






A Prospective Economic Evaluation of Rapid Endovascular Therapy for Acute Ischemic Stroke

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ABSTRACT: Background: During the Randomized Assessment of Rapid Endovascular Treatment (EVT) of Ischemic Stroke (ESCAPE) trial, patient-level micro-costing data were collected. We report a cost-effectiveness analysis of EVT, using ESCAPE trial data and Markov simulation, from a universal, single-payer system using a societal perspective over a patient's lifetime. **Methods:** Primary data collection alongside the ESCAPE trial provided a 3-month trial-specific, non-model, based cost per quality-adjusted life year (QALY). A Markov model utilizing ongoing lifetime costs and life expectancy from the literature was built to simulate the cost per QALY adopting a lifetime horizon. Health states were defined using the modified Rankin Scale (mRS) scores. Uncertainty was explored using scenario analysis and probabilistic sensitivity analysis. **Results:** The 3-month trial-based analysis resulted in a cost per QALY of \$201,243 of EVT compared to the best standard of care. In the model-based analysis, using a societal perspective and a lifetime horizon, EVT dominated the standard of care; EVT was both more effective and less costly than the standard of care (−\$91). When the time horizon was shortened to 1 year, EVT remains cost savings compared to standard of care (~\$15,376 per QALY gained with EVT). However, if the estimate of clinical effectiveness is 4% less than that demonstrated in ESCAPE, EVT is no longer cost savings compared to standard of care. **Conclusions:** Results support the adoption of EVT as a treatment option for acute ischemic stroke, as the increase in costs associated with caring for EVT patients was recouped within the first year of stroke, and continued to provide cost savings over a patient's lifetime. Clinical Trial Registration: NCT01778335

RÉSUMÉ : Évaluation économique prospective de la thérapie endovasculaire rapide dans le cas de patients victimes d'accidents ischémiques aigus. **Contexte :** C'est dans le cadre des essais ESCAPE (*Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke*) et d'une évaluation randomisée de la thérapie endovasculaire (TEV) rapide destinée aux patients victimes d'accidents ischémiques qu'ont été collectées des données portant sur le calcul des coûts de traitement pour chaque patient pris individuellement. Nous voulons présenter ici une analyse coût-efficacité de la TEV au moyen de ces données et de la méthode de simulation des chaînes de Markov, et ce, dans le cadre d'un système universel de santé à payeur unique et en recourant à une perspective sociétale valide tout au long de la vie des patients. **Méthodes :** Cette collecte de données primaires liée aux essais ESCAPE nous a permis, au cours d'une période de 3 mois, d'analyser de façon spécifique et indépendamment d'un modèle les coûts de la TEV par année de vie ajustée en fonction de la qualité (AVAQ). Nous avons ensuite fait appel à un modèle basé sur la méthode de simulation des chaînes de Markov, modèle utilisant les coûts récurrents pendant une vie et l'espérance de vie en se basant sur ce qui est disponible dans la littérature scientifique. L'état de santé des patients a été défini à l'aide des scores à l'échelle de Rankin modifiée. Enfin, l'incertitude a été explorée à l'aide d'une analyse de scénarios et d'une analyse de sensibilité probabiliste (ASP). **Résultats :** En comparaison avec la meilleure norme en matière de soins, notre analyse basée sur les essais ESCAPE d'une durée de 3 mois a permis d'établir un coût par AVAQ de 201 243 \$ en ce qui concerne la TEV. Dans une analyse basée sur un modèle, en recourant à une perspective sociétale et en fonction d'un horizon temporel couvrant une vie entière, la TEV a dépassé la meilleure norme en matière de soins en s'avérant à la fois plus efficace et moins coûteuse (- 91 \$). Lorsque cet horizon temporel a été écourté d'un an, la TEV s'est aussi révélée moins coûteuse si on la compare à la norme des soins (~ 15 376 \$ par AVAQ). Cela dit, la TEV pourrait cesser d'être synonyme de réduction de coûts en comparaison avec la meilleure norme en matière de soins si l'on admet que l'estimation de son efficacité clinique serait 4 % moindre que celle démontrée lors des essais ESCAPE. **Conclusions :** Ces résultats militent donc en faveur de l'adoption de la TEV comme traitement des accidents ischémiques aigus car l'augmentation des coûts associée aux soins prodigués aux patients ayant bénéficié de la TEV a été amortie pendant la première année consécutive à un AVC. Soulignons en outre qu'un tel traitement a continué à représenter des économies tout au long de la vie des patients.

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INTRODUCTION

The estimated annual attributable cost to incident ischemic stroke in Canada is \$2.8 billion, with the average cost per patient of \$75,353 annually.¹ The Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke (ESCAPE) trial assessed the efficacy of rapid endovascular treatment (EVT) compared to best medical treatment for acute ischemic stroke. This trial demonstrated that EVT improved functional outcomes and reduced mortality in patients with acute ischemic stroke when compared to the current standard of care.² The results from this trial have been replicated in other trials^{3–6} and demonstrate the enormous potential to reduce in the economic burden of ischemic stroke internationally.

Several economic evaluations of EVT for ischemic stroke have been published.^{7–18} Recent systematic reviews found inconsistent results from these models with some authors concluding that EVT was cost-saving (less costly and more effective) than usual care, and other studies suggesting that EVT was cost-effective (below the accepted threshold of a cost per quality-adjusted life year [QALY], but not cost savings).^{19,20} Variability between study conclusions was attributed to time horizon, model perspective, and healthcare system.

While the literature surrounding EVT for ischemic stroke has investigated both the effectiveness and the cost-effectiveness, the planned a priori economic evaluation of the ESCAPE trial has not yet been reported.² This trial-based economic evaluation is a unique contribution as it stratifies patients by mRS and utilizes micro-costed individual-level patient data. Micro-costing, the most precise form of hospital costing, gives each resource required for a patient's stay an individual unit cost.²¹ This provides individualized costing rather than estimates calculated using diagnosis or length of stay (gross costing).²¹ The subsequent Markov model builds upon these data considering patient outcomes and costs by mRS over the patient's lifetime and the micro-costed data provide a more accurate representation of the variance in direct costs of acute stroke care. The subsequent Markov model builds upon these data considering patient outcomes and costs by mRS over the patient's lifetime utilizing the micro-costed data to provide a more accurate representation of the variance in direct costs of acute stroke care.^{19,20} Thus, our objective was to determine the cost per life year gained using EVT (with or without intravenous alteplase) versus best medical treatment (intravenous alteplase if appropriate) within the ESCAPE trial and subsequently modeled over a lifetime horizon using a societal perspective.

METHODS

Overview

A cost-effectiveness analysis of EVT (with or without intravenous alteplase) versus best medical treatment (intravenous alteplase if appropriate) was conducted.²² The population for

this analysis consisted of adult patients with disabling ischemic stroke who met the inclusion criteria of the ESCAPE trial and were randomly assigned to treatment or control.² In accordance with the 2006 Guidelines for the Economic Evaluation of Health Technologies: Canada (CADTH Guidelines), a societal perspective was used in the base case, and all costs and benefits were discounted annually at 5%.²³ Health benefits were measured in life years gained and QALYs gained over a lifetime. The incremental cost per life year gained and incremental cost per QALY gained were also calculated. All costs were inflated to 2016 Canadian dollars using the Canadian consumer price index.

Trial Analysis

The duration of the trial from enrollment to final follow-up was 90 days. The 3-month costs and benefits of ESCAPE trial participants were calculated. Specifically, the average costs and benefits for the intervention and control groups were calculated. A cost per QALY and a cost per death avoided were then calculated.

Lifetime Model Structure and Validity

A decision-analytic tree (0–90 days) and Markov model (90 days–lifetime) was constructed using decision analysis software (TreeAge Pro Suite) (Figure 1). Within this model, patients with ischemic stroke are assessed in the hospital and receive either EVT or control (best medical therapy). Patients could either be alive or dead at 90 days poststroke. For those surviving, the modified Rankin Scale (mRS) was used to define patient disability or dependence (mRS 0 – no symptoms [functionally independent] to mRS 5 – severely disabled [dependent]). After 90 days, a Markov model with annual cycles was used to simulate patients until death. At the end of each cycle, patients could remain alive in the same mRS group or die.

Clinical Data Inputs

Table 1 provides the input values for the model. Both mortality and probabilities of mRS scores at 90 days for treatment ($n=165$) and control arms ($n=150$) were calculated from the ESCAPE trial data across all sites.² Deaths from 0 to 6 months included those who died in the hospital or in the community (ascertained by vital statistics). Annual ongoing risk of death by mRS was estimated from the literature.²⁴ The length of stay was calculated directly from the collected ESCAPE trial data.²

Utilities

A utility range from 0 (dead) to 1 (full health) is required to calculate a QALY. Specifically, within the ESCAPE trial, the Euroqol 5 – Dimensions (EQ-5D) questionnaire 121 was used to measure health-related quality of life at 90 days.²⁵ The United Kingdom scoring algorithm was used to calculate utility scores.²⁶

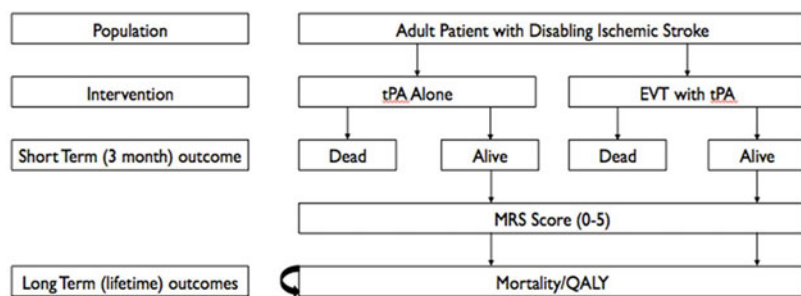


Figure 1: Model structure: decision-analytic tree and Markov state transition model.

Costs

In order to measure healthcare resource use for the first 3 months, micro-costed data were used. These data include direct patient-related costs (nurses, drugs, etc.) and operational costs that are not directly aligned to individual patient care (overhead, transportation, electrical, etc.). Individual-level data are available for all ESCAPE trial patients treated at both ESCAPE sites in Alberta (Calgary and Edmonton, $n=99$). These costing estimates represent the gold standard in costing, capture individual case variation, and offer accurate measures of precise and detailed individual patient costing.²⁷ These micro-costs were extrapolated to the remaining two-thirds of patients.

Physician costs were calculated following a standard care pathway which included physician bills, based on the Alberta Schedule of Medical Benefits,²⁸ for each point in the care pathway. The care pathway included: (1) patients arrived in the emergency room and received a consult by an emergency physician, followed by a consult with the Stroke Service team, (2) the patient would be sent for Computed Tomography Angiography (CTA) which was read by a radiologist, (3) both treatment and control groups would then receive alteplase if appropriate, and the treatment arm would also receive EVT by a neuro-interventionist (neuroradiologist, neurosurgeon, or interventional neurologist), (4) all patients were followed daily by the Stroke Service throughout their hospital stay, and (5) all patients were assessed by a psychiatrist prior to discharge.

The cost of EVT included the cost of the stent retrievers or aspiration catheters and the cost of the neuro-interventionist required to perform the procedure. Other procedure costs including additional catheters, nursing, and support staff, and room costs were captured within the micro-costing data. The cost of alteplase in both the control and EVT arms was captured within this data as an in-hospital drug cost.

The costs of tertiary care readmissions and ambulatory care usage within the first 3 months of treatment were estimated using micro-costing. Estimates were calculated for functionally independent (mRS 0–2), functionally dependent (mRS 3–5), and mRS 6 groupings rather than for each mRS score.

Annual costs (4–12 months) stratified by mRS were provided by the Economic Burden of Ischemic Stroke Study (BURST) investigators.¹ These estimates include societal costs such as lost patient productivity and unpaid caregiver time. Direct healthcare costs were also captured including hospitalization, rehabilitation, physician services, diagnostics medications, allied health professional services, homecare, medical/assistive devices, changes to residence, and paid caregiver time. Details of these costs are

reported elsewhere.¹ These costs were assumed to remain constant over time and used in the Markov model as the long-term care costs. The BURST investigators were unable to provide an estimate of mRS 5 annual costs due to a small sample size. Therefore, the difference between mRS 3 and mRS 4 was assumed to be equal to the difference between mRS 4 and mRS 5.²⁹

Validity

To assess internal model validity, simulated survival curves for EVT and control were compared. Since survival after the initial 90 days was assumed to be the same for both EVT and control arms of patients in the same mRS category, survival curves were expected to be identical between the EVT and control arms. In addition, the 3-month time frame of the trial was replicated in the model and the outputs of the model was compared to the observed trial data. Demonstration of both these outputs within the Markov model established internal validity of the model. External validity was not possible to assess as there are no long-term data for EVT outcomes in an imaging-selected patient population similar to those in the ESCAPE trial.

Uncertainty Analysis

In order to examine the impact of uncertainty on the model results, scenario analyses were conducted. In order to explore the effect of varying clinical effectiveness of EVT, a simulation was completed using the findings from other RCTs. First, the effectiveness of EVT was assumed to be equal to the Multicenter Randomized Clinical Trial on Endovascular Therapy for Acute Ischemic Stroke in the Netherlands (MR CLEAN trial) results.^{3,8} For this scenario, the probabilities of mRS score and death at 90 days were assumed to be those from the MR CLEAN trial.³ This scenario analysis simulates a smaller effect size for EVT than ESCAPE, and patients had a poorer overall prognosis in both treatment and control groups. In addition, the distribution of mRS score at 90 days from SWIFT-PRIME was modeled. This RCT resulted in greater effectiveness than demonstrated in ESCAPE trial. To further explore the impact that mRS probabilities had on the model, the relative proportions of independent and dependent survivors were varied for the EVT group. Groups were varied by percentage (e.g. 5% fewer independent and 5% more dependent survivors). Furthermore, to explore when EVT may become cost savings compared to control a time analysis was completed. The time horizon of the model was extended in monthly increments to identify the time after the intervention when EVT resulted in cost savings. Finally, a probabilistic sensitivity analysis was

Table 1: Summary of model inputs and healthcare resource use

	EVT+alteplase (tPA)							Alteplase (tPA)							
mRS	0 (n = 24)	1 (n = 34)	2 (n = 29)	3 (n = 27)	4 (n = 22)	5 (n = 11)	6 (n = 17)	0 (n = 11)	1 (n = 15)	2 (n = 17)	3 (n = 22)	4 (n = 36)	5 (n = 18)	6 (n = 28)	
mRS Prob at 90 days (SE)	0.15 (0.028)	0.21 (0.032)	0.18 (0.030)	0.16 (0.029)	0.13 (0.027)	0.07 (0.020)	0.10 (0.024)	0.07 (0.022)	0.10 (0.025)	0.12 (0.026)	0.15 (0.030)	0.24 (0.036)	0.12 (0.027)	0.19 (0.032)	
mRS CI	0.10–0.21	0.15–0.28	0.13–0.24	0.11–0.23	0.09–0.20	0.04–0.12	0.07–0.16	0.04–0.13	0.06–0.16	0.07–0.17	0.10–0.21	0.18–0.32	0.07–0.18	0.13–0.26	
Average utility at 90 days (SD)	0.86 (0.21)	0.80 (0.26)	0.77 (0.15)	0.59 (0.30)	0.26 (0.40)	0.44 (0.57)	0	0.96 (0.077)	0.87 (0.13)	0.74 (0.22)	0.54 (0.30)	0.32 (0.37)	0.38 (0.53)	0	
Prob dead (mRS 6) at 6 months*	0			0.063			—	0			0.043			—	
mRS	0 (n = 7)	1 (n = 13)	2 (n = 11)	3 (n = 7)	4 (n = 8)	5 (n = 2)	6 (n = 4)	0 (n = 3)	1 (n = 3)	2 (n = 5)	3 (n = 6)	4 (n = 15)	5 (n = 2)	6 (n = 13)	
Average tertiary care resource use at 90 days (\$)	30,795 (22,427)	27,882 (27,988)	15,914 (7625)	70,451 (53,89)	42,164 (22,47)	86,861 (86,133)	19,271 (15,794)	8935 (3332)	43,699 (65,526)	24,371 (5352)	69,859 (17,45)	45,195 (46,469)	54,742 (55,548)	12,340 (10,212)	
Average readmission cost at 90 days (\$)	4248 (10,977)			8522 (16,822)			2062 (2916)	10,555 (24,701)			9496 (34,975)			2325 (2805)	
Average number of readmissions	0.1935 (0.4016)			0.4118 (0.7123)			1.000 (1.414)	0.2727 (0.4671)			0.1739 (0.4910)			0.5000 (0.5774)	
Average LOS of readmission	14.33 (13.92)			39.00 (25.66)			6.00 (2.83)	40.33 (46.06)			46.50 (56.09)			3.00 (1.41)	
mRS	0–2 (n=12)			3–5 (n=6)			6 (n=1)	0–2 (n=3)			3–5 (n=7)			6 (n=6)	
Average ambulatory care cost at 90 days (\$)	376 (746)			484 (855)			0.00	167 (290)			652 (780)			0.00	
Average number of ambulatory care visits	1.000 (1.4771)			1.667 (2.2509)			0.00	0.6667 (1.1547)			2.8571 (2.4785)			0.00	
4–12-month societal cost†	14,883 (20,606)	16,196 (20,251)	22,821 (26,871)	30,055 (28,202)	70,478 (65,78)	110,901	—	Same as Intervention							—

CI = confidence interval; EVT = endovascular thrombectomy; mRS = modified Rankin scale; SD = standard deviation; SE = standard error; tPA = tissue plasminogen activator.

*Foothills Medical Centre and University of Alberta patients only.

†Estimated from BURST.

Table 2: Average 3-month costs and benefits calculated from the ESCAPE trial

	EVT		Control	
	N	Result (SD)	N	Result (SD)
Utility value	157	0.5901 (0.3944)	137	0.4474 (0.4218)
Average number of deaths	164	0.1037 (0.3058)	147	0.1905 (0.3940)
Index hospitalization (\$)	52	44,581 (37,956)	47	36,781 (39,400)
Cost EVT (\$)	4985		–	
Interventional radiologist (\$)	2265		–	
Emergency consult (\$)	78		78	
CTA read by radiologist	223		223	
Follow-up by stroke services (\$/ day)	45		45	
Physiatrist consult	49		49	
Readmissions (\$)	50	8924 (20,752)	38	9497 (30,423)
Ambulatory care (\$)	18	412 (760)	11	460 (674)
TOTAL COST (\$)	53,918		46,739	

EVT = endovascular thrombectomy; SD = standard deviation.

completed to examine the model uncertainty due to the variability of the micro-costing and utility data. A gamma distribution was applied to all the costing estimates and a normal distribution was used for the utility estimates.

RESULTS

Model Validation

The model replicated the 3-month trial outcomes exactly. In addition, the survival curves of each mRS stratified by EVT and control were identical after the initial 3 months. Therefore, the model simulated the expected survival establishing internal model validity. Finally, we ran our model with the inputs from the SWIFT-PRIME model¹³ and replicated the results to within 5% providing a further model and external validation.

Costs and Utility Scores

Patients who received EVT had a higher probability of being functionally independent poststroke compared to patients who received the best medical therapy (Table 1). Utility scores within mRS groups appeared similar between treatment and control groups (0.86 and 0.96 for EVT and control, respectively). For mRS 0–5 groups, utility scores ranged from 0.26 (mRS 4 EVT) to 0.96 (mRS 0 control).

Patients who received EVT in mRS groups 3–5, and 6 incurred higher tertiary care costs within the first 3 months compared to patients in the same mRS groups who received the best medical therapy (Table 1). For readmission costs, best medical therapy had higher costs for mRS 0–2, mRS 3–5, and mRS 6 patients (Table 1). Ambulatory care costs were slightly higher for functionally independent patients who received EVT compared to those who did not (\$376 compared to \$167). However, functionally dependent patients who received EVT had less ambulatory care costs compared to control (\$484 vs. \$652).

Base Case and 3-Month Results

Table 2 provides a summary of the average costs and benefits incurred by the different treatment arms within the first 3 months' poststroke. When the 3-month costs and health benefits are considered, the cost per death avoided is \$79,770, and the cost per QALY gained is \$201,243 (Table 3). Thus, while EVT is more effective, it was also associated with greater costs within the first 3 months compared to best medical therapy alone. When the time horizon is extended to the patient's lifetime and the societal perspective is adopted, overall, EVT treatment strategy dominates best medical therapy (i.e. EVT was more effective and less costly). EVT remained the dominant strategy when calculating both the cost per life year gained and the cost per QALY gained (Table 3).

Scenario Analyses

From the scenario analysis using MR CLEAN trial data,³ EVT remained the dominant treatment strategy (cost savings of –\$4464 per QALY gained with EVT compared to best standard care). Similarly, when the mRS score distribution at 90 days from SWIFT-PRIME was applied, EVT remained cost savings (–\$10547 per QALY gained when EVT is compared to standard care). When varying the mRS probabilities of the independent and dependent treatment groups, EVT remained the dominant treatment strategy at a 4% absolute change, but was no longer cost savings at a change of 5% (e.g. 5% fewer independent survivors and 5% more dependent survivors). Thus, if the real-world effectiveness of EVT 4% is less effective than the outcomes achieved in ESCAPE, EVT is no longer a cost-saving strategy although it remains economically attractive at a threshold of \$50,000 per QALY.

Time Threshold Analysis

When a time analysis was completed, EVT was associated with cost savings after the first year (Table 3). First-year costs for

Table 3: Summary of base case results and sensitivity analysis

Treatment	Cost (\$)	Average probability of being alive	Cost per death avoided	QALY	Cost per QALY gained
Three-month results from ESCAPE trial					
Control	46,739	0.81	79,770	0.11	201,243
EVT	53,739	0.90		0.15	
Treatment	Cost (\$)	Life years gained	Cost per life year gained	QALY	Cost per QALY gained
Lifetime results from model (base case)					
Control	192,426	3.69	Dominated	2.32	Dominated
EVT	192,334	5.23	(-82)	3.71	(-91)
Treatment	Cost (\$)	Life years gained	Cost per life year gained	QALY	Cost per QALY gained
Time threshold analysis (1-year results from model)					
Control	67,671	0.60	Dominated	0.34	Dominated
EVT	65,228	0.75	(-16,276)	0.50	(-15,376)

EVT = endovascular thrombectomy; QALY = quality-adjusted life year.

EVT were \$65,228 compared to \$67,671 for best medical therapy. EVT also showed a clinical benefit with greater QALYs and life years gained compared to best medical therapy.

Probabilistic Scenario Analysis

A probabilistic scenario analysis was completed and plotted (Figure 2). The majority of the simulations result in EVT being more effective than control. Fifty-four percent of simulations result in EVT being cost savings (both more effective and less costly), and only 2% of simulations suggested that EVT was inferior (both less effective and more costly) compared to best medical treatment. This variation is due to large variances in individual stroke patients and individual-level costs captured in detail with micro-costing data, as expected with a heterogeneous disease such as stroke and relatively small sample sizes is used to calculate the costing estimates (average sample size of 20 within each mRS category). When applying a willingness-to-pay threshold of \$50,000, the majority of scenarios fell below the threshold suggesting that EVT is cost-effective.

DISCUSSION

When comparing EVT to control over a lifetime horizon and using a societal perspective, EVT was associated with cost savings and an increase in effectiveness. Similar to other economic evaluations, EVT dominated, was more effective and less costly, compared to the best medical treatment strategy.

Three-month results showed that EVT was associated with greater costs and greater benefits. Specifically, the cost per death avoided was \$79,770 and the cost per QALY gained was \$201,243. Reporting of the economic outcomes completes the a priori outcome reporting of ESCAPE.²

The trial-based results highlight the increase in costs and resources required to treat patients with EVT within the first 3 months' poststroke. However, the time analysis showed that cost savings were realized within the first-year poststroke. The additional money incurred administering EVT and caring for EVT patients is recouped within the first year of stroke, and EVT continues to be cost savings over a patient's lifetime. However, if the EVT is 4% less effective than the effect size demonstrated in

ESCAPE, EVT was no longer the dominant treatment strategy. The feasible effect size is influenced by both the time to reperfusion and the quality of reperfusion. For systems of stroke care that are not able to achieve the effect size of ESCAPE, an early trial in which subsequent trials have improved upon, cost savings may not be realized.

Several other cost-effectiveness studies also reported that EVT was cost saving over a lifetime horizon compared to best medical therapy alone.^{9,11,13,14,17,18} However, some studies do not report EVT to be cost savings.^{7,8,10,12,16} Generally, the studies that did not find a cost savings used a shorter time horizon and did not consider costs borne by the patient/society (including lost patient productivity and unpaid caregiver time). Overall, all studies show that the cost per QALY gained to be less than the commonly accepted willingness-to-pay threshold of \$50,000 per QALY suggesting that EVT, if not cost savings, is still considered good-value-for-money.

The analysis presented herein used a societal perspective. It is important to note that the cost savings received from using EVT will not be entirely recouped by the healthcare system. Instead, some of the cost savings will go back to other social services, patients, and their caregivers. For example, the reduction in long-term care cost savings which, in Canada is both publicly and privately funded, will be shared by both the public purse and patient families. However, due to the limitations in the available data, the first 3 months of our model exclude costs such as caregiver burden and the economic gain of getting back to gainful employment. Thus, over time, our model will underestimate the total direct and indirect economic benefit of EVT and even more cost savings than projected within our analysis would be expected.

A major strength of our study is the use of a micro-costing approach to capture the healthcare system costs by EVT patients. This is considered the most precise form of healthcare costing and does not rely on group estimates, but rather provides individual patient-level costs.²¹ Costs reported in Table 1 are reflective of the costs borne by the ESCAPE trial participants and are not based on grouper costing estimates. Future studies and economic models could use these estimates when considering the costs of EVT.

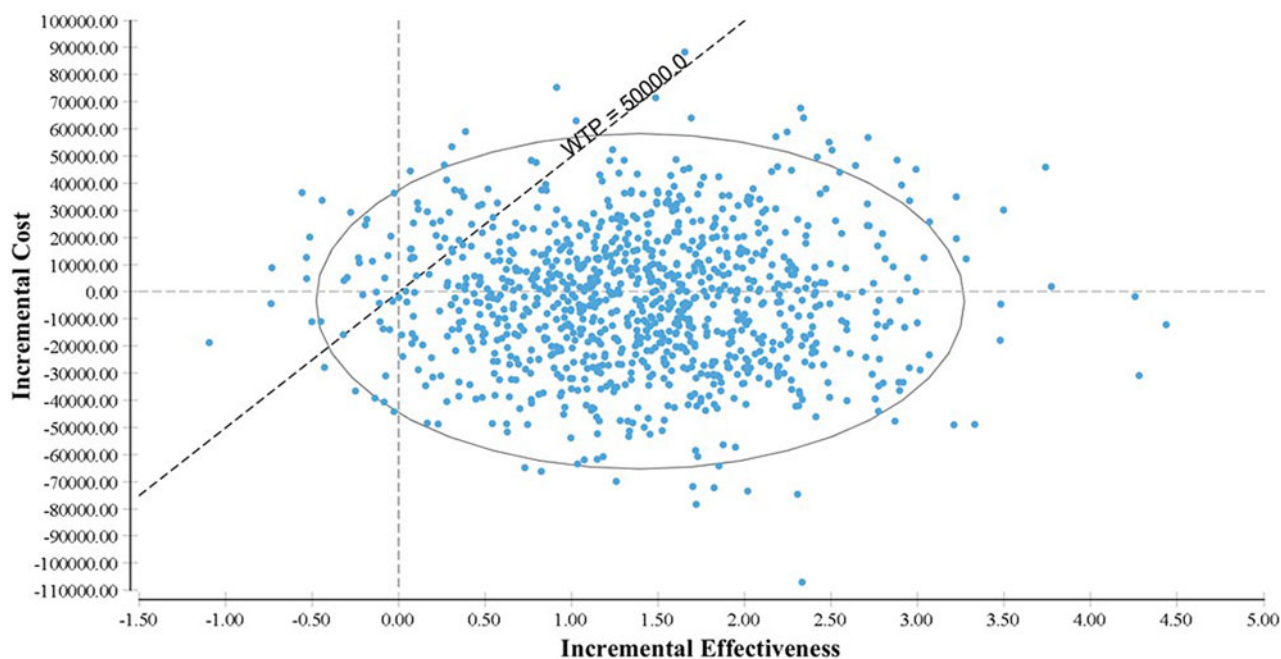


Figure Legend: WTP: Willingness to Pay Threshold = \$50,000
 Incremental effectiveness = change in QALYs
 Incremental cost = change in cost per change in QALY
 Blue dot = simulated cost per QALY (10,000)

Figure 2: Probabilistic sensitivity analysis.

This analysis indicates that the widespread implementation of EVT is associated with cost savings within a 1-year time horizon and beyond. All interventions that are both more effective and less costly should be considered for implementation by health systems. However, there are several implementation considerations that should be assessed when adopting EVT. First, the results of this model are a direct reflection of the ESCAPE trial. Our findings indicate that if systems achieve 4% less effect than observed in the ESCAPE trial, cost savings may not be achieved. Several foundational pieces of stroke care are required to achieve this result: coordination, fast door-to-needle times, comprehensive stroke teams, and a high level of expertise. Increasingly, the role of appropriate patient selection, time to reperfusion, and quality of reperfusion in achieving good outcomes, and thus achieving cost savings within the system, is being documented.^{30,31} Second, given the vast geographies in Canada, the USA, and other countries, transportation of patients to major stroke centers may also increase the costs associated with EVT. This component of the cost was not considered, and therefore could change the results of this analysis depending on the proportion of long-distance transports and the method of transportation in a given jurisdiction.

One limitation of this study was the small number of patients for which micro-costing data were obtained. Once these patients were stratified by treatment strategy and mRS score, there were several estimates with great variability within each stratum. Because Canadian and specifically Alberta data, where a universal single-payer healthcare system prevails, were used, the costs of care may not be generalizable to other locations. Similarly, this analysis assumes a base level of infrastructure is already in place. Costs for additional suites, beds, and diagnostic imaging

modalities, acute air, and ground patient transport were not captured in this analysis. These additional costs should be considered for systems where this infrastructure does not already exist.

CONCLUSIONS

Overall, EVT was shown to be a cost-saving treatment strategy. Real-world implementation factors that modify the clinical effect (time to treatment, coordination of services, technical expertise) should be the focus of healthcare systems as they implement EVT.

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STATEMENT OF AUTHORSHIP

FC provided all oversight and takes full responsibility for the research. LS, FC, and MH contributed to the conception and design. All authors critically revised the manuscript and approved the final manuscript.

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