

UC Irvine

UC Irvine Previously Published Works

Title

Stroke Warning Information and Faster Treatment (SWIFT): Cost-Effectiveness of a Stroke Preparedness Intervention

Permalink

<https://escholarship.org/uc/item/53v2475g>

Journal

Value in Health, 22(11)

ISSN

1098-3015

Authors

Stevens, Elizabeth R
Roberts, Eric
Kuczynski, Heather Carman
et al.

Publication Date

2019-11-01

DOI

10.1016/j.jval.2019.06.003

Peer reviewed



Published in final edited form as:

Value Health. 2019 November ; 22(11): 1240–1247. doi:10.1016/j.jval.2019.06.003.

Stroke Warning Information and Faster Treatment (SWIFT): Cost-effectiveness of a stroke preparedness intervention

Elizabeth R. Stevens, PhD, MPH^{1,2,*}, Eric Roberts, MPH¹, Heather Carman Kuczynski, MPH¹, Bernadette Boden-Albala, DrPH¹

¹New York University College of Global Public Health, Department of Epidemiology, New York, NY, USA

²New York University School of Medicine, Department of Population Health New York, NY, USA

Abstract

Objectives—We evaluated the cost-effectiveness of a stroke preparedness behavioral intervention study (SWIFT), a stroke intervention demonstrating capacity to decrease race-ethnic disparities in ED arrival times.

Methods—Using the literature and SWIFT outcomes for two interventions, enhanced educational (EE) materials or interactive intervention (II), we assess the cost-effectiveness of SWIFT in two ways: 1) Markov model, and 2) cost-to-outcome ratio. The Markov model primary outcome was the cost per QALY gained using the cost-effectiveness threshold of \$100,000/QALY. The primary cost-to-outcome endpoint was cost per additional patient with ED arrival <3 hours, stroke knowledge, and preparedness capacity. We assessed the ICER of II and EE versus standard care (SC) from a health sector and societal perspective using US\$ 2015, a time horizon of 5 years, and a discount rate of 3%.

Results—The cost-effectiveness of the II and EE programs were, respectively, \$227.35 and \$74.63 per additional arrival <3 hours, \$440.72 and \$334.09 per additional person with stroke knowledge proficiency, and \$655.70 and \$811.77 per additional person with preparedness capacity. Using a societal perspective the ICER for EE versus SC was \$84,643 per QALY gained and the ICER for II versus EE was \$59,058 per QALY gained. Incorporating fixed costs, EE and II

*Corresponding Author: Elizabeth R. Stevens, PhD, MPH, Department of Population Health, New York University School of Medicine, 227 E. 30th St. Rm 608, New York, NY 10016, Elizabeth.stevens@nyumc.org, Phone: 646.501.2556, Fax: 646.501.2706.
Author Contributions

ERS conceived of and designed the study, performed data collection and data analysis, and drafted the manuscript. ER performed data collection and data analysis, and contributed to manuscript preparation. HCK performed data collection and contributed to manuscript preparation. BBA conceived of and designed the study, performed data collection and data analysis, and contributed to manuscript preparation.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

No financial disclosures were reported by the authors of this paper.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

would need to administered to 507 and 1,693 or more patients, respectively, to achieve an ICER of \$100,000/QALY.

Conclusion—II was a cost-effective strategy compared to both EE and SC. However, high initial fixed costs associated with II may limit its cost-effectiveness in settings with smaller patient populations.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: .

Keywords

acute stroke; health literacy; patient education; patient-centered outcomes research; preparedness; cost-effectiveness

BACKGROUND

Stroke is a leading cause of death and serious long-term disability in the United States and globally. While primary and secondary stroke prevention remain key public health concerns, prevention remains suboptimal and stroke preparedness continues to be a priority.^{1,2}

The rapid diagnosis and treatment of acute ischemic stroke are critical in the reduction of morbidity, disability, and stroke-associated mortality. Currently, tissue plasminogen activator (tPA) is the only approved treatment for acute ischemic stroke,³ however, less than 25% of eligible stroke patients arrive to an emergency department (ED) within the 3-hour treatment window.^{4,5} Reasons for poor stroke preparedness include inadequate preparedness competency to recognize stroke symptoms and respond to stroke as an emergency.^{6–9}

A randomized controlled trial examining two stroke education focused interventions, the Stroke Warning Information and Faster Treatment (SWIFT), reported a significantly increased proportion of participants arriving <3 hours after symptom onset; approximately 50% arrived <3 hours of symptom onset compared to around 20% at baseline in both trial arms. To date SWIFT is one of the first stroke interventions demonstrating capacity to decrease race-ethnic disparities in ED arrival times.¹⁰ However, the cost of implementing this effective intervention has not yet been studied.

In this study, we present the cost-effectiveness of SWIFT comparing differences in the proportion of stroke patients arriving to the ED <3 hours, as well as, stroke knowledge and preparedness capacity.¹⁰

METHODS

Intervention and Participants

SWIFT was a controlled trial (2005–2011) that randomized 1,193 patients with an initial diagnosis of ischemic stroke or transient ischemic attack (TIA) to enhanced educational (EE) materials or interactive intervention (II). Specifically, both groups received a culturally tailored, health literature packet of preparedness focused educational materials and a medical alert bracelet. II additionally included in-hospital interactive group sessions consisting of a preparedness presentation, a stroke survivor preparedness narrative video,

and roleplaying (Figure 1). The trial had no contemporaneous “standard care” control group.^{10,11}

Patients were followed for 12 months. The primary endpoint measures were the proportion of patients arriving to the ED <3 hours after stroke onset. Compared to baseline arrival of approximately 20%, the SWIFT trial demonstrated a probability arriving at ED in <3 hours of 40.9% and 54.6% for the EE and II interventions, respectively. Secondary outcomes included pre-post intervention differences in stroke knowledge and preparedness capacity. These secondary outcomes were selected in the SWIFT study because limited stroke knowledge and preparedness capacity have been shown to be associated with poorer stroke outcomes.⁶⁻⁹ The design and key results of the SWIFT trial have been described previously.^{10,11}

Data Collection

At the time of study we documented the implementation cost of EE and II interventions including multimedia educational materials, facilitator wages, intervention time, and 1-month follow up telephone calls (Table S1). In Markov analyses, costs were estimated based on resource use derived from comparable populations of US patients. The cost of developing the content of intervention materials was not included in our analysis because these costs have already occurred and are not recoverable (in economic terminology, “sunk”) from the perspective of program dissemination. Outcome data including ED arrivals <3 hours, stroke knowledge, and preparedness capacity were collected during the trial. At baseline, 1 and 12 months, the stroke knowledge survey,¹² including an open-ended question on preparedness capacity, was verbally administered. To evaluate preparedness capacity, participants were asked to name the three most important things to say to ED staff when a stroke is suspected. A fully correct response included identification of potential stroke; report of at least one stroke symptom; and mention of either time of stroke onset, use of tissue-type plasminogen activator, or 3-hour time window.¹⁰ Model inputs for the standard care (SC) arm and stroke related resource use and utility values were derived from the literature. (Table 1)

Fixed and Variable Cost Classification

Intervention components were categorized as fixed (costs that do not change with the number of stroke patients) or variable cost inputs (costs that increase with the number of stroke patients). For example, activities related to facilitator training were generally considered fixed costs and activities related to patient-level education and follow-up were generally considered variable costs, as costs generally increased proportionally with the number patients enrolled in the program.

Cost-effectiveness

We assess the cost-effectiveness of SWIFT in two ways: 1) using a Markov model and 2) determining the cost-to-outcome ratio as compared to baseline.

We projected 5-year cost-effectiveness using a Markov model described below. We assessed the cost-effectiveness of EE compared with II and SC. The model incorporated the variable costs to assess the average cost-effectiveness per patient and the high fixed costs, which

were shared by the population, were then added separately to assess cost-effectiveness at a population level. Therefore, after the model analysis the total patient enrollment necessary to achieve cost-effectiveness was calculated. To encapsulate costs incurred by the health system and patients, our analysis adopted a limited societal perspective that included informal caretaker costs and productivity lost as well as non-medical direct costs (e.g. care facilities and paid caretakers) but did not include out-of-pocket medical costs, travel, or other non-medical direct costs. A secondary analysis was also performed using the healthcare system perspective.

We also derived the cost-effectiveness for secondary outcomes using the ratio of variable costs to program efficacy outcomes [(change in cost)/(change in effectiveness)]¹³ as compared to pre-intervention measures. The efficacy outcomes, reported in detail elsewhere,¹¹ included (1) the proportion of patients arriving to ED <3 hours after stroke onset, (2) stroke knowledge, and (3) preparedness capacity. Total costs per outcome were calculated assuming a patient population size the same as in the SWIFT trial.

Markov Model

We projected long-term cost-effectiveness of SWIFT using a Markov model, developed using TreeAge Pro Suite 2016 (TreeAge Software Inc., Williamstown, MA).¹⁴ The model and analyses were performed in April-October 2016. The model incorporated event probabilities and risk data from SWIFT and the literature to estimate quality-adjusted life expectancy, and medical costs. Model inputs can be found in Table 1.

Our Markov model used a time horizon of 5-years to capture the key clinically relevant timeframe associated with stroke recurrence. The primary end point was the incremental cost per quality adjusted life-year (QALY) gained. The model included four Markov states representing categories of modified Rankin Scale (mRS) disability scores. Each mRS score health state was assigned a health utility value which was derived from the literature.¹⁵ Patients can transition to a less severe mRS health state through recovery, remain in their current health state, transition to a more severe state through a secondary stroke, or die (Figure 2). The probabilities of transitioning between health states and mRS scores were derived from the literature (Table 1).^{16,17} Patient movement between health states was modeled using 1-month cycles for 5 years or until death.

The model was used to determine the mean total cost accrued per person receiving EE, II, and SC, as well as the mean number of QALYs gained. This allowed for the calculation of the incremental cost-effectiveness ratios (ICERs). We calculated QALYs by multiplying the time spent in each health state by corresponding utility estimates (on a scale where 1.0 = perfect health and 0.0 = death) for each stroke health state. Utility scores were derived from the literature.¹⁵ Cost-effective therapies were selected using a willingness-to-pay (WTP) threshold of \$100,000 per QALY gained. Costs and QALYs were discounted at 3% per year. All costs were converted to 2015 \$US using the consumer price index. The unit of analysis for cost-effectiveness estimates was the patient. All analyses were performed according to intention to treat. Our methods and the reporting of our results are consistent with guidelines for cost-effectiveness analyses.¹⁸

Sensitivity Analysis

In sensitivity analyses, the time horizon was set to a 10-year and a lifetime horizon to assess the long-term impact of the interventions. We performed 1-way sensitivity analyses of all model inputs (Table 1). We then employed a probabilistic sensitivity analysis of 100,000 iterations of Monte Carlo simulation.

RESULTS

SWIFT Participant Characteristics

Participants had a mean age of 63 years \pm 15, 50% were female, 17% black, 51% Hispanic, and 26% white. This was a mild stroke/TIA cohort with over 84% scoring <7 on National Institute of Health Stroke Scale.

Costs

Fixed costs for II and EE averaged \$11,542.46 and \$1,057.81, respectively. II variable costs were \$27,020.52 for 601 patients, or \$44.96 per patient. Using the total cost, including fixed and variable costs, II cost \$38,562.98, or \$64.16 per patient. EE variable costs were \$9,003.08 for 592 patients, or \$15.21 per patient. Using the total cost EE cost \$10,060.90, or \$16.99 per patient. (See supplemental Table S1)

Cost-per-outcome

At 30 days, II and EE, respectively, cost \$227.35 and \$74.63 per additional arrival <3 hours, \$440.72 and \$334.09 per additional person with stroke knowledge proficiency, and \$655.70 and \$811.77 per additional person with preparedness capacity. (Table 2)

Model analyses

Mean quality-adjusted life years (QALYs) gained for II and EE was 0.00031 and 0.00013, respectively compared to SC. Five-year costs for II, EE, and SC using a societal perspective were projected to be \$121,023, \$121,035 and \$121,045, respectively. The increased costs associated with II, EE, and SC were primarily attributable to increased tPA costs.

Using a societal perspective, the ICER for EE versus SC was \$84,643 per QALY gained and the ICER for II versus EE was \$59,058 per QALY gained.(Table 3) Using a healthcare perspective EE had an average cost of \$71,293 and an ICER of \$121,658/QALY compared to SC. II had an average cost of \$71,311 and an ICER of \$102,113 compared to EE.

Incorporating fixed costs in the societal perspective cost-effectiveness analysis, EE would need to be administered 507 patients to achieve an ICER of \$100,000/QALY. II would need to be administered to 1,693 patients to achieve an ICER of \$100,000/QALY compared to EE.

Sensitivity Analysis

The results were most sensitive to the costs associated with informal caretakers and tPA, variation in the time horizon, and the benefits of tPA.

Increasing the time horizon to 10 years and lifetime led to the ICER for II dominating both SC and EE. When incorporating fixed costs in the societal perspective 10-year horizon, EE and II would need to be administered to 24 and 267 or more patients, respectively, to achieve an ICER of \$100,000/QALY.

In the Monte Carlo simulation where all model inputs were varied across plausible distributions, at a WTP threshold of \$100,000/QALY there was a 94.9% probability that II would be cost-effective versus EE and SC, a 5.1% probability that SC would be more cost-effective than II and EE. The probability of EE being more cost-effective than both II and SC remained below 1% at all WTP thresholds.

DISCUSSION

This analysis based on SWIFT indicates that EE and II are likely to be a good value in patients who have experienced an ischemic stroke. The health benefits of the model were primarily derived from earlier thrombolysis with tPA.

While II is cost-effective when considering only variable costs, the high fixed costs associated with its implementation may be a prohibitive factor for its implementation in smaller institutions that see fewer stroke patients. Similarly, while on average II provided the greatest impact on stroke knowledge and behavioral competencies, EE was overall more cost-effective on a per outcome basis. As II implementation currently includes high-cost items such as a film customized to patient populations, it may be beneficial to manualize the intervention to decrease the initial investment burden. If the fixed costs of II cannot be successfully reduced, however, EE remains a cost-effective intervention. Therefore, in settings where II implementation is infeasible, EE should be considered as an alternative intervention.

The cost-effectiveness of EE and II holds true for both black and Hispanic patient populations, making SWIFT one of the first cost-effective behavioral interventions to reduce race-ethnic disparities in arrival times.¹⁰ In sensitivity analyses EE and II demonstrated a robust cost effectiveness across the intervention effect sizes observed among black and Hispanic patients. However, potentially due to the impact of a small sample size, II was not cost-effective among white patients. Additionally, in sensitivity analyses a greater intervention effect was observed as the age at initial stroke decreased. Therefore, the II and EE interventions are likely even more cost-effective in certain minority populations, such as Hispanic American patients who are more likely to have a stroke at an earlier age than white Americans.^{19,20}

After the 30 day follow-up call, which was designed to assess improvement in stroke knowledge and preparedness capacity and not initially intended to serve as an intervention, there was a catchup effect seen for EE. This is theorized to be an artifact of the additional stroke education received by going through the knowledge and competence questions. Due to this unintended effect and as there is a particularly high rate of stroke reoccurrence in the first month, this analysis focused primarily on the cost-effectiveness using the pre-follow-up call ED arrival data, however the cost of the follow-up calls was included in the variable

costs to be conservative. This may have biased the cost-effectiveness of II towards being more cost-effective than EE, however both II and EE would be expected to remain cost-effective compared to standard care. Additionally, the SWIFT trial observed a trend where there appeared to be an excess number of total strokes/TIA in the II compared with the EE group (187 versus 138), which was not driven by stroke mimics.¹⁰ If shown to be true, II uncovering a higher number of true strokes may indicate an improved cost-effectiveness in II beyond what is modeled.

As seen in SWIFT baseline data, significant racial and ethnic disparities exist in stroke knowledge, behavioral competencies, and ED arrivals.¹¹ Additionally, minority patients are less likely to receive tPA treatment²¹ and often have poorer stroke outcomes than white patients.^{19,20} Through its culturally tailored behavioral interventions, SWIFT represents a program that has the potential to reduce stroke outcome disparities in a cost-effective way. Thus providing an opportunity to increase health equity among stroke patients.

Continued low rates of arrival to ED under 3 hours for acute stroke suggests a need for more effective dissemination of existing materials on stroke preparedness. In the United States, about 185,000, or nearly 1 in 4 strokes annually are in people who have had a previous stroke.²² Our findings suggest that clear, simple, preparedness-focused messages, pre-discharge (and possibly follow-up reinforcement) are potentially cost-effective interventions to increase the proportion of early ED arrivals in this population. These results provide support for Brain Attack Coalition, Get with the Guidelines, and state-level certification programs that emphasize the critical role of continued stroke education.^{23–28}

Our study had several important limitations. First, the most significant limitation is in the design of the original SWIFT trial, which had no SC arm for comparison. Therefore, the literature was used to establish SC, which may not be truly reflective of the in-hospital stroke education at the study site. Similarly, the SWIFT trial did not assess the impact of the interventions on long-term survival, healthcare costs, and quality of life. To address uncertainty around these factors we examined the impact of plausible alternatives in sensitivity analyses, the results of which were similar to the result of our primary results. Second, as there is no information currently available on the long-term effectiveness of the interventions, the analysis models the impact of the interventions at a constant effect size throughout time. This may bias the results towards improving the cost-effectiveness of the interventions, however, due to the significantly higher risk of recurrent stroke within the first year after an initial stroke,¹⁷ most of the intervention benefit occurs within the first couple of years after intervention implementation. Similarly, the 5-year time horizon may be too short to capture the long-term impact of the interventions. Third, the societal perspective analysis did not include out-of-pocket medical costs, travel costs, or other non-medical direct costs beyond care facilities and paid caretakers, and is therefore limited. This likely underestimates the favorability of the intervention cost effectiveness. Fourth, approximately 10% of ischemic strokes are large vessel occlusions and eligible for thrombectomy.²⁹ Our model, however, did not include increased likelihood of earlier thrombectomy as an effect of earlier ED arrival. Thrombectomy has a treatment threshold of <6 hours since symptom onset, therefore an arrival time of <3 hours may decrease the time until thrombectomy, but is less likely to increase the total number of individuals receiving the procedure; this would

increase the potential health gains, but not costs making the model a potentially conservative estimate of the cost effectiveness. Finally, the results may not be generalizable from a mild stroke and TIA population to the larger community.

CONCLUSION

On the basis of the results of SWIFT, the implementation of II to increase stroke knowledge, behavioral competency, and secondary stroke ED arrivals <3 hours was a cost-effective strategy compared to both EE and SC. However, high initial fixed costs associated with II may limit its cost-effectiveness in settings with smaller patient populations. These findings provide support for the inclusion of a behavioral intervention in post-stroke care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding

National Institute of Neurological Disorders and Stroke grant numbers NINDS P50 NS049060-P3 and NINDS 1R01 NS072127

References

1. Miniño AM, Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2008. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2011;59(10):1.
2. Hoyert DL. 75 years of mortality in the United States, 1935–2010 NCHS data brief. 2012(88):1–8.
3. Chiu D, Krieger D, Villar-Cordova C, et al. Intravenous tissue plasminogen activator for acute ischemic stroke: feasibility, safety, and efficacy in the first year of clinical practice. *Stroke*. 1998;29(1):18–22. [PubMed: 9445322]
4. Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;363(9411):768–774. [PubMed: 15016487]
5. Kwiatkowski T, Libman R, Tilley BC, et al. The impact of imbalances in baseline stroke severity on outcome in the National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator Stroke Study. *Ann Emerg Med*. 2005;45(4):377–384. [PubMed: 15795715]
6. Boden-Albala B, Carman H, Moran M, Doyle M, Paik MC. Perception of recurrent stroke risk among black, white and Hispanic ischemic stroke and transient ischemic attack survivors: the SWIFT study. *Neuroepidemiology*. 2011;37(2):83–87. [PubMed: 21894045]
7. Skolarus LE, Zimmerman MA, Murphy J, et al. Community-Based Participatory Research: A New Approach to Engaging Community Members to Rapidly Call 911 for Stroke. *Stroke*. 2011;42(7):1862–1866. [PubMed: 21617148]
8. Dombrowski SU, White M, Mackintosh JE, et al. The stroke ‘Act FAST’ campaign: remembered but not understood? *Int J Stroke*. 2015;10(3):324–330. [PubMed: 25130981]
9. Evenson KR, Foraker RE, Morris DL, Rosamond WD. A comprehensive review of prehospital and in-hospital delay times in acute stroke care. *Int J Stroke*. 2009;4(3):187–199. [PubMed: 19659821]
10. Boden-Albala B, Stillman J, Roberts ET, et al. Comparison of Acute Stroke Preparedness Strategies to Decrease Emergency Department Arrival Time in a Multiethnic Cohort: The Stroke Warning Information and Faster Treatment Study. *Stroke*. 2015;46(7):1806–1812. [PubMed: 26069259]

11. Boden-Albala B, Stillman J, Perez T, et al. A stroke preparedness RCT in a multi-ethnic cohort: design and methods. *Contemp Clin Trials*. 2010;31(3):235–241. [PubMed: 20193777]
12. Association NS. Awareness and knowledge of stroke prevention: A study of adults, 50 years of age and over. Englewood, CO: National Stroke Association 1996.
13. Gold MR, Siegel JE, Russell LB. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
14. Sonnenberg FA, Beck JR. Markov Models in Medical Decision Making: A Practical Guide. *Medical Decision Making*. 1993;13(4):322–338. [PubMed: 8246705]
15. Greenberg D, Ginsberg G, Ziv A, et al. The Relation Between the Modified Rankin Scale (mRS) Scores and Utility Weights: Results from a Survey Among Community Dwelling Long Term Stroke Survivors. *Value in Health*.16(7):A533–A534.
16. Saposnik G, Reeves MJ, Johnston SC, Bath PM, Ovbiagele B. Predicting clinical outcomes after thrombolysis using the iScore: results from the Virtual International Stroke Trials Archive. *Stroke*. 2013;44(10):2755–2759. [PubMed: 23887844]
17. Mohan KM, Wolfe CDA, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and Cumulative Risk of Stroke Recurrence. *Stroke*. 2011;42(5):1489. [PubMed: 21454819]
18. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 2016;316(10):1093–1103. [PubMed: 27623463]
19. Trimble B, Morgenstern LB. Stroke in Minorities. *Neurol Clin*. 2008;26(4):1177–1190. [PubMed: 19026907]
20. Sealy-Jefferson S, Wing JJ, Sanchez BN, et al. Age- and ethnic-specific sex differences in stroke risk. *Gender medicine*. 2012;9(2):121–128. [PubMed: 22445684]
21. Johnston SC, Fung LH, Gillum LA, et al. Utilization of intravenous tissue-type plasminogen activator for ischemic stroke at academic medical centers: the influence of ethnicity. *Stroke*. 2001;32(5):1061–1068. [PubMed: 11340210]
22. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation*. 2017;135(10):e146–e603. [PubMed: 28122885]
23. Skolarus LE, Murphy JB, Zimmerman MA, et al. Individual and Community Determinants of Calling 911 for Stroke Among African Americans in an Urban Community. *Circulation: Cardiovascular Quality and Outcomes*. 2013;6(3):278–283. [PubMed: 23674311]
24. Goldstein LB, Edwards MG, Wood DP. Delay between stroke onset and emergency department evaluation. *Neuroepidemiology*. 2001;20(3):196–200. [PubMed: 11490166]
25. Tong D, Reeves MJ, Hernandez AF, et al. Times from symptom onset to hospital arrival in the Get with the Guidelines--Stroke Program 2002 to 2009: temporal trends and implications. *Stroke*. 2012;43(7):1912–1917. [PubMed: 22539544]
26. Morgenstern LB, Staub L, Chan W, et al. Improving delivery of acute stroke therapy: The TLL Temple Foundation Stroke Project. *Stroke*. 2002;33(1):160–166. [PubMed: 11779906]
27. Hsia AW, Castle A, Wing JJ, et al. Understanding reasons for delay in seeking acute stroke care in an underserved urban population. *Stroke*. 2011;42(6):1697–1701. [PubMed: 21546471]
28. Alberts MJ, Latchaw RE, Selman WR, et al. Recommendations for comprehensive stroke centers: a consensus statement from the Brain Attack Coalition. *Stroke*. 2005;36(7):1597–1616. [PubMed: 15961715]
29. Rai AT, Seldon AE, Boo S, et al. A population-based incidence of acute large vessel occlusions and thrombectomy eligible patients indicates significant potential for growth of endovascular stroke therapy in the USA. *J Neurointerv Surg*. 2017;9(8):722–726. [PubMed: 27422968]
30. Lacy CR, Suh D-C, Bueno M, Kostis JB. Delay in Presentation and Evaluation for Acute Stroke. *Stroke*. 2001;32(1):63. [PubMed: 11136916]
31. Qureshi AI, Kirmani JF, Sayed MA, et al. Time to hospital arrival, use of thrombolytics, and in-hospital outcomes in ischemic stroke. *Neurology*. 2005;64(12):2115–2120. [PubMed: 15985583]
32. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *The Lancet*.363(9411):768–774.

33. Saver JL, Smith EE, Fonarow GC, et al. The Golden Hour and Acute Brain Ischemia: Presenting Features and Lytic Therapy in Over 30,000 Patients Arriving Within 60 Minutes of Onset. *Stroke; a journal of cerebral circulation*. 2010;41(7):1431–1439.
34. Tsvigoulis G, Zand R, Katsanos AH, et al. Risk of Symptomatic Intracerebral Hemorrhage After Intravenous Thrombolysis in Patients With Acute Ischemic Stroke and High Cerebral Microbleed Burden: A Meta-analysis. *JAMA neurology*. 2016;73(6):675–683. [PubMed: 27088650]
35. The Nt-PASSG. Intracerebral Hemorrhage After Intravenous t-PA Therapy for Ischemic Stroke. *Stroke*. 1997;28(11):2109. [PubMed: 9368550]
36. Saver JL, Fonarow GC, Smith EE, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. *JAMA*. 2013;309(23):2480–2488. [PubMed: 23780461]
37. Reed SD, Blough DK, Meyer K, Jarvik JG. Inpatient costs, length of stay, and mortality for cerebrovascular events in community hospitals. *Neurology*. 2001;57(2):305–314. [PubMed: 11468317]
38. Steiner C BM, Weiss A. HCUP Projections: Acute Myocardial Infarction (AMI) and Acute Stroke 2004 to 2015, HCUP Projections Report # 2015–01.. 2015; <http://www.hcup-us.ahrq.gov/reports/projections/2015-01.pdf>. Accessed October 18, 2016.
39. Lekander I, Willers C, von Euler M, et al. Relationship between functional disability and costs one and two years post stroke. *PLoS One*. 2017;12(4):e0174861–e0174861. [PubMed: 28384164]
40. Skolarus LE, Freedman VA, Feng C, Wing JJ, Burke JF. Care Received by Elderly US Stroke Survivors May Be Underestimated. *Stroke*. 2016;47(8):2090–2095. [PubMed: 27387990]
41. Centers for Medicare & Medicaid Services. 2015 ASP Drug Pricing Files. 2015; <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2015ASPFiles.html>. Accessed October 18, 2016.
42. Boudreau DM, Guzauskas GF, Chen E, et al. Cost-effectiveness of recombinant tissue-type plasminogen activator within 3 hours of acute ischemic stroke: current evidence. *Stroke*. 2014;45(10):3032–3039. [PubMed: 25190439]
43. Godwin KM, Wasserman J, Ostwald SK. Cost associated with stroke: outpatient rehabilitative services and medication. *Topics in stroke rehabilitation*. 2011;18 Suppl 1:676–684. [PubMed: 22120036]
44. Choudhry NK, Avorn J, Antman EM, Schneeweiss S, Shrank WH. Should patients receive secondary prevention medications for free after a myocardial infarction? An economic analysis. *Health Aff (Millwood)*. 2007;26(1):186–194. [PubMed: 17211028]
45. Earnshaw SR, Jackson D, Farkouh R, Schwamm L. Cost-Effectiveness of Patient Selection Using Penumbra-Based MRI for Intravenous Thrombolysis. *Stroke*. 2009;40(5):1710. [PubMed: 19286581]
46. Medicare Payment Advisory Commission. A DATA BOOK: Health Care Spending and the Medicare Program. 2018; http://www.medpac.gov/docs/default-source/data-book/jun18_databookentirereport_sec.pdf. Accessed May 6, 2019.
47. Bureau of Labor Statistics. Employment and Wages In Healthcare Occupations. 2015; <https://www.bls.gov/spotlight/2015/employment-and-wages-in-healthcare-occupations/pdf/employment-and-wages-in-healthcare-occupations.pdf>. Accessed May 2, 2019.
48. Bureau of Labor Statistics. May 2018 National Occupational Employment and Wage Estimates United States. 2019; http://www.bls.gov/oes/current/oes_nat.htm. Accessed October 18, 2016.

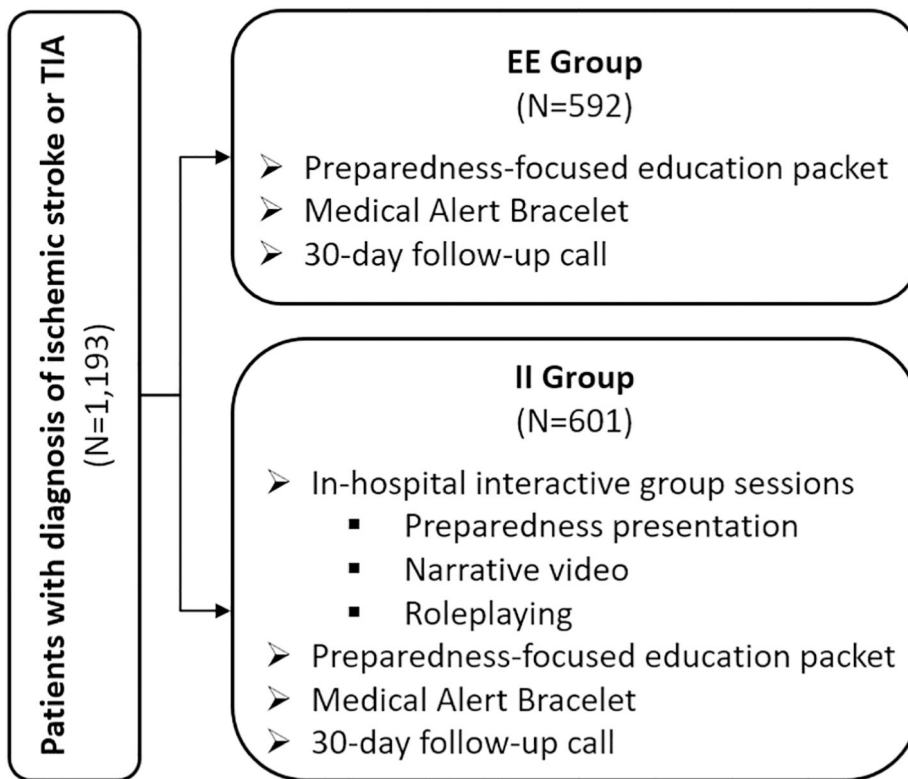


Figure 1.
SWIFT intervention study design

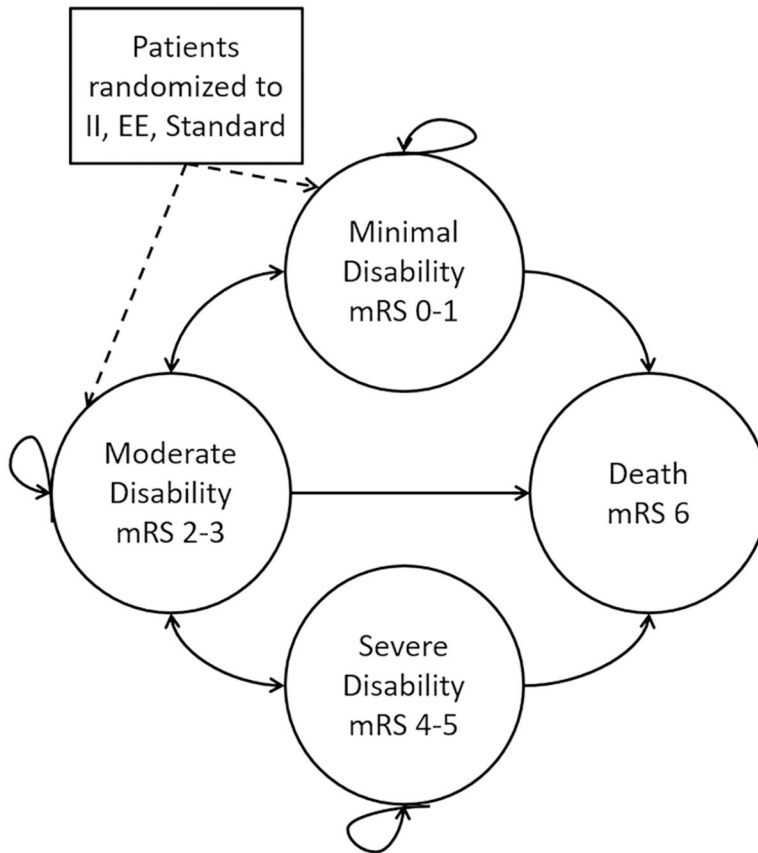


Figure 2.
Markov model structure

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Select model inputs

Parameter	Sensitivity Analysis Range			Source
	Value	Low	High	
Age at initial stroke (years)	60	49	74	SWIFT
Probability of recurrent stroke within 1 month	0.031	0.017	0.044	17
Probability of recurrent stroke within 1 year	0.111	0.09	0.133	17
Probability of recurrent stroke within 5 years	0.264	0.201	0.328	17
Probability of recurrent stroke within 10 years	0.392	0.272	0.512	17
II probability arriving at ED in <3 hours	0.5455	0.47	0.613	SWIFT
EE probability arriving at ED in <3 hours	0.4091	0.324	0.485	SWIFT
SC probability arriving at ED in <3 hours	0.25	0.117	0.336	24,25,30_32
Probability of TPA if arriving at ED in <3 hours	0.1941	0.153	0.247	33
Probability of TPA if arriving at ED in >3 hours	0.0025	0.002	0.004	33
Probability of hemorrhage with TPA	0.05	0.041	0.062	34
Probability of hemorrhage with no TPA	0.006	0.005	0.009	35
Probability of death with hemorrhage	0.217	0.182	0.261	36
Probability of death with no TPA	0.169	0.135	0.203	16
Probability of mRS 0–1 with TPA	0.283	0.251	0.336	16
Probability of mRS 2–3 with TPA	0.342	0.299	0.392	16
Probability of mRS 4–5 with TPA	0.237	0.211	0.268	16
Probability of mRS 0–1 with no TPA	0.271	0.228	0.322	16
Probability of mRS 2–3 with no TPA	0.301	0.249	0.364	16
Probability of mRS 4–5 with no TPA	0.258	0.232	0.289	16
Health Utility Value mRS 0–1	0.748	0.673	0.853	15
Health Utility Value mRS 2–3	0.395	0.329	0.472	15
Health Utility Value mRS 4–5	0.055	0.045	0.067	15
Probability of initial stroke mRS 0–1	0.556	0.443	0.655	SWIFT
Probability of initial stroke mRS 2–3	0.444	0.355	0.533	SWIFT
<i>Societal Perspective Specific Inputs</i>				
Patient hospitalization time mRS 0–1 (Days)	3.8	3.04	4.56	37,38
Patient hospitalization mRS 2–3 (Days)	4.7	3.76	5.64	37,38
Patient hospitalization mRS 4–5 (Days)	9.4	7.52	11.28	37,38
Patient care facility stay mRS 0–1 (Days)	1	0	10	39
Patient care facility stay mRS 2–3 (Days)	18	5	30	39
Patient care facility stay mRS 4–5 (Days)	144	75	250	39
Patient productivity lost mRS 0–1 (Days) *	50	10	70	39
Patient productivity lost mRS 2–3 (Days) *	39	20	50	39
Patient productivity lost mRS 4–5 (Days) *	23	10	40	39

Parameter	Sensitivity Analysis Range			Source
	Value	Low	High	
Paid caretaker time mRS 2–3 (hrs/wk) *	3	0	10	40
Paid caretaker time mRS 4–5 (hrs/wk) *	9	6	20	40
Informal caretaker time mRS 2–3 (hrs/wk)	15.4	10	30	40
Informal caretaker time mRS 4–5 (hrs/wk) Costs (\$US)	38	20	60	40
Costs (\$US)				
II variable	45	37	54	SWIFT
EE variable	15	11	20	SWIFT
Tissue plasminogen activator (tPA) - 100 mg vial	7,374	6,160	8,870	41
Hospitalization Costs mRS 0–1	7,652	6,125	9,148	37
Hospitalization Costs mRS 2–3	11,623	9,160	13,696	37
Hospitalization Costs mRS 4–5	13,589	10,928	16,058	37,42
Hospitalization Costs (death)	15,460	13,014	18,425	42
Annual Health Costs 1st yr mRS 0–1	16,463	13,170	19,756	43
Annual Health Costs 1st yr mRS 2–3	19,571	15,657	23,486	43
Annual Health Costs 1st yr mRS 4–5	22,856	18,285	27,427	43
Annual Health costs annual after 1st yr mRS 0–1	2,167	1,733	2,600	44
Annual Health costs annual after 1st yr mRS 2–3	5,394	4,315	6,473	45
Annual Health costs annual after 1st yr mRS 4–5	13,817	11,054	16,581	45
<i>Societal Perspective Specific Inputs</i>				
Care facility daily cost (per day)	1,531	500	2,000	46
Paid caretaker median hourly wage	10.77	8	20	47
US Median annual income	36,200	18,907	184,392	48

Note: Costs are reported in 2015 USD

* Productivity lost excluding hospital and care facility stays

Table 2.

Cost-effectiveness based on stroke arrival <3 hours stroke knowledge, and preparedness capacity per patient at 30 days and 12 months

Sample	Outcome	Prior to follow-up call (30 days)					12 months						
		Incremental change (per 100 events)*		Total Costs		Variable Costs		Incremental change (per 100 events)*		Total Costs		Variable Costs	
		CE ratio (\$/outcome)	95% CI	CE ratio (\$/outcome)	95% CI	CE ratio (\$/outcome)	95% CI	CE ratio (\$/outcome)	95% CI	CE ratio (\$/outcome)	95% CI	CE ratio (\$/outcome)	95% CI
II	Stroke Arrival <3hrs	28.2	120.71 to 1950.37	227.35	159.30	84.58 to 1366.6	24.9	257.79	115.93 to Dominated	180.63	81.23 to Dominated		
	Stroke Knowledge	14.6	309.88 to 762.79	440.72	308.81	217.13 to 534.48	54.7	117.20	101.7 to 138.28	82.12	71.26 to 96.89		
	Preparedness Capacity	9.8	483.04 to 1020.46	655.70	459.44	338.46 to 715.02	9.8	654.61	439.31 to 1283.8	458.68	307.82 to 899.54		
EE	Stroke Arrival <3hrs	22.8	36.36 to 85.93	74.63	66.79	32.53 to 76.9	29.0	58.56	28.43 to Dominated	52.40	17.03 to 54.71		
	Stroke Knowledge	5.1	152.44 to Dominated	334.09	298.96	136.42 to Dominated	29.9	56.83	44.5 to 78.6	50.85	23.36 to 31.33		
	Preparedness Capacity	2.1	388.33 to Dominated	811.77	726.42	347.5 to Dominated	1.0	1701.69	466.62 to Dominated	1522.77	0.89 to 0.9		
II	Stroke Arrival <3hrs	31.9	75.67 to 466.31	201.24	141.01	55.02 to 326.74	Dominated	Dominated	357.77 to Dominated	Dominated	250.68 to Dominated		
	Stroke Knowledge	10.5	280.7 to Dominated	613.32	429.75	196.68 to Dominated	11.9	539.48	226.17 to Dominated	378.00	158.47 to Dominated		
	Preparedness Capacity	13.1	312.14 to 1155.55	491.51	344.39	218.71 to 809.68	12.0	535.81	281.34 to 5612.88	375.44	197.13 to 3932.86		
EE	Stroke Arrival <3hrs	78.2	19.78 to 24.12	21.74	19.45	17.7 to 21.58	38.2	44.51	25.14 to 193.65	39.83	22.5 to 173.29		
	Stroke Knowledge	3.2	92.31 to Dominated	539.16	482.47	82.61 to Dominated	6.6	256.21	62.77 to Dominated	229.27	56.17 to Dominated		
	Preparedness Capacity	3.6	176.99 to Dominated	466.18	417.17	158.38 to Dominated	0.8	2088.52	235.45 to Dominated	1868.93	210.7 to Dominated		
II	Stroke Arrival <3hrs	22.2	90.92 to 3882.89	288.74	202.32	63.71 to 2720.68	17.7	362.99	140.19 to Dominated	254.34	98.23 to Dominated		
	Stroke Knowledge	9.4	275.64 to Dominated	685.76	480.50	193.14 to Dominated	11.2	571.07	206.9 to Dominated	400.14	144.97 to Dominated		
	Preparedness Capacity	6.8	440.94 to Dominated	948.72	664.75	308.96 to Dominated	4.5	1433.62	456.74 to Dominated	1004.52	320.03 to Dominated		
EE	Stroke Arrival <3hrs	13.6	25.6 to Dominated	124.82	111.70	22.91 to Dominated	13.6	124.82	39.48 to Dominated	111.70	35.33 to Dominated		
	Stroke Knowledge	-0.9	255.68 to Dominated	Dominated	Dominated	228.8 to Dominated	1.2	1409.53	145.81 to Dominated	1261.34	130.48 to Dominated		
	Preparedness Capacity	2.2	213.62 to Dominated	759.42	679.58	191.16 to Dominated	1.2	1431.22	211.01 to Dominated	1280.74	188.82 to Dominated		
II	Stroke Arrival <3hrs	30.8	98.63 to 406.98	208.18	145.87	69.11 to 285.16	36.8	174.26	115.68 to 353.02	122.10	81.05 to 247.36		
	Stroke Knowledge	17.4	249.73 to 701.63	368.35	258.10	174.98 to 491.62	14.5	443.06	251.78 to 1843.87	310.44	176.42 to 1291.97		
	Preparedness Capacity	8.2	505.02 to 1758.59	784.69	549.82	353.86 to 1232.22	7.2	891.81	480.99 to 6113.46	624.88	337.02 to 4283.61		
EE	Stroke Arrival <3hrs	-0.2	40 to Dominated	Dominated	Dominated	35.79 to Dominated	32.5	52.37	31.34 to 159.21	46.86	28.04 to 142.47		
	Stroke Knowledge	5.5	130.56 to Dominated	310.43	277.79	116.84 to Dominated	6.8	250.98	98.69 to Dominated	224.59	88.31 to Dominated		
	Preparedness Capacity	1.2	469.23 to Dominated	1403.41	1255.86	419.89 to Dominated	0.5	3107.47	513.25 to Dominated	2780.75	459.29 to Dominated		

Note: Dominated in 95% CI indicates a negative cost per outcome signifying that the intervention had a negative outcome impact

* For stroke knowledge and preparedness capacity this is per 100 people

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Summary of cost and clinical outcomes in the base case analysis

Table 3.

	SC	EE	Difference vs. SC	II	Difference vs. EE
Undiscounted life expectancy (years)	4.2308	4.2309	0.0001	4.2311	0.0002
Life expectancy (years) *	3.9455	3.9456	0.00012	3.9458	0.00015
QALE (QALYs) *	3.0064	3.0065	0.00014	3.0067	0.00017
Costs *	\$121,023	\$121,035	\$11.85	\$121,045	\$10.04
Incremental cost-effectiveness ratio		\$98,750 per life year gained *		\$66,933 per life year gained *	
		\$84,643 per QALY gained *		\$59,058 per QALY gained *	

* Values were discounted 3% annually. All costs are in 2015 USD.