Cost-Utility Analysis of Mechanical Thrombectomy Using Stent Retrievers in Acute Ischemic Stroke

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Background and Purpose—Recently, 5 randomized controlled trials demonstrated the benefit of endovascular therapy compared with intravenous tissue-type plasminogen activator in acute stroke. Economic evidence evaluating stent retrievers is limited. We compared the cost-effectiveness of intravenous tissue-type plasminogen activator alone versus mechanical thrombectomy and intravenous tissue-type plasminogen activator as a bridging therapy in eligible patients in the UK National Health Service.

Methods—A model-based cost-utility analysis was performed using a lifetime horizon. A Markov model was constructed and populated with probabilities, outcomes, and cost data from published sources, including 1-way and probabilistic sensitivity analysis.

Results—Mechanical thrombectomy was more expensive than intravenous tissue-type plasminogen activator, but it improved quality-adjusted life expectancy. The incremental cost per (quality-adjusted life year) gained of mechanical thrombectomy over a 20 year period was $11,651 (£7061). The probabilistic sensitivity analysis demonstrated that thrombectomy had a 100% probability of being cost-effective at the minimum willingness to pay for a quality-adjusted life year commonly used in the United Kingdom.

Conclusion—Although the upfront costs of thrombectomy are high, the potential quality-adjusted life year gains mean this intervention is cost-effective. This is an important factor for consideration in deciding whether to commission this intervention. (Stroke. 2013;46:00-00. DOI: 10.1161/STROKEAHA.115.009396.)

Key Words: cost-effectiveness ■ stents ■ stroke ■ thrombectomy ■ tissue-type plasminogen activator
associated with a 4- to 5-fold increase in the odds of good final clinical outcome, with a similar decrease in odds of death.12

Benefit of treatments is usually measured according to functional outcome at 3 months. Implementation of new treatments also depends on cost and affordability, for which a health economic study is usually needed. Stroke itself is an expensive disease in terms of its societal, personal, and financial impact. The rationalization concerning the clinical value and effectiveness of thrombectomy is guided by information regarding the benefits, risks, and costs associated. It has been suggested that although the upfront costs of thrombectomy are high, the potential reduction in morbidity can result in savings downstream both in the hospital and in the community setting, resulting in a significant reduction in the overall economic burden from stroke.

Decisions to implement new technologies in the UK National Health Service are increasingly being made taking into account economic considerations, such as cost-effectiveness and budget impact. Previous economic evaluations of thrombectomy have been undertaken in the United States and are based on single arm studies of a range of mechanical devices, now superseded in a rapidly developing field.22–25 Therefore, the purpose of this study was to model the cost-effectiveness of mechanical thrombectomy in the hyperacute management of stroke in the United Kingdom, based on a meta-analysis of the data recently published using the 5 randomized control trials, which have used predominantly stent retrievers.

Methods
This was a model-based cost-utility analysis, with outcomes measured in terms of quality adjusted life years (QALYs), 26 which are the recommended outcomes for economic evaluation in the United Kingdom.27 The number of deaths averted is also reported as an additional outcome measure.

Model Structure
A short-run decision analytic model (Figure 1A) was created to analyze data on costs and clinical outcomes within 3 months from stroke and subsequently was used to distribute a theoretical cohort of patients into 1 of 3 possible health states (see Outcomes). A long-run Markov state-transition model was then used to estimate the expected costs and outcomes over a life-time horizon of 20 years, using cycles of 3 months (Figure 1B). The analysis was undertaken from the perspective of the UK National Health Service and Personal Social Services. Costs were calculated in 2013–2014 UK pounds and are presented in US$ using an exchange rate of £1=US$1.65.28 Where appropriate, costs were converted to 2013–2014 prices using National Health Service Pay and Prices Indices.29 Outcomes are measured in terms of deaths avverted and quality adjusted life years (QALYs) gained. In the long-run model, all costs and outcomes after the first year are discounted at an annual rate of 3.5%.27

Management Strategies
Two treatment options were considered, IV-tPA alone versus mechanical thrombectomy and IV-tPA used as a bridging therapy. Only data from the recently published randomized controlled trials using predominantly stent retrievers were used (see Table 1 in the online-only Data Supplement). For both strategies, outcomes were based on modified Rankin Scale (mRS) scores measured at 90 days after stroke, which were assumed to be affected by recanalization rates and symptomatic hemorrhage rates. We assumed that all other aspects of inpatient care, including imaging and laboratory studies, would be otherwise comparable and consistent with published clinical guidelines.30

Costs
The cost of IV-tPA was estimated to be £2953 (€1214). This includes the cost of the medication (assuming an average patient weight of 76 kg)31,32 and the cost of staff time for the administration (Table II in the online-only Data Supplement). The cost of the mechanical thrombectomy was estimated to be £13,803 (€5365), including the cost of the stent, the materials, and the surgery.33,34 The cost of the procedure was calculated using a microcosting approach, multiplying the average time of an intervention for the hourly cost for each grade of personnel35 (see Table 2 in the online-only Data Supplement).

The costs for the acute management of patients in the first 3 months after stroke and the following ongoing annual costs were taken from a published report.36 Acute and ongoing costs differ according to the level of disability, measured by mRS score. Acute costs include the length of stay in the Hyper Acute Stroke Unit, in the Acute High Dependence Unit, and in the rehabilitation ward, as well as the supported discharge cost and community care costs.

The cost of a recurrent stroke has been assessed internally assuming the cost is the same in each intervention arm. Because it is not possible to predict the type and severity of a recurrent stroke and...
### Table 1. Model Parameters and Range of Values for Sensitivity Analysis: Utilities Scores, Costs, Probabilities, and Transition Probabilities

| Probabilities | Base-Case Value | Univariate Sensitivity Analysis | Distribution | Range | Alpha-Beta | Source |
|---------------|-----------------|--------------------------------|--------------|-------|------------|--------|
| mRS 0-1-2 after IV-tPA and thrombectomy | 0.46 | Dirichlet | 0–1 | 291-342 | Multiple sources |
| mRS 3-4-5 after IV-tPA and thrombectomy | 0.39 | Dirichlet | 0–1 | 247-386 | Multiple sources |
| mRS 6 after IV-tPA and thrombectomy | 0.15 | Dirichlet | 0–1 | 95-538 | Multiple sources |
| mRS 0-1-2 after IV-tPA alone | 0.26 | Dirichlet | 0–1 | 169-481 | Multiple sources |
| mRS 3-4-5 after IV-tPA alone | 0.55 | Dirichlet | 0–1 | 358-293 | Multiple sources |
| mRS 6 after IV-tPA alone | 0.19 | Dirichlet | 0–1 | 124-527 | Multiple sources |
| mRS 0-1-2 after recurrent stroke | 0.26 | Dirichlet | 0–1 | 260-740 | Short-run model |
| mRS 3-4-5 after recurrent stroke | 0.55 | Dirichlet | 0–1 | 550-450 | Short-run model |
| mRS 6-death after recurrent stroke | 0.19 | Dirichlet | 0–1 | 190-810 | Short-run model |

**If IV-tPA alone**

| mRS 0-1-2 after recurrent stroke | 0.26 | Dirichlet | 0–1 | 260-740 | Short-run model |
| mRS 3-4-5 after recurrent stroke | 0.55 | Dirichlet | 0–1 | 550-450 | Short-run model |
| mRS 6-death after recurrent stroke | 0.19 | Dirichlet | 0–1 | 190-810 | Short-run model |

**If mechanical thrombectomy**

| mRS 0-1-2 after recurrent stroke | 0.46 | Dirichlet | 0–1 | 460-540 | Short-run model |
| mRS 3-4-5 after recurrent stroke | 0.39 | Dirichlet | 0–1 | 390-610 | Short-run model |
| mRS 6-death after recurrent stroke | 0.15 | Dirichlet | 0–1 | 150-850 | Short-run model |

**Transition probabilities**

**Movement from up to end of year 1 to 3 months**

| Independent mRS 0-1-2 | | | | | | |
|----------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Independent mRS 0-1-2 | 0.955 | Dirichlet | 0–1 | 1337-63 | Ref. 33 |
| Dependent mRS 3-4-5 | 0.024 | Dirichlet | 0–1 | 34-1366 | Ref. 33 |
| Recurrent stroke | 0.013 | Dirichlet | 0–1 | 18-1382 | Ref. 33 |
| Dead mRS 6 | 0.008 | Dirichlet | 0–1 | 11-1389 | Ref. 33 |
| Dependent mRS 3-4-5 | 0.919 | Dirichlet | 0–1 | 1287-113 | Ref. 33 |
| Independent mRS 0-1-2 | 0.029 | Dirichlet | 0–1 | 41-1359 | Ref. 33 |
| Recurrent stroke | 0.013 | Dirichlet | 0–1 | 18-1382 | Ref. 33 |
| Dead mRS 6 | 0.039 | Dirichlet | 0–1 | 55-1345 | Ref. 33 |

**Movement from after year 1 to 3 months**

| Independent mRS 0-1-2 | | | | | | |
|----------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Independent mRS 0-1-2 | 0.979 | Dirichlet | 0–1 | 1371-28 | Ref. 33 |
| Dependent mRS 3-4-5 | 0.000 | Dirichlet | 0–1 | 17-1382 | Ref. 33 |
| Recurrent stroke | 0.013 | Dirichlet | 0–1 | 11-1388 | Ref. 33 |
| Dead mRS 6 | 0.008 | Dirichlet | 0–1 | 11-1388 | Ref. 33 |
| Dependent mRS 3-4-5 | 0.948 | Dirichlet | 0–1 | 1327-72 | Ref. 33 |
| Independent mRS 0-1-2 | 0.000 | Dirichlet | 0–1 | 17-1382 | Ref. 33 |
| Recurrent stroke | 0.013 | Dirichlet | 0–1 | 54-1345 | Ref. 33 |
| Dead mRS 6 | 0.039 | Dirichlet | 0–1 | 55-1345 | Ref. 33 |
| Recurrent stroke | | | | | | |
| Independent mRS 0-1-2 after IV-tPA alone | 0.834 | Dirichlet | 0–1 | 834-165 | Ref. 33, 34 |
| Dependent mRS 3-4-5 after IV-tPA alone | 0.137 | Dirichlet | 0–1 | 136-863 | Ref. 33, 34 |
| Dead mRS 6 after IV-tPA alone | 0.029 | Dirichlet | 0–1 | 28-971 | Ref. 33, 34 |
| Independent mRS 0-1-2 after IV-tPA and thrombectomy | 0.867 | Dirichlet | 0–1 | 867-132 | Ref. 33, 34 |
| Dependent mRS 3-4-5 after IV-tPA and thrombectomy | 0.104 | Dirichlet | 0–1 | 103-896 | Ref. 33, 34 |
| Dead mRS 6 after IV-tPA and thrombectomy | 0.029 | Dirichlet | 0–1 | 28-971 | Ref. 33, 34 |
therefore the correspondent treatment, the cost to treat a recurrent stroke is calculated as the mean expected cost to treat an average stroke that may not need thrombolysis or thrombectomy.

### Outcomes

Patients were categorized into 1 of 3 health outcome states based on their predicted mRS scores: independent (mRS score ≤2), dependent (mRS score 3–5), or dead (mRS=6). We assumed the patient remained in the same health state for the first 3 months. After the initial allocation of patients into mRS categories, a Markov model distributed a theoretical cohort of 1000 patients into the 3 states over time and included the additional health status of a patient having a recurrent stroke. The cohort of patients receiving the intervention treatment has been estimated using the national UK data from the stroke audit. According to the audit, 19.6% of patients eligible for thrombectomy are around 80% of those with a major occlusion (National Institute of Health Stroke Scale (NIHSS) score >16), which means 1800 patients.

QALYs combine length of life and quality of life, the latter being measured by utility scores. A utility score of 1 represents full health, whereas a score >16), which means 1800 patients.

QALYs combine length of life and quality of life, the latter being measured by utility scores. A utility score of 1 represents full health, whereas a score of 0 of death. We used the utility scores from Dorman et al., the Sandercock et al.
of 1.05 QALYs per patient over 20 years (Table 2). The additional costs were because of the cost of the device and the cost of the procedure. QALYs are higher for mechanical thrombectomy because it saves more lives, and those patients who survive are more likely to have a better health outcomes and be independent (mRS 0,1,2). Assuming a cohort of 1000 patients, the number of deaths over 20 years was 787 in patients treated with IV-tPA alone and 716 in patients treated with thrombectomy. Therefore, the mechanical thrombectomy averted 71 deaths over 20 years.

The incremental cost-effectiveness ratio of mechanical thrombectomy compared with IV-tPA was $11,651 (£7061) per QALY gained. The NMB of thrombectomy plus IV-tPA was higher than the NMB of IV-tPA alone at both the lower and upper limits of the maximum willingness to pay for a QALY, indicating that this option was preferred on cost-effectiveness ground. As expected, the probabilistic results were similar (see Table III in the online-only Data Supplement).
The results of the 1-way sensitivity analysis showed that increasing the cost of thrombectomy by 139% from $13,803 (£8365) to US $33,000 (£20,000) will make the new intervention borderline cost-effective for the lower value of the maximum willingness to pay for QALY. If the utility for the independent patients (mRS 0-1-2) were decreased from 0.74 to 0.34, then the intervention is borderline cost-effective. The results were not sensitive to changing the values of any of the other parameters included in the univariate sensitivity analysis.

The cost-effectiveness acceptability curves for the 2 interventions show that mechanical thrombectomy had 100% probability of being cost-effective at the lower and upper values of the maximum willingness to pay for QALY commonly used in the United Kingdom (Figure 2).

**Discussion**

Our principle finding is that the interventional treatment arm consisting of IV-tPA followed by mechanical thrombectomy for acute large-vessel ischemic stroke saves 1 life for every 14 thrombectomies performed, reduces disability, and is cost-effective when compared with IV-tPA alone.

Although the cost of thrombectomy is higher than that of IV-tPA initially, it leads to savings downstream in the stroke care pathway because of better outcomes. Between January and March 2014, 19,638 new cases of stroke were registered in the United Kingdom; 87.3% were ischemic strokes and 11.5% had hemorrhage. 15% of ischemic strokes registered an acute large-vessel stroke with an NIHSS score >16; therefore, thrombectomy could potentially be performed in 20% of patients who had hemorrhage. This means that in 1 year, around 1800 patients could have had a thrombectomy, for an incremental cost (budgetary impact) of $22 million (£13.4 million).

The recent Oxford Vascular study reports that each additional point in the NIHSS score can increase total costs over 5 years by 15%. Therefore, modest improved outcomes are often cost-effective from a societal perspective. These benefits need to be weighed against the procedural risks and the increased risk of symptomatic intracerebral hemorrhages. Although initially symptomatic hemorrhage appeared to be higher among those undergoing thrombectomy, subsequent studies have shown similar rates for IV-tPA and thrombectomy versus tPA alone as evident in Tables III in the online-only Data Supplement. In fact, in the studies included in this article, the average hemorrhage rates were similar (4.6% for thrombectomy versus 3.8% for IV-tPA).

Earlier this year, the first randomized controlled studies, MR CLEAN, ESCAPE, EXTEND IA, SWIFT-PRIME, and REVASCAT, demonstrate significant benefit with thrombectomy, which was contributed by the higher recanalization rate. It is likely that the development and evolution of mechanical thrombectomy in time will lead to better recanalization rates. We expect the cost of thrombectomy to decrease over time because of decreasing costs of the intervention and discounts in the device used secondary to market competition. This will improve the cost-effectiveness of the new intervention.

There is no other cost-effectiveness study for thrombectomy performed in the United Kingdom. However, similar studies have been done in the United States based on single-arm studies, which also demonstrated cost-effectiveness of $16,001 per QALY gained. $12,120 per QALY gained, and $9,386 per QALY gained. Patil et al focussed on patients whom could receive treatment within 8 hours but were not eligible for IV-tPA. Nguyen-Huynh et al studied patients beyond 3 hours and who were then offered mechanical thrombectomy or antiplatelet therapy and supportive care. However, Kim et al looked at a similar question to ours, that is, the use of IV-tPA as a bridging therapy to mechanical thrombectomy versus IV-tPA alone. However, their data were based on the Multi-MERCI study using the Merci retrieval systems (Concentric, s-Hertogenbosch, Netherlands), as well as some use of intra-arterial thrombolysis and angioplasty. As mentioned earlier, stent retrievers have been shown to be significantly better than the Merci retrieval system. The advantage of this study is that we have used data from randomized controlled trials predominantly using stent retriever devices. Despite several differences among cost-effectiveness studies, all have concluded that mechanical thrombectomy is cost-effective compared with medical therapy.

The analysis has several limitations. In the absence of data, we have assumed the probability of a recurrent stroke is the same irrespective of the level of disability after initial stroke, when we might expect the probability of recurrent stroke to be higher among the more disabled. The results of our sensitivity analysis showed that our conclusions were not sensitive to this assumption.

The analysis was undertaken from the perspective of the UK National Health Service. A wider perspective, such as a societal one, would also include impacts on the rest of society, including patients, families, and business. Given that stroke is the leading cause of disability in the United Kingdom, it is likely that the cost savings attributable to mechanical thrombectomy would be greater than demonstrated if costs from other viewpoints were included.
Summary

We have demonstrated in this first cost-effectiveness study that the use of predominantly stent retrievers in mechanical thrombectomy after IV-tPA is cost-effective in the United Kingdom, based on current data. However, we hope that this study will supplement the recently published randomized controlled trials together with evidence demonstrating an increasing prevalence of stroke among young adults to assist healthcare commissioners regarding purchasing and investing in this new aspect of acute stroke services.

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Disclosures

T. Sunderland is a permanent employee of Boehringer Ingleheim. The other authors report no conflicts.

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Cost-Utility Analysis of Mechanical Thrombectomy Using Stent Retrievers in Acute Ischemic Stroke
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### Table I: Summary of mRS outcomes from five randomised control trials.

| Trial:          | Intervention group | mRS 0-2 | mRS 3-5 | mRS 6 | Total | Haemorrhage rate (%) | References |
|-----------------|--------------------|---------|---------|-------|-------|-----------------------|------------|
| MR CLEAN        | Thrombectomy       | 76      | 108     | 49    | 233   | 7.7                   | 7          |
|                 | tPA                | 51      | 157     | 59    | 267   | 6.4                   | 7          |
| ESCAPE          | Thrombectomy       | 87      | 60      | 17    | 164   | 3.6                   | 8          |
|                 | tPA                | 43      | 76      | 28    | 147   | 2.7                   | 8          |
| EXTEND 1A       | Thrombectomy       | 25      | 7       | 3     | 35    | 0                     | 9          |
|                 | tPA                | 14      | 14      | 7     | 35    | 6                     | 9          |
| SWIFT-PRIME     | Thrombectomy       | 59      | 30      | 9     | 98    | 0                     | 10         |
|                 | tPA                | 33      | 53      | 12    | 98    | 3                     | 10         |
| REVASCAT        | Thrombectomy       | 45      | 39      | 19    | 103   | 4.9                   | 11         |
|                 | tPA                | 29      | 58      | 16    | 103   | 1.9                   | 11         |
| **Total number of** | **Thrombectomy** | **292** | **244** | **97** | **633** | **29**              |            |
| **patients**    | tPA                | **170** | **358** | **122** | **650** | **25**              |            |
| **mean figures** | **Thrombectomy**  | **46%** | **39%** | **15%** | **100%** | **4.6**             |            |
|                 | tPA                | **26%** | **55%** | **19%** | **100%** | **3.8**             |            |
Table II: Detailed breakdown costs for iv TPA and iv Thrombectomy

| Cost of IV-tPA | Cost (US $ 2014) | Reference |
|----------------|------------------|-----------|
| Cost of Alteplase | $950.40 | 31 |
| Staff time | | |
| 5 min additional nurse time | 14.01 | 29,33 |
| 190 min registrar time | 378.02 | 29,33 |
| 50 min consultant time | 194.76 | 29,33 |
| 5 min routine observation by senior nurse | 2.66 | 29,33 |
| 12 additional set of observation at 5 min each | 233.71 | 29,33 |
| 5 hours 1:1 Senior nurse care | 1,168.54 | 29,33 |
| 10 min overnight senior nurse care | 11.49 | 29,33 |
| Total cost of administration | 2,003.19 | |
| Total cost IV-tPA | 2,953.59 | |

| Cost of Thrombectomy | Cost (US $ 2014) | Reference |
|----------------------|------------------|-----------|
| Cost of material | | |
| device | 7,566.08 | 36-37 |
| guidecatheter | 159.73 | 36-37 |
| guidewire | 168.14 | 36-37 |
| microcatheter | 672.54 | 36-37 |
| stent thrombectomy | 3,154.21 | 36-37 |
| aspiration catheter | 840.68 | 36-37 |
| Total cost of material | 12,561.37 | |
| Surgery Staff         | Cost (US $ 2014) | Reference |
|-----------------------|------------------|-----------|
| Surgeon               | 411.93           | 29, 36-37 |
| Radiographer          | 108.87           | 29, 36-37 |
| Instrument Nurse      | 64.73            | 29, 36-37 |
| Circulating Nurse     | 61.79            | 29, 36-37 |
| Circulating Nurse     | 61.79            | 29, 36-37 |
| Anaesthesist          | 411.93           | 29, 36-37 |
| Anaesthetic Nurse     | 120.64           | 29, 36-37 |

**Total cost of surgery**  
1,241.68

**Total cost of Thrombectomy**  
13,803.04
Table III: Probabilistic sensitivity analysis results: Expected values per 1,000 patients. Costs are based on 2013-14 prices. The Net Monetary Benefit is calculated at the lower and upper limits of the willingness to pay for a QALY, which in the UK are $33,000 (£20,000) and $49,500 (£30,000) respectively.

|                  | IV-tPA       | M. Thrombectomy | Difference  |
|------------------|--------------|-----------------|-------------|
| Costs (95% CI)   | $52,849,215  | $64,887,437     | $12,038,222 |
|                  | ($51,073,057 - $53,837,494) | ($63,546,387 - $65,957,721) | ($10,462,678 - $14,155,764) |
| QALYs (95% CI)   | 3,723        | 4,677           | 954         |
|                  | (3,590-3,988) | (4,617-5,068)   | (753-1352)  |
| ICER (95% CI)    |              |                 | $12,614     |
|                  |              |                 | ($9,043 - $15,988) |
| Net Monetary Benefit |        |                 |             |
| Lower            | $70,002,953  | $89,457,959     |             |
| Upper            | $131,429,037 | $166,630,656    |             |