Published in final edited form as:

Stroke. 2015 July ; 46(7): 1870–1876. doi:10.1161/STROKEAHA.115.009779.

Cost-Effectiveness of Intraarterial Treatment as an Adjunct to Intravenous Tissue Plasminogen Activator for Acute Ischemic Stroke

Michelle H Leppert, MD, MBA, Jonathan D Campbell, PhD, Jennifer R Simpson, MD, and James F Burke, MD, MS

Department of Neurology (M.H.L., J.R.S.), and Pharmacy (J.D.C.), University of Colorado, Aurora; and the Stroke Program (J.F.B.), University of Michigan, Ann Arbor

Abstract

Background and Purpose—The objective of this study was to determine the cost-effectiveness of intraarterial treatment within the 0- to 6- hour window after intravenous (IV) tissue plasminogen activator (tPA) within 0- to 4.5-hours compared to IV tPA alone, in the US setting and from a social perspective.

Methods—A decision analytic model estimated the lifetime costs and outcomes associated with the additional benefit of intraarterial therapy compared to standard treatment with IV tPA alone. Model inputs were obtained from published literature, the MR CLEAN study, and claims databases in the United States. Health outcomes were measured in quality adjusted life years (QALYs). Treatment benefit was assessed by calculating the cost per QALY gained. One-way and probabilistic sensitivity analyses were performed to estimate the overall uncertainty of model results.

Results—The addition of intraarterial therapy compared with standard treatment alone yielded a lifetime gain of 0.7 QALY for an additional cost of \$9,911, which resulted in a cost of \$14,137 per QALY. Multivariable sensitivity analysis predicted cost-effectiveness (\$50,000 per QALY) in 97.6% of simulation runs.

Conclusion—Intraarterial treatment after IV tPA for patients with anterior circulation strokes within the 6 hour window is likely cost effective. From a societal perspective, increased investment in access to intraarterial treatment for acute stroke may be justified.

Keywords

stroke; endovascular treatment; tissue- type plasminogen activator; cost-effectiveness

Correspondence to: Michelle H. Leppert, MD University of Colorado Anschutz Medical Campus, Department of Neurology, Mail Stop B182, RC-2, Rm 5104, 12700 E 19th Ave, Aurora, CO 80045, Tel: 919-906-2068, Fax: 303-724-4764, Michelle.Leppert@ucdenver.edu.

Disclosures:
None.

Introduction

Until recently, intravenous (IV) tissue plasminogen activator (tPA) administered within 4.5 hours of symptom onset was the only therapy supported by randomized clinical trials to reduce long term disability in acute ischemic stroke.¹ Intraarterial therapy (IAT), either through local delivery of thrombolytic agents or mechanical thrombectomy has been tested in various capacities over the last two decades and resulted in considerable controversy.^{2,3} Completed after the emergence of more effective thrombectomy devices, the recent MR CLEAN trial provides credible evidence for the clinical effectiveness of IAT for the treatment of proximal arterial occlusion in the anterior circulation within 6 hours after symptom onset, largely in patients that have already received IV tPA.⁴⁻⁶

While the results of MR CLEAN demonstrated the effectiveness of IAT, IAT is a costly therapy requiring expensive devices and medications, highly trained proceduralists, peri-procedural support from interventional teams including anesthesiology and close post-procedure monitoring. Consequently, assuming IAT is effective, the question remains whether it is cost-effective. Prior attempts to address this question, due to the lack of efficacy data, were based on rates of revascularization to predict clinical outcome at 90 days.⁷ This model attempts to determine whether these cost-effectiveness estimates are robust by analyzing the economic value of IAT based on the clinical outcomes directly seen in MR CLEAN.

Methods

Overview

A decision analytic model was programmed in Microsoft Excel to analyze the cost-effectiveness of using IAT (i.e. arterial catheterization with delivery of a thrombolytic agent, mechanical thrombectomy or both) in addition to standard care (i.e. treatment with intravenous IV tPA within 4.5 hours) as compared to standard care alone. Eligible patients had an acute ischemic stroke caused by a proximal intracranial occlusion of the anterior circulation within 6 hours after symptom onset, following the inclusion criteria of MR CLEAN.⁸ A Markov state transition model was developed to represent the clinical outcomes over time in acute stroke patients and simulated a cohort of patients presenting to the emergency department with acute ischemic stroke and meeting the criteria for IAT (Figure 1). Finally, lifetime cost (broken down into acute care and long term care cost), quality adjusted life years (QALY), and life years for each treatment group from the time of stroke until death was calculated.

Model Structure

Patients entered the model at stroke onset, at which point they either received IAT with standard care or standard care alone. All patients were then subsequently assigned an initial modified Rankins score (mRS); mRS 0 with no symptoms, mRS 1 with no significant disability, mRS2 with minor disability, mRS3 with moderate disability, mRS 4 with moderated to severe disability, mRS 5 with severe disability, and mRS 6 or death. The cycle length was 1 year with time horizon of 30 years. At the end of each cycle patients remained

in their current health state, died, or suffered a recurrent stroke after which they were reallocated to a lower health state with equal probability of recurrent stroke death. Of note, patients were not further stratified by the presence of symptomatic intracranial hemorrhage in the IAT or standard care group as there were no statistical difference in the rates of hemorrhage between the two arms in the MR CLEAN trial.⁸ Death whether by stroke or other causes was the only absorbing state, after which patients were excluded from the model.

Input Parameters

Primary model input parameters were drawn from published literature and costs from the National Inpatient Sample (NIS).⁹ (Table 1) Whenever possible, this study relied on assumptions used in prior peer-reviewed cost-effectiveness analyses to enhance the validity of these findings as well to maximize their comparability to other stroke treatments.

Transitional probabilities

All patients were assumed to be 65 years old at the time of index stroke. This was the mean age enrolled in the MR CLEAN trial.⁸ Mortality rates from the index stroke, and functional outcomes (mRS 0 to 5) after 90 days were also based on the results of that trial. Stroke recurrence rate was estimated at 5.1 % a year associated with recurrence stroke mortality of 19% according to published literature.¹³

Patients after the index stroke were assumed to have an all-cause mortality higher than the average population.^{12, 13} Age specific mortality rates were obtained from life tables from the US National Vital Statistics report.¹⁴ Probability of death from all causes was obtained by multiplying the mortality rate by the relative death hazard ratios reported by Samsa et al. according to the mRS at 90 days.¹² Life years were discounted at 3% per year.¹⁵

Quality-of-life estimates for stroke survivors were based on published utility values stratified by mRS and summed over the lifetime of the patient to obtain QALY estimates.¹²

Costs

Cost of the index stroke were derived from previous literature using US nationwide estimates of Medicare Costs.¹⁶ These costs were broken down by dispositions after the index stroke, including “dead at discharge”, “discharge to skilled nursing facility”, or “discharge to home or home health services”. Based on the definition of the mRS, these dispositions were assigned mRS 6 for dead at discharge, mRS 4–5 for discharge to skilled nursing facility and mRS 0–3 for discharge to home or home health services.¹⁰ The additional cost of administering tPA was estimated by the difference between the cost of acute ischemic stroke (AIS) without tPA from the cost of AIS with tPA, in the absence of complications, using diagnosis related groups (DRGs) 63 and 66 respectively.¹⁷ A similar method was used to calculate the additional cost of IAT. It was the difference between the cost of IAT and the cost of AIS with tPA, both in the absence of complications using DRGs 27 and 66 respectively. Recurrent stroke hospitalization costs were derived from previous models obtained from an economic study that assessed these costs at 5 major academic centers.¹⁸ Annual posthospitalization costs were obtained from Earnshaw et al.¹⁰ All costs

are discounted by 3% per year.¹⁵ All costs prior to 2012 were inflated to 2012 dollars according to the medical care component of the Consumer Price Index.¹⁹

Outcomes Assessment

Utility for each mRS ranged from 0 to 1. Whereas a utility value of 1 represents perfect health or no loss of utility and 0 is death or no utility whatsoever. Respective utility values were multiplied to the life years spent in that health state and summed over the lifetime of the patient to obtain QALYs. Utility values were obtained from published literature, based partly on patient surveys.¹²

The incremental cost and QALY between IAT and standard therapy were assessed. The incremental cost-effectiveness ratio (ICER) was obtained by dividing the cost difference by the difference in QALY. Interventions were considered cost-effective if the ICER was less than or equal to the conventional threshold of \$50,000.¹⁸ Interventions were considered borderline if the ICER was between \$50,000 and \$100,000.

Sensitivity Analysis

To estimate the overall uncertainty of model results, deterministic one-way sensitivity analysis was performed. Parameters analyzed included clinical efficacy (percentage of patients reporting each mRS at 90 days for each treatment arm), acute stroke mortality rate, acute stroke care cost, tPA treatment cost, IAT cost, annual posthospitalization cost, recurrent stroke cost, mortality of recurrent stroke, utilities, and death hazard ratios (Figure 2). Values derived from the MR CLEAN trial, outcome utilities, recurrent stroke probability and death with recurrent stroke probability were varied by their 95% confidence intervals, death hazard ratios were varied based on consensus of an expert panel, and all cost variables were varied by 50% in either direction.

In addition to one way sensitivity analysis, we wanted to determine how much worse IAT could have performed but still produced a cost-effective ICER. We constructed three hypothetical worse outcomes representing, least unfavorable, unfavorable and most unfavorable scenarios for IAT performance by assuming worse outcomes in none to mild disability states at 90 days. This was accomplished by setting each mRS 0 to 2 at its 10th, 5th, and 1st percentile based on its beta distribution, representing least unfavorable, unfavorable and most unfavorable outcomes respectively (Supplementary Figure I). Then the total difference was redistributed evenly among mRS 3 to 6, so that the sum of all outcomes still added to 1, Table 2. Finally, the ICER in each instance was calculated by comparing to the base case for standard therapy alone.

Monte Carlo simulation was also performed in which all variables in the one way sensitivity analysis were varied simultaneously. We assumed clinical 90 day mRS outcomes followed a Dirichlet distribution, which allows for the multivariate generalization of the beta distribution. Proportion of patients receiving tPA, incidence of recurrent stroke, utility and recurrent stroke mortality followed a beta distribution. All costs were varied using a normal distribution (assuming 50% in each direction as the 95% confidence interval). Relative mortality risk for each mRS after the index stroke was varied using the log normal scale.

The analysis was run 10,000 times to capture stability in the results. Uncertainty was represented using a scatter plot (Figure 3).

Results

Base Case Analysis

For the base case, standard therapy yielded 3.10 QALYs at a total lifetime cost of \$130,144. In comparison, IAT in addition to standard therapy yielded 3.80 QALYs at a total lifetime cost of \$140,055. Therefore IAT resulted in a lifetime gain of 0.7 QALYs at an additional cost of \$9,911, which represented an additional cost of \$14,137 for each QALY gained (Supplementary Table I).

One-Way Sensitivity Analysis

The tornado diagram illustrates the effects of varying input parameters on the ICER or cost per QALY (Figure 2). Overall, the one way sensitivity analysis showed that variation of each assumption from their minimum to maximum values still resulted in QALYs gained and cost savings. Across all parameter ranges, ICERs were within the acceptable limits of cost-effectiveness, defined as willingness to pay (WTP) of less than \$50,000/QALY. Of all parameters, the variable with the largest impact on the ICER across the range of values explored in sensitivity analysis was the probability of standard treatment producing an outcome of mRS 4 (30.2%). The upper bound probability (35.8%) produced an ICER of \$157 and the lower bound probability (25%) of \$22,467. The ICER was most impacted by the outcomes of each treatment arm producing mRS 4, 3, and 5 at 90 days in addition to the cost of IAT and the annual posthospitalization cost for mRS 4–5.

When compared to the standard care arm, the least unfavorable, unfavorable and most unfavorable scenarios produced ICERs of \$41,816, \$56,146, and \$132,128 respectively. In each hypothetical worse case scenario, IAT continued to produce a benefit in QALYs when compared to standard therapy alone; 0.28 for least unfavorable, 0.21 for unfavorable and, 0.09 for most unfavorable. In the least unfavorable scenario IAT continued to be a fully cost-effective therapy. However, in the most unfavorable scenario IAT only produces a marginal benefit over standard therapy.

Multiway Probabilistic Sensitivity Analysis

The results of the multiway probabilistic sensitivity analysis are shown in Figure 3. In 19% of the simulation runs, IAT was the dominant strategy with a lower cost and higher QALYs compared to standard treatment alone. In 79% of the simulation runs, IAT was more costly but also more effective than standard treatment alone. Overall, in 97.6% of simulation runs, IAT was recommended, meaning it was either the dominant strategy or was preferred over standard therapy alone at a WTP threshold of \$50,000/QALY. In only 1.4% of the runs was standard therapy more effective than the addition of IAT. The cost-effectiveness acceptability curve in Figure 4 shows the cost-effectiveness of IAT as a function of the WTP threshold.

Discussion

The addition of IAT surpassed conventionally accepted cost-effectiveness thresholds, leading to better outcomes at a cost of \$14,137 for each QALY gained in the base case. This conclusion held up to significant variation in modeling assumptions. When pessimistic functional outcome distributions for IAT were compared to standard therapy, IAT remained cost-effective in the least unfavorable and unfavorable scenarios. IAT remained cost-effective at a WTP threshold of \$50,000/QALY even when the number needed to treat (NNT) to produce a mRS of 0–2 was increased to 20 in the least unfavorable outcome and at a WTP threshold of \$100,000/QALY when the NNT was increased to 26 in the unfavorable outcome, compared to the NNT of 7 in MR CLEAN itself. Given that the recent ESCAPE and EXTEND-IA trials had NNT of 4 and 3 respectively, these assumptions are particularly pessimistic and support the idea that IAT is likely cost effective.^{20, 21}

There have been previous models which predicted the cost-effectiveness of IAT.⁷ Due to the previous lack of positive randomized clinical trials, past studies used results from the single arm trials such as MERCI to predict clinical outcomes based on the rates of recanalization.^{3,22} This study had the benefit of a randomized clinical trial (MR CLEAN) with clinical outcomes as a primary end point. Hence, direct measurements of outcomes were used and not extrapolated from clinical outcomes of reperfusion rates. In spite of these differences in methodology, the results were largely concordant with prior IAT ICERs: \$12,000²³ for mechanical thrombectomy within 8 hours compared to no treatment and \$16,000 for mechanical thrombectomy compared to patients who received IV tPA within 3 hours.²⁴

If the efficacy of IAT demonstrated in MR CLEAN is supported by future trials, the data suggest that there is a strong societal rationale for investment in IAT systems of care. Not only does IAT results in improvement in clinical outcomes for a relatively large subset of patients at high risk for disability, but the net costs of IAT appear to be within the bounds of conventional cost-effectiveness thresholds, even under pessimistic assumptions. Thus, even if costs-per-acute-treatment increased substantially, it is likely that IAT would still be a relatively good investment. This suggests that even costly investments in the capital needed to support IAT systems of care (e.g. telemedicine, transport networks) may also be good investments from a societal perspective. Similarly, initiatives to improve patient recognition of stroke symptoms and self-efficacy to seek emergent medical care as well as physician educational initiatives may also prove to be wise investments. Finally, future research that results in more expensive IAT protocols (e.g. more costly devices or imaging protocols) or which targets patient populations resulting in moderately less efficacy than was seen in MR CLEAN may also be cost-effective and should be explored.

The real world cost implications of IAT remain to be seen. This study does not account for some important costs such as infrastructure, service redesign or specialist training. While the overall cost per QALY is reasonable for IAT, inefficient system changes may entirely erode this advantage. Conversely, it may be the case that the real world cost implications of IAT may be even greater than seen here — overall hospitalization costs and rehabilitation costs may be lower in IAT patients due to their improved functional outcomes. Moreover, it is

conceivable that the infrastructure benefits used to deliver IAT may have broader benefits leading to more general improvement in acute ischemic stroke care.

There are some limitations to this study. The acute treatment costs for IAT and IV tPA were updated using the NIS data to reflect the current market. However, there were not more updated studies for costs reflecting the index stroke, or recurrent stroke. Hence these estimates were inflated from previous literature and may not as closely estimate current market values. Updated studies estimating costs for long term stroke care were also unavailable. Previous neurologic cost-effective models (i.e. Earnshaw et al.) have based estimates on figures by Caro et al., which estimated lifetime cost of stroke care using a Stroke Treatment Economic Model using unit costs from the United Kingdom in 1996.²⁵ Lifetime cost of stroke estimates are also used in cardiology cost-effectiveness models which have looked at medications such as Ximelgatran or Dabigatran for preventing strokes in atrial fibrillation.^{26, 27} These estimates were fivefold higher and derived from looking at the cost of post stroke care in the Rochester Stroke Registry from 1937 to 1989.²⁸ Other lifetime strokes cost estimates from Taylor et al. were in the same range as the neurology models but were derived from Medicare claims data in 1987 using the National Medical Expenditure Survey.²⁹ In lieu of more updated figures, estimates from Earnshaw et al. were used and inflated to 2012 dollars. The data suggest that regardless of which of these costs is most accurate, IAT is likely cost-effective, but a better understanding of the costs of care is likely necessary to intelligently evaluate the cost-effectiveness of more marginally cost-effective treatments.

In conclusion, IAT is likely cost effective for patients with anterior circulation strokes and proximal occlusion within the 6 hour window in addition to standard medical therapy. From a societal perspective, we will have to start changing the mindset behind stroke care. Providers can no longer stop at administering IV tPA, but patients with suspected anterior infarcts must also have vessel imaging to see if they would be a candidate for IAT. Furthermore it will involve widening the network of comprehensive stroke centers so that patients meeting the criteria can have prompt access to IAT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

None.

Sources of Funding

Supported by the National Institute of Health to J.F.B.

References

1. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013; 44:870–947. [PubMed: 23370205]

2. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized control trial: Prolyse in acute cerebral thromboembolism. *JAMA*. 1999; 282:2003–2011. [PubMed: 10591382]
3. Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi-MERCI trial. *Stroke*. 2008; 39:1205–1212. [PubMed: 18309168]
4. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Eng J Med*. 2013:893–903.
5. Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al. Endovascular treatment for acute ischemic stroke. *N Eng J Med*. 2013:904–913.
6. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. *N Eng J Med*. 2013:914–923.
7. Chen M. Cost-effectiveness of endovascular therapy for acute ischemic stroke. *Neurology*. 2012; 79(suppl 1):S16–S21. [PubMed: 23008392]
8. Berkhermer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. *NEJM*. 2015; 372:11–20. [PubMed: 25517348]
9. HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality. 2012. <http://hcupnet.ahrq.gov/>. Accessed January 7, 2015
10. Earnshaw SR, Jackson D, Farkouh R, Schwamm L. Cost-Effectiveness of Patient Selection Using Penumbra-Based MRI for Intravenous Thrombolysis. *Stroke*. 2009; 40:1710–1720. [PubMed: 19286581]
11. Chambers MG, Koch P, Hutton J. Development of a decision analytic model of stroke care in the United States and Europe. *Value Health*. 2002; 5:82–97. [PubMed: 11918824]
12. Samsa GP, Reutter RA, Parmigiani G, Ancukiewicz M, Abrahamse P, Lipscomb J, et al. Performing Cost-Effectiveness Analysis by integrating Randomized Trial Data with a Comprehensive Decision Model: Application to Treatment of Acute Ischemic Stroke. *J Clin Epidemiol*. 1999; 52:259–271. [PubMed: 10210244]
13. Fagan SC, Morgenstern LB, Petitta A, Ward RE, Tilley BC, Marler JR. Cost-Effectiveness of tissue plasminogen activator for acute ischemic stroke. *Neurology*. 1998; 50:883–890. [PubMed: 9566367]
14. Arias E. United States life tables, 2006. *Natl Vital Stat Rep*. 2010; 58:1–40.
15. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke. The Framingham Study. *Stroke*. 1982; 13:290–295. [PubMed: 7080120]
16. Reed SD, Blough DK, Meyer K, Jarvik JG. Inpatient costs, length of stay, and mortality for cerebrovascular events in community hospitals. *Neurology*. 2001; 57:305–314. [PubMed: 11468317]
17. Boudreau DM, Guzauskas GF, Chen E, Lalla D, Tayama D, Fagan SC, et al. Cost-Effectiveness of Recombinant Tissue Type Plasminogen Activator Within 3 Hours after Acute Ischemic Stroke. *Stroke*. 2014; 45:3032–3039. [PubMed: 25190439]
18. Tung CE, Win SS, Lansberg MG. Cost-Effectiveness of tissue-type plasminogen activator in the 3- to 4.5- hour time window for acute ischemic stroke. *Stroke*. 2011; 42:2257–62. [PubMed: 21719767]
19. Consumer Price Index. 2014. Available at <http://www.bls.gov/cpi/>. Accessed August 9, 2014
20. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. *N Eng J Med*. 2015; 372:1019–1030.
21. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. *N Eng J Med*. 2015; 372:1009–1018.
22. Smith WS, Sung G, Starkman S, Saver JL, Kidwell CS, Gobin YP. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. *Stroke*. 2005; 36:1432–1438. [PubMed: 15961709]

23. Patil CG, Long EF, Lansberg MG. Cost-Effectiveness analysis of mechanical thrombectomy in acute ischemic stroke. *J Neurosurg*. 2009; 110:508–513. [PubMed: 19025358]
24. Kim AS, Nguyen-Huynh M, Johnston SC. A cost utility analysis of mechanical thrombectomy as an adjunct to intravenous tissue type plasminogen activator for acute large-vessel ischemic stroke. *Stroke*. 2011; 42:2013–2018. [PubMed: 21636817]
25. Caro JJ, Huybrechts KF. Stroke Treatment Economic Model (STEM): predicting long-term costs from functional status. *Stroke*. 2005; 36:305–314.
26. Freeman JV, Zhu RP, Owens DK, Garber AM, Hutton DW, Go AS, et al. Cost-Effectiveness of Dabigatran Compared with Warfarin for Stroke Prevention in Atrial Fibrillation. *Ann Int Med*. 2011; 154:1–11. [PubMed: 21041570]
27. O'Brien CL, Gage BF. Cost-Effectiveness of ximelagatran for stroke prophylaxis in chronic atrial fibrillation. *JAMA*. 2005; 293:699–706. [PubMed: 15701911]
28. Leibson CL, Hu T, Brown RD, Hass SL, O'Fallon WM, Whisnant JP. Utilization of acute care services in the year before and after first stroke: A population-based study. *Neurology*. 1996; 46:861–869. [PubMed: 8618713]
29. Taylor TN, Davis PN, Torner JC, Holmes J, Meyer JW, Jacobson MF. Lifetime cost of stroke in the United States. *Stroke*. 1996; 27:1459–66. [PubMed: 8784113]

Figure 1.

Model Structure. Decision analytic tree and Markov state transition model. A patient enter the model when he or she is admitted to the hospital and receives either intravenous tPA with or without intraarterial treatment. At the end of each annual cycle after the initial stroke, the patient may remain in the same health state, have a recurrent stroke and transition to a lower health state or die. This applies to patients with any mRS outcome, but is only illustrated for mRS 2 in this figure.

AIS- Acute Ischemic Stroke, IA- Intraarterial, tPA- tissue Plasminogen Activator, mRS- modified Rankin's Score, hrs- hours

Figure 2.

One-way sensitivity Analysis: effects of parameter variation on the incremental cost-effectiveness ratio using intraarterial treatment in addition to standard treatment. Dark bars represents the upper bound, light bars represents the lower bound. Baseline incremental cost per QALY -\$14,140. IA- intraarterial, mRS- modified Rankins Score.

Figure 3.

Multiway probabilistic sensitivity analysis. Incremental cost-effectiveness scatter plot of patients treated with Intraatrial intervention in addition to standard care compared to standard care alone. Dotted line represents an incremental cost per QALY of \$50,000. Points to the right of the dotted line are considered cost-effective. Each gray dot represents a simulation run. The black dot represents the base-case result \$9,911 and 0.7 QALYs. QALY-quality adjusted life year.

Figure 4. Cost-effectiveness acceptability curve. The curve represents the probability that IAT in the 0 to 6 hour window is cost-effective for each willingness to pay threshold. IAT- Intraarterial treatment.

Table 1**Base-Case Values and Ranges of Plausible Values**

Model Input	Standard Treatment (Range)	IAT (Range)	Reference
Probability of			
tPA	0.903 (0.864-0.935)	0.871 (0.825-0.911)	MR CLEAN ⁸
mRS0	0.001 (0.000-0.00665)	0.030 (0.0122-0.0554)	
mRS1	0.062 (0.0938-0.120)	0.090 (0.0568-0.130)	
mRS2	0.132 (0.0942-0.175)	0.210 (0.160-0.264)	
mRS3	0.162 (0.120-0.208)	0.180 (0.133-0.232)	
mRS4	0.302 (0.249-0.358)	0.220 (0.169-0.275)	
mRS5	0.121 (0.0848-0.163)	0.060 (0.0938-0.333)	
Death	0.220 (0.173-0.271)	0.210 (0.160-0.264)	
Model Input	Base Case	Range	Reference
Cost-Acute (mRS range)			
Acute stroke mild (0–3)	\$7,411	(\$3,705-\$11,116)	Earnshaw et al ¹⁰
Acute stroke severe (4–5)	\$11,287	(\$5,643-\$16,930)	
Acute stroke death (6)	\$13,160	(\$6,580-\$19,740)	
Additional cost of tPA treatment	\$6,892	(\$3,446-\$10,338)	NIS ⁹
Additional cost of IAT	\$14,405	(\$7,202-\$21,607)	
Cost-Long term (mRS Range)			
Recurrent Stroke Hospitalization	\$20,106	(\$10,053-\$30,159)	Chambers et al ¹¹
Annual Posthospitalization (0–3)	\$6,523.15	(\$3,261-\$9,784)	Earnshaw et al ¹⁰
Annual Posthospitalization (4–5)	\$17,704.00	(\$8,852-\$26,556)	
Utility			
mRS0	0.80	(0.64-1)	Samsa et al ¹²
mRS1	0.80	(0.64-1)	
mRS2	0.65	(0.52-0.78)	
mRS3	0.50	(0.4-0.6)	
mRS4	0.35	(0.28-0.42)	
mRS5	0.20	(0.16-0.24)	
Death	0.00	–	
Death hazard ratios			
mRS0	1	(1-1.2)	Samsa et al ¹²
mRS1	1	(1-1.2)	
mRS2	1.11	(0.89-1.3)	
mRS3	1.27	(1.02-1.52)	
mRS4	1.71	(1.37-2.05)	
mRS5	2.37	(1.90-2.84)	
Probability of			
Recurrent Stroke	0.052	(0.0416-0.0624)	Fagan et al ¹³
Death with recurrent Stroke	0.19	(0.152-0.228)	

Model Input	Base Case	Range	Reference
Discount Rates			
Cost	0.03	–	Samsa et al ¹²
Outcomes	0.03	–	

All Costs were converted to 2012 dollars by using the medical care component of the Consumer Price Index.

tPA- tissue plasminogen activator, IAT- Intraatrial treatment, mRS- modified Rankin's Score

Table 2

Hypothetical Worse Performance for MR CLEAN, based on mRS outcomes at 90 days

IA + Standard Treatment Probability of	Base Case	Least Unfavorable	Unfavorable	Most Unfavorable
mRS0	3.0%	1.4%	1.2%	0.9%
mRS1	9.0%	6.1%	5.7%	4.9%
mRS2	21.0%	16.8%	16.0%	14.6%
mRS3	18.0%	20.2%	20.5%	21.2%
mRS4	22.0%	24.2%	24.5%	25.2%
mRS5	6.0%	8.2%	8.5%	9.2%
Death	21.0%	23.2%	23.5%	24.2%
NNT	7	20	26	71

mRS- modified Rankins Score. NNT – number needed to treat for one patient to have a mRS of 0–2.