changing repeatedly over a 15-month period. This caused uncertainty among hospital and ambulance staff about where potential stroke patients should be treated, both

during and after implementation.[231] This combination of factors reduced the likelihood of patients being treated in a HASU (including many patients who were eligible for HASU care), and delivery of evidence-based care varied more across the system. Taken together, this helps explain why patients in Greater Manchester were less likely to receive evidence-based care.[231]

Greater Manchester B was simpler and more inclusive than its predecessor and was associated with a significant increase in the proportion of stroke patients being treated in a HASU. In addition, change leaders learned from previous experiences, drawing on service reviews to drive change, and they 'held the line' in insisting on there being a single launch date. Finally, an **ODN** became a key support in embedding the new system post-implementation, facilitating regular audits and systemwide discussions needed to maintain effective system operation.[226] This ODN has subsequently become the current Greater Manchester ISDN.

Lessons from centralising acute stroke services in London and Greater Manchester

If MT is to be provided safely and effectively to stroke patients across the English NHS, regional acute stroke systems will need to be developed and reorganised so that units have the necessary capacity to deliver MT 24/7 and so that all patients can access these units in a timely manner.[105 107] Delivering this will require major system change, similar in complexity to the changes described in this chapter. Several important lessons for future reconfigurations to deliver MT may be drawn from these experiences.

Although this research extended understanding of the implementation and impact of centralised stroke services, other forms of centralisation exist and may be relevant when planning service models for delivering MT. Examples include where 'spoke' services carry out initial assessment and treatment of patients before transfer to a specialist centre, and full co-location of hyperacute care and acute rehabilitation. Furthermore, it should be noted that London and Greater Manchester are large, urban areas; therefore, the degree to which our findings can be applied to more rural contexts is limited.

We present clear evidence that models that prioritise delivery of an intervention that benefits only a small proportion of stroke patients (e.g. as Greater Manchester A did with its 'thrombolysis window') reduce the likelihood of systemwide improvement. Planners should therefore ensure that optimising access to MT is not at the expense of other interventions that offer significant benefit to all stroke patients, especially access to organised stroke care/HASUs.

Centralisation of the acute pathway – whether to increase access to HASUs or CSCs – will result in increased travel times for many stroke patients, particularly in rural settings. We found that patients and carers are willing to travel for longer if the new system delivers better care and outcomes. However, planners should engage actively with patient and public views on proposed changes to ensure that future models are considered acceptable and do not disadvantage specific groups.

To ensure selection of a suitable service model, local planners should combine systemwide, 'top-down' authority with 'bottom-up' clinical leadership. This can help align multiple stakeholders to overcome likely resistance to change. Use of top-down authority has also been observed internationally, where regional politicians in Central Denmark stood firm on their planned number of regional specialist stroke centres in the face of opposition from a local hospital that wished to host its own centre.[212]

Engaging relevant stakeholders across the system (including hospital and ambulance services, payers, patients, the public, and patient and public representatives) can support systemwide ownership of proposed changes. The value of engagement is also identified in international experience of reorganising services in Ontario and providing integrated stroke services in the USA (Florida, Massachusetts, New Mexico and New York), which describes how local champions (clinical or non-clinical) can facilitate widespread support for the system.[222] In contrast, in Central Denmark, change leaders rejected engagement (e.g. with patient representatives, professional organisations, primary care, and municipal level of governance), and this change saw an unexpectedly large increase in referrals and lack of awareness of the new system outside hospital services.[212]

Collecting and sharing evidence (e.g. local reviews, national audit and independent research) should be used to drive and sustain change. International experience reflects this, with local inspection and accreditation identified as supporting ongoing compliance and improvement.[221, 222]

Clear specification – of both service model and implementation approach – may support better understanding and uptake of the new system. Use of quality standards linked to financial incentives increases the likelihood of services delivering evidence-based care. International experience also supports this, noting how regionwide pathway guidelines for services[212, 221, 222] and implementation[221] facilitated a shared understanding of the system among staff and across organisations.

Although phased approaches are common in quality improvement activities, the experience presented here suggests that a single launch date for a new system offers clarity for hospital and ambulance staff. A phased approach was used when reorganising Central Denmark's stroke system, with gradual closure of beds over a 20-month period, but the impact of this was not evaluated.[212]

Hands-on facilitation by networks – e.g. through on-site project management and central oversight of timelines – provides the operational capacity and impetus to ensure timely delivery of change. Independent evidence (through audit or evaluation) can help sustain a model that seems to be working well or build a case for further change where necessary. Finally, change is not a one-off: assessing the evidence and responding accordingly might result in further change; internationally, the Ontario changes were used as a platform to develop new research to generate new evidence, which was felt to be key to ongoing development of the system.[221]

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10 Establishing a regional thrombectomy service

Don Sims

Key points

- Staff across the care pathway, including those who interpret **CTA**s and assess patient suitability in referring centres, must be trained with the new skills to deliver **MT**.
- A clear idea of total costs and how many thrombectomies are required to deliver a financially sustainable service is crucial.
- Necessary infrastructure must be planned, including access to biplane neuroangiography equipment and sufficient capacity at the **CSC** to manage patients transferred from other hospitals.
- Engaging ambulance services with tools to identify possible **LAO**s out of hospital and convey them directly to a 'mothership' may be crucial in future.
- Appropriate system governance is required to review outcomes and feed back results and timings to referrers to ensure the pathway is safe and efficient.

Mechanical thrombectomy is particularly challenging to deliver, because it is a specialised, time-critical intervention requiring a significant-sized team that must be available in a timely manner to maintain an effective service. In contrast to other stroke service developments, such as **IVT**, MT is much more complex as it requires collaborative working across multiple sites and specialties, including interventional neuroradiology and anaesthesia, which have until recently had little involvement in the management of **AIS**.

Many of those setting up a MT service will be familiar with initiating an IVT service, so it offers a good starting point for comparison. Office-hours IVT services were often started in trusts after the stroke specialist nurse and stroke consultants attended a single training day. Negotiation with radiology was needed to get **CT** scans performed immediately, and staff on stroke wards required training in monitoring and managing complications after IVT. From this platform, services were extended around the clock, often involving consultants who were not necessarily stroke specialists but were keen to support delivery of this innovative treatment.

Mechanical thrombectomy requires many more specialist staff to run often entirely new rotas out of hours, with the training for interventionists unfamiliar with the procedure requiring years rather than days. Like thrombolysis, MT also has to be delivered as soon as possible to preserve as much brain parenchyma as possible, and the mantra of 'time is brain' remains crucial. An additional challenge is that while IVT is delivered in all ASCs, MT can currently be delivered only in a much more limited number of CSCs in hospitals with neuroscience centres with an on-site interventional neuroradiology service (just 26 in the UK at the time of writing). This therefore requires assessment and rapid onward transfer of significant numbers of potentially unstable patients to MT centres.

Neuroradiology staffing

Personnel costs make up most of the NHS budget, and staffing a service is the biggest challenge faced, because MT requires additional staff across a number of disciplines and a skill mix that is already in short supply. It is difficult to exactly specify the additional staffing needed to establish or expand a MT service, because every hospital has different configurations of existing staff depending on the other specialties and services they offer. A CSC within a aneuroscience centre that already does significant volumes of interventional work will have different needs to smaller centres, but nevertheless many similarities and parallels can be drawn.

For the procedure itself, the overwhelming majority of current CSCs and most future centres will need consultant **INR**s trained in the intervention; however, credentialling for staff from other specialties is being made available by the General Medical Council. Although an initial office-hours service can be supported by three or four INRs, a sustainable 24/7 rota requires at least five or more likely six operators to ensure the service is resilient. Too many operators on a MT rota can also cause issues if the number of cases is insufficient for the staff to maintain the skills required. If a new MT service is set up in

a CSC without a neuroscience centre run by trained interventionists from other specialties only doing MT for acute stroke, the level of activity to maintain competence will need to be agreed and monitored.

Depending on the number of existing INRs present in the CSC, some would need an additional two to four consultants. In addition, neurointerventional nurses are needed to support the procedure, as is a radiographer trained in the use of biplane digital subtraction angiography. Anaesthetic support is also needed to safely deliver MT; although many patients do not require escalation to a general anaesthetic, it can be hard to determine this prior to the procedure. Currently, our experience has been that about 50% of patients have required a general anaesthetic, either initially or during the procedure, and we have had a neuroanaesthetist and an **ODP** available for all procedures. However, there is wide variation in the use of general and local anaesthesia in the UK.[193]

The limited number of neuroanaesthetists is nearly as challenging as the shortage of INRs in the UK. Other teams with whom we work confirm that the anaesthesia required for MT is not particularly complex, so although services should be led by a neuroanaesthetist, the procedure itself could be delivered by a general anaesthetist. This still requires support from an ODP, who are also in short supply in the UK.

The need for MT to be done in a timely manner means that staff cannot, for the most part, be used for other services without jeopardising the timely delivery of MT. Our service needed additional nurses and radiographers knowing that the frequency they would be called in would greatly increase but that they could stay on existing aneurysm coiling rotas, which can usually be delayed for more urgent stroke cases. However, as the anaesthetic team was already fully occupied undertaking other resident roles, we needed a completely new rota specifically for MT so the costs in our centre (Queen Elizabeth Hospital, Birmingham) were high, although this may not be the case elsewhere.

Stroke staffing

Procedures have to be in place to determine whether the patient is still suitable for MT on arrival and to ensure that appropriate acute care is started for a potentially unstable group of patients after MT. The decision to proceed to MT is complex and should be made jointly between a stroke physician and INR, supported by appropriate imaging if not already undertaken in the referring centre, such as **CTP**.

Patients require care for at least 24 hours following the procedure. Some centres have been successfully undertaking MT followed by immediate repatriation, bypassing the need for stroke team and **ASU** involvement at the CSC. However, we believe that this model of care carries risks due to the lack of close involvement of a stroke physician and team in the peri-procedural period.

Stroke teams also have a potential peri-procedural role in cases where the MT is proceeding under only light sedation. A stroke team assessment of the patient's clinical status (by stroke specialist nurse or consultant) can help INRs determine whether any remaining vessel occlusion after a partially successful procedure is worth pursuing due to residual neurological deficit, potentially reducing the risk of the procedure continuing unnecessarily if the symptoms are sufficiently resolved. Our practice has been that when the procedure tends towards an hour with no improvement or when the total time from onset passes the 6-hour window, the decision to continue or abandon the procedure is made jointly between the interventionist and stroke physician.

Post-procedure, a joint decision is again needed about the type and timing of antiplatelet therapy, as research trials in this area have yet to be done. A judgement is needed based on how much instrumentation was required, whether lysis was given, and the patient's risk factor profile for bleeding complications.

Finally, although many patients have near full or significant improvement immediately after MT, a significant proportion do not. Some patients will still have the total anterior circulation stroke that was originally threatened, and a few will have symptomatic haemorrhagic transformation or need subsequent decompressive hemicraniectomy, necessitating neurosurgical involvement. As most MT is carried out in CSCs with onsite neurosurgery, it seems counterintuitive to repatriate early, only for the patient to need to return for hemicraniectomy. Our opinion therefore remains that, in most cases, 24 hours post-procedure on our ASU to allow for repeat CT and check the potential need for other interventions is appropriate before repatriation to the referring hospital ASC, even if this is a comparatively rare occurrence.

We have based our service on the expectation that about 4 hours of stroke consultant time is needed per MT case. This includes initial discussion of the patient with the referrer

right through to the patient arriving on the ASU after their post-procedure CT, as well as the governance to maintain a safe service. In centres with a tier of middle-grade medical staff, it may be that this can be reduced, but certainly in our centre, like many others, it remains a consultant-delivered service from all involved specialties.

Staffing an expanded ASU, with the additional trained nurses competent in post-MT care, is also essential, as are the therapy requirements that go with acute specialist care. The additional bed capacity needed for any individual CSC that delivers MT is difficult to generalise. It depends particularly on two factors – the total number of MTs being provided and especially how many are referrals external to the CSC and the average length of stay at the MT centre. For our service to date, one additional HASU bed has been needed per 100 MTs undertaken annually.

Financial implications

The delivery of successful MT offers a real potential for saving hospital bed-days in acute and rehabilitation hospitals. The total savings dwarf the cost of the intervention when the reductions in social care costs and informal care costs are also taken into account. However, from a single trust perspective, the finances are much more challenging and need to be considered before starting the service. An overall reduction in total acute hospital stay for a typical MT patient compared with an untreated similar case is very likely. Our own internal audit suggests this may work out at an average of 3 days or more in reduced acute hospital stay per treated patient. Although this sounds promising, it is not the complete story, because this is the saving on a CSC's length of stay for patients treated with MT who would normally have presented to their front door. Most CSCs serve a MT catchment area well in excess of their local catchment and will be receiving many, if not most, patients from external ASCs. The savings will still be accrued in total length of stay, but the CSC is now looking after patients on its ASU that it normally never would have seen, and, even with prompt repatriation on day one or two, these are all extra bed-days in the CSC that need to be accommodated in any business case. The NHS overall and, most importantly, patients will undoubtedly benefit from a regional MT service in terms of less disability and shorter lengths of stay, but individual CSCs must recognise that they may need significantly more ASU beds – with all the associated staff – to deliver these savings.

All of these factors mean that the business case for MT, especially for an individual trust, is finely balanced and needs careful planning not just internally but also with neighbouring trusts and NHS England Specialised Commissioning. It is not possible to generalise costs for individual centres because of the range of variables involved and the different starting points for each centre. The economies of scale play an important role in finding the balance or break-even point. Our internal calculations suggest a break-even point at about 250–300 MT cases at the current English tariff. This would change with different tariffs and would be more favourable if MT devices were 'excluded' from the tariff or if costs come down, either because of competition between device providers or increased use of cheaper aspiration catheters.

Because MT will require new rotas of staff available at a moment's notice, most costs are incurred up-front. In England, the income from MT is set by Specialised Commissioning and is paid on a per-patient basis. This means that once the service is set up, we have estimated that about 75% of all eligible patients in our catchment would need to be receiving MT for the costs to be covered by the tariff. It is particularly important for individual trusts to calculate this correctly. Whatever clinicians feel about the market model, if you get these calculations for MT wrong and rotas of staff are in place but the cases do not present (for whatever reason), unrecovered costs can amount to millions of pounds a year. For the time being, this risk is mitigated by the present arrangement for Specialised Commissioning to agree with CSCs a 'floor' for annual activity based on projected growth, while not also imposing a 'ceiling' for paid activity – a significant safeguard to assist medium-term planning. As stated earlier, it is very difficult to make generalisable statements about costs and bed-days, but we calculated that a CSC probably needs one extra bed per 100 externally referred MTs, but centres treating a much higher proportion of their own patients may be able to save this by reducing their overall length of stay for stroke.

Finally, there was much discussion about how to introduce the service – either 24/7 immediately or in stages. After a 9 am-5 pm start, centres may consider phased increases in service hours. Again, individual circumstances and local staffing issues may dictate the model, but, from a purely financial perspective, a model that was functional and responsive 7 days a week until 8 pm or midnight was barely cheaper than a full 24/7 service, so we have elected to move straight to the latter once all staff were in post. Such a rapid transition may not be feasible for centres starting from a lower baseline for staffing.

Working with referrers

Ideally, all eligible stroke patients would be conveyed by ambulance directly to a CSC, but this would require accurate recognition of patients with LAO by ambulance paramedics, which is currently not feasible (**see Chapter 4**) and would require substantial reconfiguration of our current service. Service modelling (**see Chapter 3**) suggests this would not be sustainable for most centres. For the foreseeable future, therefore, patients will still have to be selected for urgent transfer from ASCs to CSCs, which need to be able to work effectively with referring hospitals in their region or network (Box 8), and, for some regions, this may also involve transport by air ambulance or dedicated retrieval teams.

Box 8. Requirements for CSCs working with referring ASCs

- Clear and rapid pathways for referral
- Engagement with ambulance trusts
- Correct infrastructure for rapid imaging transfer
- Clinical skills in all ASUs for caring for repatriated MT patients
- Agreements on patients being transferred with thrombolysis with alteplase often still running (unless tenecteplase becomes more widespread)
- Trained staff to support the unstable patients and any infusions during transfer

Agreed pathways for immediate repatriation should be in place for patients whose symptoms have resolved on arrival or in whom MT is not felt to be indicated due to futility or other issues, although in our experience this is infrequent.

Regardless of the referral model, repatriation pathways and escalation policies need to be firmly in place. The lessons from longstanding similar issues in neurosurgery and more recently with major trauma centres need to be learnt if a CSC is to avoid congestion.

Comprehensive stroke centres that take significant numbers of additional patients for MT must ensure that those new patients and also the majority of patients who normally present to their front door but are not candidates for MT still have access to usual ASU-level stroke care. Delays in repatriation of referred MT patients, even by a day or two, have the potential to quickly overwhelm a service, especially regarding their ASU capacity and therefore access. Care is also needed to avoid the development of a two-tier service between those who receive MT and those who do not.

With regard to repatriation, we are referring patients back to a local ASC-level bed, so some medical instability should not be a barrier. We are also referring patients back to the team that initially referred them, who will likely have another MT-eligible patient to send soon, so co-operative working is encouraged. Unlike in the funding agreement with major trauma, the accepting ASC will (under current arrangements in England) receive a full stroke tariff despite not having the patient back until they are 1–2 days into their pathway, having already received some costly interventions in the CSC.

Our experience to date suggests that clinical acceptance of a patient for repatriation is the easiest step, with physical location of a bed on the stroke unit at the referring ASC usually the barrier to the smooth flow of patients. Other issues, such as patients refusing to return to a referring ASC and difficulties accessing local **ESD** services from a more distant hospital, are rarely a major issue, but do occur. Financial penalties for not taking back a patient who is ready are popular among some clinicians but in practice are difficult to facilitate in a system where the MT tariff is controlled by Specialised Commissioning. Small financial penalties do not, of course, create beds.

For a 24/7 service to function and flourish, prompt repatriation is vital and may prove to be the issue that grinds otherwise functioning networks to a halt. If staffing a service remains the biggest challenge to starting 24/7 services, repatriation is the biggest challenge to keeping it running, and it needs to be explicitly addressed within regional networks from the outset.

Infrastructure

It is easy to concentrate on changes in the CSC providing the service, but critical parts of the pathway occur outside the CSC. Many ASCs across a network need to change practice to allow them to identify all potentially eligible patients with LAO in a timely manner. Sometimes the stroke decision-maker (for IVT and also now for MT) is at home out of hours, and decision-making processes are reliant on non-specialists such as medical or **ED** registrars. Many centres in the UK have saved costs by exporting their out-of-hours radiology reporting service to an external provider. These changes do not provide a strong foundation to prompt decision-making based on clinical assessment and accurate and timely **NCCT**/CTA reports (or, in some cases, advanced brain imaging).

Expecting CSCs to accept all potential MT cases seems impractical given the difficulty non-specialists (and sometimes specialists) have in making a clear diagnosis of stroke, never mind one with a likely LAO. All currently available pre-hospital LAO scales have significant false-positive rates (see **Chapter 4**). For a hub-and-spoke model to be sustainable, some screening out of non-stroke patients and stroke patients without LAO needs to occur (see **Chapter 3**). Our view, in discussion with referring centres, is that the decision-maker (often a stroke physician) has to be trained to a level where they can interpret a NCCT/CTA to determine if there is a LAO in an ischaemic stroke patient. Otherwise CSCs risk being overwhelmed with mimics and patients with non-LAO strokes. It is not feasible with current UK neuroradiology consultant numbers for all CTAs obtained in referring ASCs to be immediately reported and reviewed by **CSC** neuroradiologists.

Conclusion

It is vital to ensure that appropriate staff across the care pathway are trained with the new skills required to deliver MT, including the ability to interpret CTAs and assess suitability of patients in referring ASCs. An appropriate governance structure is required to review outcomes and to feed back the results and timings to referrers to ensure the pathway is efficient. The tariff for MT is significant, but so are the start-up costs, most of which occur prior to launch. A clear idea of total costs and how much activity is required to deliver a financially sustainable service is crucial, which is very dependent on local circumstances. Planning the necessary infrastructure is essential, including access to a biplane imaging intervention suite and sufficient CSC capacity to manage patients transferred from other hospitals.

11 Developing a business case for mechanical thrombectomy

Marcus Bradley and Carolyn Roper

Key points

- Define the clinical model before any modelling and development to give the programme a clear anchor from which to make assumptions and maintain a consistent thread through all work.
- Engage key internal and external stakeholders early, including stroke team, interventional neuroradiology, anaesthesia and theatre services, local ambulance service, local stroke network and IT services.
- Consolidate existing or *ad-hoc* service before considering expansion.
- Phase the development of the service as a manageable operational approach; accept that some assumptions about future phases will need to be revisited before the entire service expansion to 24/7 is complete and use good governance and steering groups to oversee this.
- Brief key senior decision-makers as the business case is being developed and understand their requirements and any concerns before the business case enters the approval process.

Introduction

In 2016, NHS England began a commissioning process for the provision of **MT** to patients in England. This was in response to a series of clinical trials that demonstrated conclusively that MT was both effective and safe for patients with **AIS** due to a **LAO** in the anterior circulation. The magnitude of this task is enormous given that this is a highly specialised procedure performed by a small number of **INR**s working in teams based only in neuroscience centres. To support such a service requires a fundamental restructuring of regional stroke services and expansion of the trained workforce.

North Bristol NHS Trust (NBT) hosts the regional adult neuroscience service and provides MT for a population of 2.4 million in a largely rural setting across Gloucestershire, Wiltshire, Somerset and Bristol. Prior to NHS England initiating formal commissioning, the stroke and interventional neuroradiology team at NBT had developed the *ad-hoc* capacity to deliver MT for the patients in this region within the constraints of available resources. This was possible because of a pre-existing stroke and cardiac network, which was tasked with implementing the National Stroke Strategy in 2008 and increasing uptake of **IVT** . This provided a network of stroke physicians, a digital infrastructure for image sharing, and a regional clinical forum to examine the latest evidence, including the evolving field of MT, and also provided the impetus to develop the service to date.

During this period, the trust consolidated services on one site in a new hospital and provided new facilities from which the acute stroke service could be run.

The stroke network offered insight into future developments in the treatment of stroke, informing the design of the new hospital, which included two biplane angiography suites suitable for neurointerventional procedures.

North Bristol NHS Trust background

North Bristol NHS Trust had an established MT service that treated approximately 100 patients in 2018 and, before service development work started, provided a service that operated 9 am-4 pm Monday to Friday – the level of service that could be provided by the neuroradiology and stroke workforce at that time. At that point, there had been no specific capacity investment in the MT service, and activity had been accommodated within existing resources.

In April 2018, NHS England requested that neuroscience centres develop a plan for the delivery of a 24/7 stroke MT service. The NBT management team requested a clear service development plan and investment business case to support delivery of such a service over the next 5 years. The 2021/22 NHS tariff for providing MT is £12,543 (MT tariff [YA13Z] only, and this does not include any market forces factor).

A programme started that culminated in substantial agreed investment in the MT service. In this chapter, we describe our experience in developing a business plan that gave the trust confidence to invest in the service development. The programme of work was underpinned by two key factors: getting the right information in the business case to facilitate approval and ensuring that this information was underpinned by good governance and decision-making.

Framing the business case

A good business case provides decision-makers with a clear vision of the service it intends to achieve and the investment required succinctly summarised as 'a written argument that is intended to convince a decision-maker to approve a course of action'. It is important to consider the audience reading and approving the business case, their varying knowledge of MT services, and the elements that need to be covered in order to agree the case for investment. The following aspects were included:

- A description of MT and the commissioning rationale, including the compelling evidence of clinical and cost-effectiveness
- Alignment of the MT service to the wider NHS, local **STP** and the trust's strategy, goals and mission
- A clear clinical, operational and financial case that supported a structured argument for investment
- Involvement of all stakeholders in development and agreement of the service model and key planning assumptions, such as projected activity growth
- Key milestones to achieve the service development and enablers of and risks to delivery
- What the service would bring to the organisation's financial bottom line and any mitigation that might increase the pace at which the service yields a positive return on the investment
- The impact on other services, both internally and externally.

Good governance

A Stroke Thrombectomy Steering Group was established, which oversaw development of the MT service plan and maintained focus and resource on this service development. This group was chaired by the trust's chief operating officer who acted as the programme senior responsible officer, spanned several divisions (neurosciences, critical care and imaging), and included key decision-makers capable of progressing decisions on business cases.

The function of the group was threefold:

- To support cross-divisional development and agreement of an investment business case
- To support implementation of the service development and changes
- To raise the profile of the service and prepare stakeholders prior to the business case being submitted for approval.

Cross-divisional commitment was ultimately required to expand the service, so it was imperative that all divisions were represented and contributed to service planning. Activities included reaching agreement on key activity and growth assumptions and on the timescales for delivery. Minutes from steering group meetings provided an audit trail of key planning decisions. A number of individuals working on the steering group were representatives at the key trust executive meetings that gave final approval of the business case. Early involvement equipped them to comprehensively present and field questions during the approval process.

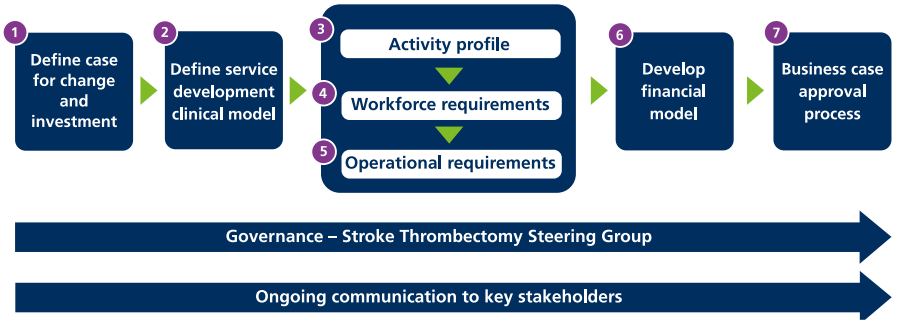
The level of investment required was significant – more than £2 million for the first stage of service development – and required approval at trust board level.

Business case development process

Figure 24 shows the process that was followed, which combined the pragmatic application of best practice in service development and business case development methods to ensure the business case progressed quickly.

Figure 24. Business case development process.

Zoom in



Be clear on the starting position and case for investment

Information from internal governance processes and from cases submitted to **SSNAP** should be used as a baseline to understand the number of potential MT patients. In developing the business case, we drew on our existing knowledge and experience of delivering MT, which supported the development of referral pathways from the **ED** and the wider network and had already optimised referral methods, scanning protocols and anaesthetic support.

One of the first actions was to clearly describe the current service and inform relevant stakeholders in the trust of the rationale for developing a sustainable expanded service. This included highlighting that MT was now an NHS England-commissioned service.

Clearly articulate the clinical development process

The case for investment had to be underpinned by clinical consensus on a well-articulated pathway. The option to expand immediately to a 24/7 service was discounted at an early stage due to the national shortage of INRs and stroke physicians. A phased approach was preferred, so work focused on how to structure the phasing, with options considered against the following criteria:

- Sustainable clinical services
- Maximise currently available interventional neuroradiology capacity
- Stroke network readiness to identify and refer patients for MT (expected referral volume for each centre *versus* actual referral volume to date)
- Workforce availability
- Cost-effectiveness – investment *versus* return.

The MT steering group's recommended approach to service expansion was to stabilise the current service, with three phases of expansion:

- Phase 1 – stabilisation of current service (9 am–4 pm Monday–Friday) and expansion to 8 am–8 pm Monday–Friday
- Phase 2 – 8 am–8 pm 7-day service
- Phase 3 – 24-hour 7-day service.

This phasing was used as the framework to build the activity profile and subsequent interventional neuroradiology, **ITU** and **ASU** bed capacity. Once this approach had been defined, it was agreed that a full business case covering all three phases would be difficult to produce due to workforce uncertainty and further detailed work on workforce rotas and models. To enable activity modelling, estimated start dates for each phase were defined, based on current workforce intelligence, with the caveat that these would be reviewed in the future. The goal was to complete Phase 3 within five years – in line with NHS commissioning intentions – with intermediate stages implemented as service development permitted.

Profile the activity in the clinical development model

As with any activity modelling, various assumptions had to be defined and agreed by the steering group. For the purposes of modelling potential activity, an agreed catchment from which most patients would be referred was defined as the Severn region, which aligned with the major trauma and neuroscience centre footprint. This was tested against historic activity and confirmed as a reasonable modelling assumption.

The incidence of confirmed stroke across the Severn region served by our service was shown from SSNAP data to be about 4,500 per year. A 10% eligibility threshold was applied based on current criteria for treatment, assuming that both the necessary imaging at referring sites and the MT service were in operation 24/7. This provided a best-case total service volume for a 24/7 service, which was adjusted using the following factors to model the rate at which activity would grow:

- Rural geography of the Severn network, including the impact of transfer time
- The hours of service available for each phase of service development
- The impact of increased awareness of the NBT stroke MT service at referring hospitals and embedding of referrals pathways.

Describe the workforce required to deliver the service

The business case identified all staff groups required to support a sustainable service and Phase 1 expansion. As NBT is an established neuroscience centre and already a training centre for INRs, this allowed clinical fellows to develop skills and the potential to meet local recruitment when the service needed to expand. This has meant that NBT has been able to encourage future trainees to further their careers within the department.

The NBT stroke and interventional neuroradiology teams worked closely together on the MT pathway, and the business case included tandem recruitment to develop all arms of the service. In reality, it was difficult to align this recruitment with the plan, and some steps were undertaken out of sequence to ensure that good candidates could be recruited.

A detailed analysis to develop specialties other than interventional neuroradiology to provide MT was not considered necessary, as it was anticipated that INRs would also be required to provide aneurysm coiling. However, the role of credentialling for other professionals was seen as an important option if rota gaps need addressing in the future. A 24/7 service will require six **WTE** INRs.

Set the operational requirements and impact

Defining the potential impact on other services was essential to give the wider organisation understanding and assurance about the impact of increasing MT work. The key operational areas affected were:

- Increased numbers coming through the ED. All external referrals would be met by the stroke team in ED, having had **CT** and **CTA** at the referring centre.
- Access to interventional neuroradiology angiography suite capacity and delivery of other interventional and diagnostic neuroradiology activity alongside provision of emergency access.
- ITU and ASU bed capacity, which was closely linked to the assumed length of stay for MT patients. We assumed that patients outside of NBT's local catchment area would return to their local stroke unit within 72 hours of MT – or earlier if clinically appropriate. Precise modelling depended on the number of local ASU beds, average length of stay, and agreements for transfer and repatriation of patients to adjacent **ASC**s. For example, an ASC admitting 1,000 patients annually, with an average length of stay of 2.5 days and 85% occupancy, may need about eight ASU beds. Adding 350 external MT referrals would require an additional 3–4 beds.

The two key operational protocols underpinning the service were those detailing the referral and repatriation processes. We were able to utilise the Severn Network repatriation policy already in place for major trauma and other tertiary services. The referral criteria aligned to Specialist Commissioning referral criteria and included clear imaging requirements for CTA to be uploaded via an established cloud-based image-sharing system supporting the regional **IVT** service.

Most MT referrals will present to other hospitals and require a secondary transfer, and increasing numbers being transferred for MT would impact on the ambulance service, with additional Category 2 ambulance transfers within the region and displacement of ambulances. All activity assumptions and referral procedures were shared with the ambulance service from the outset to facilitate their negotiations with NHS England regarding increased activity.

Develop the financial case

A full financial assessment was undertaken, including a full cost and income modelling exercise. The information generated from the financial model was summarised as a comparison of cost per case against tariff plus market forces factor and specialist centre top-up. The following costs per case were calculated to assess the impact of the service development:

- Current baseline service activity and costs
- Sustainable service requirements and activity levels
- Phase 1 service requirements and the profile of phased activity.

This helped to identify the volume required to support a break-even Phase 1 service and when this could be expected. The modelling suggested that, with a tariff income of £13,400 plus adjustments including market forces factor, and an 8 am-8 pm 5-day service in Phase 1, including interventional neuroradiology and the anaesthetic team, about 220 cases per annum would be needed to break even (40% of final planned activity).

Submit the business case for approval

Given the strategic significance of this development, it was agreed that all investments should be set out in one phased business case to provide optimum strategic oversight for the trust. The final investment value set out in the full business case for Phase 1 required approval at all key trust governance meetings and ultimately from the trust board. Early engagement was essential to a 'no surprises' approach, with members of the steering group represented on all these groups who were able to present and support the case for investment.

The business case was approved by the NBT board in October 2018 and has been implemented. The Stroke Thrombectomy Steering Group has continued to review progress against predicted activity and a 7-day service started on 1 January 2021, with expansion to 24/7 planned for first quarter in 2022/23. Stroke thrombectomy is a key strategic trust priority, and this will ensure that momentum remains behind this project through to successful completion.

12 Delivering mechanical thrombectomy during the COVID-19 pandemic

Wazim Izzath, Norman McConachie, David Hargroves

Key points

- Increased public awareness is needed to ensure patients with acute stroke symptoms continue to seek immediate medical attention during pandemic waves.
- Routine rapid testing at initial presentation should be incorporated into the acute stroke patient pathway.
- Infection control measures and streamlined regional pathways should be developed to minimise delays in assessment, diagnosis and imaging, image and patient transfer, treatment and post-procedural care.
- Angiography suites with negative pressure ventilation and/or anaesthetic rooms within interventional suites should be used wherever possible.
- Future increased incidence of **COVID-19** may impact workforce, and alternative local and regional working arrangements should be established to ensure continuity of **MT** service provision.

Introduction

In December 2019, an atypical pneumonia, now called COVID-19, emerged in Wuhan, China,[232] and was confirmed in January 2020 to be caused by a novel coronavirus now named **SARS-CoV-2**.[233] The disease began to spread within China and then to other countries, with the first documented case of COVID-19 in the UK confirmed on 31 January 2020. The **WHO** declared the outbreak as a pandemic on 11 March.[234] On 23 March 2020, the UK Government announced a partial lockdown to contain the spread of COVID-19, with subsequent lockdowns and varying restrictions in place across the UK to the time of writing in December 2021.

Subsequently, the presentation of stroke altered during the first wave of the pandemic, and changes have had to be made to stroke pathways. This chapter considers the impact of COVID-19 on presentation, management and outcomes of stroke, focusing on MT, and the implications for the future management of **LAO** stroke.

COVID-19-associated coagulopathy and stroke

Although COVID-19 was initially viewed as a respiratory disease, it quickly became clear that it had serious vascular effects, akin to those observed with the original **SARS** and **MERS** outbreaks.[235] Like the pathogens involved in these earlier diseases, SARS-CoV-2 binds angiotensin-converting enzyme 2, an intrinsic membrane protein with enzymatic activity that is expressed widely, including in endothelial cells and the heart, and which physiologically counters activation of the renin-angiotensin-aldosterone system.[235] Initial infection with COVID-19 produces lung inflammation that progresses to a cytokine storm in the most severe cases.[235] The spectrum of disease seen with SARS-CoV-2 includes frequent involvement of the haemostatic system, coagulopathy and a procoagulant endothelial phenotype. This is thought to result from the severe proinflammatory response and endothelial activation/damage, associated with elevations of fibrinogen and D-dimer/fibrin/fibrinogen degradation products that are associated with systemic hypercoagulability and frequent venous thromboembolic events.[235] Patients often have mild thrombocytopenia, increased platelet consumption and increased platelet production.[235]

Worldwide experience of stroke and COVID-19

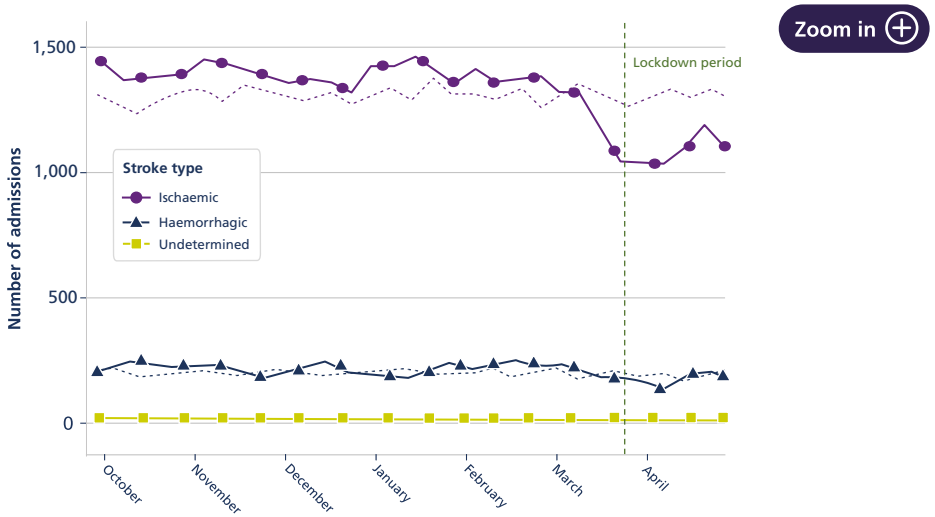
Increased incidence of stroke in COVID-19 patients

Given the endothelial dysfunction, hypercoagulability and exacerbation of underlying pre-existing risk factors seen with COVID-19,[236–239] multiple institutions across the world reported an increased incidence of stroke in COVID-19 patients and that the disease is an independent risk factor for **AIS** and LAO. For example, rates of ischaemic stroke were 2.5% in an Italian study and 1.65% (versus 0.2% in patients with influenza) in New York hospitals.[234, 240, 241] Furthermore, LAOs were demonstrated in atypical locations and in younger patients.[238]

Reductions in UK stroke admissions during the pandemic

Paradoxically, as the pandemic progressed, multiple studies and reports from around the world indicated that fewer patients with acute stroke presented to **ED**s,[242–247] resulting in decreased rates of stroke admissions, **IVT** and MT during the early stages of the COVID-19 pandemic. An NHS England internal analysis using faster secondary uses services (a secure data warehouse that stores patient-level information in line with national standards and applies complex derivations to support national tariff policy and secondary analysis) suggested an approximate 25% drop in stroke admissions and a 40–50% drop in ED attendances for stroke/**TIA** during the initial surge period. A reduction in stroke admissions was also observed in national data from **SSNAP** – the registry of patients with acute stroke admitted to hospital in England, Wales, and Northern Ireland, which largely continued during the pandemic, albeit initially with a reduced core minimum COVID-19 dataset.[248] Comparing SSNAP data for patients admitted to 114 hospitals with acute stroke between 1 October 2019 and 30 April 2020 and equivalent periods in the 3 prior years, Douiri *et al* identified a 12% reduction in admissions during the 23 March–30 April 2020 lockdown compared with the same period in the 3 previous years (6,923 *versus* 7,902) (**Figure 25**).[249]

Figure 25. Weekly numbers of admission for stroke from 1 October 2019–30 April 2020 (solid lines) compared with the previous 3 years (dotted lines). Reproduced from Douiri *et al* (2021).[249]



As the incidence of acute stroke is unlikely to have changed markedly during the pandemic[249] (indeed the opposite may be true given the COVID-19-associated coagulopathy described earlier[250]), other factors, notably behavioural change and isolation, may have led to this reduction.[251–255] Firstly, advice to the public during the first wave was to avoid going to hospital unless absolutely necessary to reduce pressure on the NHS.[250] Some people with acute stroke symptoms followed this advice but were anxious and aware of the risk of acquiring COVID-19 in hospitals during the first wave of the pandemic.[250] Some people 'just coped' at home, some may have misinterpreted or dismissed their symptoms, and others may have died without seeking help.[250] There may also have been reluctance from healthcare staff in the community to refer patients with minor stroke into hospital services.[248] Secondly, neurological symptoms in some patients may have been missed due to 'masking' when they had severe respiratory illness due to COVID-19,[256–258] particularly in those requiring endotracheal intubation. Finally, minor stroke symptoms were likely to have been overlooked in care home residents,[258] and, even when they were identified, many patients with poor prognosis had 'do not transfer to hospital' orders in place.

To understand the impact of COVID-19 specifically on MT service provision in the UK, a survey was undertaken in 2020, with responses from 27 out of 28 CSCs.[259] This identified a 28% decrease in the number of MTs reported in April 2020 compared with the first three months of the year. Any downturn in MT activity proved to be confined to the first wave and short-lived, with activity sustained during the second wave in autumn–winter 2020–21.[260, 261] Most MT centres rapidly adapted their practices to ensure that delivery of time-critical MT and other vital neurointerventional procedures continued during the pandemic. Nine out of 24 UK centres split their **INR** consultant staff into two or three discrete rotas to limit cross-infection and ensure continuation of regional MT services. Others reported changes made to the working environment, include working from home (remote reporting of diagnostic neurological studies) and transitioning all **MDT** meetings into a virtual setting.[259] The proportion of successful procedural outcomes (defined as TICI 2B-3) did not significantly alter during the first 4 months of 2020 (range 79–84%). A similar unchanged rate of successful procedural outcome was reported by colleagues in France and Germany.[255, 262]

Changes to the stroke pathway in the UK due to COVID-19

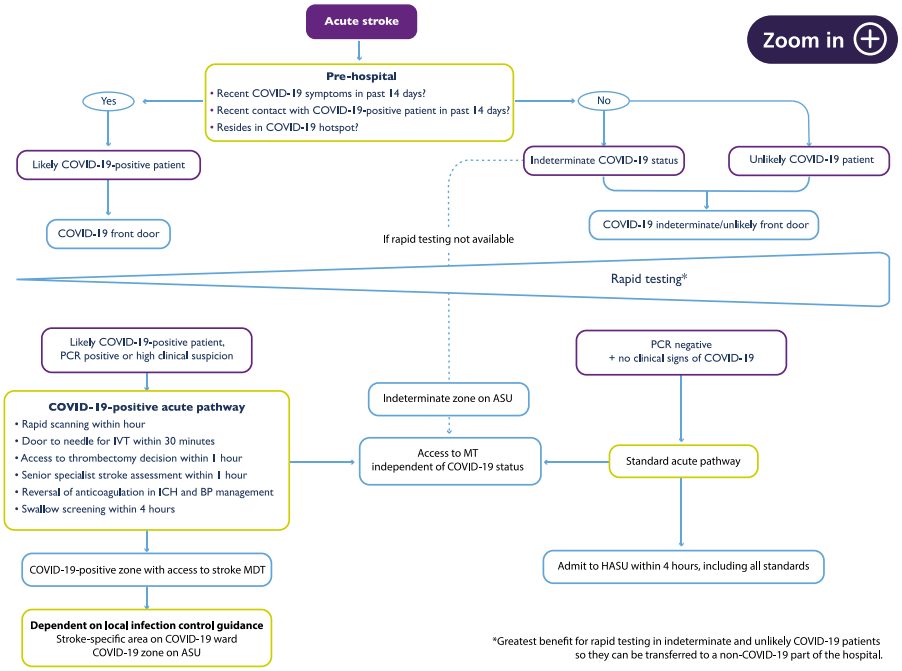
With strokes continuing to be a medical emergency during the pandemic, stroke teams had to modify pathways to enable prompt treatment. Oxford **AHSN** and **GIRFT**, with the support of **BASP**, developed practical guidance to help stroke teams across England deliver high-quality care drawing on local adaptations by individual stroke units at the start of the pandemic; key recommendations are described here.[248, 263]

The ability to deliver timely and effective care has to be balanced with minimising the risk of infection with COVID-19 between patients and the clinical team,[248, 264, 265] and infection control remains a primary concern. All acute stroke patients whose COVID-19 status is unknown should receive a rapid test on admission, particularly patients with LAO who may require MT,[248] although this is still not routine in many centres, with many patients waiting 24 hours for results of **PCR** testing as lateral flow tests are not considered sufficiently reliable for hospital use. Staff should also be tested regularly, but infection prevention and control must continue irrespective of the presence of antibodies from previous infection or vaccination, as this does not guarantee immunity or prevention of re-infection or transmission.[248] Given the potential for widespread contamination of patient rooms or environments, effective cleaning and decontamination are vital.[266] The Oxford AHSN/GIRFT guidance included a suggested pathway for managing acute stroke patients when rapid testing is available (**Figure 26**).[248]

We recommend incorporating rapid **RT-PCR** testing (with some point-of-care options providing results in 20 minutes) into the MT patient pathway, preferably at the time of initial admission/assessment. Where a PCR test result is not available, centres are encouraged to use a screening questionnaire prior to transfer and at the start of MT to risk-stratify patients with respect to likelihood of having active COVID-19 infection.[259] Consider using chest CT as a screening test only in patients with a high likelihood of COVID-19 infection when an alternate definitive diagnostic rapid PCR test is unavailable and there are significant clinical respiratory symptoms/signs.

Examining patients in **PPE** is challenging, as verbal and non-verbal communication are difficult.[267] PPE is uncomfortable, cumbersome, and difficult to don and doff, affecting clinicians' ability to examine patients[267] and slowing down normal procedures. Visors and masks hide clinicians' facial expressions, and full PPE may alarm and distress patients already frightened by their condition and being in hospital without the usual support of family or friends.

Figure 26. Pathway for acute stroke patients when rapid testing is available.[248]

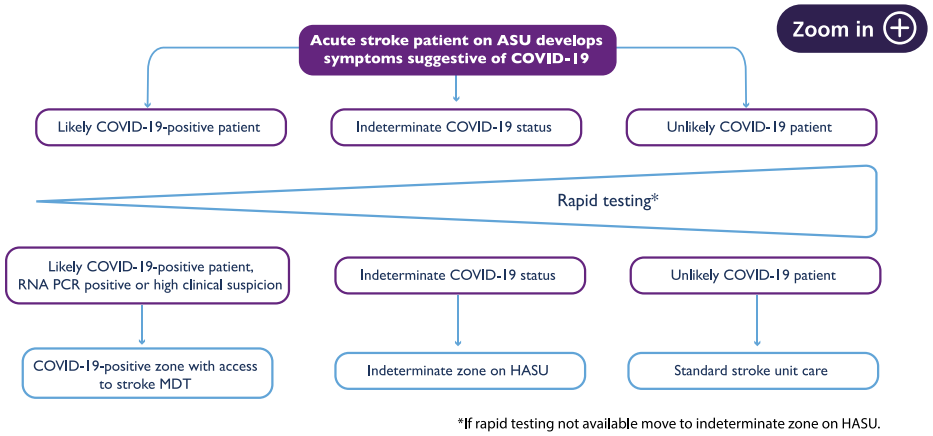


In an era of face coverings and virtual communications, careful attention needs to be given to the quality of communication with patients, carers and other staff.[248] Personal protective equipment makes taking a history and obtaining consent from the patient difficult. It is vital therefore to speak slowly and use non-verbal cues.[248] For patients unable to communicate following their stroke, the absence of visitors due to social distancing measures means that clinicians have to rely on telephone and video calls to obtain a history and consent for procedures. When visiting is restricted, stroke teams should consider adopting a system where the healthcare team call relatives on a daily basis.[248]

Patients may develop stroke without having COVID-19, because of COVID-19, or coincidentally with COVID-19. Patients with acute stroke who are COVID-19-positive should be cared for on COVID-19 ward areas. A non-COVID-19 stroke pathway should ideally be created for patients without COVID-19, with separate consultation spaces, scanners, wards and an interventional suite,[268] but this is unlikely to be feasible for

most hospitals in the UK. Some stroke patients may have asymptomatic COVID-19 infection or be diagnosed with COVID-19 later during the stroke pathway, and **Figure 27** demonstrates a suggested pathway in these circumstances.[248]

Figure 27. Consensus pathway for patients who begin to show symptoms of COVID-19 once they are already in the stroke unit.[248]



Current infection control measures are sufficient to minimise viral transmission with case rates at the time of writing; however, when levels of circulating virus are high in age groups typically in hospital, it may be necessary to revert to measures from the height of the pandemic: minimising face-to-face contact using telemedicine, reducing footfall between departments and teams, and reducing the number of **HCP**s in contact with a patient.[248] Daily in-reach of the stroke **MDT** – virtual wherever possible – is vital for patients in different areas of the hospital.[248] Senior stroke specialists should review patients and CT images via telemedicine to inform decision-making around interventions and transfer for MT.[263] If a patient's COVID-19 status is unknown, it is reasonable to intervene if they would otherwise be eligible and on the basis that they are infected rather than delay intervention while awaiting a test result.[248, 268] Adjustments to the MT pathway are described subsequently.

COVID-19-positive patients requiring stroke unit care should be managed in a dedicated COVID-19 ward or area. Stroke teams may need to work across two or more areas within a hospital or between COVID-19 and non-COVID-19 sites, and nursing and therapy HCPs may need to be upskilled to deliver stroke specialist care through virtual consultations.

As stroke is a recognised complication of COVID-19, stroke teams should advise other specialties on identifying stroke in patients with COVID-19, what to do if an inpatient with COVID-19 is suspected to have had a stroke, and what response and support to expect from the stroke team.[248]

Managing patients in the intervention suite

It is unrealistic for most trusts to designate COVID-19 and non-COVID-19 intervention suites and batching of COVID-19-positive patients at the end of the day is unworkable due to the timeframes in which MT is effective, so rapid cleaning protocols are needed.[248] There may be specific challenges with transferring confirmed or suspected COVID-19-positive patients to a CSC for MT; however, COVID-19-positive patients should not be disadvantaged.[248] Systems that share images and use artificial intelligence can support early referral for MT.[263]

COVID-19 impact on peri- and post-procedural care

Utility of general anaesthesia and patient recovery

As most patients eligible for MT have an uncertain COVID-19 status, **ESMINT**, **SNIS** and **SNACC** recommend lowering the threshold for performing the procedure under **GA**. This is particularly the case where consensus between the neurointerventionalist and anaesthetist highlights a significant risk of intraprocedural conversion from local to GA.[259, 269–271] As endotracheal intubation is an aerosol-generating procedure, it is advisable that this is performed in a negative-pressure environment (e.g. anaesthetic bay) where possible without incurring significant delay.[259] When intubation is performed in the angiography suite, it is advisable that all healthcare personnel in the room don **enhanced PPE** (N95, FFP3 or equivalent air filtration masks, surgical gown, face shield/goggles and gloves).[259] Designated areas for PPE donning and doffing must be defined to minimise contamination risk.[271]

Both ESMINT and SNIS recommend, where possible, that extubation of patients should be performed in negative pressure environments, which can include using the angiography suite if this is the only area with negative pressure ventilation. Effective decontamination procedures within the angiography suite must be instituted with guidance from local infection control teams.[259]

When there are moderate or high levels of virus circulating in the community, we advocate limiting the number of personnel within the angiography suite to only essential staff required to perform the procedure.[270] When there is requirement for stroke physician input or advice, this can be delivered via means of remote consultation.

Post-procedural care

Now that rapid testing is widely available, PCR results will enable transfer to appropriate COVID-19 or non-COVID-19 HASU wards by the time post-procedural recovery is completed in most cases. If rapid testing is not available, one approach is to risk-stratify patients into an isolation bed or COVID-19-suspected bed for 24 hours pending RT-PCR results before transfer to a COVID-19 or non-COVID-19 ward.[272] Centres should have a clear immediate post-procedural care pathway to minimise the risk of cross-infection.

COVID-19 impact on wider service

If COVID-19 rates in a region rise substantially, it may be necessary to split consultant INR teams into separate rotas to limit cross-infection and ensure continuation of an MT service – a change one-third of UK **CSC**s made during the first wave of the pandemic. MT centres should consider revising MT **SOP**s to include responses to changing levels of COVID-19 infection rates in the community. This is in line with published ESMINT guidance and will help to ensure MT services are sustained.[259] All healthcare personnel involved in the provision of MT should be vaccinated against COVID-19, unless contraindicated. Where geography allows, CSCs should seek to establish collaborative arrangements with adjacent CSCs that permit cross-cover in the event of a service being rendered unavailable by a COVID-19 outbreak among staff. Whereas closure of angiography suites for servicing can be anticipated and planned for, outbreak closures are likely to be at short notice and **ISDN**s will have a key role in ensuring continuity of MT service for their catchment through such collaborative arrangements.

Lessons learned and future directions

Given the probability of further waves of COVID-19 and to ensure patient pathways minimise delays, we recommend mandatory rapid PCR testing at the time of initial presentation within locoregional SOPs, procedures to minimise patient transfer times, and streamlining of workflows, with the inclusion of appropriate PPE and infection control measures as per local institutional policies. Furthermore, we recommend minimising the number of healthcare personnel required within the angiography suite to provide MT and, where there is potential to adversely impact service provision due to increased COVID-19 incidence (hospital or community), we advocate consideration of splitting teams to ensure the MT service is maintained. Another issue highlighted from experiences shared during the pandemic is the need to develop future angiography suites with negative-pressure ventilation and or the availability of a dedicated anaesthetic bay within interventional suites. A second on-site MT-suitable angiographic suite will facilitate MT availability in general but particularly under the circumstances of a COVID-19 or other infectious disease peak.

Finally, we note that 14 out of 24 CSCs reported impeded MT service development due to the impact of COVID-19.[259] As we emerge from the pandemic in the UK, there is a critical need to catch up and regain the momentum of expanding MT provision.

Conclusion

A co-ordinated response to the COVID-19 and future pandemics requires:

- Increased public awareness to ensure that patients with acute stroke symptoms seek immediate medical attention
- Incorporating routine rapid testing into the acute stroke patient pathway at initial presentation
- Incorporating infection control measures and streamlined regional pathways to minimise delays in assessment, diagnosis/imaging, image and patient transfer, treatment and post-procedural care
- The development of angiography suites with negative pressure ventilation and/or anaesthetic rooms within interventional suites
- Establishing alternative regional arrangements to ensure continuity of MT service provision if future increased incidence of COVID-19 impacts workforce.

Trial acronyms and abbreviations

Trial acronyms

BASICS	Basilar Artery International Cooperation Study
BEST	Acute Basilar Artery Occlusion: Endovascular Interventions vs Standard Medical Treatment
DAWN	DWI or CTP Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo
DEFUSE	Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution
DIRECT-MT	Direct Intraarterial Thrombectomy in Order to Revascularize Acute Ischemic Stroke Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: a Multicenter Randomized Clinical Trial
DIRECT-SAFE	A Randomized Controlled Trial of DIRECT Endovascular Clot Retrieval Versus Standard Bridging Thrombolysis With Endovascular Clot Retrieval
EASI	Endovascular Acute Stroke Intervention
ENDO-LOW	Endovascular Therapy for Low NIHSS Ischemic Strokes
ESCAPE	Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times
EXTEND-IA	Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial
EXTEND-1A-TNK	Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke
HERMES	Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials
IMS	Interventional Management of Stroke
LASTE	Large Stroke Therapy Evaluation
MOSTE	Minor Stroke Therapy Evaluation
MR CLEAN	Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in The Netherlands
NINDS	National Institute of Neurological Disorders and Stroke trial of tissue plasminogen activator for acute ischaemic stroke
NOR-TEST	Norwegian Tenecteplase Stroke Trial
PASTA	Paramedic Acute Stroke Treatment Assessment
PISTE	Pragmatic Ischaemic Thrombectomy Evaluation
REVASCAT	Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within 8 hours of Symptom Onset
SONIIA	Sistema Online d'Informació de l'Ictus Agut
STOP-Stroke	Screening Technology and Outcome Project in Stroke Study
SWIFT	Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke
SWIFT-DIRECT	Solitaire With the Intention For Thrombectomy Plus Intravenous t-PA Versus DIRECT Solitaire Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke
SWIFT-PRIME	Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke
TENSION	Efficacy and safety of thrombectomy in stroke with extended lesion and extended time window
TESLA	Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke
THERAPY	The Randomized, Concurrent Controlled Trial to Assess the Penumbra System's Safety and Effectiveness in the Treatment of Acute Stroke
THRACE	Mechanical Thrombectomy After Intravenous Alteplase Versus Alteplase Alone After Stroke

Other acronyms and abbreviations

AHA	American Heart Association
AHSN	academic health science network
AIS	acute ischaemic stroke
AMPDS	Advanced Medical Priority Dispatch System
ASC	acute stroke centre
ASPECTS	Alberta Stroke Program Early CT Score
ASU	acute stroke unit
AVVV	Ataxia, Visual disturbances, Vertigo, Vomiting
BASP	British Association of Stroke Physicians
BCIS	British Cardiovascular Intervention Society
BCS	British Cardiovascular Society
BP	blood pressure
CCG	clinical commissioning group
CCU	coronary care unit
CO_2	carbon dioxide
COVID-19	coronavirus disease 2019
CSC	comprehensive stroke centre
CT	computed tomography
CTA	computed tomography angiography
CTA-CS	computed tomography angiography collateral scoring
CTA-SI	computed tomography angiography source images
CTP	computed tomography perfusion
DA	direct aspiration
DGH	district general hospital
DIDO	door-in-door-out
DSC	district stroke centre
DWI	diffusion-weighted imaging
ECG	electrocardiogram
ED	emergency department
EEG	electroencephalogram
ESC	European Society of Cardiology
ESD	early supported discharge
ESMINT	European Society of Minimally Invasive Neurological Therapy
ESO	European Stroke Organisation
FAST	Face Arm Speech Test
FAST-ED	Field Assessment Stroke Triage for Emergency Destination
FLAIR	fluid-attenuated inversion recovery
GA	general anaesthesia
GCS	Glasgow Coma Scale
GFAST	Gaze–Face–Arm–Speech–Time
GIRFT	Getting It Right First Time
HCP	healthcare professional
HASU	hyperacute stroke unit
HRG	healthcare resource group
ICA	internal carotid artery
ICER	incremental cost-effectiveness ratio
ICS	integrated care system
INR	interventional neuroradiologist
IPR	individual patient record
IQR	interquartile range
ISDN	Integrated Stroke Delivery Network
ITU	intensive therapy unit
IVT	intravenous thrombolysis
LAO	large artery occlusion
LKW	last known well
MCA	middle cerebral artery
MDT	multidisciplinary team
MEND	Miami Emergency Neurological Deficit
MERCI	Mechanical Embolus Removal in Cerebral Ischemia
MERS	Middle East respiratory syndrome
MI	myocardial infarction
MINAP	Myocardial Ischaemia National Audit Project
MIP	maximum intensity projection

MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
mRS	modified Rankin scale
MT	mechanical thrombectomy
NCCT	non-contrast computed tomography
NIAP	National Infarct Angioplasty Project
NICE	National Institute for Health and Care Excellence
NIHSS	National Institutes of Health Stroke Scale
NMB	net monetary benefit
NNT	number needed to treat
ODN	operational delivery network
ODP	operating department practitioner
OR	odds ratio
PACS	picture archiving and communication system
PCR	polymerase chain reaction
PPCI	primary percutaneous coronary intervention
PPE	personal protective equipment
PSC	primary stroke centre
QALY	quality-adjusted life-year
RACE	Rapid Arterial oCclusion Evaluation scale
RAPID	RApid processing of PerfusIon and Diffusion
RCT	randomised controlled trial
ROSIER	Recognition of Stroke in the Emergency Room
RT-PCR	reverse transcriptase polymerase chain reaction
SARS	severe acute respiratory syndrome
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SEAT	stroke emergency assessment team
sICH	symptomatic intracerebral haemorrhage
SITS	Safe Implementation of Treatment in Stroke
SNACC	Society for Neuroscience in Anesthesiology & Critical Care
SNIS	Society of NeuroInterventional Surgery
SOP	standard operating procedure
SR	stent retriever
SSCA	Scottish Stroke Care Audit
SSNAP	Sentinel Stroke National Audit Programme
STEMI	ST elevation myocardial infarction
STP	sustainability and transformation partnership
SU	stroke unit
TICI	Thrombolysis in Cerebral Infarction Scale
WHO	World Health Organization
WTE	whole-time equivalent
WTP	willingness to pay

Useful resources

Learning from Stroke
Lessons from stroke reconfiguration in London and Greater Manchester
View website

Stroke in Stoke
A resource for patients, their families and carers, and staff looking after patients with stroke or conducting research related to stroke
View Website

Mechanical thrombectomy for ischaemic stroke
A guide to training of interventional radiologists from the Royal College of Radiologists
View guide

2021 consensus guidance from BASP, BSNR, ICSWP, NACCS, and UKNG to support safe provision of mechanical thrombectomy services for patients with acute ischaemic stroke
Download guidance

Training guidelines for endovascular ischemic stroke intervention
An international multi-society consensus document
Download training guidelines (Word)

Standards for European training requirements in interventional neuroradiology
From UEMS Division of Neuroradiology, UEMS Interventional Radiology Division, European Society of Neuroradiology (ESNR), European Board of Neuroradiology (EBNR) and European Society for Minimally Invasive Neurological Therapy (ESMINT)
Download standards (PDF)

BSNR training guidance for mechanical thrombectomy
Produced by members of the UK Neurointerventional Group and British Society of Neuroradiologists, March 2016
Download standards (PDF)

European Society of Minimally Invasive Neurological Therapy (ESMINT)
Recommendations for optimal interventional neurovascular management in the COVID-19 era
Download recommendations (PDF)

Guide on adapting stroke services during the COVID-19 pandemic and reshaping them afterwards
Developed by Oxford AHSN and GIRFT
Download guidance (PDF)

Guide to support stroke teams in restoration and recovery phase of the COVID-19 pandemic
Developed by Oxford AHSN and GIRFT
Download guidance (PDF)

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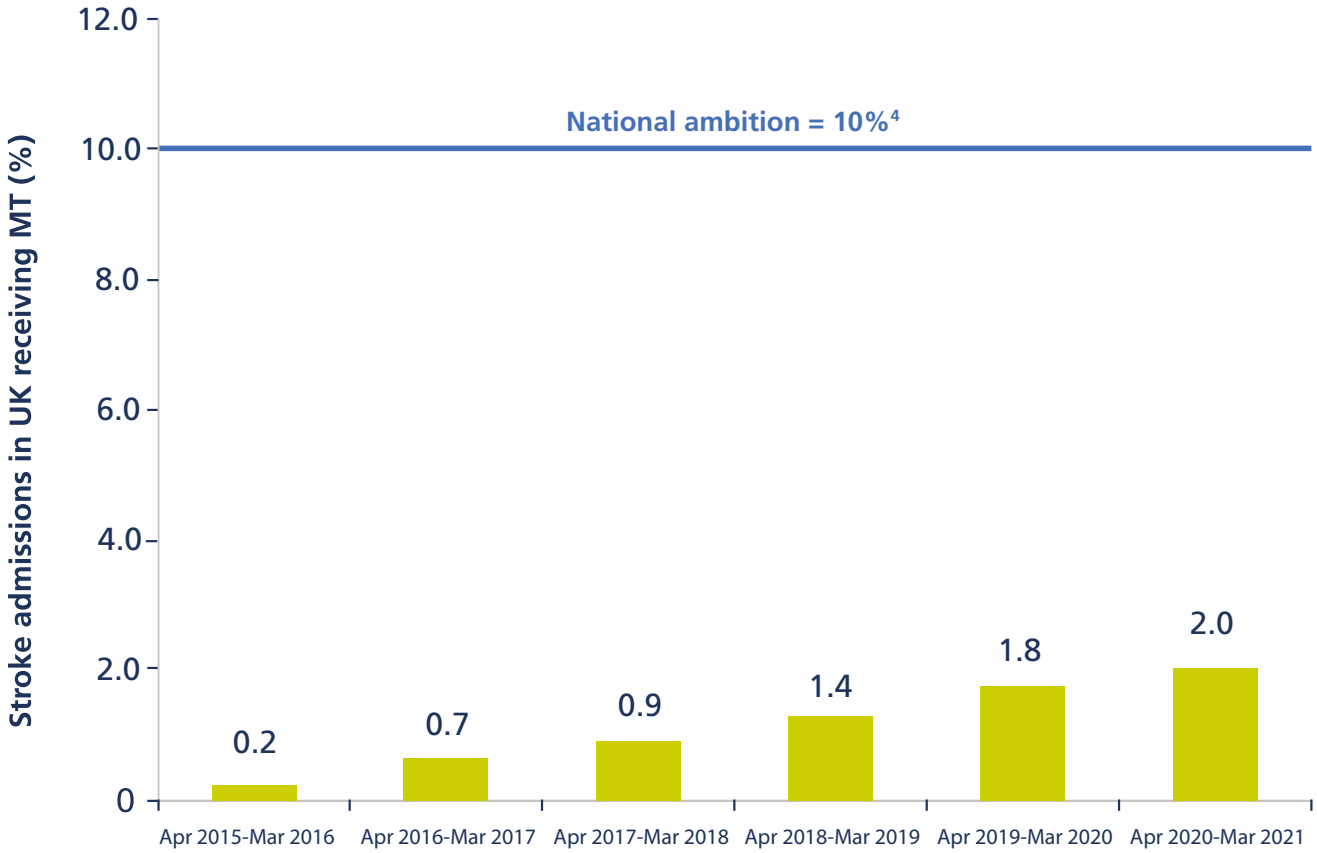
Figure 1



	Apr 2015-Mar 2016	Apr 2016-Mar 2017	Apr 2017-Mar 2018	Apr 2018-Mar 2019	Apr 2019-Mar 2020	Apr 2020-Mar 2021
Thrombectomies (n)	150	604	800	1,222	1,607	1,711
National denominator (N)*	85,014	85,870	87,166	88,089	89,280	87,507

Figure 3

Study	MT		Standard care		OR, random, 95% CI
	Events	Total	Events	Total	
ESCAPE	87	164	43	147	2.7 (1.7 to 4.4)
EXTEND-IA	25	35	14	35	3.8 (1.4 to 10.2)
MR CLEAN	76	233	51	267	2.1 (1.4 to 3.1)
PISTE	17	33	12	32	1.8 (0.7 to 4.8)
REVASCAT	45	103	29	103	2.0 (1.1 to 3.5)
SWIFT-PRIME	59	98	33	93	2.8 (1.5 to 4.9)
THERAPY	19	50	14	46	1.4 (0.6 to 3.3)
THRACE	106	200	85	202	1.6 (1.1 to 2.3)
Total (95% CI)		**916**		**925**	**2.1 (1.7 to 2.5)**
Total events	**434**		**281**		

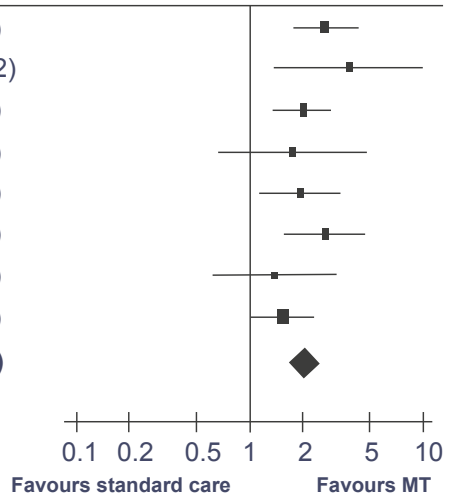


Figure 4

Study	MT		Standard care		OR, random, 95% CI
	Events	Total	Events	Total	
ESCAPE	17	164	28	147	0.5 (0.3 to 0.9)
EXTEND-IA	3	35	7	35	0.4 (0.1 to 1.6)
MR CLEAN	49	233	59	267	0.9 (0.6 to 1.4)
PISTE	7	33	4	32	1.9 (0.5 to 7.2)
REVASCAT	19	103	16	103	1.2 (0.6 to 2.6)
SWIFT-PRIME	9	98	12	97	0.7 (0.3 to 1.8)
THERAPY	6	50	11	46	0.4 (0.2 to 1.3)
THRACE	24	202	27	206	0.9 (0.5 to 1.6)
Total (95% CI)		**918**		**933**	**0.8 (0.6 to 1.1)**
Total events	**134**		**164**		

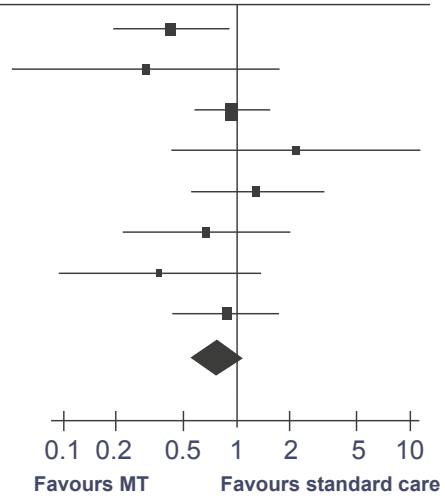


Figure 5

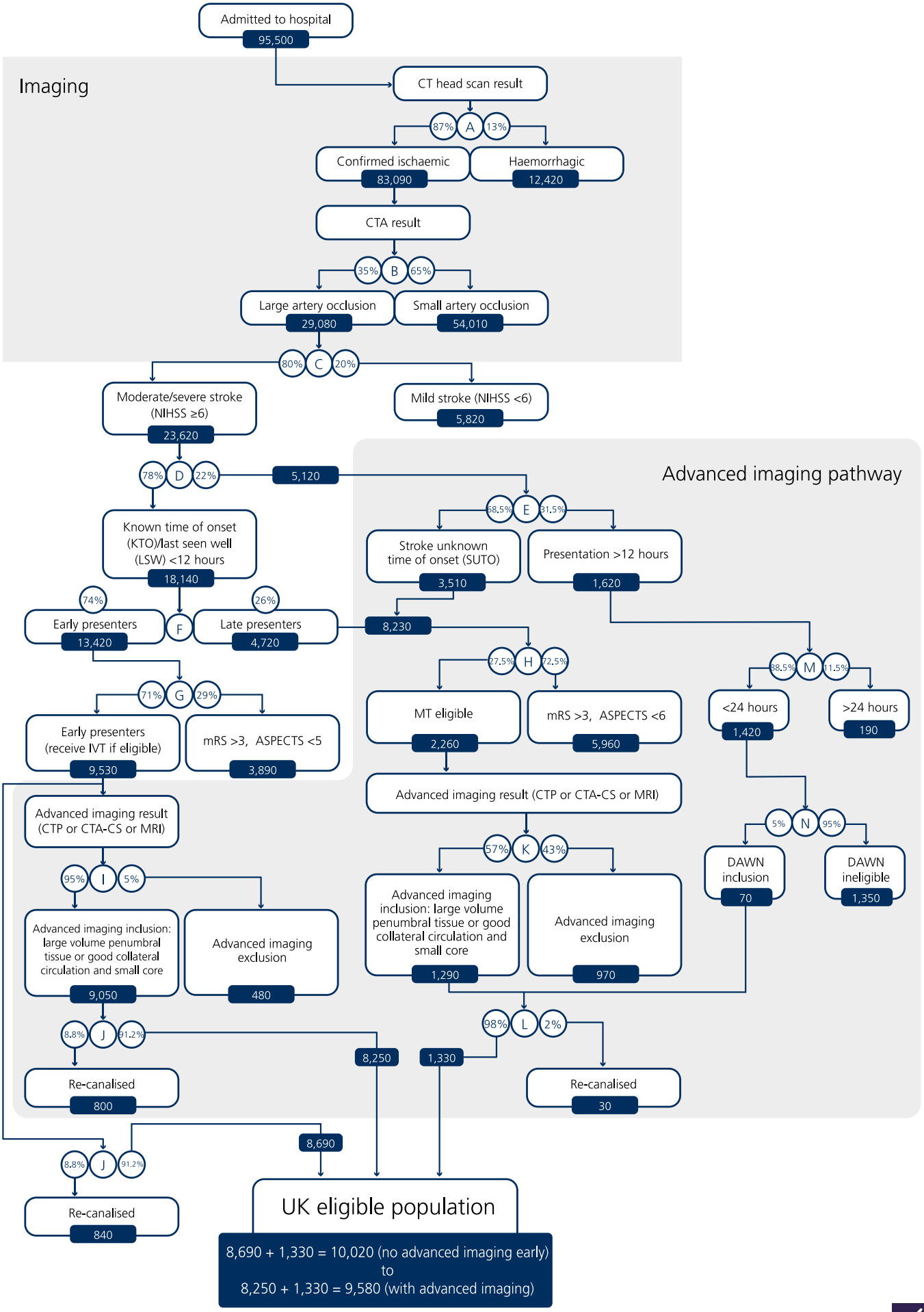

Admitted to hospital
95,500
Imaging
CT head scan result
87%
A
13%
Confirmed ischaemic
83,090
Haemorrhagic
12,420
CTA result
35%
B
65%
Large artery occlusion
29,080
Small artery occlusion
54,010
80%
C
20%
Moderate/severe stroke (NIHSS ≥6)
23,620
Mild stroke (NIHSS <6)
5,820
78%
D
22%
5,120
Advanced imaging pathway
68.5%
E
31.5%
Known time of onset (KTO)/last seen well (LSW) <12 hours
18,140
Stroke unknown time of onset (SUTO)
3,510
Presentation >12 hours
1,620
74%
Early presenters
13,420
F
26%
Late presenters
4,720
8,230
27.5%
H
72.5%
38.5%
M
11.5%
71%
G
29%
MT eligible
2,260
mRS >3, ASPECTS <6
5,960
<24 hours
1,420
>24 hours
190
Early presenters (receive IVT if eligible)
9,530
mRS >3, ASPECTS <5
3,890
Advanced imaging result (CTP or CTA-CS or MRI)
Advanced imaging result (CTP or CTA-CS or MRI)
5%
N
95%
95%
I
5%
57%
K
43%
DAWN inclusion
70
DAWN ineligible
1,350
Advanced imaging inclusion: large volume penumbral tissue or good collateral circulation and small core
9,050
Advanced imaging exclusion
480
Advanced imaging inclusion: large volume penumbral tissue or good collateral circulation and small core
1,290
Advanced imaging exclusion
970
98%
L
2%
8.8%
J
91.2%
8,250
1,330
Re-canalised
800
Re-canalised
30
8,690
8.8%
J
91.2%
Re-canalised
840
UK eligible population
8,690 + 1,330 = 10,020 (no advanced imaging early)
to
8,250 + 1,330 = 9,580 (with advanced imaging)

Figure 6

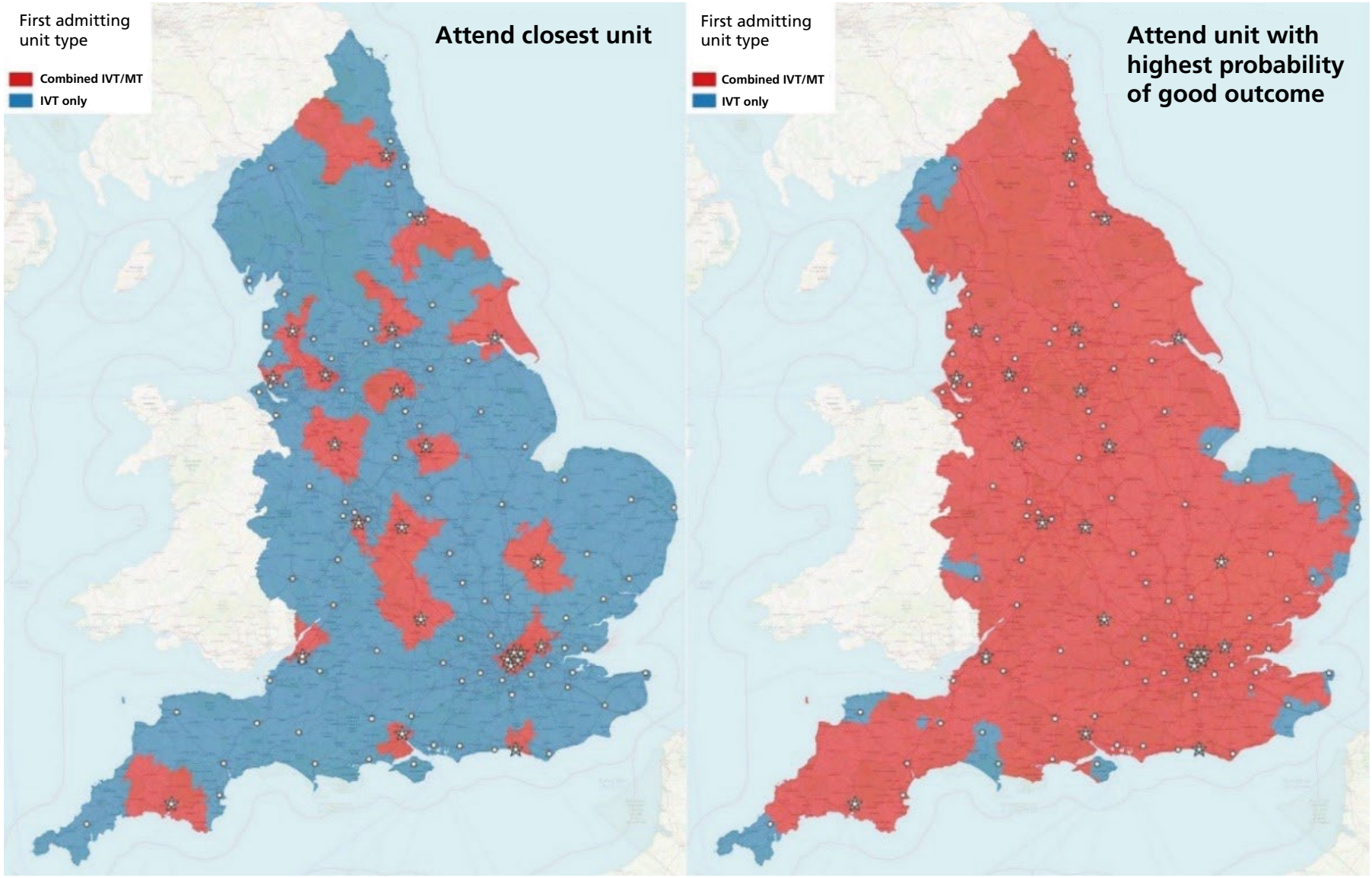

First admitting unit type
Combined IVT/MT
IVT only
Attend closest unit
First admitting unit type
Combined IVT/MT
IVT only
Attend unit with highest probability of good outcome

Figure 7

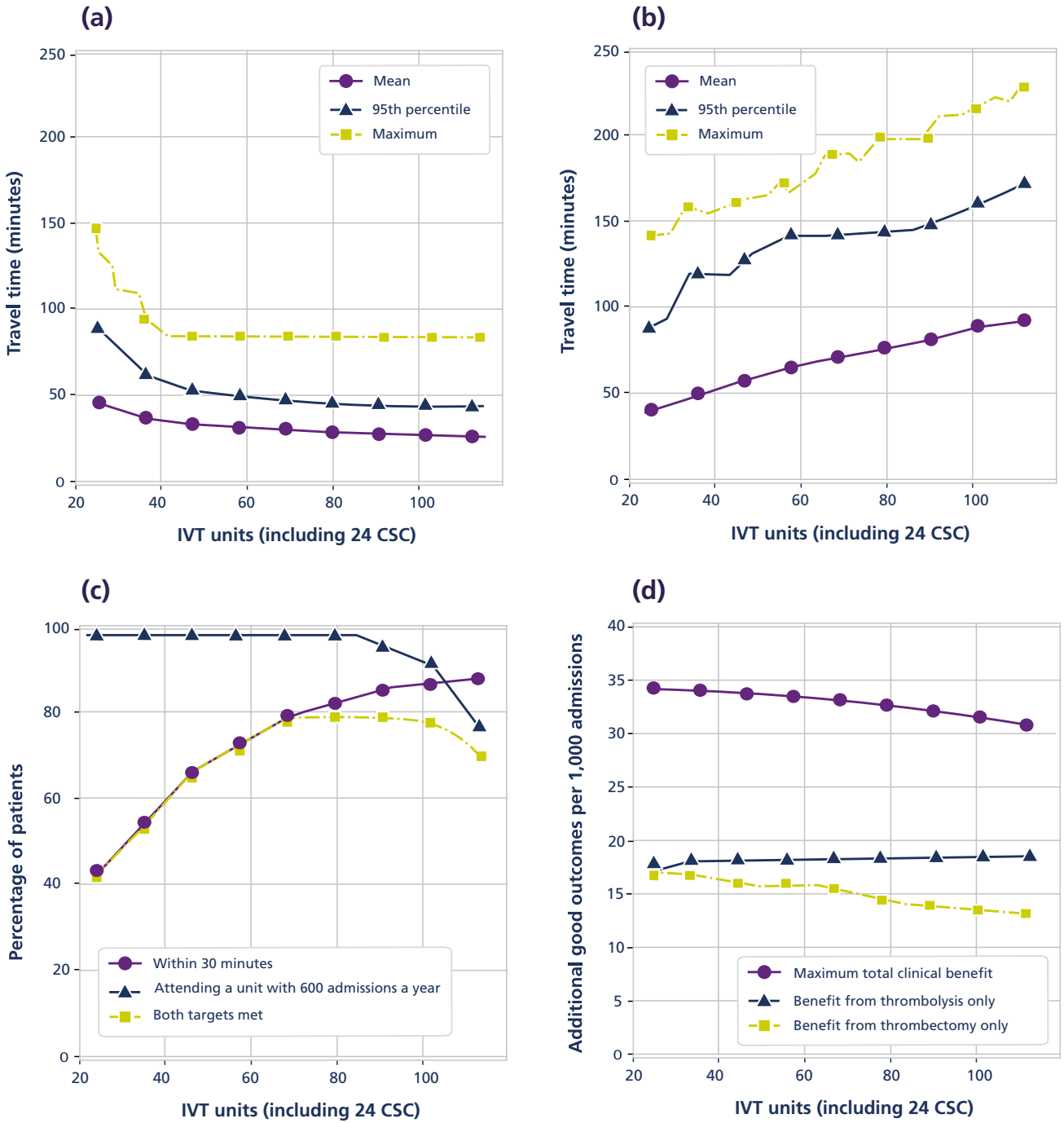

(a)
Travel time (minutes)
250
200
150
100
50
0
20
40
60
80
100
IVT units (including 24 CSC)
Mean
95th percentile
Maximum
(b)
Travel time (minutes)
250
200
150
100
50
0
20
40
60
80
100
IVT units (including 24 CSC)
Mean
95th percentile
Maximum
(c)
Percentage of patients
100
80
60
40
20
0
20
40
60
80
100
IVT units (including 24 CSC)
Within 30 minutes
Attending a unit with 600 admissions a year
Both targets met
(d)
Additional good outcomes per 1,000 admissions
40
35
30
25
20
15
10
5
0
20
40
60
80
100
IVT units (including 24 CSC)
Maximum total clinical benefit
Benefit from thrombolysis only
Benefit from thrombectomy only

Figure 8

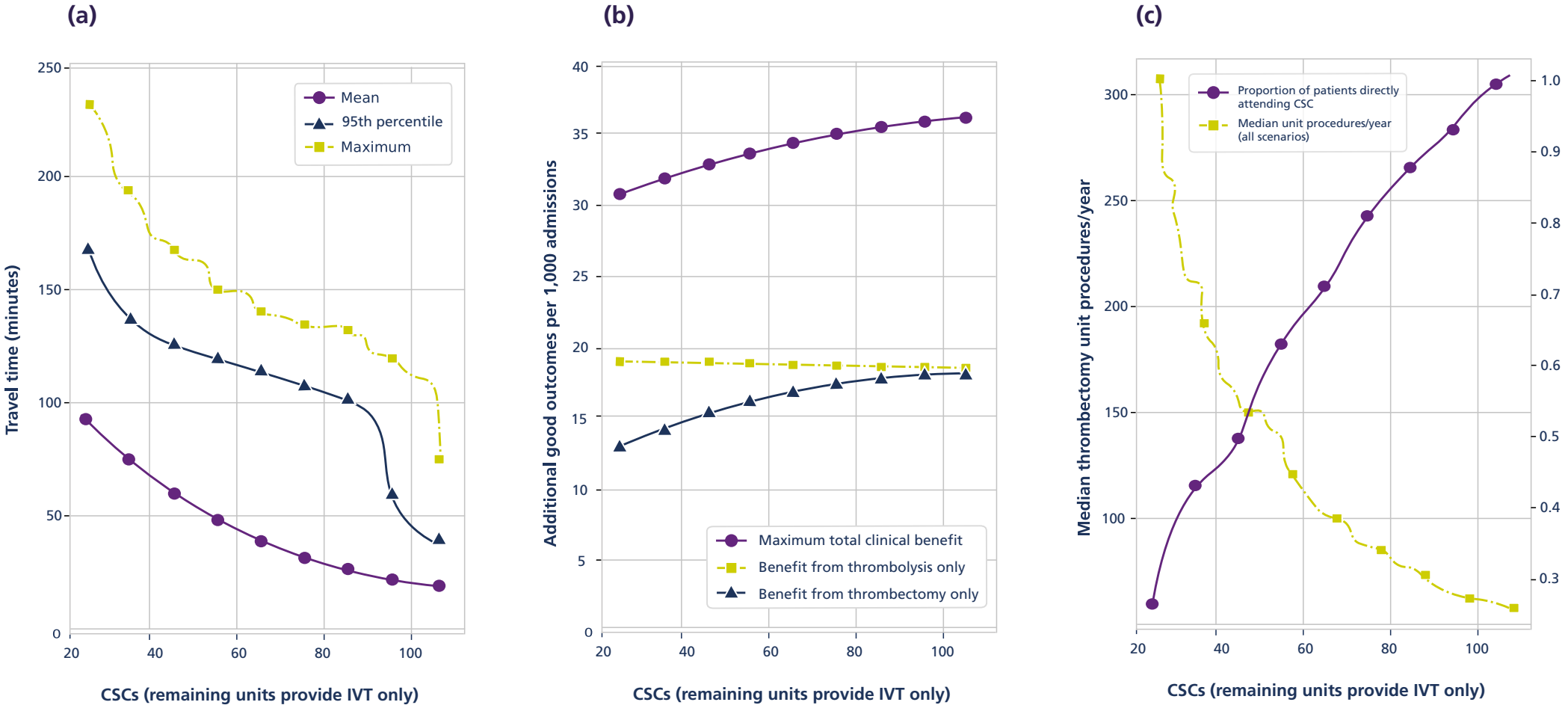

(a)
Travel time (minutes)
250
200
150
100
50
0
20
40
60
80
100
CSCs (remaining units provide IVT only)
Mean
95th percentile
Maximum
(b)
Additional good outcomes per 1,000 admissions
40
35
30
25
20
15
10
5
0
20
40
60
80
100
CSCs (remaining units provide IVT only)
Maximum total clinical benefit
Benefit from thrombolysis only
Benefit from thrombectomy only
(c)
Median thrombectomy unit procedures/year
300
250
200
150
100
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
20
40
60
80
100
CSCs (remaining units provide IVT only)
Proportion of patients directly attending CSC
Median unit procedures/year (all scenarios)

Figure 9

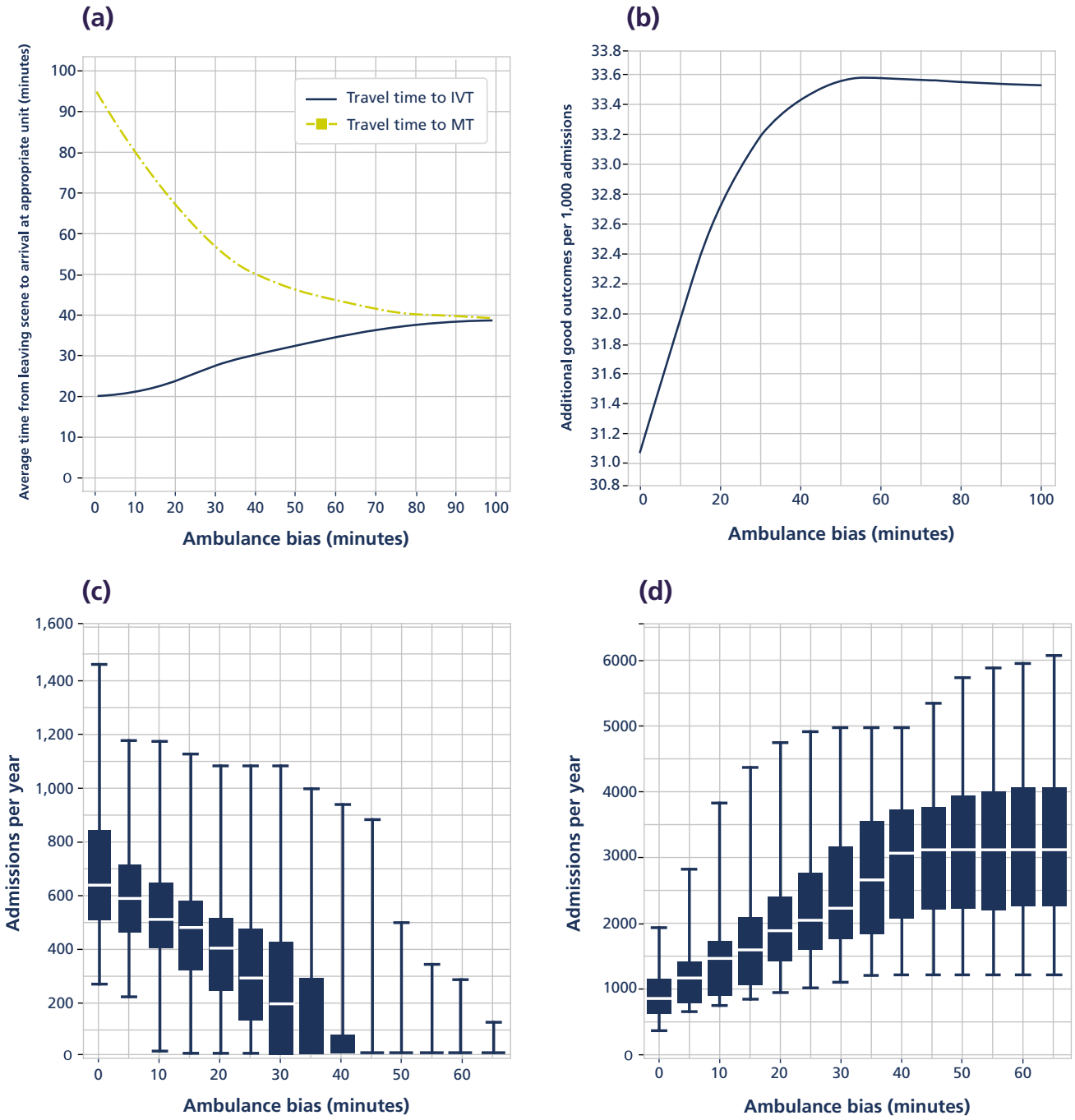

(a)
Average time from leaving scene to arrival at appropriate unit (minutes)
Travel time to IVT
Travel time to MT
Ambulance bias (minutes)
(b)
Additional good outcomes per 1,000 admissions
Ambulance bias (minutes)
(c)
Admissions per year
Ambulance bias (minutes)
(d)
Admissions per year
Ambulance bias (minutes)

Figure 10

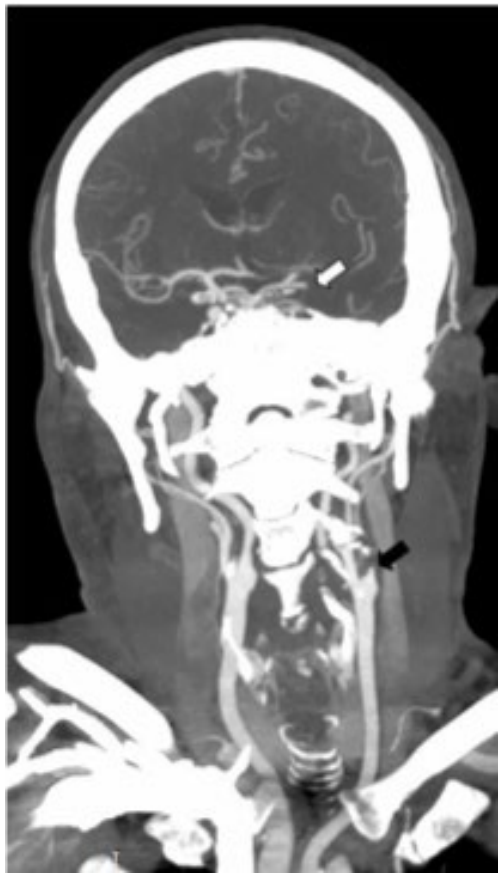


Figure 11

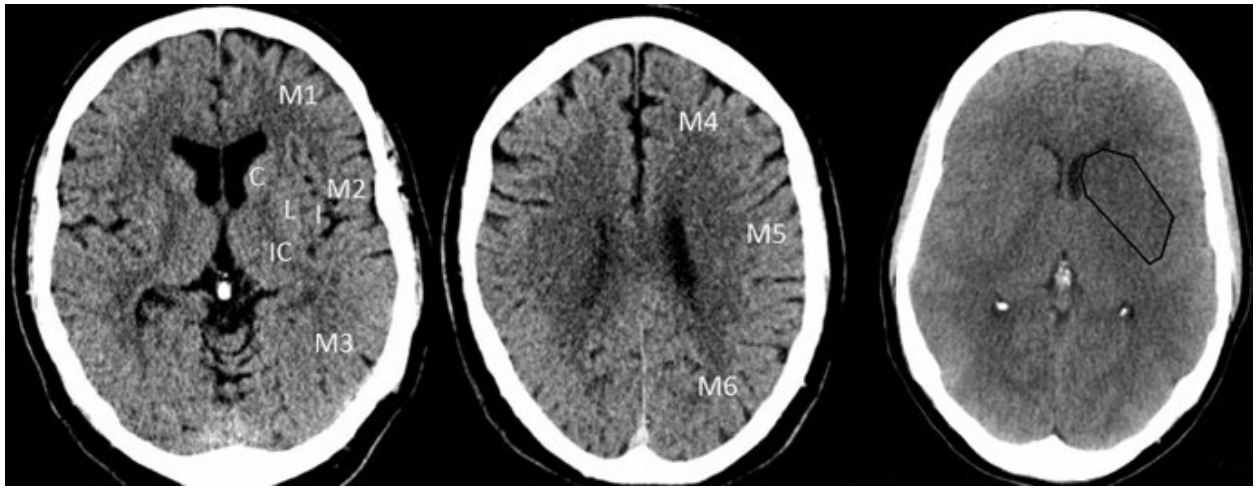


Figure 12

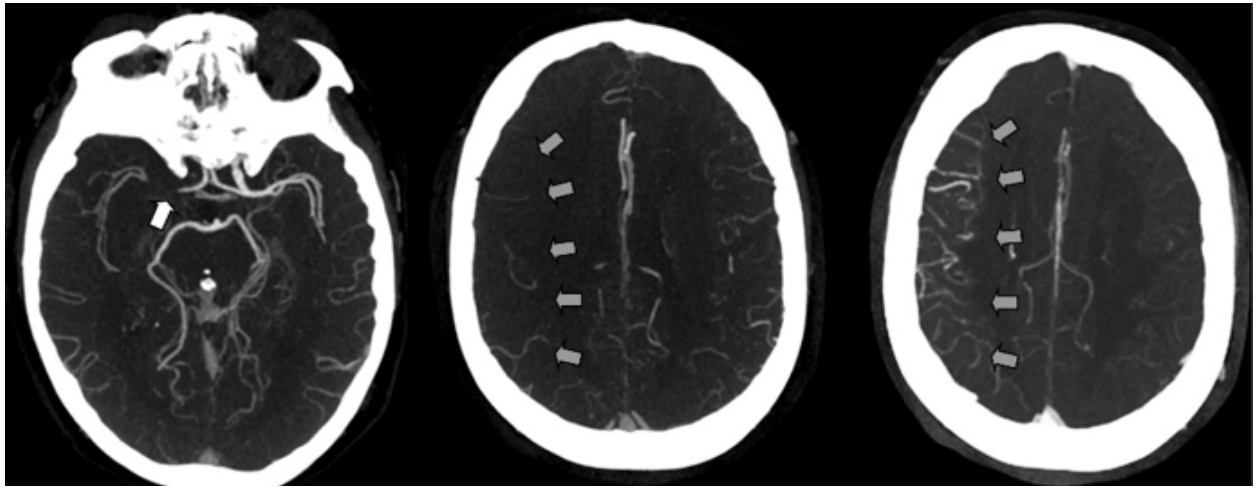


Figure 13

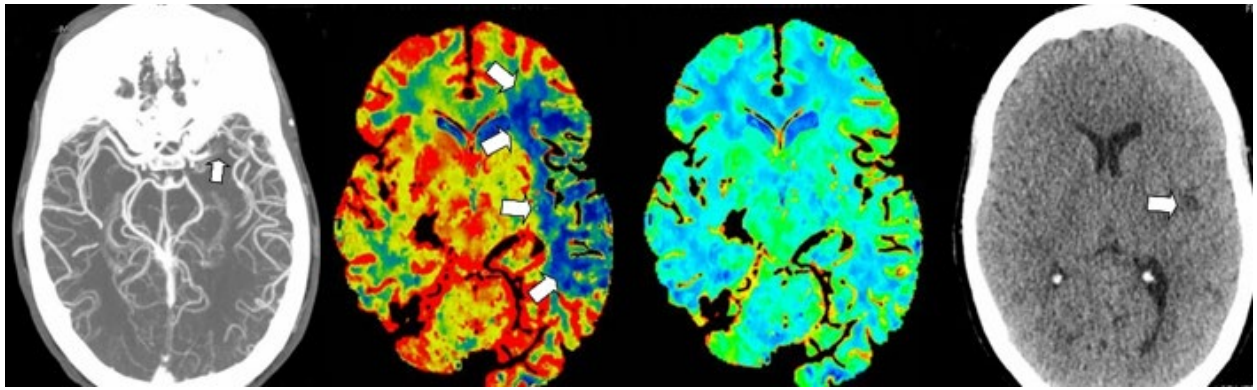


Figure 14

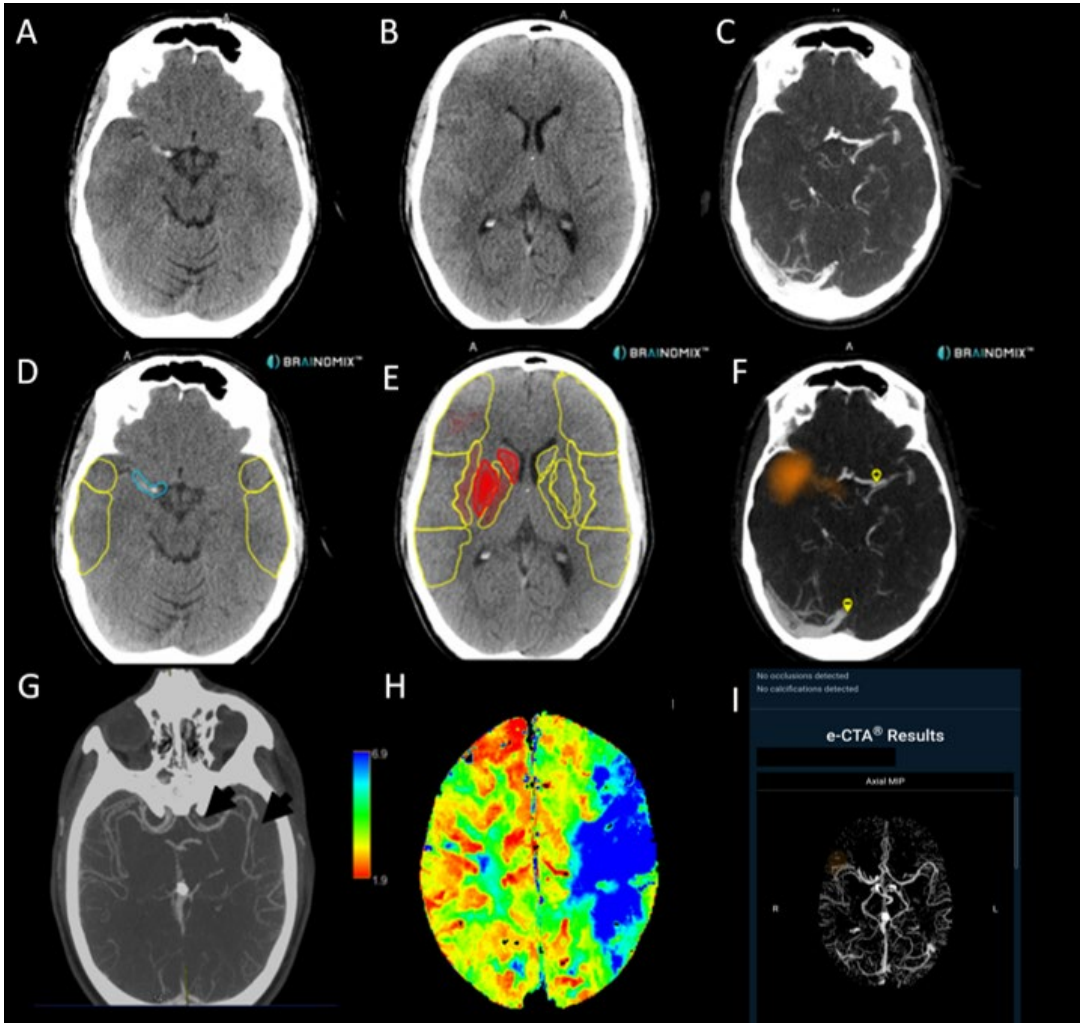

A
B
C
D
BRAINOMIX
E
BRAINOMIX
F
BRAINOMIX
G
H
6.9
1.9
I
No occlusions detected
No calcifications detected
e-CTA® Results
Axial MIP
R
L

Figure 15

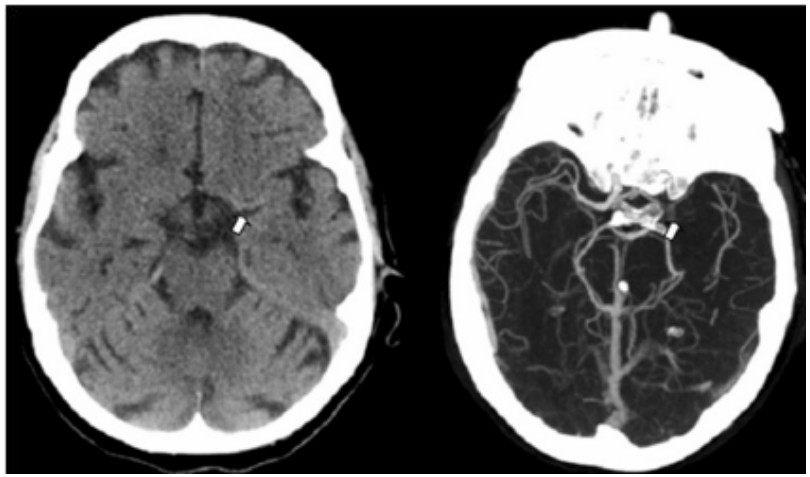


Figure 16

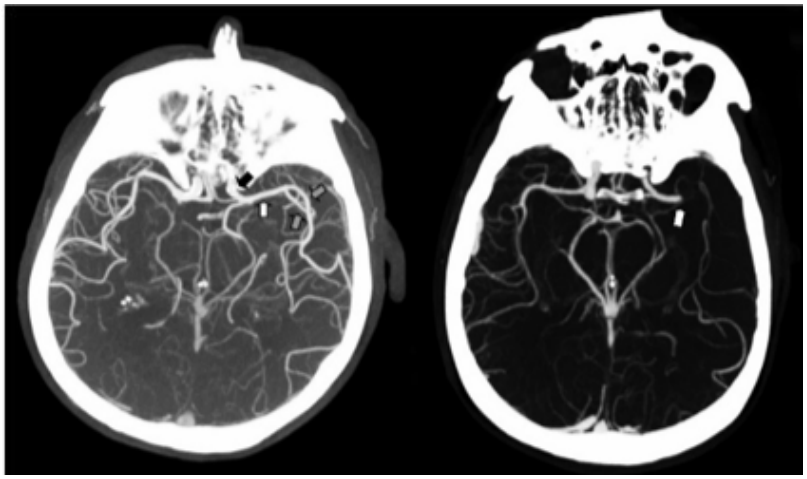


Figure 17

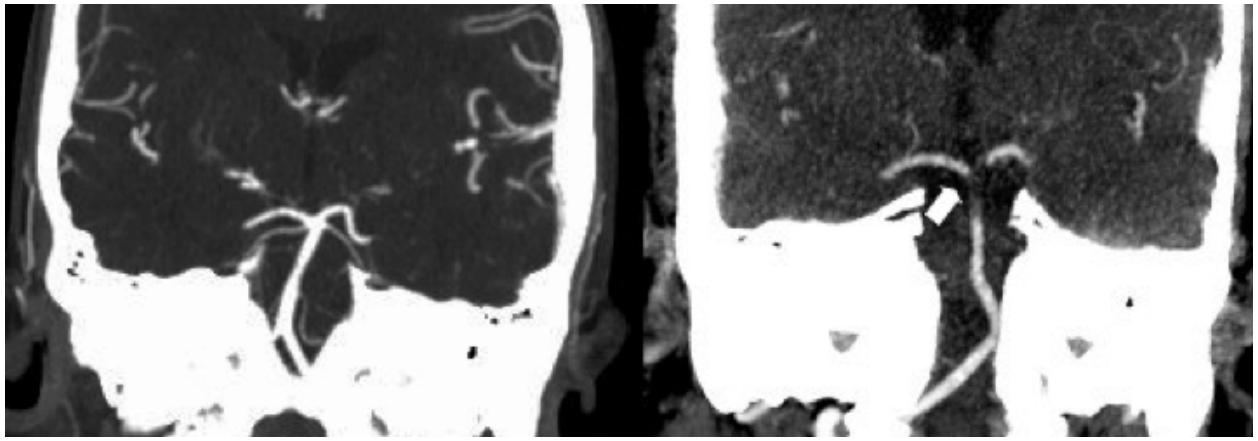


Figure 18

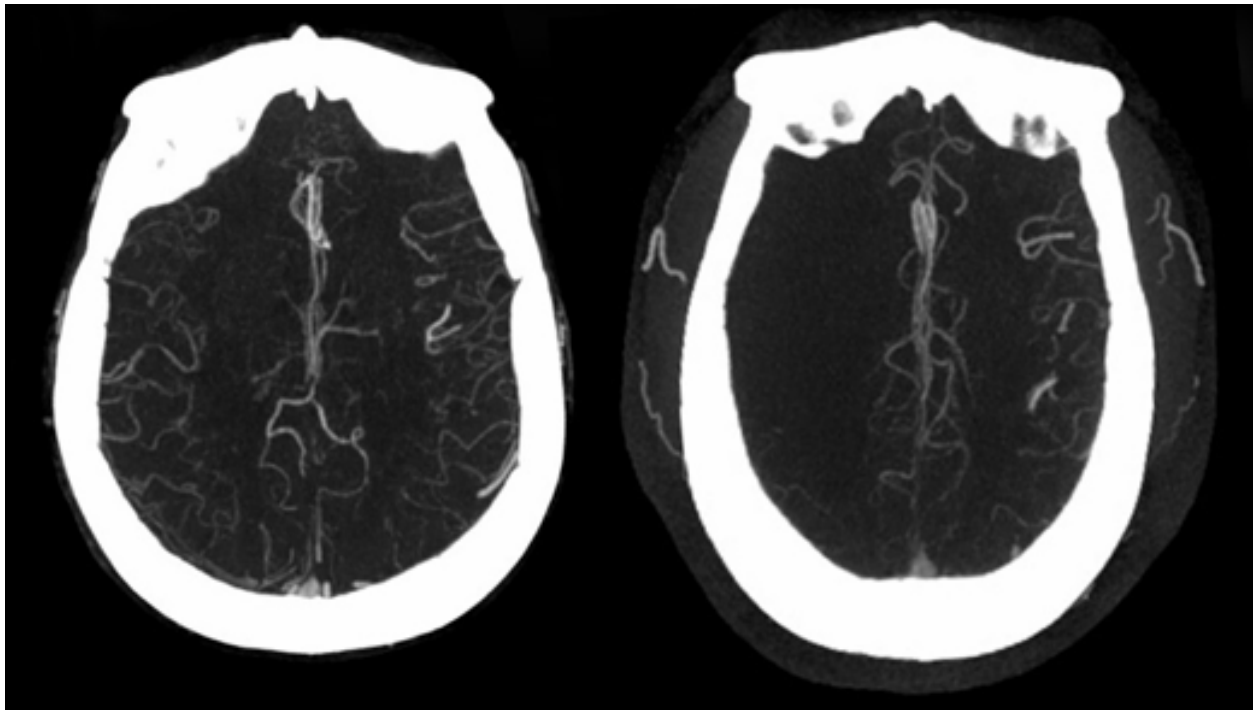


Figure 19

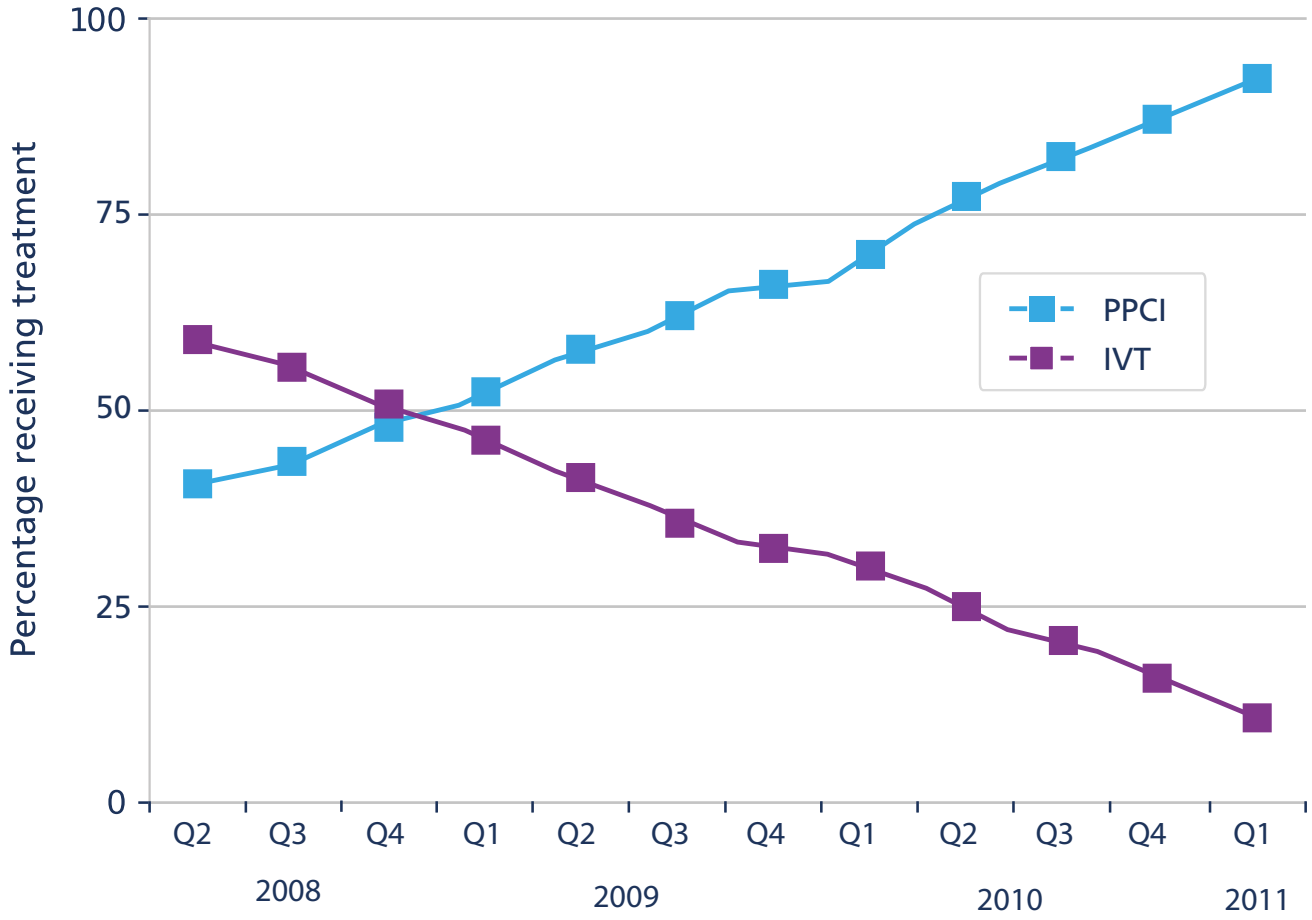

Percentage receiving treatment
100
75
50
25
0
PPCI
IVT
Q2
Q3
Q4
Q1
Q2
Q3
Q4
Q1
Q2
Q3
Q4
Q1
2008
2009
2010
2011

Figure 20

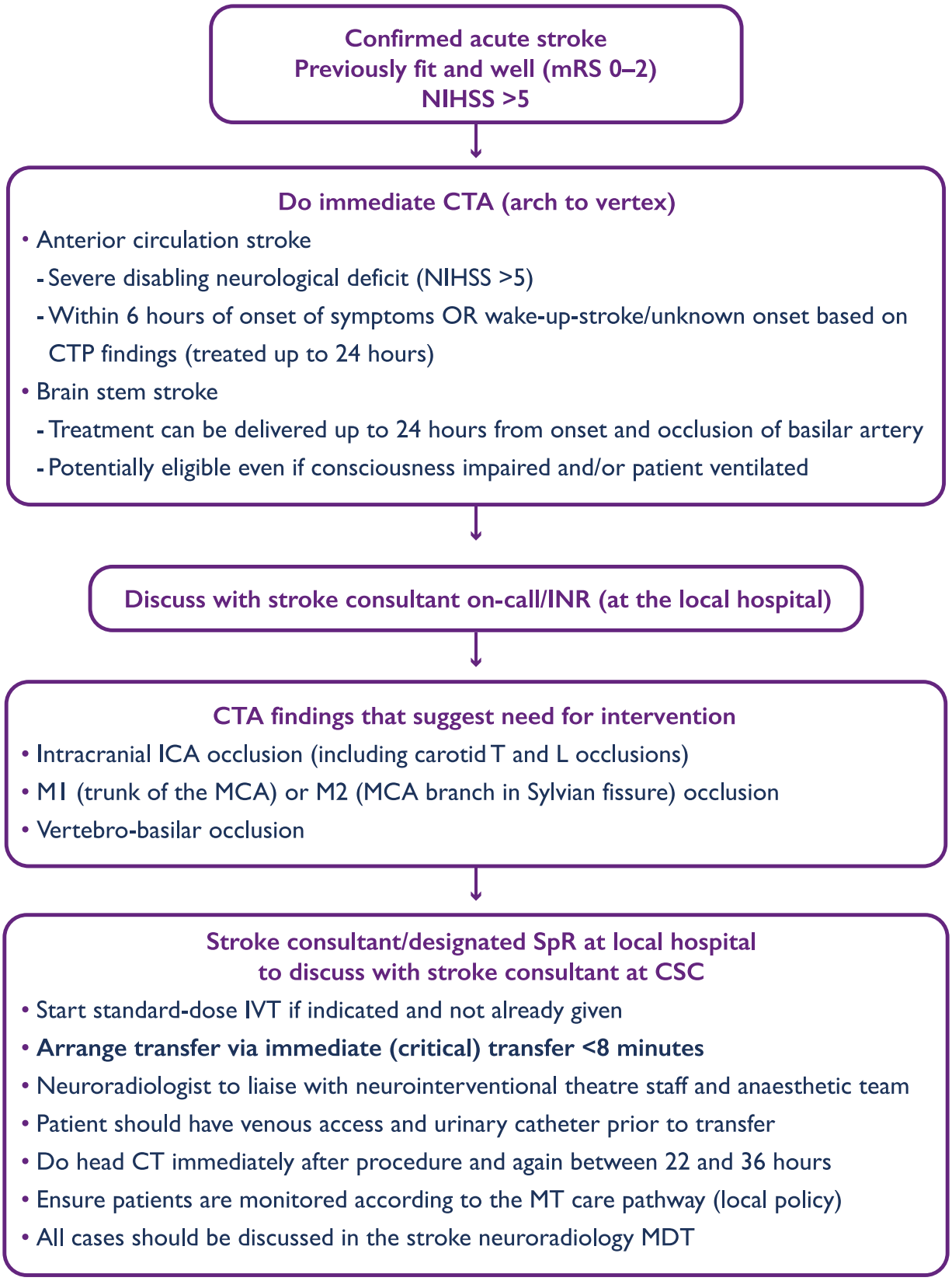

Confirmed acute stroke
Previously fit and well (mRS 0–2)
NIHSS >5
Do immediate CTA (arch to vertex)
• Anterior circulation stroke
- Severe disabling neurological deficit (NIHSS >5)
- Within 6 hours of onset of symptoms OR wake-up-stroke/unknown onset based on CTP findings (treated up to 24 hours)
• Brain stem stroke
- Treatment can be delivered up to 24 hours from onset and occlusion of basilar artery
- Potentially eligible even if consciousness impaired and/or patient ventilated
Discuss with stroke consultant on-call/INR (at the local hospital)
CTA findings that suggest need for intervention
• Intracranial ICA occlusion (including carotid T and L occlusions)
• M1 (trunk of the MCA) or M2 (MCA branch in Sylvian fissure) occlusion
• Vertebro-basilar occlusion
Stroke consultant/designated SpR at local hospital to discuss with stroke consultant at CSC
• Start standard-dose IVT if indicated and not already given
• Arrange transfer via immediate (critical) transfer <8 minutes
• Neuroradiologist to liaise with neurointerventional theatre staff and anaesthetic team
• Patient should have venous access and urinary catheter prior to transfer
• Do head CT immediately after procedure and again between 22 and 36 hours
• Ensure patients are monitored according to the MT care pathway (local policy)
• All cases should be discussed in the stroke neuroradiology MDT

Figure 21

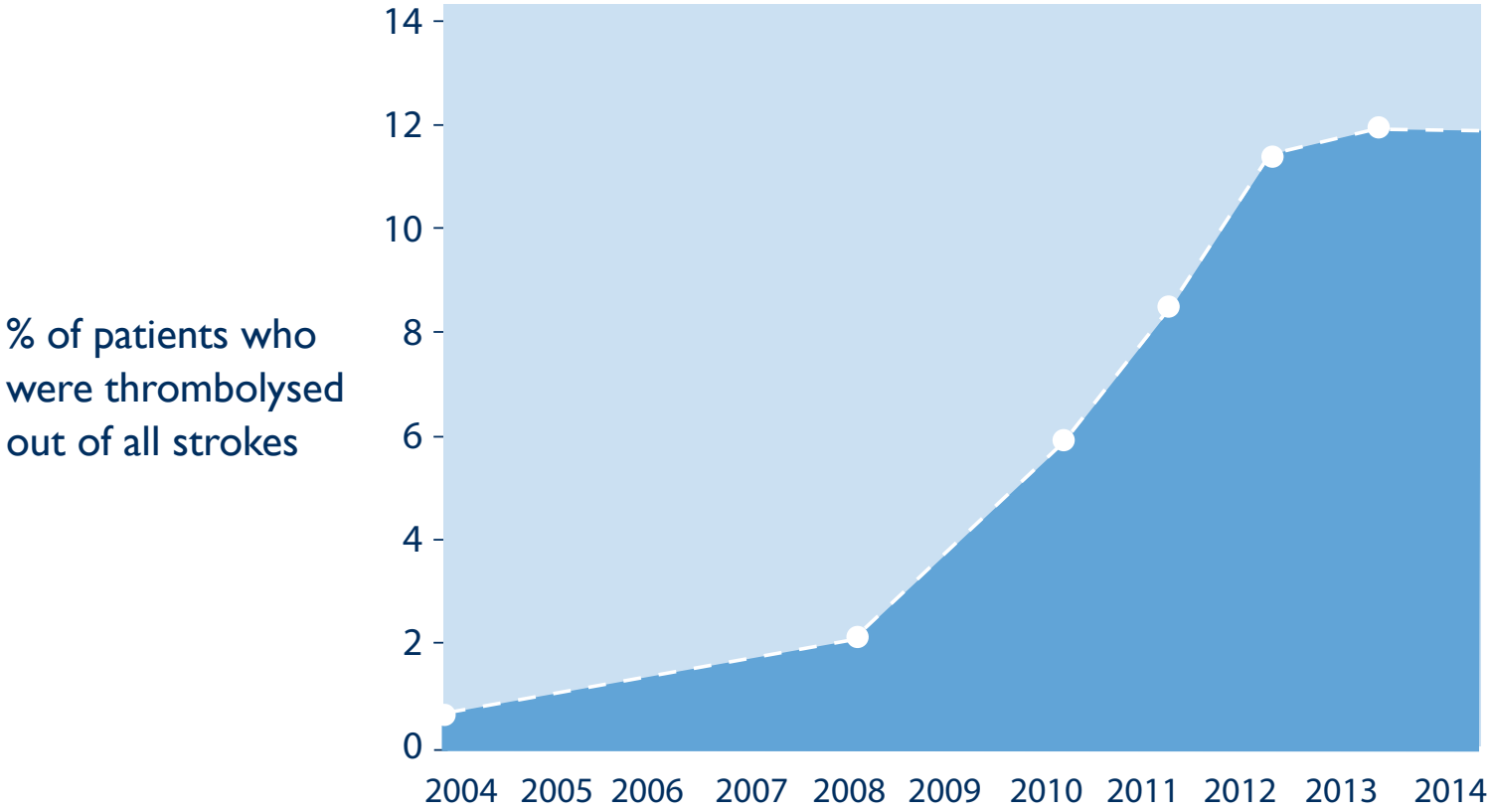

% of patients who were thrombolysed out of all strokes
14
12
10
8
6
4
2
0
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014

Figure 22

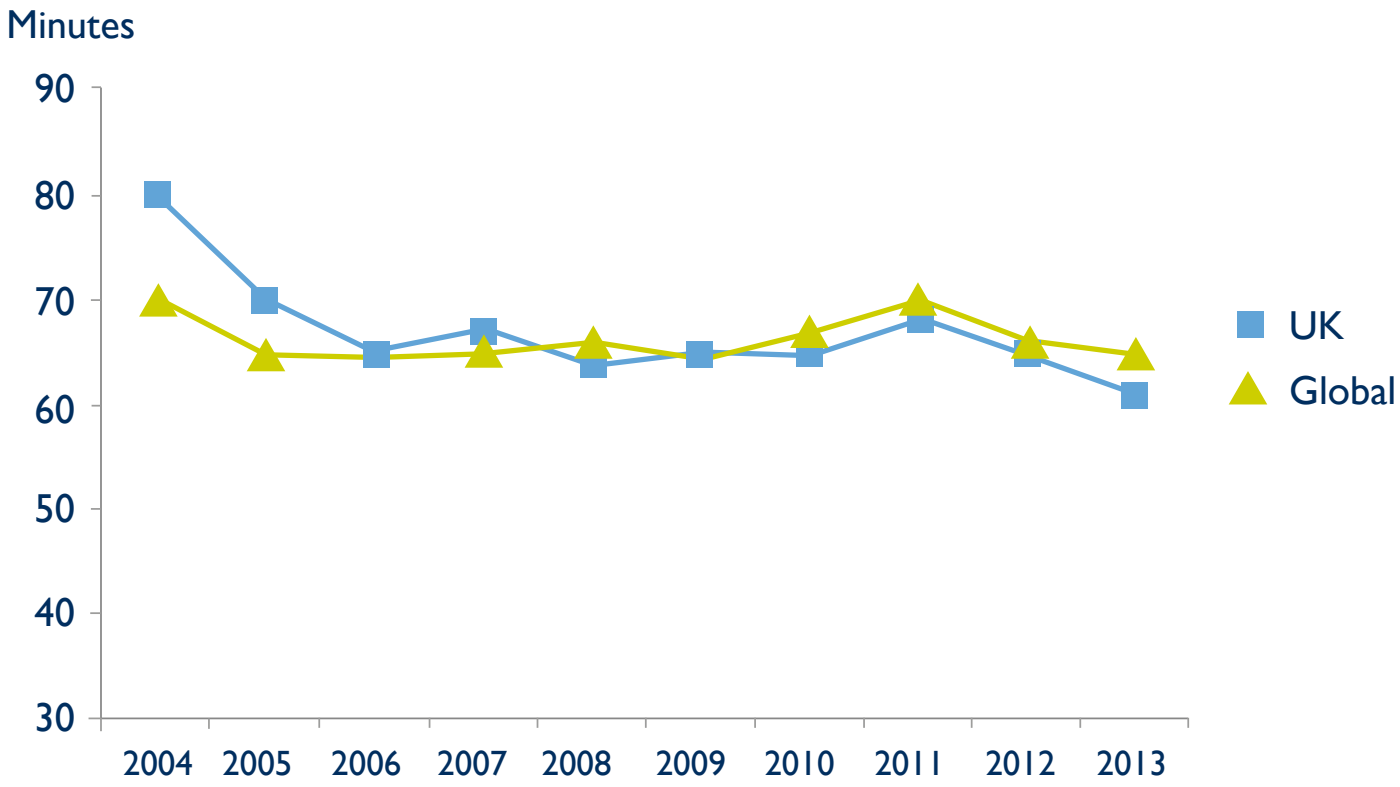
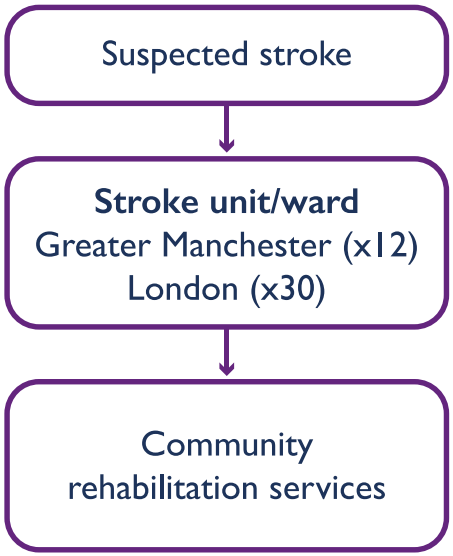
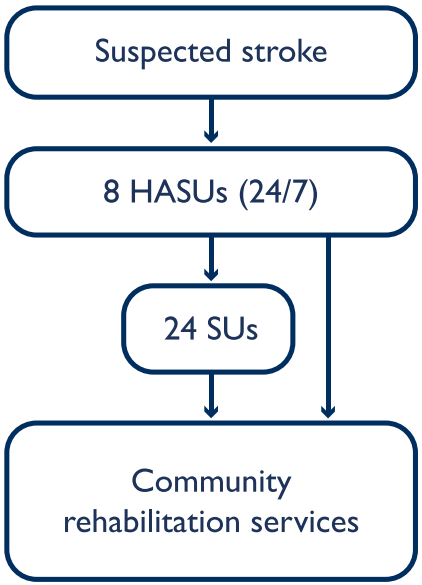

Minutes
90
80
70
60
50
40
30
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
UK
Global

Table 6

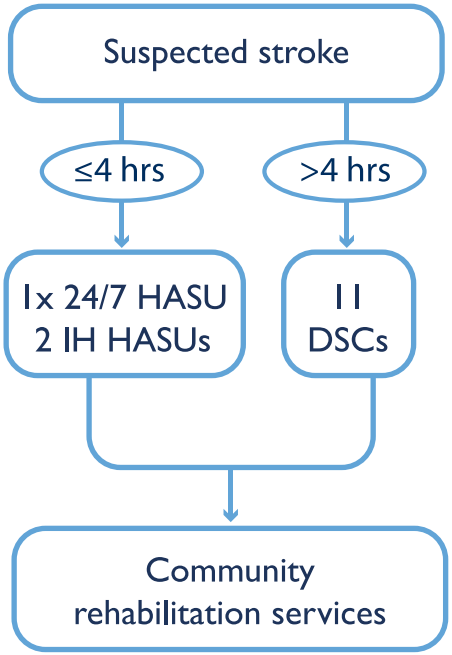
1A



1B



1C



1D

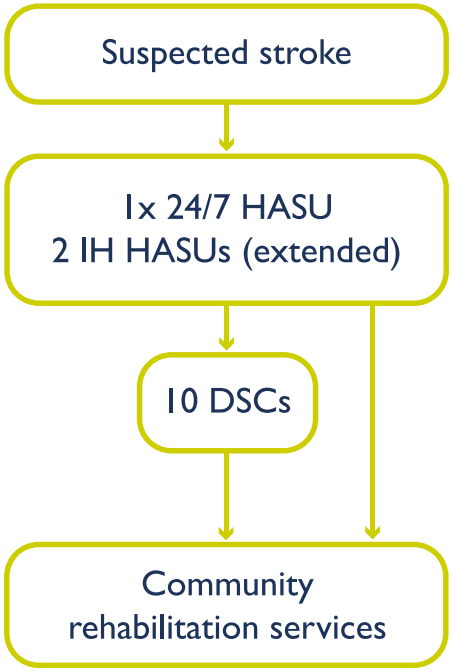


Figure 23

Decision to change		• **London:** Led by regional authority; 'holding the line', e.g on model • **GMA:** Led by network; 'consensus' approach • **GMB:** Led by commissioners; 'holding the line', e.g. on implementation approach
Decision on which model to implement		• **London:** Simple, inclusive model • **GMA:** More complex, less inclusive model • **GMB:** Less complex and more inclusive than GMA; more in line with London
Implementation approach		• **London:** 'Big bang' implementation; accreditation – standards linked to financial levers; hands-on facilitation • **GMA:** Pilot, then phased; no accreditation or financial levers; platform to share learning • **GMB:** 'Big bang' implementation; no accreditation or financial levers; hands-on facilitation, post-implementation
Implementation outcomes		• **London:** HASUs provide interventions; 93% treated in HASU • **GMA:** HASUs provide interventions; DSCs vary; 39% treated in HASU • **GMB:** HASUs provide interventions; 86% treated in HASU
Intervention outcomes	Clinical interventions	• **London: More likely** than elsewhere overall • **GMA: No more likely** than elsewhere overall (except HASUs) • **GMB: More likely** than elsewhere overall
	Clinical outcomes	• **London:** LOS = ↓ (1.2 days per patient); mortality = ↓ (96 lives per annum) • **GMA:** LOS = ↓ (2 days per patient); mortality = no significant difference • **GMB:** LOS = ↓ (1.5 days per patient); mortality = ↓ in HASUs (68 lives per annum)
	Cost effectiveness	• **London:** Cost = ↑; QALYs = ↑; NMB >0 • **GMA:** Cost = ↓; QALYs = ↑; NMB >0 • **GMB:** Cost = ↑; QALYs = ↑; NMB <0
	Patient and carer experience	London and GMA: • Good experience overall • Clear communication needed at each stage

Figure 24

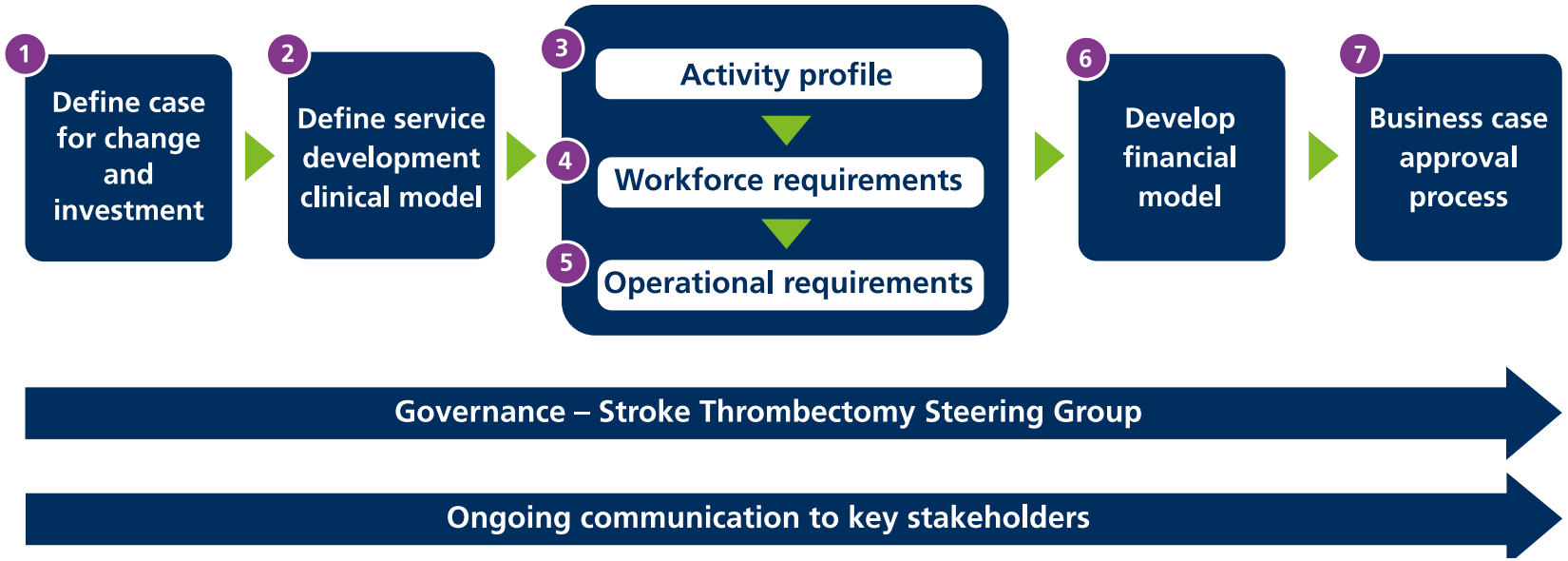

1
Define case for change and investment
2
Define service development clinical model
3
Activity profile
4
Workforce requirements
5
Operational requirements
6
Develop financial model
7
Business case approval process
Governance – Stroke Thrombectomy Steering Group
Ongoing communication to key stakeholders

Figure 25

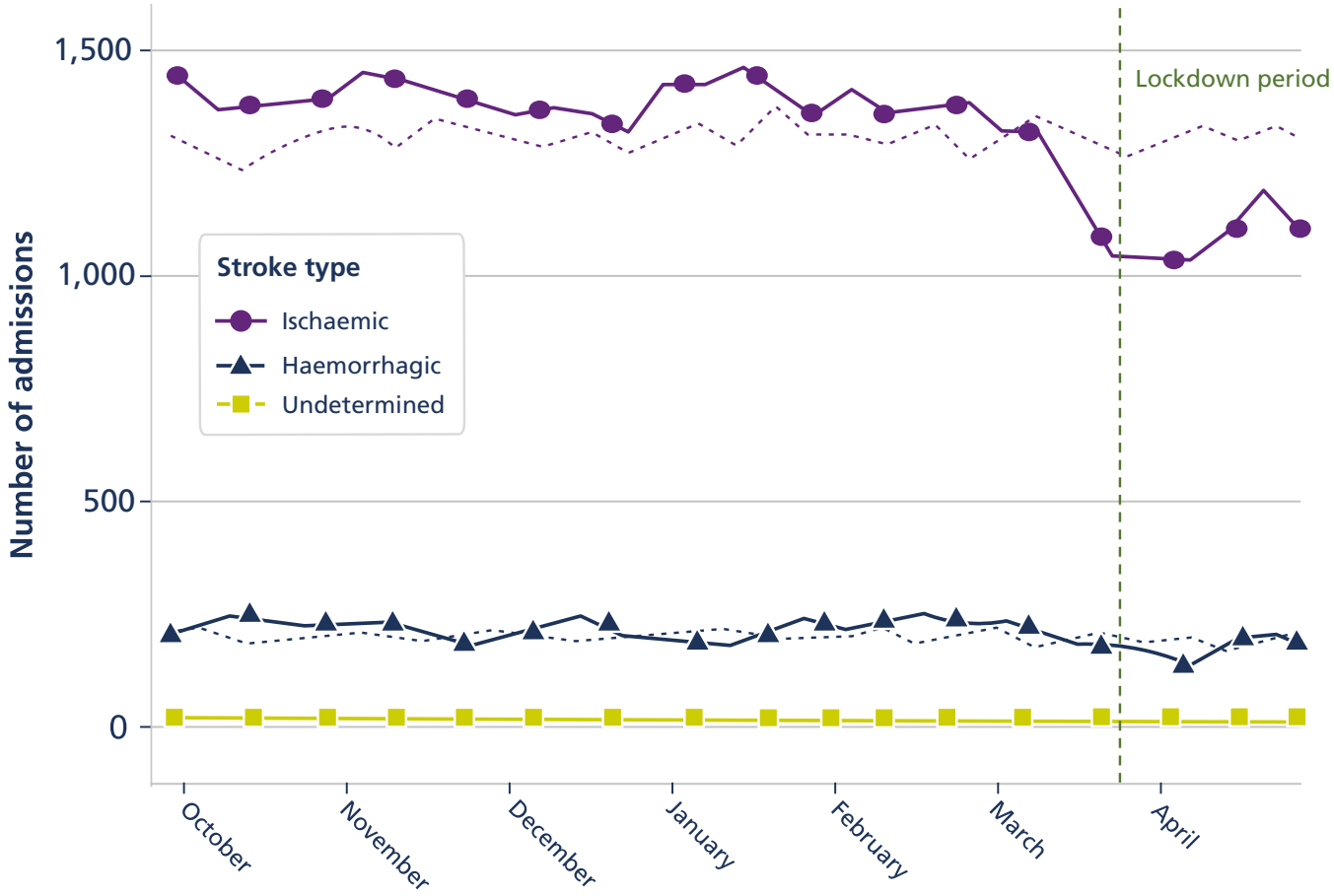
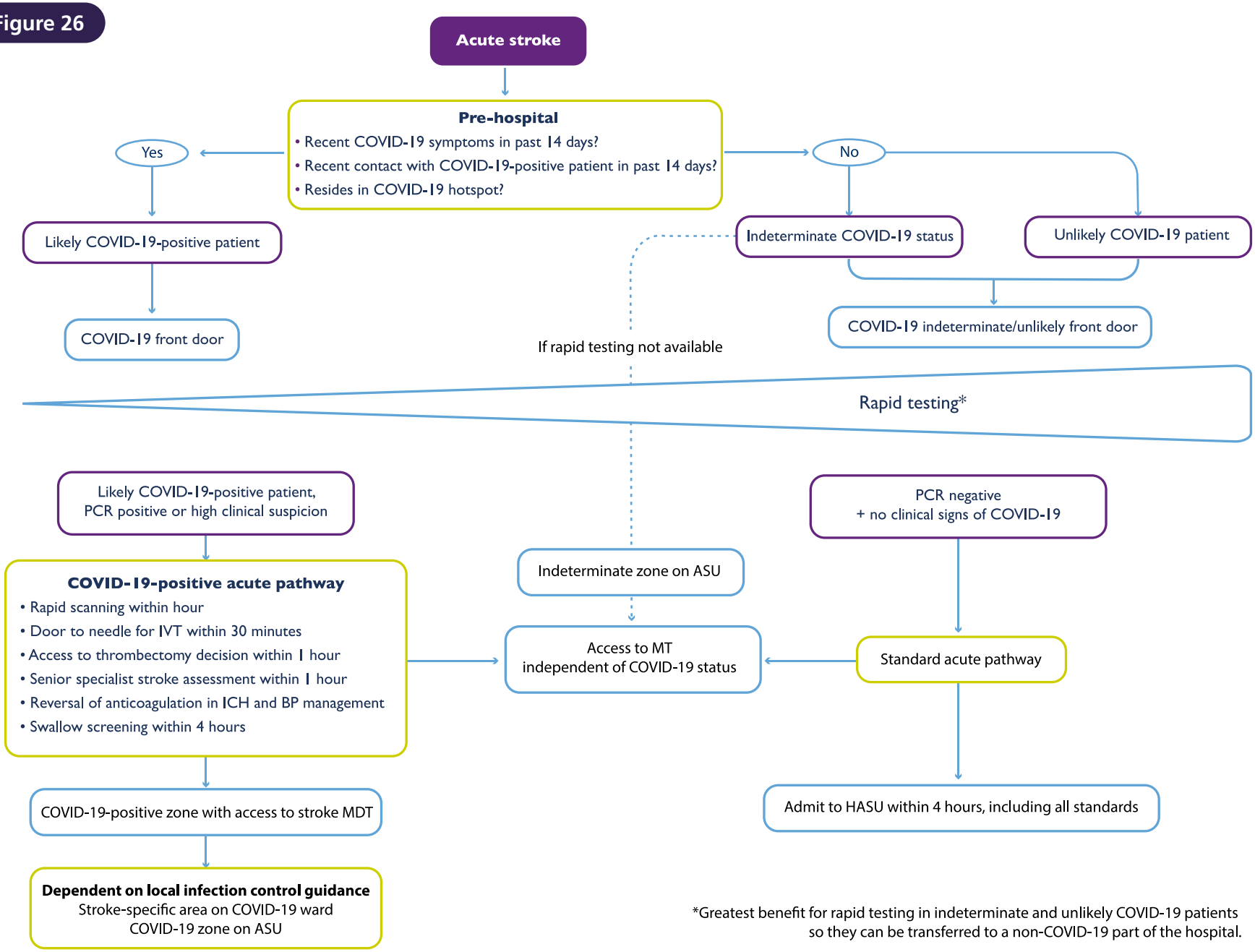
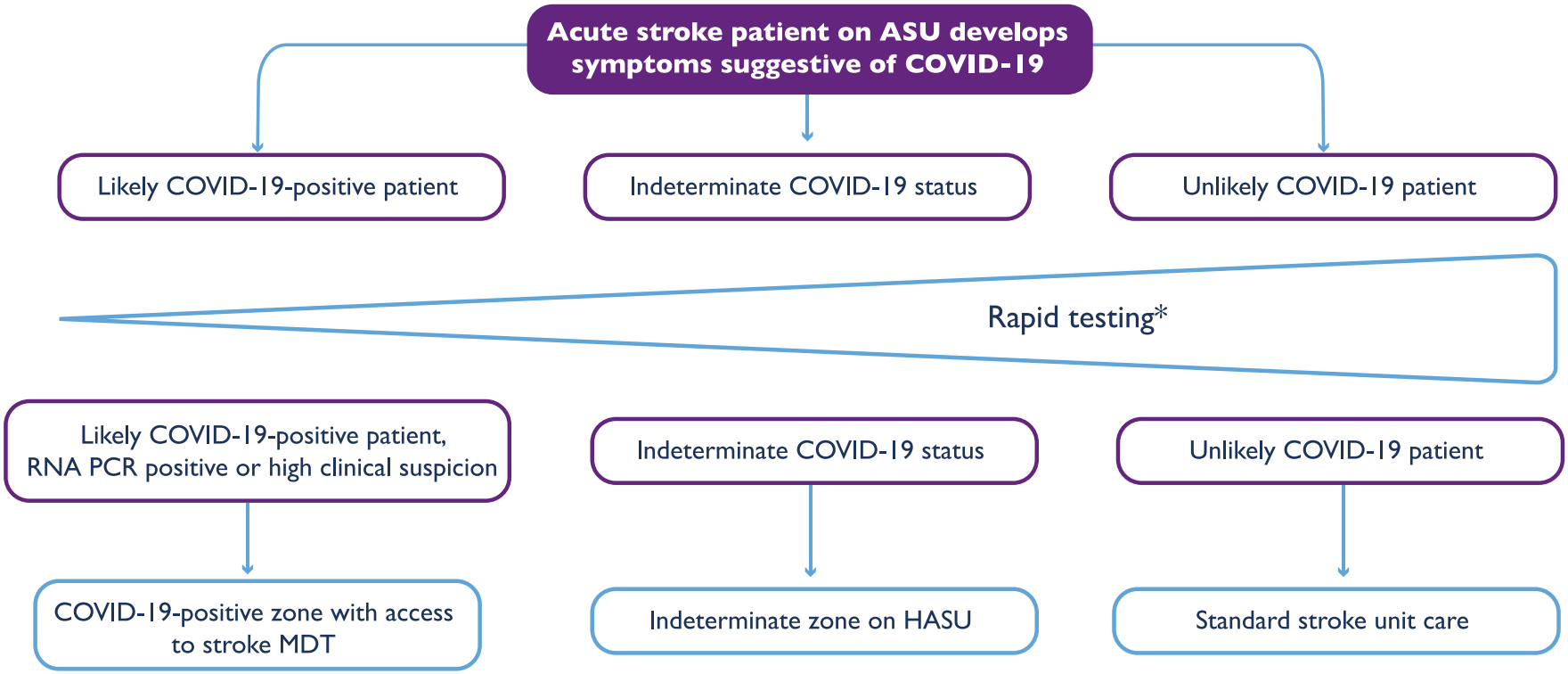

1,500
1,000
500
0
Number of admissions
Lockdown period
Stroke type
Ischaemic
Haemorrhagic
Undetermined
October
November
December
January
February
March
April

Figure 26



*Greatest benefit for rapid testing in indeterminate and unlikely COVID-19 patients so they can be transferred to a non-COVID-19 part of the hospital.

Figure 27



*If rapid testing not available move to indeterminate zone on HASU.

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