

Exploring the Cost-Effectiveness of Mechanical Thrombectomy Beyond 6 Hours Following Advanced Imaging in the United Kingdom

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Background and Purpose—In the United Kingdom, mechanical thrombectomy (MT) for acute ischemic stroke patients assessed beyond 6 hours from symptom onset will be commissioned up to 12 hours provided that advanced imaging (AdvImg) demonstrates salvageable brain tissue. While the accuracy of AdvImg differs across technologies, evidence is limited regarding the proportion of patients who would benefit from late MT. We compared the cost-effectiveness of 2 care pathways: (1) MT within and beyond 6 hours based on AdvImg selection versus (2) MT only within 6 hours based on conventional imaging selection. The impact of varying AdvImg accuracy and prior probability for acute ischemic stroke patients to benefit from late MT was assessed.

Methods—A decision tree and a Markov trace were developed. A hypothetical United Kingdom cohort of suspected stroke patients aged 71 years with first event was modeled. Costs, health outcomes, and probabilities were obtained from the literature. Outcomes included costs, life years (LYs), quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios. Probabilistic sensitivity analyses were performed. Various scenarios with prior probabilities of 10%, 20%, and 30%, respectively, for acute ischemic stroke patients to benefit from late MT, and with perfect accuracy, 80% sensitivity, and 70% specificity of AdvImg were studied.

Results—Incremental cost-effectiveness ratios resulting from our deterministic analyses varied from \$8199 (£6164) to \$49 515 (£37 229) per QALY gained. AdvImg accuracy impacted the incremental cost-effectiveness ratio only when its specificity decreased. Over lifetime horizons, all scenarios including late MT improved QALYs and LYs. Depending on the scenario, the probabilistic sensitivity analyses showed probabilities varying between 46% and 93% for the late MT pathway to be cost-effective at a willingness to pay threshold of \$39 900 (£30 000) per QALY.

Conclusions—Late MT based on AdvImg selection may be good value for money. However, additional data regarding the implementation of AdvImg and prior probability to benefit from late MT are needed before its cost-effectiveness can be fully assessed. (*Stroke*. 2019;50:3220-3227. DOI: 10.1161/STROKEAHA.119.026816.)

Key Words: advanced imaging ■ cost-effectiveness ■ stroke ■ thrombectomy ■ United Kingdom

Recently, 2 prospective randomized control trials demonstrated superior health benefits of mechanical thrombectomy (MT) beyond 6 hours from symptom onset (late MT) plus standard medical care versus standard medical care alone in acute ischemic stroke (AIS) patients. Patient selection was based on advanced imaging (AdvImg), namely perfusion imaging with computed tomography (CT) or magnetic resonance.^{1,2} As new evidence emerged, policymakers updated their recommendations and the National Health Service (NHS) England issued a document in March 2018 announcing that MT would be routinely commissioned provided it can be

achieved within 6 hours of the onset of stroke.³ Furthermore, NHS England will commission MT until 12 hours where AdvImg indicates substantial salvageable brain tissue.³

In the vast majority of the randomized clinical trials establishing the benefit of MT in AIS patients, CT followed by CT angiography (CTA) were the imaging modalities used to assess the brain tissue and intracranial vessels.⁴ In the United Kingdom (UK), as in western countries, the standard diagnostic imaging workup in centers performing MT within 6 hours since stroke onset closely matches the imaging techniques used in these clinical trials.^{5,6} AdvImg, by allowing

Received May 6, 2019; final revision received July 31, 2019; accepted August 20, 2019.

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The online-only Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.119.026816>.

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DOI: 10.1161/STROKEAHA.119.026816

brain perfusion assessment, can more accurately assess the volumes of the infarct core and, above all, salvageable brain tissue (penumbra). It is, therefore, expected to better identify AIS patients with large vessel occlusion who will benefit from late MT in clinical practice. The accuracy of imaging differs across technologies or remains unknown for devices under development. In addition, evidence is limited regarding the proportion of patients who would benefit from late MT.^{7,8} In fact, this proportion is influenced by the different inclusion criteria used in trials. Since the availability of AdvImg is expected to influence future care of AIS patients, the aim of this study was to explore the cost-effectiveness of 2 care pathways or strategies for patients presenting with a suspected stroke in the UK: (1) MT within and beyond 6 hours, up to 24 hours, based on AdvImg selection versus (2) MT only within 6 hours based on conventional imaging selection (ie, CT and CTA). We also assessed the impact of jointly varying the AdvImg accuracy and the prior probability for AIS patients to benefit from late MT.

Methods

The authors declare that all supporting data are available within the article and its [online-only Data Supplement](#).

General Description of the Study Methodology

The formal steps of modeling were followed with conceptualizing, scoping, structuring, populating, analyzing, and addressing uncertainty.^{9,10} A decision-analytic model was designed in Microsoft Excel to analyze and compare the cost-effectiveness of 2 care pathways for the population of suspected stroke patients: (1) allowing MT within and beyond 6 hours, up to 24 hours, from symptom onset based on AdvImg selection versus (2) MT only within 6 hours from onset and based on conventional imaging selection with CT and CTA. The first care pathway will be referred to as AdvImg with early and late MT (AIELMT), whereas the second one will be referred to as CT-CTA with early MT (CCEMT). We also assessed the impact of jointly varying the AdvImg accuracy and the prior probability for AIS patients to benefit from late MT. The CCEMT pathway represented the standard UK pathway of the past few years: suspected stroke patients receive a CT and CTA systematically precedes MT. AIS patients whose onset is beyond 6 hours or unknown after CT assessment (ie, not receiving MT) will not receive CTA. The remainder of the AIS patients not receiving MT may, or not, have been assessed by CTA. The 2 care pathways were compared based on their respective diagnostic and subsequent treatment options. In addition to the treatments that were explicitly modeled (IV-tPA [intravenous tissue-type plasminogen activator] and MT), we assumed that patients received standard medical care (including antiplatelet therapy, blood pressure management, complication prevention, and rehabilitation).

A hypothetical UK cohort of suspected stroke patients aged 71 years with a first-ever stroke was modeled. A literature search was performed to populate the input parameters, and clinical experts were consulted to ascertain some of them. Using 2 time-horizons of, respectively, 3 months and lifetime, costs, quality-adjusted life years (QALYs), and life years (LY) were calculated for each care pathway. Costs and effects were discounted at 3.5%. The perspective was the UK NHS which did not include societal costs. No ethics approval was needed.

Model Structure

Decision Tree

A short-run decision tree model (Figure 1A) was built to predict the costs and clinical outcomes at 90 days after the first suspected stroke. A hypothetical cohort of initially independent patients (ie, with a

modified Rankin Scale [mRS] of 0–2) was distributed at 90 days into 1 of 4 possible subgroups, as follows: recovered (mRS 0), independent (mRS 1 or 2), dependent (mRS 3, 4, or 5) and dead (mRS 6). Treatment effects were assumed to occur during the acute phase. From the initial cohort of suspected stroke patients, hemorrhagic stroke patients, and nonstroke patients (tumors, other conditions) were assumed to have the same health outcomes in the CCEMT strategy as in the AIELMT strategy and were, therefore, not modeled in detail. Furthermore, we assumed that AdvImg performs as good as unenhanced CT in diagnosing hemorrhagic strokes and equal or better than CT+CTA in identifying nonstrokes. Clinical judgment was assumed to complement CT and AdvImg. The probabilities for a patient to end up in each group (ie, recovered [mRS 0], independent [mRS 1 or 2], dependent [mRS 3, 4, or 5], or dead [mRS 6]) at 90 days were calculated using data provided by trials and registries. We applied the probabilities reported in Table I in the [online-only Data Supplement](#).

Markov Model

Data from the short-run model related to AIS patients fed into a long-run Markov state-transition model (Figure 1B) built to predict, from initial diagnosis, the lifetime costs, and outcomes. The model was based on 3-month cycles and ran until all patients died to reflect a lifetime time horizon (150 cycles appeared adequate for this purpose). Given the data available, patients in mRS 0 and mRS 1–2 were grouped together in mRS 0–2 in the Markov model. It was assumed that patients in mRS 0–2 and mRS 3–5 could move between these states only during the first year, due to deterioration or rehabilitation. Patients experiencing a recurrent stroke could either maintain the status they were in before recurrence or deteriorate. Previous studies indicated that dependent patients (mRS 3–5) have increased mortality compared to independent patients (mRS 0–2).^{11,12} We used a 1.29 hazard ratio for mRS 0–2 and a 3.33 hazard ratio for mRS 3–5 compared with UK population averages (see Table II in the [online-only Data Supplement](#)). We used UK life tables for age- and sex-adjusted all-cause mortality rates applying from year 2 onwards. As the life table data from the UK were truncated at 100 years, the mortality starting at 101 years was kept constant and equal to the mortality at 100 years.

Patients experiencing a recurrent stroke were managed based on the same strategy as during their initial stroke. If an independent patient experienced a recurrent stroke, the probabilities of remaining in mRS 0–2, moving to mRS 3–5, or dying were the same as the probabilities after the initial stroke. However, a dependent patient experiencing recurrent stroke could only remain in the dependent state or die. Furthermore, the probability of an individual in the dependent state to die from recurrent stroke was assumed to be the same as that of an independent patient experiencing recurrent stroke. Based on previous studies,^{13,14} the risk of recurrence was assumed to be equal for mRS 0–2 and mRS 3–5. A maximum of 1 recurrent stroke per patient per 3-month cycle was assumed. The transition probabilities can be found in Table I in the [online-only Data Supplement](#).

Modeling AdvImg Accuracy in the AIELMT Strategy

Late MT after 6 hours from onset was only possible if it was indicated by AdvImg; therefore, only patients in the AIELMT strategy could undergo late MT. The choice was made to model late MT for AIS patients who did not receive IV-tPA previously (see Figure 1A). In the decision tree, the value of similar input parameters in the 2 strategies was kept equal, except for parameters related to MT beyond 6 hours. As such, AdvImg was assumed to have the same accuracy as CT+CTA to refer patients to MT until 6 hours from onset, and the model was structured to investigate the difference in effects and costs driven by performing late MT (AIELMT path) versus no late MT (CCEMT path). For this reason, the uncertainty regarding the benefits of MT was explicitly modeled only after 6 hours from onset. The accuracy of AdvImg beyond 6 hours was varied (see section about simulated scenarios). Health outcomes of late MT at 90 days (AIELMT strategy) were stratified according to the ability of AdvImg to correctly identify AIS patients for late MT. Outcomes were simulated for true positive, false positive, false negative, and true negative patients (Table III in the [online-only Data Supplement](#)). Outcomes

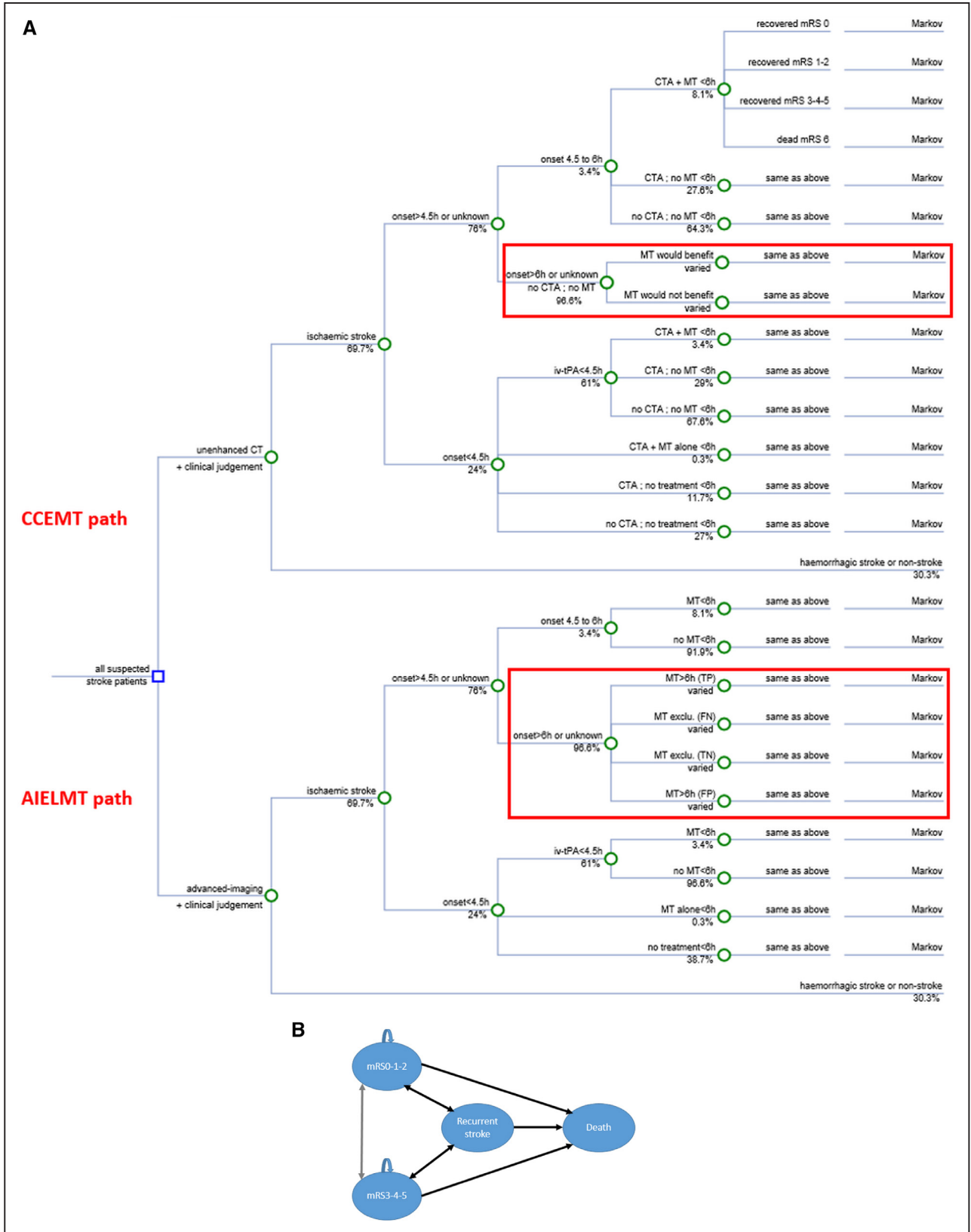


Figure 1. Structure of the decision tree model and Markov model. **A**, Decision tree model representing the diagnostic, acute treatment and outcomes at 90 d after initial stroke. **B**, Markov model reflecting long-term expectations for post-initial stroke patients. AdvImg indicates advanced imaging; AIELMT, AdvImg with early and late MT; CCEMT, CT-CTA with early MT; CT, computed tomography; CTA, CT angiography; FN, false negative; FP, false positive; IV-tPA, intravenous tissue-type plasminogen activator; mRS, modified Rankin Scale; MT, mechanical thrombectomy; TN, true negative; and TP, true positive.

for false positive patients were based on the outcomes for true negative patients but corrected for the risk of procedural complications.¹⁵ It was assumed that all false positive AIS patients, irrespective of the stroke severity, had an equal mortality risk due to complications (see Table IVa and IVb in the [online-only Data Supplement](#)).

Costs and Resource Use

All costs were calculated in British pounds (£) for the year 2018 and presented in US\$ using an exchange rate of £1=US\$1.33. Costs originating from previous years were inflated based upon the pay and price index for Hospital and Community Health Services for 2017.¹⁶ The inflation factor from 2016 to 2017 (1.018) was used to inflate costs to 2018. Costs and resource used in the model are presented in Table I in the [online-only Data Supplement](#). The imaging cost of identifying the nonischemic stroke patients (nonstroke and hemorrhage) was computed to account for the cost difference between the diagnosis by CT-CTA and AdvImg (Figure 1A). The cost of IV-tPA consists of drug acquisition and drug administration. Details about the calculations can be found in Table Va and Vb in the [online-only Data Supplement](#). Based on clinical expert review, the cost of MT was sourced from a microcosting study¹⁴ and inflated to 2018. The mean acute costs incurred during the first 90 days after AIS and the mean 3-monthly long-term healthcare costs were found to be specific to the severity of the outcome (mRS) in the literature. These costs included nurse visits, general practitioner visits, emergency care, outpatient visits, day cases, and hospitalizations. CT costs were deducted from the costs of the first 3 months since the found estimates already included initial diagnostic tests for a suspected stroke. The cost of a recurrent stroke, including the cost of the 3 following months, was based upon the findings of the short-run model and was assumed to be specific to either the CCENT strategy or AIELMT strategy. Therefore, it represents the deterministic estimate of the cost to identify and treat an average ischemic stroke according to the care pathways defined in the decision tree. Costs incurred in the future were assumed to be similar to those incurred in the present and the first 3 months following a recurrent stroke to be equally costly as the 90 days following the initial stroke.

Utilities/Quality of Life

Utilities were assigned to each of the 3 possible health states of the mRS based on a study by Wardlaw et al¹⁷ who performed a review of utilities used in previous economic evaluations. Utility values ranged from 0.71 for mRS 0–2 to 0.20 for mRS 3–5 to 0 for mRS 6. The utility of a recurrent ischemic stroke was derived from the short-run model and, therefore, assumed to be specific to the CCENT strategy and AIELMT strategy. Utilities were varied according to a beta distribution (see Table I in the [online-only Data Supplement](#)).

Simulated Scenarios

In line with the principles of economic evaluations of diagnostic technologies, we ran scenario analyses on 2 important parameters, test accuracy, and prior probability to benefit from late MT, to assess their impact on the cost-effectiveness of the AIELMT strategy. Because evidence regarding the effectiveness of late MT is lacking due to the experimental nature of the indication, we simulated different proportions of patients potentially benefitting from an intervention beyond 6 hours from onset. As such, 3 scenarios were simulated in which the prior probability of benefitting from MT (before AdvImg information is obtained) was varied from 10% to 20% and 30% (Table). The prior probability was defined as the probability for an AIS patient imaged beyond 6 hours after onset to benefit from late MT. In the CCENT path, patients with an onset above 6 hours (therefore not receiving MT) were split between those who would theoretically benefit from late MT and those who would not, based on the prior probability. Patients in the AIELMT strategy were, in theory, referred to late MT according to the AdvImg preprocedural findings. CT perfusion is the most commonly used AdvImg technique in the diagnosis of AIS patients. Its accuracy was reported mainly when image acquisition occurred within the 6-hour window from onset with a mean sensitivity of 80% and a mean specificity of 95%.¹⁸ We assumed that the sensitivity of AdvImg beyond 6 hours would not go below the sensitivity reported for testing within 6 hours and used 80% as the minimal value in our scenario analysis. Specificity was tested for its impact on the cost-effectiveness

Table. Parameters for the 9 Scenario Analyses Based on Pairwise Variation of Prior Probability and AdvImg Accuracy

Set of Parameters for the 9 Scenario Analysis	Prior Probability=30%	Prior Probability=20%	Prior Probability=10%
Perfect AdvImg test	Scenario 1	Scenario 2	Scenario 3
	TP=0.3	TP=0.2	TP=0.1
	FN=0	FN=0	FN=0
	FP=0	FP=0	FP=0
	TN=0.7	TN=0.8	TN=0.9
AdvImg test with a sensitivity of 80% and a specificity of 100%	Scenario 4	Scenario 5	Scenario 6
	TP=0.24	TP=0.16	TP=0.08
	FN=0.06	FN=0.04	FN=0.02
	FP=0	FP=0	FP=0
	TN=0.7	TN=0.8	TN=0.9
AdvImg test with a sensitivity of 100% and a specificity of 70%	Scenario 7	Scenario 8	Scenario 9
	TP=0.3	TP=0.2	TP=0.1
	FN=0	FN=0	FN=0
	FP=0.21	FP=0.24	FP=0.27
	TN=0.49	TN=0.56	TN=0.63

AdvImg indicates advanced imaging; FN, false negative; FP, false positive; TN, true negative; and TP, true positive.

results and was set to a minimum value of 70%. Therefore, we simulated a perfect AdvImg test (sensitivity=specificity=100%), a test with reduced sensitivity to 80% (and 100% specificity) and a test with reduced specificity to 70% (and 100% sensitivity). The probability to be referred to late MT based on AdvImg, therefore, varied according to 9 scenarios based on the pairwise combination of prior probability and accuracy of imaging (Table).

Sensitivity Analysis

A probabilistic sensitivity analysis (PSA) was performed to assess the impact of the uncertainty around the input parameter values. This was implemented by assigning a distribution to each parameter to represent the uncertainty around its mean value. A random value was sampled from each distribution, and the results were calculated using the set of sampled values. This process was repeated in 3000 simulations per scenario to generate 3000 estimates of the costs, QALYs, and LY in each scenario of each strategy. This number of simulations matched the number needed to obtain stable estimates. The proportion of simulations when the AIELMT path had the highest net monetary benefit was calculated for a range of values of the willingness to pay for a QALY. The results were presented with cost-effectiveness acceptability curves. Each curve represented the probability that the AIELMT strategy was cost-effective compared with the CCENT strategy at different thresholds for cost-effectiveness.

Results

At 90 days after the initial AIS, most AIELMT scenarios (1, 2, 3, 4, 5, 6, 7, and 8) increased the proportions of fully recovered patients, decreased mortality, and generally improved outcomes on the mRS scale, compared with the CCENT strategy. Scenario 9 (sensitivity 100%; specificity 70%) increased mortality (because of MT-related mortality risk in false positive patients) at 90 days but still increased QALYs. The distribution of AIS patients across the mRS scale at 90 days was used

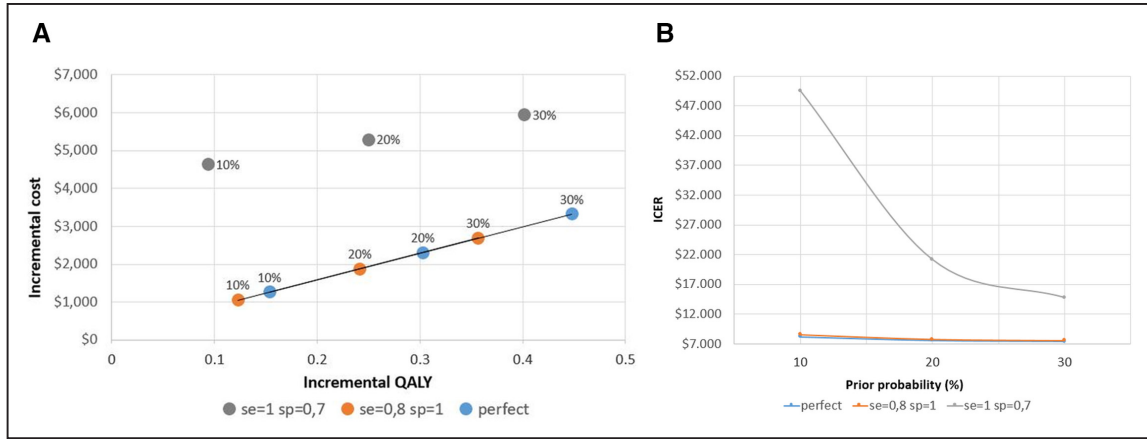


Figure 2. Lifetime results for the 9 scenarios. **A**, Cost and quality-adjusted life year (QALY) differences between computed tomography (CT)–CT angiography with early mechanical thrombectomy (CCEMT) and advanced imaging with early and late MT (AIELMT) strategy for the 9 scenarios. % refers to the prior probability to benefit from late MT. **B**, Incremental cost-effectiveness ratio (ICER) at lifetime time horizon for different levels of advanced imaging accuracy. Se indicates sensitivity; and Sp, specificity.

as the starting point in the Markov model and can be found in Table VI in the [online-only Data Supplement](#).

At lifetime horizon, in the 9 scenarios, the AIELMT strategy was associated with a health gain, ranging from 0.09 to 0.45 QALYs, per AIS patient. It was also associated with a higher cost per AIS patient, ranging from \$1051 (£790) to \$5932 (£4460) (Table VII in the [online-only Data Supplement](#)). QALYs and LYs are higher in the AIELMT path as this strategy saves lives and improves health outcomes on the mRS scale compared with the CCEMT strategy. The incremental long-term costs were induced by the cost of MT and the longer survival of patients in the AIELMT strategy. A higher prior probability of benefitting from late MT led to higher additional costs and more QALYs in the AIELMT strategy.

Based on a lifetime horizon, there is a similar linear relationship between the incremental costs and incremental QALYs in the 6 scenarios of the perfect test and the reduced sensitivity test (Figure 2A). Although incremental costs and incremental QALYs increase as the prior probability increases, the incremental cost-effectiveness ratios (at different prior probabilities) for the perfect test and the reduced

sensitivity test remain almost equal. In the reduced specificity scenario, when increasing the prior probability, incremental effects are increasing faster than incremental costs, which results in a lower lifetime incremental cost-effectiveness ratio (cost per QALY gained) as the prior probability rises (\$49 515 [£37 229] at 10%, \$21 156 [£15 906] at 20%, and \$14 765 [£11 101] at 30%; Figure 2B). In the reduced specificity scenario, when the prior probability increases, smaller impacts are observed on costs, as the frequency of false positive goes down. Details about the incremental cost-effectiveness ratios at 90 days and lifetime related to both the LYs and QALYs can be found in Table VIII in the [online-only Data Supplement](#).

Probabilistic sensitivity analyses confirmed that the higher the prior probability, the higher the cost difference and the effect difference between the 2 care pathways, with increased costs and effects observed in the AIELMT strategy (Figure 3A). Furthermore, at a constant prior probability, the cost difference increased in the case of the decreased specificity test but stayed quasisimilar for both the perfect and decreased sensitivity test (Figure 3B).

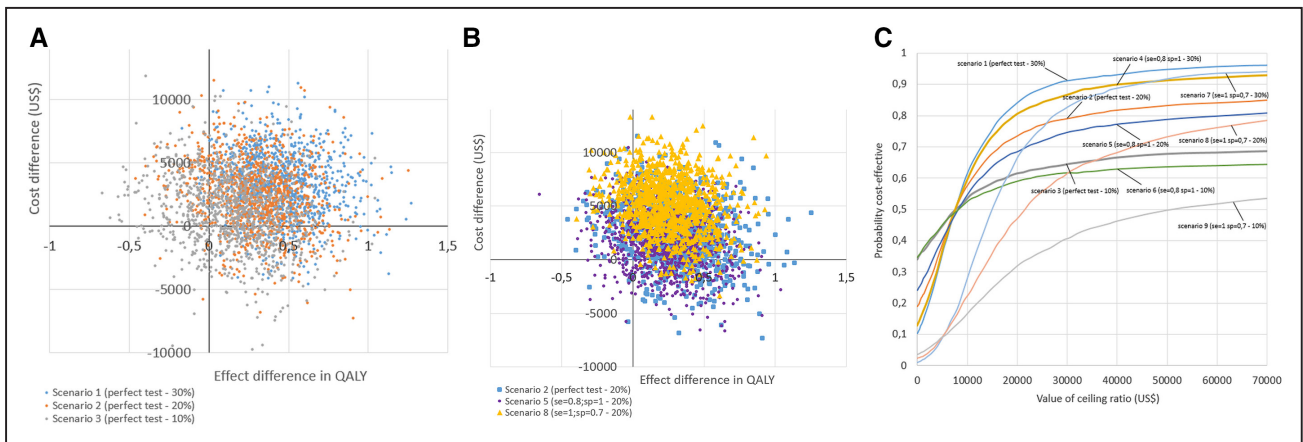


Figure 3. Results of the probabilistic sensitivity analyses. **A**, Monte Carlo simulations of incremental cost per quality-adjusted life year (QALY) gained of advanced imaging with early and late mechanical thrombectomy (AIELMT) in 3 scenarios of perfect test and different prior probability. **B**, Monte Carlo simulations of incremental cost per QALY gained of AIELMT in 3 scenarios of a 20% prior probability and different imaging accuracy. **C**, Cost-effectiveness acceptability curves showing the probability that the AIELMT pathway is cost-effective at different values of willingness to pay for a QALY, for the 9 scenarios compared to the computed tomography (CT)–CT angiography with early mechanical thrombectomy (CCEMT) pathway (CCEMT pathway curves not shown).

The cost-effectiveness acceptability curves for the AIELMT strategy show that, at a willingness to pay of \$39 900 (£30 000), the probability of being cost-effective was above 46% in the 9 scenarios (Figure 3C). With reduced specificity, the probability of the AIELMT strategy to be cost-effective at low willingness to pay thresholds dropped substantially.

Discussion

Our main finding is that AdvImg, by extending the time window beyond 6 hours (up to 24 hours) for MT, improves health outcomes but increases costs when compared with conventional imaging (CT+CTA) coupled to MT up to only 6 hours from symptom onset. Incremental cost-effectiveness ratios resulting from our deterministic analyses varied from \$8199 (£6164) to \$49 515 (£37 229) per QALY gained. This study suggests that late MT based on AdvImg selection is cost-effective in the UK. However, at a willingness to pay threshold of \$39 900 (£30 000), the probability of an AIELMT strategy to be cost-effective varies widely across scenarios.

Since the evidence regarding the probability to benefit from late MT based on AdvImg criteria is limited, extensive scenario and uncertainty analyses were performed. These analyses showed that reduced specificity of AdvImg reduces the cost-effectiveness. However, the magnitude of this impact decreases as the prior probability for AIS patients to benefit from late MT increases. These findings suggest that advanced neuroimaging should focus on excluding patients without sufficient salvageable tissue to avoid unnecessary interventions and make the benefit of (late) MT worth the considerable resource utilization.

Compared with previous economic studies that assessed the value of MT after IV-tPA versus IV-tPA alone,^{14,19–21} our study presents comprehensive results about the cost-effectiveness of an integrative UK care pathway that combines AdvImg and all possible subsequent early and late acute treatments. Despite methodological differences, our results on the value of late MT are consistent with the results published by Pizzo et al.¹⁹ who demonstrated that MT performed between 6 and 24 hours after onset is cost-effective in the UK. To the best of our knowledge, our study is the first to explore the combined impact of uncertainty from imaging accuracy and prior probability on the cost-effectiveness of late MT.

Our results may have important policy implications. Commissioning criteria for late MT by NHS England are based on the identification of substantial salvageable brain tissue up to 12 hours after onset by perfusion or multiphase CTA.³ Strong evidence about the accuracy of these imaging techniques for late MT referral is crucial to ascertain whether the NHS policy commissions a cost-effective practice. As shown above, a decreased specificity might considerably lower the probability for an AIELMT strategy to be cost-effective. Strong evidence also implies the assessment of technology-specific preprocedural findings in terms of their ability to predict clinical outcomes. Quantification of the amount of salvageable brain tissue required before neurointervention and definition of the target in terms of clinical outcomes per

patient might be needed to clarify the commissioning policy. Once this is clear, the AIELMT pathway may be implemented.

Implementation of the AIELMT pathway will have considerable consequences for the NHS in terms of number of patients treated and costs. From April 2016 to March 2017, 85 122 cases of strokes were reported in the UK, Wales, and Northern Ireland.²² Assuming that 85% of those were ischemic,³ we estimated about 72 350 AIS patients. According to the probabilities used in our model, 76% of these patients (about 55 000) were imaged beyond 4.5 hours, and 97% of the latter (about 53 350) were imaged beyond 6 hours from onset. Applying a prior probability of 20%, a decreased sensitivity of 80%, and a perfect specificity, about 8500 of these patients would receive MT, should the infrastructure and manpower allow this capacity. Compared with data on recent care (2016–2017),²² in which 580 MT were performed, the incremental budget impact of performing AdvImg and late MT would be around \$93 (£70) million.

However, providing widely accessible AdvImg is likely to be an organizational challenge for the NHS, for 2 reasons. First, AdvImg would probably be available only at comprehensive stroke centers. Assuming that around 25% of stroke patients would be directly attending a comprehensive center (providing MT) and 75% first attending a local acute stroke unit (providing IV-tPA only),²³ a major question arises on how to handle the stroke patients at local units providing only CT and CTA and whether to transfer them to a comprehensive center. Second, there is currently no emergency transfer infrastructure supporting a system based on widely accessible AdvImg and MT. So, probably more realistically, only those directly attending a comprehensive stroke center will have access to AdvImg and late MT. This illustrates the challenge of embedding new technologies in the existing healthcare system and the need for the organization of stroke care to evolve. In that respect, the optimal ratio of comprehensive stroke centers versus local acute stroke units should be determined.

We acknowledge limitations in our study. First, our model combines treatment outcomes per time since onset from different studies investigating slightly different AIS populations. Given the model structure, it was impossible to use inputs based on one single comprehensive source of treatment outcomes. To overcome this limitation, comprehensive real-world data are needed, especially regarding the first 3 months after AIS onset. However, since this limitation influences equally, the 2 strategies of our comparison, the incremental results of our model are not affected. More importantly, the outcomes of the DAWN trial (Diffusion Weighted Imaging or Computerized Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) were used, that included 5% of patients who received IV-tPA in the intervention arm and 13% in the control arm. This contrast slightly influences our incremental results by underestimating the value of the AIELMT pathway. Second, we conservatively assumed no difference between the AdvImg and CT-CTA strategies regarding the ability to detect stroke mimics. Inclusion of an improved ability by AdvImg to detect stroke mimics would have resulted in a more favorable estimated cost-effectiveness. Third, although we used the best available cost data for

generalizability,²⁴ these were based on a patient population presenting with a history of atrial fibrillation.

We explored the value of AdvImg for late MT. Beyond our investigation, crucial research questions remain to assess the comprehensive value of AdvImg and how it could improve the early stroke care pathway. First, with a single image acquisition, AdvImg might save time and diagnose more patients within the 4.5- and 6-hour window, compared with CT+CTA and, in turn, refer more patients to treatment. Second, AdvImg might offer increased accuracy within the 6-hour window compared with the currently used imaging techniques. Since the accuracy of AdvImg in AIS is specific to the lesion type and size, to the location of the lesion in the brain, and to the time since onset, assessing the full value of AdvImg along the stroke care pathway is challenging. Third, further clinical research regarding the percentage of patients likely to benefit from late MT is needed to optimize the stroke care pathway in the UK.

Finally, although US dollar equivalents are provided, this analysis does not reflect the US healthcare costs and is not generalizable to the US healthcare setting. Although diagnostic and treatment guidelines for AIS patients are similar in the United States and the UK, the reported mean lifetime cost of AIS is \$140 000 in the United States,²⁵ which is 2.33× our UK estimate. Based on exploratory analyses, the remuneration of physicians and the cost of hospitalization and IV-tPA are the main contributors to the cost difference (data not shown). These observations suggest that AdvImg and late MT would be more cost-effective in the United States than in the UK.

Conclusions

Based on these exploratory results, referring AIS patients to MT beyond the 6-hour window by means of AdvImg may be good value for money in the UK. However, additional data regarding the prior probability to benefit from late MT and the accuracy of imaging for AIS patients is needed before MT can be widely implemented in clinical practice.

Sources of Funding

The project leading to this publication has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 668142. However, this body had no role in study design, data collection and analysis, or preparation of the article.

Disclosures

None.

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