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Age-specific Cost Effectiveness of Using Intravenous Recombinant Tissue Plasminogen Activator for Treating Acute Ischemic Stroke

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Abstract

Introduction—Studies have demonstrated that intravenous recombinant tissue plasminogen activator (IV rtPA) is a cost-effective treatment for acute ischemic stroke. Age-specific cost effectiveness has not been well examined. This study estimated age-specific incremental cost-effectiveness ratios (ICERs) of IV rtPA treatment versus no IV rtPA.

Methods—A Markov model was developed to examine the economic impact of IV rtPA over a 20-year time horizon on four age groups (18–44, 45–64, 65–80, and ≥81 years) from the U.S. healthcare sector perspective. The model used health outcomes from a national stroke registry adjusted by parameters from previous literature and current hospitalization costs in 2013 U.S. dollars. Long-term annual costs and quality-adjusted life years (QALYs) in the years after a stroke were discounted at 3% per year. Incremental costs, incremental QALYs, and ICERs were estimated and sensitivity analyses were conducted between 2015 and 2017.

Results—Use of IV rtPA gained 0.55 QALYs and cost $3,941 more than no IV rtPA for stroke patients aged ≥18 years over a 20-year time horizon. IV rtPA was a dominant strategy compared to no IV rtPA for patients aged 18–44 and 45–64 years. For patients aged 65–80 years, IV rtPA gained 0.44 QALYs and cost $4,872 more than no IV rtPA (ICER=$11,132/QALY). For patients aged ≥81 years, ICER was estimated at $48,676/QALY.

Conclusions—IV rtPA saved costs and improved health outcomes for patients aged 18–64 years and was cost effective for those aged ≥65 years. These findings support the use of IV rtPA.

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SUPPLEMENTAL MATERIAL

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INTRODUCTION

Stroke is a serious disease with high costs and high rates of death and disability. About 6.6 million U.S. adults have had a stroke, and the cost of stroke in the U.S. was $33 billion in 2012.[1] Intravenous recombinant tissue plasminogen activator (IV rtPA, alteplase), the only intravenous or intra-arterial medication approved by the U. S. Food and Drug Administration, is recommended for treatment of acute ischemic stroke by the American Heart Association and American Stroke Association (AHA/ASA).[2]

Previous research has shown that IV rtPA is a cost-saving or cost-effective treatment.[3–8] For example, a 1998 study showed that IV rtPA is a cost-saving treatment.[3] A more recent study published in 2014 by Boudreau et al.[4] confirmed that the use of IV rtPA within 3 hours after stroke onset saved costs and improved health outcomes. In 2009, AHA/ASA guidelines were updated to recommend the use of IV rtPA between 3 and 4.5 hours after an acute ischemic stroke onset.[9] Two subsequent studies showed that IV rtPA injection between 3 and 4.5 hours after stroke onset was cost effective.[6,8]

Although evidence exists that IV rtPA is a cost-saving or cost-effective treatment within both of the time frames described, the cost effectiveness of this treatment for people of different ages has not been thoroughly examined. Using data from a national stroke registry and information about current hospitalization costs, this study estimates the age-specific incremental cost-effectiveness ratios (ICERs) of IV rtPA treatment compared to no IV rtPA in the U.S.

METHODS

The Models

Based on a Markov model from Boudreau and colleagues,[4] a decision tree model was developed for this study. A U.S. healthcare sector perspective with a 20-year time horizon was used.[10] All costs were reported in 2013 U.S. dollars. Costs were adjusted by using Medical Care Consumer Price Index data from the U.S. Bureau of Labor Statistics, if needed.[4,11] All health outcomes and costs were discounted at a 3% rate.[12] All analyses with the decision tree model were performed in TreeAge Pro, version 2016, between 2015 and 2017.

A decision tree was adapted to simulate health status 3 months after discharge from hospitalization for acute ischemic stroke (Figure 1).[4,8,13] Possible outcomes were nondisabled, disabled, and death. The modified Rankin Scale, which is used to measure the level of disability of stroke patients, was used to define these outcomes. Specifically, scores 0–2 were used for the outcome of nondisabled (no or minor disability), scores 3–5 were used for the outcome of disabled (moderate to severe disability), and a score of 6 was used for the outcome of death.[14] For patients who were nondisabled or disabled 3 months after discharge, a Markov model was used to simulate long-term health status and change in health status because of a recurrent stroke or non-stroke death over a 20-year time horizon.[10] Time cycle in the model was 1 year.[15,16] Patients stayed at their original health status until they experienced a recurrent stroke or non-stroke death.[4,8] Patients who had a recurrent

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stroke could move to the disabled or death health status. This study assumed that patients with recurrent stroke do not receive IV rtPA and that patients cannot move from disabled to nondisabled health status.[4,8] Models were generated for patients in four age groups: 18–44, 45–64, 65–80, and ≥81 years.

Data

Data on the health status of patients were taken from the Paul Coverdell National Acute Stroke Program (PCNASP) for 2012–2013. The PCNASP tracks and measures acute stroke care in the U. S. and works to improve the quality of care for stroke patients.[17] It is funded and supported by the U.S. Centers for Disease Control and Prevention.[17] This study defined the IV rtPA group as patients who received IV rtPA at the PCNASP reporting hospitals. The no IV rtPA group was defined as follows: (1) IV rtPA was not initiated for the patient at the reporting hospital, (2) no IV rtPA was initiated at an outside reporting hospital, and (3) no intra-arterial catheter-based reperfusion was given at the reporting hospital.

Since the PCNASP is not an RCT but a registry, characteristics of patients in the IV rtPA group and the no IV rtPA group were significantly different. For example, patients in the IV rtPA group were younger and typically had experienced a more severe stroke than those in the no IV rtPA group. Because this study was designed to compare patients who received IV rtPA to those who could have received this treatment but did not, a propensity score matching technique was used to match the characteristics of the two groups. Patients' age, gender, and stroke severity, using the NIH Stroke Scale, were controlled.[18] Although propensity score matching has a disadvantage that any bias associated with latent covariates may endure even after the matching,[19] propensity score matching is a common approach to evaluate effects of treatment.[20] NIH Stroke Scale characterizes the initial evaluation of stroke patients before treatment. The percentages of patients in each group who were nondisabled or disabled or who died during hospitalization by IV rtPA status were compared using matched samples (N=7,418).

This study estimated the probabilities of being disabled or dying at 3 months after discharge by using the PCNASP data that included the probabilities of being disabled or dying during hospitalization and the previous literature (Table 1).[3] An extrapolation technique was used for the estimations. The validity of categorization of modified Rankin Scale was guaranteed by a similar distribution of modified Rankin Scale scores within each category between IV rtPA and no IV rtPA groups.[4,8]

This study applied age-specific baseline mortality from the U.S. life tables[21] to the Markov model for patients at 3 months after a stroke. For patients who were nondisabled or disabled, mortality was adjusted using the mortality hazard ratio from previous literature.[22,23]

Costs of acute care for acute ischemic stroke during initial hospitalization were estimated by using the 2010–2013 Market-Scan Commercial Claims and Encounters Inpatient Database and Medicare Supplemental and Coordination of Benefits Database.[24,25] This database has been used to analyze the costs of ischemic stroke, and the authors' cost estimates were consistent with the literature.[24,26–29] This study applied the estimated age-specific acute care costs using the database. The cost for patients who were nondisabled was defined as the

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average per person inpatient payment for patients discharged to home after hospitalization. The cost for patients who were disabled was defined as the payment for those discharged to any destination except home. The cost for patients who died was defined as the average per person inpatient payment for patients who died at a hospital. These definitions came from Earnshaw et al.[30] Annual costs beginning at 3 months after a stroke for nondisabled and disabled patients are taken from the previous literature.[30]

Quality-adjusted life years (QALYs) were used as a measure of health outcome. Estimates of mean QALYs for nondisabled and disabled stroke patients were taken directly from a previous study.[4]

Sensitivity Analysis

One-way sensitivity analyses as well as probabilistic sensitivity analyses were performed to confirm the robustness of the cost-effectiveness results. One-way sensitivity analyses were conducted with each input using ranges shown in Tables 1 and 2. Input parameters for the top ten causes of variability in ICERs are shown in tornado diagrams by age group. This study reported 95% CIs for each health outcome and developed cost-effectiveness acceptability curves using the results of probabilistic sensitivity analyses. The curves demonstrated the probability of IV rtPA being cost effective compared to no IV rtPA at a range of willingness-to-pay per QALY, which is called the cost-effectiveness threshold. This study used $50,000 per QALY and $100,000 per QALY as cost-effectiveness thresholds.[32,33] Technical details about probabilistic sensitivity analyses are presented in the Appendix (available online).

RESULTS

Use of IV rtPA increased QALYs and decreased costs for patients aged 18–44 and 45–64 years (Table 3). For patients aged 65–80 and ≥81 years, IV rtPA increased both QALYs and costs. ICERs were $11,132 per QALY for those aged 65–80 years (95% CI= −$821, $41,255 per QALY) and $48,676 per QALY for those aged ≥81 years (95% CI= −$488,562, $537,997 per QALY). For all patients aged ≥18 years, ICER was $7,134 per QALY (95% CI= −$7,057, $59,807 per QALY).

In the one-way sensitivity analyses, models for patients aged 18–44, 65–80, and ≥81 years were most sensitive to the probability of death for no IV rtPA group (Appendix Figure 1, available online). The probability of death for IV rtPA group had the largest effect on the models for patients aged 45–64 years. In the probabilistic sensitivity analyses, results of ICERs by each age group were examined using cost-effectiveness acceptability curves (Appendix Figure 2, available online). The curves for two age groups, aged 18–44 and 45–64 years, showed a 100% probability that IV rtPA treatment was cost effective at the $50,000 per QALY threshold. In other words, based on the model, the additional cost of IV rtPA treatment compared with no IV rtPA is always less than $50,000 per QALY for those age groups. For patients aged 65–80 years, there was a 97% probability that IV rtPA was cost effective at $50,000 per QALY and a 98% probability that it was cost effective at $100,000 per QALY. For patients aged ≥81 years, the cost-effectiveness acceptability curves demonstrated a 47% probability that IV rtPA was cost effective at $50,000 per QALY. In

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other words, there was a 47% probability that the cost of IV rtPA compared with no IV rtPA was less than $50,000 per QALY. For this age group, there was a 75% probability that IV rtPA was cost effective at $100,000 per QALY. For all age groups, the probability that IV rtPA is cost effective is 96% at $50,000 per QALY and 99% at $100,000 per QALY.

DISCUSSION

This study demonstrated that IV rtPA was either a costsaving or cost-effective strategy for treating patients with acute ischemic stroke, but that ICERs varied by age. Overall, ICER was $7,134 per QALY for patients who received IV rtPA compared with those who did not. These findings are consistent with previous research.[3,4,8] In the U.S., the use of IV rtPA within 3 hours after stroke onset is known to be a cost-saving treatment, whereas the use of IV rtPA between 3 and 4.5 hours after stroke onset is a cost-effective approach.[3,4,8] Boudreau and colleagues[8] have also shown that IV rtPA between 3 and 4.5 hours after stroke onset is cost saving for people aged <65 years. The findings from this study confirm that IV rtPA is a cost-saving treatment for patients aged 18–44 and 45–64 years. A Chinese study of the cost effectiveness of IV rtPA treatment within 4.5 hours of stroke onset showed that this treatment led to an ICER of $2,380 per QALY gained in a 30-year time horizon.[13]

For patients who could be treated with IV rtPA within 3 to 4.5 hours after stroke onset, the effectiveness of IV rtPA was not ascertained for patients aged >80 years in the 2013 AHA/ASA guideline.[2] The 2016 AHA/ASA guideline, however, suggested that IV rtPA for patients aged >80 years can be as effective as in younger patients.[34] The Food and Drug Administration label for rtPA still mentions that the risks of IV rtPA treatment may increase for patients aged >75 years, and the treatment should be initiated within 3 hours.[34] Baseline results showed that IV rtPA treatment was still cost effective for patients >80 years, using a $50,000 per QALY threshold. However, the probabilistic sensitivity analysis predicted cost effectiveness of IV rtPA in 47% of simulation runs with the same threshold. This study also found that about 29% of patients in the 2012–2013 PCNASP who received IV rtPA were older than 80 years. As the U.S. population continues to age, improving access to IV rtPA among elderly stroke patients will become a significant public health issue.

Developing stroke systems of care that include emergency medical service partners, developing protocols for IV rtPA delivery, and expanding the use of telemedicine and helicopter transport for stroke patients could improve access to IV rtPA, assuming that patients activate emergency care in a timely manner.[35–37] However, these strategies might require additional costs, which were not considered in the current study.[17,36,38] For instance, to help build state-based stroke registries as part of the PCNASP, the U.S. Centers for Disease Control and Prevention funded six state health departments (Georgia, Massachusetts, Michigan, Minnesota, North Carolina, and Ohio) about $600,000 annually from 2007 to 2012.[17] Future research could assess the costs needed to implement programs that improve access to IV rtPA.

Since 2015, treatment for large vessel occlusions with mechanical endovascular reperfusion (MER) has emerged as a standard of care for selected patients.[2,39–43] In appropriate patients, MER has been shown to reduce disability and mortality.[39–43] However, AHA/ASA

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recommends that patients who are eligible for IV rtPA should receive the treatment, even if they receive MER later.[2] Early studies demonstrated that for some patients IV rtPA +MER is a lifetime dominant strategy in a Swedish setting compared to the standard of care (IV rtPA only).[44] In the U.S. setting, MER treatment within the 0 to 6-hour window after IV rtPA within 0 to 4.5-hour window is a lifetime cost-effective strategy for 65-year-old patients with acute ischemic stroke caused by a proximal intracranial occlusion.[45]

This study has several strengths. First, it used national registry data to examine the cost effectiveness of IV rtPA treatment in a real-world setting, which was identified as a research gap.[4] Thus, the results could provide reasonable parameters for further economic evaluations of public health programs that support IV rtPA treatment. Another strength is the use of current data. MarketScan data for 2010–2013 were used to estimate acute care costs for stroke patients, and the PCNASP data for 2012–2013 were used to estimate health outcomes. Both the MarketScan database and the PCNASP data have information about a large number of stroke patients.[24] This study also used recognized modeling techniques, Markov models for recursive disease process simulation.[46] This study also provided results from one-way and probabilistic sensitivity analyses, which supported the robustness of the findings. Another strength of this analysis is that it showed that the age of the patient could affect the cost effectiveness of IV rtPA treatment in the U.S. Investigation of variances by age and ways to improve the cost-effectiveness ratio for particular age groups is an important area for future research.

Limitations

This study also has several limitations. Although sample characteristics between the IV rtPA and no IV rtPA groups were matched, there could be other factors that affected health outcomes after stroke onset (e.g., baseline pre-stroke disability, the presence of serious comorbidities) but these factors could not be accounted for. This study also did not consider the time window of when IV rtPA was injected because of data limitation. However, it is reasonable to assume that data from a national stroke registry in 2012–2013 represents patients who received IV rtPA within 0 to 4.5 hours after stroke onset and is not limited to those who received IV rtPA within 0 to 3 hours after stroke onset. It is because the data were collected after AHA/ASA released its extended time window recommendation in 2009.[9] Still, some patients may have received IV rtPA after 4.5-hour time window. Late treatment might decrease the health benefits of IV rtPA among the IV rtPA group.

Although this study attempted to use most plausible data, some input parameters may have an issue with possible bias. For instance, use of the Medical Care Consumer Price Index for inflation adjustment has been reported to be a biased measure of overall medical inflation.[47] However, the index is still widely used. Also, using payment data as a proxy for acute treatment costs is a limitation of this study, because payments by private insurers may exceed the costs of providing care and are also generally higher than Medicare payments. This study used input parameters, such as QALYs and a mortality rate, from different sources, which may not necessarily be consistent. The Markov model is limited because the history of a disease cannot affect its prognosis with the model.[46] An RCT, which can provide the strongest evidence of the treatment efficacy, could be an alternative. However,

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because long-term RCT data including both efficiency and costs information are not available, a simulation model is the best possible option. A stroke patient with recurrent strokes may have higher annual costs after discharge and a higher mortality rate than a patient with a first-ever stroke. The Markov model also did not consider the time dependency of input parameters. This study allowed variations by age in the efficacy of acute care and prognosis only up to 3 months after stroke onset because of limited data. However, cost effectiveness could vary by age because of other age-related factors, such as treatment efficacy after 3 months, and annual treatment costs after discharge. Thus, the variation of ICERs by age may be underestimated.

CONCLUSIONS

This is the first study to demonstrate the cost effectiveness of IV rtPA using the real-world registry data in the U.S. The findings in this study provide age-specific information about the cost effectiveness of IV rtPA treatment for patients who experience an acute ischemic stroke. IV rtPA treatment saves money and improves health outcomes for stroke patients aged 18–64 years. For patients aged ≥65 years, IV rtPA treatment is a cost-effective strategy compared to no IV rtPA. These findings, which used current data in a real-world setting, support the importance of promoting IV rtPA treatment for stroke patients for all adults of all ages.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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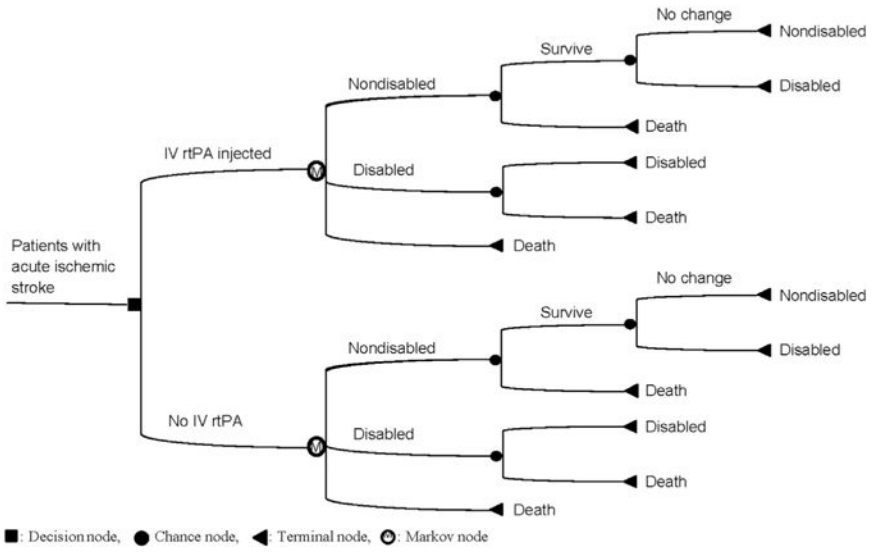

Figure 1.

Decision tree for cost-effectiveness analyses of IV rtPA use for patients with acute ischemic stroke.

IV rtPA, intravenous recombinant tissue plasminogen activator.

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Table 1

Probabilities of Health Status of Acute Ischemic Stroke Patients at 3 Months After Hospital Discharge, by Age

Age group/health status	No IV rtPA group, % (95% CI)	IV rtPA group, % (95% CI)
18–44 years		
Disabled	39 (34, 42)	25 (21, 30)
Death	10 (3, 16)	6 (1, 11)
45–64 years		
Disabled	40 (37, 41)	25 (23, 27)
Death	19 (16, 23)	17 (13, 20)
65–80 years		
Disabled	44 (43, 46)	34 (33, 36)
Death	27 (23, 31)	27 (23, 31)
≥81 years		
Disabled	46 (45, 48)	42 (40, 44)
Death	42 (37, 47)	40 (35, 45)
Total		
Disabled	43 (42, 44)	33 (32, 34)
Death	28 (26, 30)	27 (24, 29)

Note: Health status defined by mRS (scores 3–5 for disabled and 6 for death). Because data on mRS were only collected at hospital discharge from the PCNASP, probabilities at discharge from the PCNASP were adjusted to probabilities at 3 months after stroke onset by using the ratios from Fagan et al.[3].

IV rtPA, intravenous recombinant tissue plasminogen activator; mRS, modified Rankin Scale.

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Table 2

Clinical Parameters, Costs, and Health Outcomes Used in the Cost-Effectiveness Model

Inputs	Parameters for baseline[a]	Parameters for probabilistic sensitivity analyses		Reference
		M (SD)	Distribution	
Annual clinical parameters				
Probabilities of stroke recurrence	0.0498 (0.0446–0.055)	0.050 (0.002)	β	Hong et al.[31]
Mortality hazard ratio: nondisabled	1.1 (1–1.7)	1.183 (0.117)	Normal	Stahl et al.,[22] Boudreau et al.[4]
Mortality hazard ratio: disabled	2.5 (1.7–3.8)	2.583 (0.350)	Normal	Eriksson et al.[23]
Acute care cost (2013 U.S.$)				
No IV rtPA group				
18-44 years				
Nondisabled	18,215 (17,751–18,679)	18,215 (155)	γ	MarketScan 2010–2013[25]
Disabled	34,724 (32,588–36,859)	34,724 (712)	γ	MarketScan 2010–2013[25]
Death	44,658 (37,805–51,510)	44,658 (2,284)	γ	MarketScan 2010–2013[25]
45–64 years				
Nondisabled	16,163 (15,997–16,330)	16,163 (56)	γ	MarketScan 2010–2013[25]
Disabled	27,436 (26,878–27,995)	27,436 (186)	γ	MarketScan 2010–2013[25]
Death	40,105 (37,727–42,484)	40,105 (793)	γ	MarketScan 2010–2013[25]
65–80 years				
Nondisabled	13,250 (13,043–13,457)	13,250 (69)	γ	MarketScan 2010–2013[25]
Disabled	17,334 (16,980–17,687)	17,334 (118)	γ	MarketScan 2010–2013[25]
Death	23,415 (21,943–24,887)	23,415 (491)	γ	MarketScan 2010–2013[25]
≥81 years				
Nondisabled	13,087 (12,811–13,362)	13,087 (92)	γ	MarketScan 2010–2013[25]
Disabled	15,408 (15,150–15,667)	15,408 (86)	γ	MarketScan 2010–2013[25]
Death	19,616 (18,612–20,620)	19,616 (335)	γ	MarketScan 2010–2013[25]
IV rtPA group				
18–44 years				
Nondisabled	28,027 (25,899–30,155)	28,027 (709)	γ	MarketScan 2010–2013[25]
Disabled	39,764 (34,476–45,053)	39,764 (1,763)	γ	MarketScan 2010–2013[25]
Death	48,995 (27,693–70,297)	48,995 (7,101)	γ	MarketScan 2010–2013[25]
45–64 years				
Nondisabled	26,998 (26,106–27,889)	26,998 (297)	γ	MarketScan 2010–2013[25]
Disabled	40,007 (37,858–42,156)	40,007 (716)	γ	MarketScan 2010–2013[25]
Death	38,996 (32,566–45,427)	38,996 (2,144)	γ	MarketScan 2010–2013[25]
65–80 years				

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Inputs	Parameters for baseline[a]	Parameters for probabilistic sensitivity analyses		Reference
		M (SD)	Distribution	
Nondisabled	22,728 (21,443–24,014)	22,728 (429)	γ	MarketScan 2010–2013[25]
Disabled	27,141 (25,502–28,780)	27,141 (546)	γ	MarketScan 2010–2013[25]
Death	31,629 (26,936–36,323)	31,629 (1,565)	γ	MarketScan 2010–2013[25]
≥81 years				
Nondisabled	24,276 (22,062–26,490)	24,276 (738)	γ	MarketScan 2010–2013[25]
Disabled	24,440 (23,095–25,785)	24,440 (448)	γ	MarketScan 2010–2013[25]
Death	27,674 (24,561–30,787)	27,674 (1,038)	γ	MarketScan 2010–2013[25]
Annual cost after hospital discharge (2013 U.S.$)				
Nondisabled	5,714 (4,571–6,856)	5,714 (381)	γ	Earnshaw et al.[30]
Disabled	14,635 (11,708–17,562)	14,635 (976)	γ	Earnshaw et al.[30]
Health outcomes				
QALYs: nondisabled	0.84 (0.66–0.92)	0.823 (0.043)	β	Boudreau et al.[4]
QALYs: disabled	0.47 (0.24–0.66)	0.463 (0.070)	β	Boudreau et al.[4]
Discount rate (%)	3 (2.4–3.6)	3 (0.2)	Uniform	Assumption

[a]Numbers in parentheses show sensitivity range for one-way sensitivity analyses. Sensitivity ranges are ±20% for discount rate and annual costs after hospital discharge.

IV rtPA, intravenous recombinant tissue plasminogen activator; QALYs, quality-adjusted life years.

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Table 3

Costs and QALYs with IV rtPA for Acute Ischemic Stroke Over a 20-Year Time Horizon Compared With No IV rtPA, by Age Group

	Costs, 2013 U.S. $ (95% CI)			QALYs (95% CI)			
Age, years	IV rtPA	No IV rtPA	Difference (A), IV rtPA – no IV rtPA	IV rtPA	No IV rtPA	Difference (B), IV rtPA – no IV rtPA	Cost-effectiveness ICER (A/B), $/QALY (95% CI)
18–44	156,187 (148,378, 162,646)	161,917 (153,322, 169,171)	−5,730 (−14,360, 2,236)	10.10 (9.27, 10.39)	8.95 (8.08, 9.34)	1.15 (0.39, 1.90)	IV rtPA dominant (−24,579, 1,841)
45–64	130,546 (114,782, 141,203)	134,127 (115,845, 146,716)	−3,581 (−9,159, 2,131)	7.97 (6.86, 8.48)	7.01 (5.96, 7.55)	0.96 (0.47, 1.38)	IV rtPA dominant (−14,211, 1,902)
65–80	86,264 (65,015, 106,127)	81,392 (58,462, 103,375)	4,872 (−126, 9,189)	4.48 (3.12, 5.48)	4.05 (2.78, 5.02)	0.44 (0.05, 0.81)	11,132 (−821, 41,255)
≥81	47,277 (33,966, 59,413)	38,370 (25,496, 50,821)	8,907 (5,526, 11,683)	1.50 (0.74, 2.10)	1.32 (0.67, 1.87)	0.18 (−0.06, 0.42)	48,676 (−488,562, 537,997)
Total	93,268 (42,787, 139,748)	97,209 (35,170, 140,909)	3,941 (−3,018, 9,126)	5.02 (1.44, 7.01)	4.47 (1.28, 6.44)	0.55 (0.10, 0.86)	7,134 (−7,057, 59,807)

Note: Data were analyzed by 20-year time horizon or until age 100 years. 95% CIs are estimated from Monte Carlo simulation with 10,000 iterations.
ICER, incremental cost-effectiveness ratio; IV rtPA, intravenous recombinant tissue plasminogen activator; QALYs, quality-adjusted life years.