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Endovascular Therapy (mechanical thrombectomy) for Ischemic Stroke

A Health Technology Assessment and Implementation Analysis

The Health Technology Assessment Unit, University of Calgary

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Abbreviations

ADAPT	Direct aspiration first-pass technique
AMSTAR	A Measurement Tool to Assess Systematic Reviews
BCBS TEC	Blue Cross Blue Shield Technology Evaluation Centre
BCEHS	British Columbia Emergency Health Services
CADTH	Canadian Agency for Drugs and Technology in Health
CASP	Critical Appraisal Sills Programme
CHEC	Consensus on Health Economic Criteria
CT	Computed Tomography
CTA	CT Angiography
CTAF	California Technology Assessment Forum
ER	Emergency room
EUnetHTA	European Health Technology Assessment Network
EVT	Endovascular therapy
FAST	Face-arm-speech-test
HQO	Health Quality Ontario
HTA	Health technology assessment
KGH	Kelowna General Hospital
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
NICE	The National Institute for Health and Care Excellence
QALY	Quality-adjusted life year
RCH	Royal Columbia Hospital
RCT	Randomized control trial
sICH	Symptomatic intracranial hemorrhage
TIAs	Transient Ischemic Stroke
tPA	Tissue plasminogen activator (alteplase)
VGH	Vancouver General Hospital
VicGH	Victoria General Hospital

Executive Summary

This report presents the findings and conclusions of a HTA and implementation analysis on the use of EVT for acute ischemic stroke in British Columbia. The primary policy question is: Should endovascular therapy (mechanical thrombectomy) (EVT) for the treatment of acute ischemic stroke be publicly funded in BC's health authorities?

Background: Ischemic stroke occurs when a blood clot blocks a blood vessel in the brain, preventing blood, and the nutrients it carries, from flowing into the brain. Stroke can be very debilitating with some patients able to continue their daily lives and others become confined to bed. The mortality rate is approximately 13%. In 2012, there were approximately 4900 incident cases of stroke in BC. Current care for ischemic stroke patients is tissue plasminogen activator, which dissolves the blood clot, and helps restore blood flow to the brain.

Issue: EVT is an emerging treatment option for ischemic stroke patients, and is now included in the Canadian Hyperacute Stroke Care Guidelines (establishing EVT as best practice). The procedure begins with an arterial puncture, typically in the groin, and the insertion of a delivery catheter through the femoral artery(1). The catheter is then advanced to the site of the occlusion using x-ray guidance. A guidewire with a thrombus retrieval device attached is then introduced through the delivery catheter and brought to the site of the blockage. The thrombus is then physically removed by the thrombus retrieval device, and blood flow is restored to the brain (recanalization). Eligibility criteria include: an ischemic stroke caused by a blockage in the main cerebral artery, CT or MR angiography to confirm the size and location of the occlusion(1), a favourable imaging profile defined by an ASPECTS score > 4 and evidence of moderate or good collateral, and time from onset within the required timeframe. The timeframe required varies by centre however, the Canadian guidelines recommend the procedure within 6 hours of symptom onset.

Methods: This HTA was completed following best-practice in evidence gathering and synthesis. This includes:

- A critical appraisal and summary of existing clinical effectiveness systematic review
- A systematic review of the cost-effectiveness literature
- An environmental scan of published HTAs, websites of HTA agencies, and emails to public health contacts in all Canadian provinces
- Key informant interviews with physicians and administrators across the province
- A systematic review of stroke patient experiences with traveling for care
- Focus groups with BC patients regarding their experience with traveling for care through the Patient Voices Network
- Implementation scenario development

Key Findings:

EVT resulted in approximately 2.23 times more patients with functional independence, no increases in sICH and non-statistically significant decreases in mortality. Based on the available evidence, EVT is clinically effective with no increases in adverse events. From the cost effectiveness studies, all studies suggested that with a time frame of at least 1 year, EVT is cost effective using a willingness to pay threshold of $50,000 per quality-adjusted life year (QALY).

HTAs completed in other jurisdictions conclude that EVT is clinically effective, cost-effective and support adoption in appropriate patients selected by an experienced clinician carried out by appropriately trained specialists with regular experience in intracranial endovascular interventions, in appropriate facilities and with neuroscience support. In Canada, of the eight provinces that responded, all of them, except for Prince Edward Island (PEI), are currently offering EVT within their province and actively seeking to expand coverage to the entire province.

In BC, currently three hospitals [Vancouver General, Royal Columbia, Victoria General] are treating ischemic stroke patients with EVT. Key informants highlighted challenges to the development of EVT including: the geography of BC making transport to an EVT centre challenging within a 6-hour time-window, the location and lack of staff to support 24/7 service, and the demand for interventional suites. Patients identified considerations including timely transportation, costs, effective repatriation, and information exchange. Patients also noted the experience of rapid transport to a major centre is frightening for families and they are deeply appreciative of efforts to include them in the family member's care.

Four implementation scenarios were considered to represent a broad range of adoption possibility. The four scenarios include:

Scenario	Clinical Impact	Budget Impact
I. No EVT	• Number of patients treated with EVT: 0 • mRS distribution: same as current practice	• Estimated budget impact: $0.0M
II. VGH, RCH and VicGH continue to operate "as is" without patient transport coordination	• Number of patients treated with EVT: 311 • 54 more independent survivors compared to current care	• Estimated budget impact: $5.6M
III. VGH, RCH and VicGH operating with increased catchment due to coordinated transport system	• Number of patients treated with EVT: 445 • 79 more independent survivors compared to current care	• Estimated budget impact: $10.7M
IV. VGH, RCH, VicGH, and Kelowna General Hospital (KGH) operating with increased catchment due to coordinated transport system	• Number of patients treated with EVT: 445 • 79 more independent survivors compared to current care	• Estimated budget impact: $10.4M (excluding program development costs that may be required in Kelowna)

1.0 Purpose

The purpose of this health technology assessment (HTA) is to summarize the current evidence on endovascular therapy (mechanical thrombectomy [EVT]) for acute ischemic stroke. The report summarizes evidence on the effectiveness, cost-effectiveness, patient experience and system

feasibility of EVT in comparison to available alternatives for acute ischemic stroke. Based on the evidence, reasonable implementation scenarios are presented with feasibility considerations.

2.0 Research Questions

The primary policy question is:

- Should endovascular therapy (mechanical thrombectomy) (EVT) for the treatment of acute ischemic stroke be publicly funded in BC?

The primary research objectives are:

- To determine the safety and effectiveness/efficacy of EVT for the treatment of acute ischemic stroke
- To determine the cost-effectiveness of EVT for the treatment of acute ischemic stroke
- To determine the burden of illness, patterns of care and capacity in British Columbia (BC) as it relates to EVT and the treatment of acute ischemic stroke
- To understand patient experiences of travelling to receive specialized care and document considerations to inform possible implementation
- To determine possible budget impacts of possible EVT implementation scenarios

3.0 Background Information

3.1 Stroke

Stroke occurs when blood flow to the brain is disrupted resulting in a reduction of oxygen and nutrients flowing to the brain(2). This ultimately leads to cell death and reduced brain function. There are two types of stroke: hemorrhagic stroke and ischemic stroke. Ischemic stroke ranges from transient and mild (transient ischemic attack) to severe and fatal(2). The mechanism of the stroke differentiates the type of stroke. Hemorrhagic stroke occurs when an artery to the brain breaks open, resulting in bleeding into the brain whereas an ischemic stroke occurs when a blood clot blocks a blood vessel in the brain. This physical blockage prevents blood, and the nutrients it carries, from flowing into the brain. When the blockage is transient lasting minutes, and most often less than half an hour, the patient rapidly recovers from their neurological deficits and the event is termed a transient ischemic attack, or “mini-stroke”. The remainder of this report will focus on ischemic strokes specifically(3).

3.2 Ischemic Stroke Symptoms and Diagnosis

Symptoms of ischemic stroke depend upon which part of the brain is affected. The most common symptoms are identified using the face-arm-speech-test (FAST), which is a tool that has been developed to enable medical first responders, EMTs, paramedics and members of the public to recognize acute stroke quickly and efficiently(4). Facial asymmetry, drooping of one arm and disturbance of speech are some of the indications of a stroke that are included in the checklist. The Heart and Stroke Foundation has launched a national campaign to help educate Canadians on the signs of stroke with radio and online segments, highlighting the importance of acting FAST(2).

Diagnosis of the type of stroke is critical in order to assess eligibility of the patient for various stroke treatments. Specifically, hemorrhagic stroke cannot be treated with alteplase (tissue plasminogen activator (tPA)) whereas ischemic stroke is optimally treated with tPA for appropriate patients(4). The only dependable method of differentiation between hemorrhagic and ischemic is through brain imaging techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)(4).

3.3 Ischemic Stroke Burden

The incidence of stroke in Canada is estimated to be 50,000 annually, and is the third leading cause of death in Canada(2). Of these strokes, about 80% are ischemic(5). It is estimated that stroke costs the Canadian economy $3.6 billion each year(2). In British Columbia, strokes cause a significant amount of death and disability. In 2012 there were approximately 4,900 cases of hospitalized stroke in BC(6). The mortality rate for these cases is 13%(6). Estimates from the BC Ministry of Health show that there were approximately 5,500 stroke cases in BC in 2015.

3.4 Outcomes of Ischemic Stroke

One of the primary outcomes of an ischemic stroke is a change in functional status. Clinicians and researchers commonly use the modified Rankin Scale (mRS) to differentiate patient functional status. This scale has seven levels (0-6) where 0 is no symptoms and 6 is death(7). Functional independence is defined as levels 0-2, and functional dependence is defined as levels 3-5 (Table 1). Physical changes associated with stroke include: aphasia (communication difficulties), vision loss, hemiparesis (one sided paralysis or weakness), dysphagia (swallowing

difficulties), imbalance or incoordination, and hemi-sensory loss (reduced or absent sensation on one side of the body) (2).

Table 1 modified Rankin Scale (mRS) Levels(7)

	Level	Level Description
Functional independence	0	No symptoms
	1	No significant disability despite symptoms; able to carry out all usual duties and activities
	2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
Functional dependence	3	Moderate disability; requiring some help, but able to walk without assistance
	4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
	5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
	6	Dead

3.5 Ischemic Stroke Treatment Options

The current standard of care for ischemic stroke patients is tPA which is administered through an IV into the arm(8). tPA dissolves the thrombus which helps restore the blood flow to the brain. Within 4.5 hours of stroke onset, tPA can be administered; however, there is strict eligibility criteria that ischemic stroke patients must meet before receiving the treatment. Some of the exclusion criteria include surpassing the time window or evidence of an intracranial hemorrhage(9).

3.6 Emerging Ischemic Stroke Treatment Options

The emerging treatment in ischemic stroke care is endovascular therapy or mechanical thrombectomy (EVT). This treatment begins with an arterial puncture, typically in the groin, and the insertion of a delivery catheter through the femoral artery(1). The catheter is then advanced to the site of the occlusion using x-ray guidance. A guidewire with an attached thrombus retrieval device is then introduced through the delivery catheter and brought to the site of the blockage. The thrombus is then physically removed by the thrombus retrieval device, and blood flow is restored to the brain (recanalization). Patients usually have local anesthetic, but general anesthesia may be used. tPA is often administered prior to treatment.

Eligibility criteria include: an ischemic stroke caused by a blockage in the main cerebral artery, CT or MR angiography to confirm the size and location of the occlusion(1), a favourable imaging profile defined by an ASPECTS score >4, evidence of moderate or good collateral, and time from onset within the required timeframe. The timeframe required varies by centre with some stroke centres in Canada only providing patients with EVT if the procedure can be done within 3.5 hours. Others have pushed the time limit to 12 hours of stroke symptom onset. The best outcomes are achieved if the procedure is done rapidly, ideally within 90 minutes of the baseline CT or MR scan.

EVT is now included in the Canadian Hyperacute Stroke Care Guidelines establishing EVT as best practice in Canada (10). The guidelines further specify that EVT should be offered within a coordinated system of care, that patient selection should be based on CT head and CT Angiography (CTA), and that eligible patients should be treated within six hours of symptom onset(10). The guidelines recommend EVT be available both to patients who are and are not eligible for IV tPA. For patients who are eligible for both treatments, the guidelines recommend treating the patient with IV tPA while preparing the angiography suite for EVT. In regards to device selection, the guidelines recommend retrievable stents as the first-choice EVT device; however, other devices may be used based on local protocols and expertise. Finally, the guidelines state that elective general anesthesia and intubation should not be used in most patients.

There are several different techniques and thrombus retrieval devices available (Table 2) (11).

Table 2 Summary of Clot Retrieval Devices (11)

	Name	Manufacturer	Device Type	Health Canada Approval Date	Currently used in Canadian Practice	Cost (2016 $CDN)
Licensed in Canada	Penumbra Aspiration System	Penumbra Inc.	Aspiration Catheter	2008-10-09	Yes	1,973.68*
	Solitaire 2 Revascularization Device	Medtronic	Stent Retriever	2015-09-09	Yes	4,985.00
	Trevo ProVue Retrieval System	Stryker	Stent Retriever	2013-04-25	Yes	5,950.00
Not licensed in Canada	• MERCI Coil (Concentric Medical Inc.) [no longer authorized for sale in Canada] • Aperio Thrombectomy Device (Acandis GmbH & Co KG) • EmboTrap Revascularization Device (Neuravi Ltd.) • ERIC Retrieval Device (MicroVention Europe) • MindFrame Capture LP Revascularization Device (Medtronic) • pREset LT Device (Phenox GmbH) • REVIVE Self Expanding Thrombectomy Device (Medos International SARL)					

*Estimated from literature

4.0 Clinical Effectiveness: Critical Analysis of Published Systematic Review and Meta-Analysis

Summary

- We completed a critical appraisal of a systematic review published in December 2015
- The systematic review is of high quality
- Eight RCTs were identified in the review; however, the analysis of this report only includes the five completed trials with the current protocol for EVT and new generation of stent retrievers
- EVT resulted in approximately 50% more patients with functional independence, no increases in sICH and non-statistically significant decreases in mortality
- Authors concluded that EVT should be considered as a primary treatment option for appropriately selected ischemic stroke patients

4.1 Purpose:

To assess the clinical effectiveness of EVT.

4.2 Methods:

A recent systematic review and meta-analysis of randomized control trials (RCT) of EVT in comparison with best medical treatment for acute ischemic stroke was identified(12). A quality assessment was completed using a validated tool (A Measurement Tool to Assess Systematic

Reviews" (AMSTAR) (13)). AMSTAR assesses literature search quality and reporting standards, while addressing questions on study design, methods, and publication bias. A summary of the review and meta-analysis findings was completed. An update search ran from April 2105 to June 2016 to ensure that all current evidence was captured; no additional RCTs were identified.

4.3 Results:

The systematic review and meta-analysis by Balami et al. was published in December, 2015. (12). The study was deemed to be of high quality (Table 3). The primary aim of this study was to compare thrombolysis to EVT for acute ischemic stroke treatment.

Table 3 AMSTAR Checklist for Systematic Review of EVT Effectiveness(13)

Question	Inclusion (Yes, No, Can't Answer, Not Applicable)
1. Was an "a priori" design provided?	Yes
2. Was there duplicate study selection and data extraction?	Yes
3. Was a comprehensive literature search performed?	Yes
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes
5. Was a list of studies (included and excluded) provided?	Yes
6. Were the characteristics of the included studies provided?	Yes
7. Was the scientific quality of the included studies assessed and documented?	Yes
8. Was the quality of the included studies used appropriately in formulating conclusions?	No
9. Were the methods used to combine the findings of studies appropriate?	Yes
10. Was the likelihood of publication bias assessed?	Yes
11. Was there conflict of interest included?	Yes
Total Score:	**10/11**

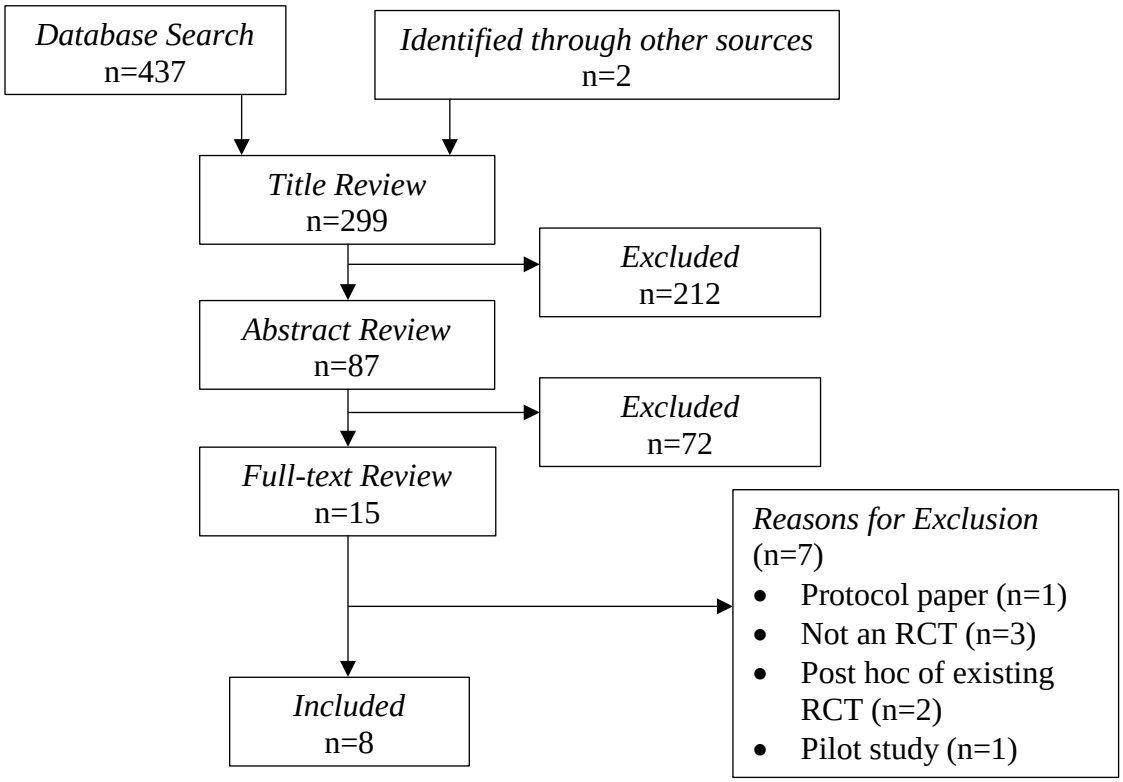
The systematic review searched Medline, EMBASE, Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials from January 1995 to May 2015(12). Terms capturing the disease (e.g. brain ischemia, acute ischemic stroke, cerebral infarction, etc.), the intervention (e.g. endovascular therapy, mechanical thrombectomy, etc.), and study design (randomized control trial) were combined using the Boolean operator "AND". Titles and abstracts were reviewed independently by four reviewers. Full text review and data extraction was completed independently by five reviewers. Table 4 summarizes the inclusion/exclusion criteria applied.

Table 4 Inclusion and Exclusion criteria used by Balami et al.(12)

Inclusion Criteria	Exclusion Criteria
• RCT published in peer reviewed journal • Study population >20 participants • Patients had acute ischemic stroke due to major vessel occlusion and had received treatment with endovascular intervention, IV thrombolysis or best medical care, or endovascular treatment with IV thrombolysis • Major vessel occlusion was confirmed by CT angiography or MR angiography • Studies used old and/or new generation EVT devices in at least 25% of cases • The studies reported the following outcomes: functional outcome (mRS), all-cause mortality, symptomatic intracerebral hemorrhage, and risk estimate	• Not RCT or not published in peer review journal • <20 study participants • Patients had acute ischemic stroke not due to major vessel occlusion and did not receive treatments with endovascular intervention, IV thrombolysis or best medical care, or endovascular treatment with IV thrombolysis • CT angiography or MR angiography not used to confirm major vessel occlusion • Studies that did not use old or new generation EVT devices – pure manipulation of the clot with a guide wire, without use of EVT device, was not considered EVT • Did not report the following outcomes: functional outcome (mRS), all-cause mortality, symptomatic intracerebral hemorrhage, and risk estimate

Two hundred and ninety-nine studies were reviewed after de-duplication (Figure 1). During title and abstract review, fifteen studies were selected by reviewers and proceeded to full text review. Eight studies were included in the final data extraction and analysis (14-21).

Figure 1 Flowchart of Included and Excluded Studies from Balami et al.(12)



The included studies were: IMS III, MR RESCUE, SYNTHESIS, ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT, and SWIFT PRIME. The primary outcome used for the meta-analysis was clinical function independence (mRS 0-2) at 90 days(12). Secondary outcomes include: spontaneous intracerebral hemorrhage (sICH) and all-cause mortality. Studies varied with respect to study location, number of participants, and mean age. Table 5 summarizes the eight RCTs.

Table 5 Summary of Included RCTs in Clinical Effectiveness Systematic Review

Acronym	Location	Population	Intervention	Comparator	Primary Outcome	N
IMS III, 2013 (14)	North America, Europe, Australia	• Age 18-82 • tPA within 3 hours after symptom onset • NIHSS ≥ 10 • Score of 8 to 9 with CT angiographic evidence on occlusion of the first segment of the middle cerebral artery, internal carotid artery, or basilar artery	• All participants received IC tPA at a standard dose • Those with treatable vascular occlusion received endovascular intervention with either the Merci receiver, Penumbra System, Solitaire stent, or endovascular delivery of tPA by means of the MicroSonic SV infusion system or microcatheter • Procedure began within 5 hours of stroke onset	IV Tpa	Proportion of participants with mRS≤2: 40.8% EVT group and 38.6% in control group. Difference was not significant, and trial was stopped early due to futility.	• Intervention: 434 • Control: 222
MR RESCUE, 2013 (15)	North America	• Age 18-85 • NIHSS of 6-29 • Large vessel, anterior-circulation ischemic stroke • Patients who were treated with IV tPA without successful recanalization were eligible if MR or CT angiography after the treatment showed a persistent target occlusion	• Mechanical embolectomy with either the Merci Retriever or Penumbra system	Standard medical therapy	Unadjusted mRS at 90 days: Embolectomy, Penumbral=3.9; Standard Care Penumbral=3.4; Embolectomy, Nonpenumbral=4.0, Standard Care, Nonpenumbral=4.4 No significant difference	• Intervention: 70 • Control: 57

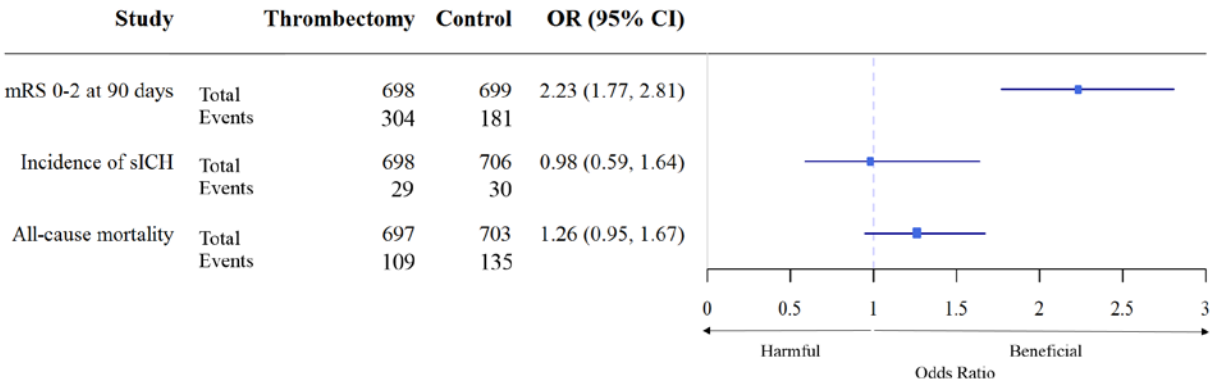
SYNTHESIS, 2013 (16)	Europe	• Age 18-80 • Intracranial hemorrhage ruled out • Sudden focal neurological deficit attributable to cerebral stroke • IV tPA within 4.5 hours of symptom onset • EVT within 6 hours of symptom onset	• Patients assigned to treatment group did not receive IV tPA • Pharmacologic or mechanical thrombosis or both • Pharmacologic thrombosis with microcatheter • Mechanical thrombosis could involve use of micro-guidewire to facilitate disintegration, systems to capture and extract, or more complex systems to crush and aspirate thrombus • Solitaire, MERCI, Penumbra and Trevo retrievers used	IV tPA	Odds ratio of mRS at 90 days without disability (0-1): 0.82 (0.53 to 1.27). Adjusted odds ratio: 0.71 (0.44 to 1.14)	• Intervention: 181 • Control: 181
ESCAPE, 2015 (17)	North America, Europe, South Korea	• 18+ • Functioning independently (Barthel Index >90) • IV tPA within 4.5 hours of ischemic stroke symptom onset • CT and CTA performed to identify patients with a small infarct core, occluded proximal artery in the anterior circulation, and moderate-to-good collateral circulation	• Endovascular treatment plus guideline-based care (intravenous tPA) • Solitaire stent retriever used	Guideline based care alone	MRS at 90 days: adjusted odds ratio 3.1 (2.0-4.7)	• Intervention: 165 • Control: 150
EXTEND-IA, 2015 (18)	Australia and New Zealand	• Could receive IV tPA within 4.5 hours of ischemic stroke onset • Occlusion of the internal carotid artery, or the first or second segment of the middle cerebral artery • Established with CTA • Endovascular therapy initiated within 6 hours and completed within 8 of stroke onset • No restrictions on age or severity • MRS<2	• TPA (0.9mg per kg) plus endovascular therapy • Solitaire stent retriever used	TPA-only	Median reperfusion at 24 hrs – adjusted odds ratio 4.7 (2.5 to 9.0)	• Intervention: 35 • Control: 35

MR CLEAN, 2015 (19)	Europe	• 18 years of age or older • Acute ischemic stroke • Intracranial occlusion in the anterior circulation artery • Intraarterial treatment within 6 hours of stroke onset • Occlusion of the distal, middle, or anterior cerebral artery • Established with CTA, MRA, DSA • Score of >2 NIHSS	• Arterial catheterization with microcatheter to the level of occlusion and delivery of a thrombolytic agent, mechanical thrombectomy, or both • Intra-arterial treatment (IAT): Intra-arterial tPA or urokinase, and/or mechanical treatment	Standard of care	MRS Adjusted odds ratio: 1.67 (1.21 to 2.30)	• Intervention: 233 • Control: 267
REVASCAT, 2015 (20)	Spain	• 18-85 years • Occlusion in the proximal anterior circulation • Treated within 8hrs of symptom onset • MRS <1 • NIHSS >6	• Medical therapy (including intravenous tPA when eligible) and endovascular treatment with the Solitaire stent retriever	Medical therapy alone	MRS at 90 days: adjusted odds ratio 1.7 (1.04 to 2.7)	• Intervention: 103 • Control: 103
SWIFT PRIME, 2015 (21)	North America and Europe	• Age 18-80 • Acute Ischemic Stroke • MRS <1 • NIHSS >8 • tpA within 4.5 hours • Harbor imaging confirmed occlusions of proximal, anterior circulation arteries • Do not have a large, established care infarct • Treatment within 6 hours of symptom onset	• Neurovascular thrombectomy with Solitaire FR or Solitaire 2 and IV tPA	IV tPA alone	MRS at 90 days – odds ratio not reported (median 3 vs 2)	• Intervention: 98 • Control: 98

Figure 2 summarizes the results from the 2015 trials sub group analysis from the meta-analysis (ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT, and SWIFT PRIME). The three earlier trials are not presented in this figure, as they were deemed to not be reflective of current practice and utilized the older generation of technology (complete pooled analysis in Appendix A). For this sub group analysis, a fixed effect model was used.

Based on the pooled meta-analysis, the odds of being functionally independent with EVT are 2.23 times greater than the odds of being functionally independent with current care (12). There is no difference in the incidence of sICH, and the findings of a mortality benefit with EVT are not statistically significant.

Figure 2 Results of Primary and Secondary Outcomes of the Meta-Analysis



4.4 Limitations

The systematic review and meta-analysis by Balami et al. was the highest quality, most current assessment of clinical effectiveness identified in the search. This study includes all RCTs examining the use of EVT for acute ischemic stroke from January 1995 to May 2015. However, as the 3 pre-2015 trials do not use the current technology and practice, the meta-analysis of the 2015 trials was presented as the base case with a complete meta-analysis of all 8 trials (pre-2015 and 2015) assessed in sensitivity analysis.

The Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration pooled patient-level data from the five 2015 trials (as opposed to the aggregate data pooled in our analysis). The results of the two approaches are very similar: OR of 2.35 (95% CI:

1.85-2.98; p<0.0001) for functional independence (mRS score 0-2) at 90 days (22) and non-significant findings for incidence of sICH and mortality.

4.5 Conclusion:

Overall, the systematic review was deemed to be of high quality, and an updated search did not identify any new trials. The conclusion from the systematic review and meta-analysis was that there are improved functional outcomes when using EVT compared to the standard of care alone for treatment of ischemic stroke(12). The secondary analysis showed that EVT did not increase the risk of symptomatic intracranial hemorrhage (sICH). There is a trend towards decreased 90-day mortality with EVT although the finding was not statistically significant. These results were reflected in both the overall analysis and the sub group analysis of the 2015 trials. Authors concluded that EVT should be considered as a primary treatment option for ischemic stroke patients.

5.0 Cost-effectiveness: A Systematic Review of the Literature

Summary

- We completed a systematic review of the cost-effectiveness of EVT for ischemic stroke
- 16 studies were identified including 9 cost effectiveness analyses and 7 cost analyses; the cost-effectiveness models used a combination of the old and new generation stents thus an analysis of the 5 studies considering the new generation stents was completed.
- For the cost analyses, most studies suggested that EVT with a stent retriever was the most expensive treatment option, but also resulted in the best clinical outcomes
- From the cost effectiveness studies, all studies suggested that with a time frame of at least 1 year, EVT is cost effective using a willingness to pay threshold of $50,000 per quality-adjusted life year (QALY).

5.1 Purpose:

To establish the cost-effectiveness of EVT compared to the standard of care for patients with acute ischemic stroke.

5.2 Methods:

A systematic review of the cost effectiveness of EVT was performed. MEDLINE, EMBASE, HTA Database, NHSEED and EconLit were searched from inception until June 3, 2016. A librarian developed the search strategy. Terms capturing the process of EVT (e.g. thrombectomy, clot retrieval, stent-assisted, clot disruption) were combined using the Boolean operator “OR”.

Terms reflecting the health state (ischemia, brain, cerebral, stroke) were also combined using the Boolean operator "OR". To capture economic evaluations in our search, terms such as "cost", "economic" and "cost-effectiveness" were combined. Studies were limited to those including human models and availability in either English or French language. The detailed search strategy is in the Appendix B.

The abstracts were screened in duplicate. Abstracts proceeded to full text if they were: economic evaluations of EVT, cost-analysis of EVT, or business cases for EVT. Abstracts were excluded if they: were not economic evaluations, stroke treatment other than EVT, and did not include patients with ischemic stroke. All abstracts selected by either reviewer were included in the full-text review. Full text articles were also screened independently and in duplicate. Discrepancy between reviewers was resolved through consensus (κ=0.849). Table 6 shows a full break down of the inclusion/exclusion criteria.

Table 6 Inclusion/Exclusion Criteria for Systematic Review of Cost-effectiveness Analyses

Inclusion Criteria	Exclusion Criteria
• Economic Evaluations (Cost-effectiveness, cost-utility, cost-minimization, cost-benefit) • Cost-analysis • Business cases • Rapid EVT, mechanical thrombectomy, etc. • Ischemic stroke	• Other study designs • Not rapid EVT (other stroke treatments) • Not ischemic stroke (thrombectomy for other parts of the body or other types of stroke)

For all studies, author, year, country, population, type of model, perspective, model details (time horizon, discount rate), outcome assessed, input details (clinical and cost inputs), source of clinical inputs, currency, primary result, assessment of uncertainty and general conclusions were extracted in duplicate using a standardized data extraction form. Discrepancies between reviewers during data extraction were resolved through consensus.

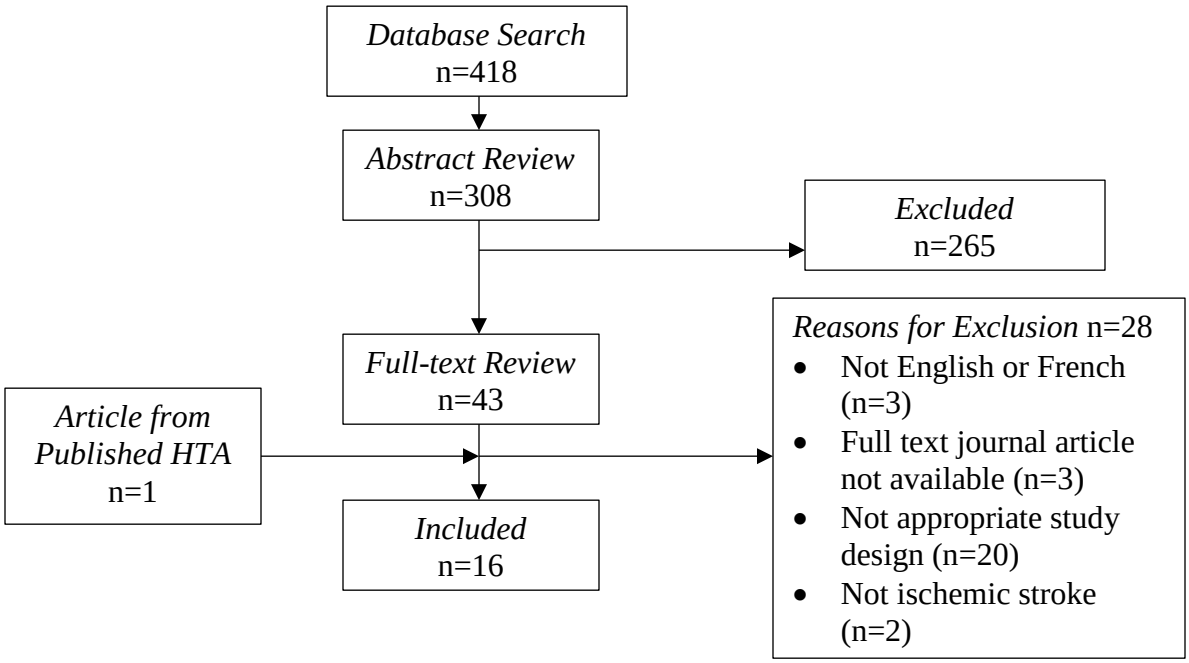
To assess the quality of the economic evaluations the Consensus on Health Economic Criteria (CHEC) checklist was applied(23). Quality assessment was completed in duplicate with discrepancies being resolved through discussion. Using this checklist, each study was assessed based on whether or not they fit the nineteen recommended criteria (e.g. appropriate valuation of outcomes, sensitivity analysis, appropriate economic study design). For each criterion, a study

was assigned one point for appropriately addressing the criterion, and 0 points if it did not. For certain criterion, not applicable (N/A) was assigned to studies that were cost-analyses versus cost-effectiveness studies. A final tally out of a possible 19 points was calculated for each study. All studies were of moderate to high quality. A breakdown of the quality assessment can be found in Appendix B, Table 1.

5.3 Results:

A total of 418 abstracts were identified with the literature search, 308 were reviewed after de-duplication. Of those abstracts, 265 were excluded and 43 proceeded to full-text review (Figure 3). One study was added through hand searching. Ultimately, sixteen studies were included (3, 24-38). Appendix B, Table 2 provides a summary of all of the identified studies' characteristics.

Figure 3 Flowchart of Included and Excluded Studies



5.3.1 Cost-analysis

Seven studies performed cost-analyses and reported different costs for providing EVT. The studies are grouped into three broad categories:

Cost of device/Approach: Three studies reported the cost of the devices and the cost of different approaches for performing EVT (31, 32, 35). Comai et al. included cost inputs for all angiographic devices used to perform EVT in order to compare direct aspiration first-pass technique (ADAPT) and stent-assisted thrombectomy (includes catheter and stent retriever). The differential cost between the ADAPT technique and the stent-assisted technique is €-2,747.82 (2013 Euros) ($-4,084.71 CDN 2016), with an estimated cost saving of €32,226 (2013 Euros) ($47,904.89 CDN 2016)(32). Turk et al. (2014) analyzed the total procedural cost, including costs of procedural complication. The average costs of EVT using a stent retriever and EVT using a Penumbra aspiration catheter were compared. The results showed an incremental cost of $4,862.91 (2012 USD) for the stent retriever compared to Penumbra(31). Lastly, Turk et al. (2015) reported the average total cost for three patient groups: patients treated with the Penumbra aspiration catheter approach, patients treated with the stent-retriever approach, and patients treated with the ADAPT technique. The average cost for Penumbra was $47,673, stent-retriever was $46,735 and ADAPT was $31,716 (2013 USD)(35). The difference in average total costs between the Penumbra and stent retriever groups was not significant. Authors suggested that the increased costs in the Penumbra system compared to stent retriever group may be attributable to a higher primary device success rate when using a stent retriever, as well as the requirement for fewer and cheaper additional devices in the case of failure.

Procedural device cost of EVT: One of the included studies had the primary objective of determining the procedural device cost of EVT(28). Total procedural device cost was calculated using list prices for the devices used (catheters, thrombectomy devices, guide wires, etc.); however, consumable goods, staff, and imaging equipment costs were not included. In comparison to previous technologies, procedural device cost using Solitaire or Trevo stent retrievers for EVT was significantly higher than performing thrombectomy with a non-stent retriever. While cost of EVT was $13,419 (2014 USD) compared to $9,308 (2014 USD), the use of the stent retrievers provided significantly higher rates of complete reperfusion(28).

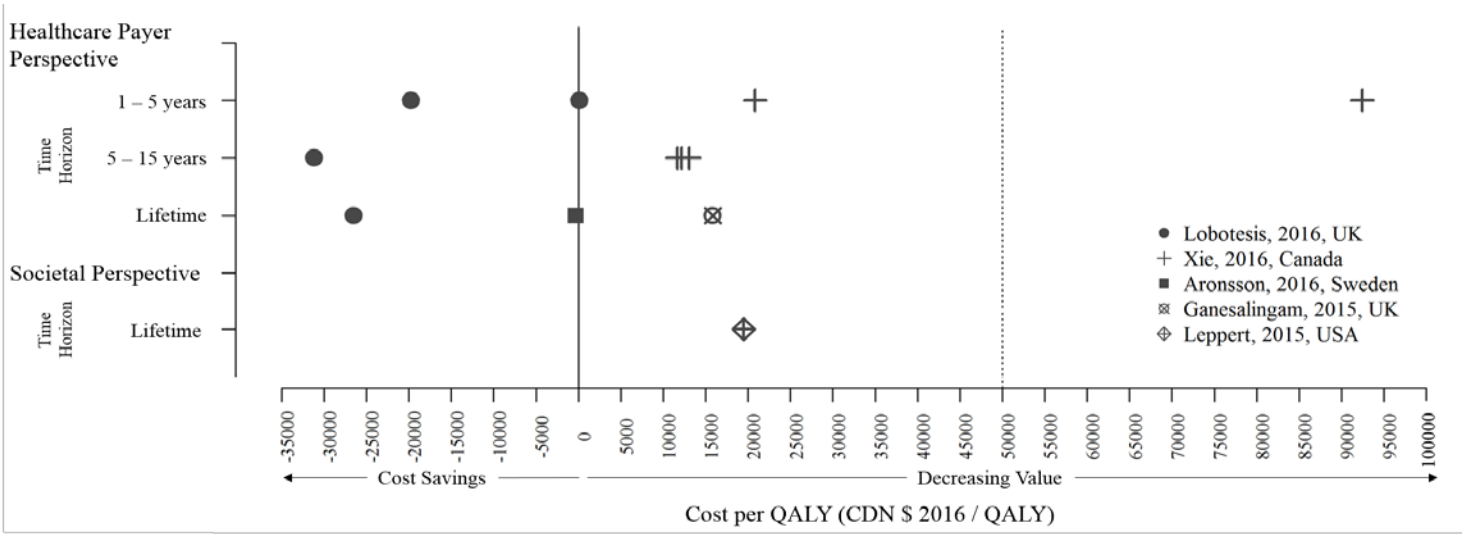
Hospitalization costs of EVT: Three studies reported the hospitalization costs for patients treated with EVT (26, 29, 30). All studies were from the USA. The costs in this analysis included cost of discharge location, hospital charges and cost of EVT therapies. The study by Brinjikji et al. compared the cost of EVT with the average Medicare reimbursement payment ($36,999 vs $22,075 (2008 USD))(26). Cost estimates were based on the mean cost-to-charge ratio for each patient's hospital, and total hospital charges were used. All costs were inflated to 2008 USD. The authors conclude that although Medicare payments have not been adequate in reimbursing the hospitalization costs, the improved patient outcomes associated with EVT may compensate this later through decreases in long-term costs. Simpson et al. compared costs for patients treated with EVT and patients treated with IV tPA alone, and found that EVT patients incurred $9,500 (2012 USD) more in costs than tPA patients(29). Lastly, Rai et al. found a net financial gain of $476 (2008 USD) associated with EVT, compared to the net financial loss of $1,752 (2008 USD) associated with tPA; however, these results were not significant(30).

5.3.2 Cost-effectiveness

Nine of the sixteen included studies reported the cost-effectiveness of EVT (3, 24, 25, 27, 33, 34, 36-38); however, only five of the studies were based off the 2015 clinical evidence(33, 34, 36-38). Of these five studies, two are from the UK, one is from Sweden, one is from Canada, and one is from the USA. Four of the studies considered a public-payer perspective, and only one considered a societal perspective. Further, four of the five studies considered a lifetime horizon. None of these studies included pre-hospital transportation costs. The primary outcome for these studies was the cost per quality adjusted life year (cost per QALY). Several studies reported multiple cost-effectiveness ratios resulting from sensitivity analyses varying the time horizon. Figure 4 plots the reported cost per QALY in 2016 Canadian Dollars for the five recent studies (a figure including all nine of the identified studies can be found in Appendix B). The cost-effectiveness ratios are grouped by time horizon used in each analysis; all cost-effectiveness ratios reported in each study are included with the symbol representing the study. From the figure, two of the studies (four data points) found a cost-savings for EVT(36, 37). The remaining studies found a positive cost per QALY associated with EVT(33, 34, 38). When the commonly adopted threshold of $50,000 per QALY gained is considered, all but one of the cost-effectiveness ratios are more attractive than $50,000 per QALY.

The estimate greater than $50,000 per QALY is from the Canadian study at a 1-year time horizon using a Healthcare Payer Perspective(38). While this estimate is greater than $50,000 per QALY, the authors determined that this value dropped below the threshold by a three-year time horizon. All other estimates from this study using 3, 5, 10 and 15-year time horizons are less than $50,000 per QALY. The overall conclusion from this Canadian study were that EVT is cost-effective compared with IV thrombolysis alone for acute ischemic stroke patients.

Figure 4 Summary of Cost per QALY Findings



5.4 Limitations:

Due to the lack of variation in the incremental cost-effectiveness ratios by context, the presence of a Canadian cost-effectiveness study (Ontario), as well as the comparison of Ontario estimates with unpublished estimates available from Alberta, a primary economic model was not developed. Furthermore, because BC does not have activity based costing, a BC specific direct hospital cost estimate could not have been determined. The effectiveness of EVT has also not been measured in the BC context meaning that the same trial-based estimates of effectiveness would be the most appropriate estimate. Using the trial-based effectiveness and the activity-based costing from the ESCAPE trial is the same methodology utilized by the six identified cost-effectiveness studies above, as well as the unpublished Alberta economic model. Overall, it is highly unlikely that a model incorporating BC would yield different results as the physician fee and stent costs are comparable to both the Ontario and Alberta estimates.

5.5 Conclusions:

The cost-effectiveness studies of EVT for ischemic stroke are generally of good quality and a robust body of evidence has been reported (9 cost-effectiveness studies and 7 costing studies). Of the studies that reported costs associated with EVT only, most acknowledged that EVT with a stent retriever resulted in the highest hospitalization and procedural costs; however, these devices were also associated with improved patient outcomes. EVT appears to be good value for money when a threshold of $50,000 per QALY gained is adopted. All reported cost-effectiveness ratios were less than $50,000 per QALY except when a time horizon of one year and a public payer perspective were used in the Canadian context. Two studies using effectiveness from the 2015 trials, adopting a public perspective and a variety of time horizons, reported cost-savings when using EVT.

6.0 International Scan

Summary

- Four large health technology assessment organizations and Google were searched for evidence syntheses on EVT
- Seven reports were identified: two from Canada, two from Australia, one from the USA, one from the UK and one from Europe
- The reports pre-2015 noted that insufficient evidence was available and new evidence was emerging
- All of the reports capturing the 2015 RCTs concluded that EVT appeared safe and clinically effective
- Those that examined costs also noted that EVT appeared cost-effective
- Several reports also noted the need for appropriate selection of patients by an experienced clinician and that EVT should only be carried out by appropriately trained specialists with regular experience in intracranial endovascular interventions, with appropriate facilities and neuroscience support

6.1 Purpose

To synthesize existing evidence syntheses on EVT for acute ischemic stroke, and provide insight into the international use of EVT.

6.2 Methods

A grey literature search was performed. Grey literature, including four large health technology assessment organizations (the National Institute for Health and Care Excellence (NICE), the Canadian Agency for Drugs and Technology in Health (CADTH), the California Technology

Assessment Forum (CTAF), and the Blue Cross Blue Shield Technology Evaluation Centre (BCBS TEC)) and Google were searched up until August 9, 2016. Search terms included "mechanical thrombectomy", "endovascular therapy", and "acute ischemic stroke." HTAs were also identified from the published literature during the systematic review of the cost effectiveness, both from the HTA Database and other published sources (see section 3.2 for the systematic review methodology). Only reports published in French or English were included.

6.3 Results

Seven technology briefs were identified (1, 11, 39-43). Two other reports were identified, but were excluded as they were not published in English or French. Of the seven identified technology syntheses, five were completed after the 2015 trials had been published. The five reports were described as: "technology brief", "rapid review", "technology assessment" and "procedural guidance." Most studies varied in terms of primary objectives and methodology. A narrative summary follows and data from each report are synthesized in Table 7. A table capturing the two reports completed prior to the 2015 trials can be found in Appendix C.

Table 7 HTA and evidence synthesis reports identified

Organization, Year, Country	Type of Report	Search Dates	Device(s) Evaluated	Patient Selection	Evidence	Conclusions
HealthPACT, 2015, Australia (40)	Technology Brief	Not reported	Solitaire Neurovascular Remodeling Device, TREVO stent retriever, APERIO, pREset, EmboTrap, Sofia	5-10% of ischemic stroke patients. Eligibility largely based on EXTEND-IA inclusion criteria.	• 1 systematic review • 1 meta-analysis • 5 RCTs • 1 cost utility analysis • 1 HTA	"The evidence to date demonstrates a clear benefit in terms of recovery time and functional outcomes for the small population (up to 10%) of acute ischemic stroke patients who satisfy the inclusion criteria for both pharmacological thrombolysis and mechanical thrombectomy. This procedure should only be offered as part of comprehensive stroke, neuro-intervention and imaging services."
CADTH, 2015, Canada (41)	Rapid Response	1 January 2010 to 16 July 2015	MERCI retriever, Penumbra System, TREVO stent retriever, and Solitaire Neurovascular Remodeling Device	Adult patients who have undergone ischemic stroke whose clots have been visualized using either CTA or MRA, and were treated with EVT.	• 7 meta-analyses • 2 systematic reviews • 5 economic evaluations • 5 cost analyses • 3 evidence based guidelines	"Although IV thrombolysis remains the first-line treatment for patients presenting within 4.5 hours of onset of AIS symptoms, EVT offers a viable option for patients who present outside this time window, are contraindicated to IV thrombolysis, or have large vessel occlusions."
HQO, 2016, Canada (43)	Health Technology Assessment	1 January 2005 to 11 March 2015	Solitaire Neurovascular Remodeling Device	Patients with acute ischemic stroke caused by proximal anterior circulation intracranial occlusion in the internal carotid artery, M1 or M2 middle cerebral artery, or A1-anterior cerebral artery. Patients who presented in hospital up to 12 hours after symptom onset and were treated with mechanical thrombectomy.	• 5 RCTs • 5 cost utility analyses	"We found that [newer EVT devices] improved patients' ability to live independently after a stroke caused by a blockage in a large artery. They were as safe as current treatment options, and they were also cost effective."

NICE, 2016, UK (1)	Interventional procedure guidance	Database inception to 28 May 2015	Penumbra Aspiration Pump, Solitaire Neurovascular Remodeling Device, Acandis APERIO, Revive SE, pREset, MERCI retriever, TREVO stent retriever	Patients with acute ischemic stroke treated with mechanical thrombus retrieval.	• 2 systematic reviews • 8 RCTs • Specialist advisors	"Current evidence on the safety and efficacy of mechanical clot retrieval for treating acute ischemic stroke is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit." "Selection of patients for mechanical thrombus retrieval for treating acute ischemic stroke should be done by clinicians experienced in the use of thrombolysis for stroke and in interpretation of relevant imaging. The procedure should only be carried out by appropriately trained specialists with regular experience in intracranial endovascular interventions, with appropriate facilities and neuroscience support."
EU Net HTA, 2016, European Union (11)	Rapid Assessment	1 January 2005 to August 2015	SOFIA, Trevo stent retriever, EmboTrap, ERIC, REVIVE SE, Solitaire Neurovascular Remodeling Device, MindFrame Capture, pREset, Amperio thrombectomy device	Not reported	• 8 RCTs	"…mechanical thrombectomy is of benefit, in terms of morbidity and function and, perhaps, generic quality of life, in selected patients with anterior circulation acute ischemic stroke, treated with second-generation (stent retriever) thrombectomy devices after having first received IV tPA, where appropriate. There is currently insufficient evidence to determine the applicability of this evidence to the much larger, heterogeneous cohort of patients with ischemic stroke who are treated in the real-world setting and who may be ineligible for IV tPA, who arrive outside the time window for treatment and/or who are managed in non-specialized institutions or units."

6.3.1 Australia HealthPACT

The 2015 report by HealthPACT examined the use of other EVT technologies for acute ischemic stroke(40). This report covered cost infrastructure and economic consequences, ethical, cultural, access or religious considerations, and safety and effectiveness.

For the cost infrastructure and economic consequences, it was estimated that the cost of consumables was approximately $10,690 and that most of the required infrastructure already exists in tertiary hospital stroke units(40). For the economic evaluation, authors also examined a cost-utility analysis from the UK, a Canadian HTA and unpublished economic data from EXTEND-IA trial. Authors did not identify any ethical, cultural or religious considerations, but did note that there may be access implications as only large tertiary centres with stoke units would be able to provide this service. Specifically, there would be reduced access for rural and remote patients. Authors examined an existing rapid review and further examined the five 2015 RCTs to examine the safety and effectiveness of the device. Overall conclusions drawn indicate that the results presented support EVT in appropriately selected patients, and that EVT should only be offered as part of a comprehensive stroke program with neuro-intervention and imaging support.

6.3.2 Canadian Agency for Drugs and Technologies in Health (CADTH)

The 2015 rapid review by CADTH focused on the safety and effectiveness of the technology and the cost-effectiveness(41). For the safety and effectiveness, authors identified two systematic reviews and seven meta-analyses. There were mixed results within these studies; however, authors discussed that this may be due to the increased use of second generation EVT devices in the recently published trials. For the cost-effectiveness, authors examined 4 cost-effectiveness/cost-utility studies, which all had an incremental cost-effectiveness ratio of <$16,000(41). Conclusions were in favour of EVT in appropriately selected patients.

6.3.3 Health Quality Ontario (HQO)

In 2016, HQO published a full HTA on EVT in patients with acute ischemic stroke(43). A systematic review of safety and effectiveness, as well as economic literature was conducted; a Canadian specific cost-effectiveness model was also completed.

For the clinical evidence review, five RCTs were identified. All five studies were considered to be high quality evidence, and showed improved functional independence at 90 days. Authors noted the importance of process times and imaging prior to treatment for potential EVT patients. Overall conclusions from the study were that there was high quality evidence showing a significant difference in functional independence in patients who received EVT(43). There was moderate quality evidence regarding mortality, symptomatic intracranial hemorrhage, quality of life, and reperfusion rates. There was also low quality evidence showing higher recanalization rates in EVT patients.

From the economic evaluation review, five cost utility analyses were identified(3, 24, 25, 27, 34). All included studies concluded that EVT for acute ischemic stroke patients was cost effective. From the authors' primary economic evaluation, authors calculated that the cost per QALY gained of EVT in the Canadian context and using a public payer perspective was $11,990(43). All of the five identified cost-utility analyses, as well as the author's primary economic evaluation are included in section 3.3.1 of this report.

6.3.4 National Institute for Health and Care Excellence (NICE)

In 2016, NICE updated their interventional procedure guideline regarding the use of EVT for treating acute ischemic stroke(1). This report examined the procedure technique, efficacy, and safety. For the efficacy, a systematic review was conducted and eight RCTs were identified. From the literature, EVT was shown to improve functional outcomes at 90 days post stroke and there was no significant difference in mortality at 90 days between the treatment groups(1). Furthermore, there were no significant differences in seven day mortality, rates of symptomatic intracerebral hemorrhage, or reports of large or malignant cerebral artery stroke between groups(1). Overall recommendations from the committee were in support of the use of this procedure given that standard arrangements are in place for clinical governance, consent and audit. Other recommendations were that patient selection should be done by experienced clinicians using diagnostic imaging, and that only appropriately trained specialists with regular experience should carry out the procedure. More specifically, NICE recommended that EVT only be provided by "appropriately trained specialists with regular experience in intracranial endovascular interventions, with appropriate facilities and neuroscience support"(1).

6.3.5 European Health Technology Assessment Network (EUnetHTA)

Similarly to the above reports, in 2016 the EUnetHTA released a rapid assessment on EVT for ischemic stroke(11). The focus of the report was on clinical effectiveness and safety. A total of eight RCTs were identified. Again, authors noted that the evidence suggests that EVT is not associated with lower (or higher) mortality at 90 days compared to the control group(11). However, significantly more patients had an independent functional status at 90 days compared when treated with EVT compared to the control group. Authors concluded that EVT has a beneficial effect on morbidity and function, and health related quality of life in appropriately selected patients treated with a second generation device(11).

6.4 Conclusions

Seven evidence syntheses reports were identified. Of those, five synthesis reports included the 2015 RCTs on EVT. All of the reports described the clinical effectiveness of the technology, but differed in regards to their publication year and inclusion/exclusion criteria. All of the recent studies concluded that there was sufficient evidence to support the use of EVT for treating ischemic stroke. Some of the reports also noted that EVT appeared to be cost effective. Three of the reports noted the need for appropriate selection of patients, appropriately trained clinicians, with EVT only be offered as part of comprehensive stroke, neuro-intervention and imaging services.

7.0 Jurisdictional Scan

Summary

- Clinicians and/or administrators involved in stroke care from each of the provinces were contacted with an email survey
- Questions focused on the use of EVT in the province, the locations and restrictions on access, the implementation and transportation strategies currently in place, and other acute ischemic stroke treatment options
- Seven of the provinces responded to the email survey
- All of the provinces that responded except for Prince Edward Island (PEI) are currently offering EVT within their province

7.1 Purpose

To assess the current state of EVT use for treating ischemic stroke across Canada

7.2 Methods

To gain an understanding of how ischemic stroke is treated across the country, emails to clinicians and health ministry employees were sent out to contacts in all of the Canadian provinces. Contacts were sent a follow up email one month after the initial email. All responses were collated and summarized. The questions included were:

1) Is rapid endovascular therapy used as a treatment option in your province?
2) If so, in which locations and under what conditions?
3) What implementation and transportation strategies are being used to treat ischemic stroke patients with rapid endovascular therapy?
4) What other treatment options are available in your province?

7.3 Results

Responses were received from seven of nine provinces contacted (nonresponse from Manitoba, Newfoundland and Labrador). Table 8 provides a summary of the question responses by province. PEI is the only province not currently offering EVT. Most of the provinces report that they are considering transportation and expansion strategies.

Table 8 Results of Jurisdictional Scan by Province

Province	Currently using EVT?	Where?	Implementation and transport strategies	Other treatment options
Alberta	Yes	Comprehensive stroke centres in Calgary and Edmonton	Current discussion on appropriate transport for rest of province. All patients being transferred to Calgary and Edmonton via 'Fast Stroke" protocol.	IV tPA
Saskatchewan	Yes	Royal University Hospital in Saskatoon	Provincial coordination of acute stroke treatment through the Saskatchewan Acute Stroke Pathway. Only currently being used for patients with large vessel occlusions with treatment determined by ESCAPE trial criteria.	tPA and all endovascular therapies.
Manitoba	No response			
Ontario	Yes	10 hospitals, dependent on clinical and imaging features 6 of 10 centres offer 24-hour care	Uses provincial telestroke network (27 enabled sites) to identify eligible EVT patients and help coordinate transports. Patients can only travel a maximum of 2 hours. Air transport is decided on a case by case basis. Current discussions focusing on bypassing local hospitals and shifting to direct transport to EVT site. Paramedic protocols are expanding. Currently, in order to be eligible for EVT, patients must receive EVT within 3.5 hours of stroke symptom onset. This is being expanded to 4.5 hours as the province gains experience.	IV tPA
Quebec	Yes	4 tertiary care centres	Most patients are transported by Ambulance. If a patient is coming from the far north, a plane would be used. Most of these patients are out of the timeframe for IV tPA, but if they arrive within 12 hours they are still candidates for EVT.	IV tPA

New Brunswick	Yes	Saint John comprehensive stroke centre (serves southwestern New Brunswick)	Patients are bypassed to hospital on activation of a code stroke. Rapid CT/CTA with tPA and EVT given as appropriate. Current discussion about accepting patients from central parts of the province.	IV tPA
Prince Edward Island	No	-	Two designated hospitals equipped and staffed to administer tPA. Paramedics and ambulance response system are trained and equipped to deal with acute stroke. Ambulance provides direct transport to stroke centre if acute stroke is suspected. Current discussions on increasing the number of people who experience signs of stroke and call 911.	tPA
Nova Scotia	Yes	Halifax (Queen Elizabeth II Health Sciences Centre)	Nova Scotia Stroke System comprised of seven district stroke programs. Programs include: ambulance bypass policies, thrombolysis protocols, multidisciplinary stroke unit care, and rapid access TIA clinics. Currently working on making EVT routinely available for patients living in Central Management Zone. A few patients from other Zones have been transported to the Halifax Infirmary for EVT. This has only been done on an ad hoc basis using road and air transport (helicopter and fixed-wing). A more formal provincial policy for EVT is currently being developed by the Central Management Zone Stroke Program, the Nova Scotia Health Authority, and Nova Scotia Emergency Health Services. Currently, only for patients who meet the eligibility criteria provided in the Canadian Stroke Best Practice Recommendations.	tPA is delivered in 10 Nova Scotia hospitals. Follow up care offered at 7 Acute Stroke Units.
Newfoundland and Labrador	No response			

7.4 Conclusions

Seven provinces responded to the email survey. All of the provinces that responded except for PEI are currently offering EVT, while all of the provinces (PEI inclusive) are currently using tPA as a treatment option for ischemic stroke. Alberta, Ontario, New Brunswick and Nova Scotia all specified that they are currently working on increasing access to EVT and formalizing transportation plans. Several provinces have used telestroke networks and 'fast stroke' protocols to increase patient access.

8.0 Current British Columbia Context

Summary

- Ten key informant interviews were conducted by a qualitative researcher to gain insight into the current BC experience with EVT and the key factors for its successful implementation
- Currently three BC hospitals (Vancouver General, Royal Columbia, Victoria General) are treating ischemic stroke patients with EVT
- Several challenges, barriers and facilitators for the successful implementation were identified including geographic concerns and appropriate credentialing for EVT interventionists

8.1 Purpose

To understand the BC experience with EVT to date and to determine the burden of illness, patterns of care and capacity in BC as it relates to using EVT for the treatment of ischemic stroke.

8.2 Methods

Key informant interviews were done to collect information to describe the current social context in BC. Ten interviews were conducted with thirteen individuals (one interview was done with a group of three individuals) between June and July 2016. The interviews included three individuals from Calgary, three from Stroke Services BC, four from Vancouver Island Health, one from Vancouver General Hospital, one from the Royal Columbian Hospital, and one individual from Northern Health. All participants had a range of health care experience (seven physicians and six health care administrators). A purposive sampling strategy was used with a goal of trying to speak with people who could provide insights into different parts of the ischemic stroke patient care pathway. A focus was placed on the pre-hospital part of the pathway

given the importance of the time window. An effort was made to speak with individuals from all the BC health regions, with a specific emphasis to speak to those that are providing EVT.

A semi-structured interview guide was developed for the interviews. This guide evolved over the course of the interviews, as questions were refined to reflect what had been learned through the previous interview(s). All of the interviews were audiotaped with the consent of the interview participants and detailed notes were taken. Using the qualitative analysis methods of constant comparative analysis, the notes were reviewed to identify key themes related to the policy questions being posed.

8.3 Findings

8.3.1 EVT for ischemic stroke in BC: current state

Stroke Service BC's planning for EVT has been going on several years, with the momentum picking up in early 2015. EVT is currently being provided in three locations, with Victoria just beginning to provide EVT for Island residents (4 cases as of July 1, 2016). Table 9 summarizes the current state.

Table 9 Current use of EVT in BC

Hospital	Number of EVT cases as of July 22, 2016	Catchment
Vancouver General Hospital	150	1.5 million people
Royal Columbia Hospital	50-60	1.5 million people
Victoria General Hospital	4	500,000 people

Vancouver General Hospital: Vancouver General Hospital (VGH) in central Vancouver (Vancouver Coastal Health Authority) has done approximately 150 EVT cases over the past year, and serves a population of about 1.5 million people. This hospital has been doing EVT for more than a decade, but has experienced an increase in the past 2-3 years. In the past, VGH had been using stent retrievers to remove clots, but now aspiration is their first line of treatment. Interviewees noted that this technology was easier to use ("less technical and fiddly") and estimated that in less than 10% of cases would a stent retriever be required. As a comprehensive stroke centre, the VGH stroke neurology group has been very good at the triaging and transfer of patients. A model similar to other major stroke centres, such as Calgary, has been adopted whereby patients bypass smaller hospitals and are directly transported to VGH. VGH is part of a telestroke network, which enables videoconferencing with outside centres. This has been used to

see patients and assess their eligibility for EVT before transport. A formal stroke call model has been in place since January 2016.

Royal Columbia Hospital: Royal Columbia Hospital (RCH) in New Westminster (Fraser Health Authority) has completed 50-60 cases in 2016, and could increase to 100 cases/year in their catchment area. This hospital serves approximately 1.5 million people. Over the past five years, a strong stroke program has developed at RCH, and the hospital now has a stroke-neurology team. Those interviewed felt that a great deal of work is required to develop a 'fast stroke protocol' for Fraser Valley. This will require coordination between the 13 hospitals in Fraser Health, and ensuring that the RCH Emergency Room (ER) has the capacity to handle the increased number of cases if EMS bypasses local hospitals.

Victoria General Hospital: Victoria General Hospital (VicGH) (Vancouver Island Health Authority) has performed 4 EVT cases as of July 2016. All were successful. The hospital serves a health region of approximately 500,000. Southern Vancouver Island has an older population, consisting of about three times as many 80 year olds as the national average. However, this population tends to be very active and healthy. VicGH has a history of working to prevent strokes by providing follow up care after Transient Ischemic Strokes (TIAs) through their 'Stroke Assessment Unit'. Despite this, interviewees noted there are approximately 890 ischemic strokes on Vancouver Island per year, indicating that the expected number of patients to benefit from EVT would be 80 to 100 per year. There was considerable support among interviewees to provide EVT on Vancouver Island. Neurologists and interventional radiologists on Vancouver Island are interested in increasing their capacity to provide quality EVT to island residents, and are actively building their brain health and stroke program. There are now two stroke units (one in Victoria and one in Nanaimo). There are six general interventional radiologists based in Victoria on a 24/7 call rotation, providing services for the entire island. The Vancouver Island Health Authority now has system-wide CT and CTA protocols in place with seven sites offering these services across the island. There is coordinated imaging and electronic health records across the island, meaning that the stroke team has instant access to the history and current imaging of stroke patients.

8.3.2 Moving towards a more coordinated, provincial model for EVT

Currently, residents outside of the lower mainland do not have access to EVT. There is considerable support, across interviewees, for implementing a coordinated provincial stroke program, and having national collaboration. It is important to work together across health region and provincial boundaries, as the closest location for EVT may be in a neighboring health region or province.

VGH and RCH are beginning to work together in a more coordinated fashion to serve the lower mainland population. To date, there have been no (or very few) patients from the Northern, Interior, or Vancouver Island health authorities treated with EVT at either VGH or RCH. Interviewees noted that considerable work still needs to be done at these centres to optimize service provision and British Columbia Emergency Health Services (BCEHS) coordination. Additionally, interviewees stated that conversations are beginning between the Interior Health Authority and Calgary regarding the possibility of having patients travel to Alberta for care and between the Northern health authority and Edmonton.

8.3.3 Current Challenges in BC EVT Development

Interviewees described a number of challenges regarding EVT development in BC. Some of these are similar to challenges in other jurisdictions, while others are more BC specific.

One challenge that was noted by interviewees is the cost of the procedure. Interviewees noted that funding is required to cover stent retrievers and/or thrombus aspiration devices and related disposables, on call staff including interventionists, neurologists, strokes nurses and CT/CTA technicians, and patient transportation. In order to ensure that EVT is done well, some interviewees acknowledged that there should be a push towards a mechanism that includes province wide oversight, coordination, good data management, and a sustainable funding model.

Geography, particularly in the northern part of the province, was noted as a challenge. This is further challenged by BCEHS transport and the availability of air ambulances specifically. The optimal approaches for treatment and transportation are still being worked out. For instance, depending on where a patient presents and the distance to the EVT site, it may be beneficial to complete the CT/CTA and start tPA locally prior to transportation. Alternatively, if the patient is not significantly further from the EVT site compared to the closest CT/CTA site, direct transport may be preferred. Alongside transportation protocols, repatriation must also be considered.

However, interviewees noted significant work has been put into this due to the limited number of beds in outlying areas and the lack of transport.

24/7 service provision was also noted as a challenge. Many of the non-EVT sites do not have a CT/CTA technician on call to provide 24/7 service. A unique challenge for Vancouver is that many of the required staff cannot afford to live in Vancouver, making it difficult for the staff to be on call from home and for 24/7 service to be provided.

The lack of interventionists who are trained to do EVT poses an additional challenge for BC. For instance, some interviewees felt there is a need to provide EVT in the Interior (Kelowna or Kamloops) due to the transport times to Vancouver; however, neither site appears to be moving towards providing EVT at present. In addition, interviewees noted that there is a lack of clarity about the expertise and training required to carry out the EVT procedure. Some felt that the procedure should only be completed by neuro-interventional radiologists whereas others felt that interventional radiologists, with training and mentorship, are able to competently complete the procedure.

Lastly, interviewees noted that EVT will also increase pressure on intervention suites, as clinicians seek to fit EVT into existing processes and infrastructure. Because of this, it is important to consider how the EVT-site can triage to optimize the use of its suites. Several interviewees commented that to address the noted challenges, there is a required cultural shift to acknowledge stroke as an emergency and the importance of time-to-door; some likened it to reacting similarly to heart attacks.

8.3.4 Increasing Capacity for EVT in BC

Given the challenges highlighted by interviewees, several key areas were identified as requiring capacity increases in order to provide high quality EVT in BC as part of a provincial stroke program/initiative:

- Enhanced BCEHS transportation system: Interviewees seemed unfamiliar with available transport and commented that there was little coordination and availability of air and helicopter transport. Interviewees felt that the transport system improves the provision of access to the communities that are only accessible via air and water transport.

- Appropriate credentialing: Some interviewees felt that standardization and clarity about what training it takes to do EVT was required. In general, most neuro-interventionists in Canada become skilled either through a radiology residency followed by neuroradiology fellowship training, or neurosurgery residency followed by endovascular fellowship training. In the US, some radiologists are becoming skilled from body interventional training followed by stroke training. In Canada, 'body' fellowship programs have varied amounts of neuro included. As previously noted, there is a lack of agreement within the community regarding what training is required. A standard for neuro-interventional radiology was recently published, but does not appear to be universally accepted across the broader medical community. The standards document suggests at least one year of additional training following neuro-radiology training. A number of interviewees, both in AB and BC, suggested that the best way to learn to do EVT is through practice. Opportunities for skilled body interventionists or neurosurgeons to work with a skilled neuro-interventionists to learn and practice the required technique may be appropriate. Mentorship within the BC EVT sites may also be appropriate in order to ensure that all sites meet the minimal acceptable level and reach a level of training that is deemed satisfactory.
- Hospital infrastructure requirements: Required infrastructure may include additional procedure rooms and capacity in step-down units as many patients will not require ICU care.

8.4 Conclusions

"What we know from tPA, and it's been proved over and over again, time is brain. The earlier tPA is administered, the better the patient outcome. The same thing will hold true for EVT."

Overall concluding thoughts from the interviewees were that a coordinated, appropriately resourced provincial program that has functional relationships with neighbouring provinces and territories is required; health region and provincial boundaries are arbitrary when the goal is to get a patient to the closest appropriate location for diagnosis and treatment as quickly as possible. An efficient, finely tuned, ischemic stroke care pathway that starts from when the patient first experiences stroke symptoms and goes through to smooth repatriation is also needed. Due to the time window, every step along the pathway is important, with transportation being a critical

consideration. There is a need to be careful that excellence of the EVT itself does not obscure the view of the rest of the pathway. Process improvement based on outcome evaluation should remain a focus.

9.0 Patient Perspectives

Summary

- We completed a systematic review of the stroke patient experiences with travelling for care and focus groups with patients
- Two studies were identified: in both studies, patients showed a strong preference for returning home as soon as possible following treatment
- From the focus groups, communication and information exchange was identified as the dominant theme, with communication between major centres and local health professionals often described as lacking
- Policies and protocols need to maintain enough inherent flexibility to enable responsiveness to patient needs and goals
- Process improvement is needed if patients are to have access to treatments such as EVT, where there is a defined time window

9.1 A Systematic Review of the Literature

9.1.2 Purpose

To understand the experience of being treated away from home or the experience with travelling for care from the perspective of stroke patients and/or their families.

9.1.3 Methods

A systematic review of stroke patient perspectives on willingness to travel and be treated away from home was completed. MEDLINE, Cochrane Central Register, Cochrane Database of Systematic Reviews, HTA Database, EMBASE, and CINAHL, were searched from inception until June 8, 2016. The search strategy was developed by a library and information specialist. Terms capturing the disease (e.g. ischemic, stroke, attack, etc.) were combined using the Boolean operator “and” with terms reflecting the patient experience of traveling away from home for treatments (e.g. travel, medical tourism, patient transfer, choice behavior, etc.). These results were then focused to include only qualitative studies by using terms such as “qualitative research”, “interviews”, and “grounded theory.” Results were filtered to exclude non-human studies. The full search strategy can be found in Appendix D.

The abstracts were screened in duplicate by independent reviewers. Abstracts were assessed using the following inclusion criteria developed *a priori*: individuals diagnosed with stroke; report on stroke patient (or family member) experience being treated away from home or their experience with travelling for care treatment; original qualitative research; human studies; and adult participants. Abstracts were excluded if they did not meet the above inclusion criteria, or if they: did not report results from the patient perspective; or reported primarily quantitative data. Abstracts included by either reviewer proceeded to full-text review; consensus was not required. This abstract screen was intentionally broad to ensure that all relevant literature was captured.

Studies included after the first screen proceeded to full-text review by two independent reviewers. Studies were included if they met all of the inclusion criteria and did not meet any of the exclusion criteria presented in Table 10. Reference lists for the included studies were hand-searched to ensure that all relevant articles were included. Quality of the included studies was also assessed independently and in duplicate using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist(44).

Table 10 Inclusion and Exclusion Criteria for Systematic Review of Stroke Patient Experiences with Being Treated Away from Home or Travelling for Care

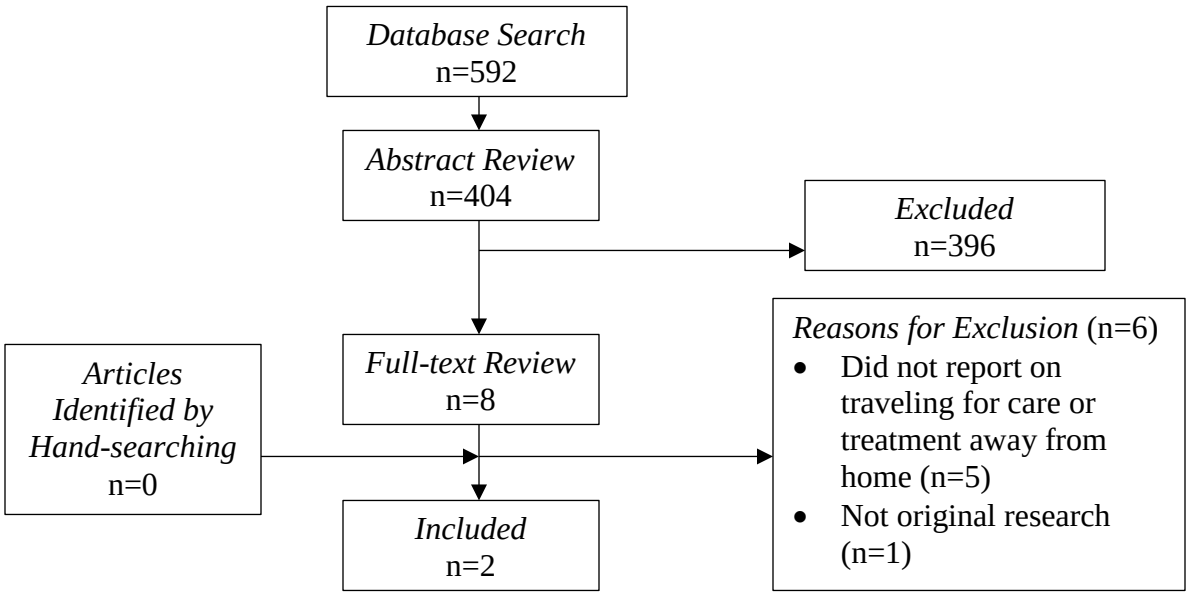
Inclusion Criteria	Exclusion Criteria

• Stroke patients
• Report on at least one of the following:
  o Experience being treated away from home
  o Experience with travelling for care
• Original qualitative research
• Full-text available
• Adult participants
• Human studies
	• Not stroke patients
	• Did not report on patient perspective
	• Physician accounts of patient experience
	• Other study designs
	• Abstracts, posters, editorials, opinions
	• Patients <18 years of age

9.1.4 Results

404 abstracts were retrieved, after de-duplication (Figure 5). During abstract review, eight abstracts were selected by the reviewers and continued to full-text review. Only two studies were included in the final dataset. Studies were excluded mainly for two reasons: did not report experience with travelling for treatment or being treated away from home (n = 5), and did not report primary data from a qualitative study (n = 1).

Figure 5 Flowchart of Included and Excluded Studies



Characteristics of the selected two studies are summarized in Table 11 and the findings of these studies are narratively synthesized below. Results from this quality assessment analysis can be found in Table 12.

Table 11 Summary of included studies by year

Author, Year of Publication, Country	Journal	Study Design	Participant Selection	Participant Inclusion Criteria	Participants Exclusion Criteria	Participant Characteristics	Findings
Gregory, 2010, USA (45)	Top Stroke Rehabilitation	Face-to-face interviews with questionnaire adapted from previous validated instrument.	Patients admitted to hospital with the primary diagnosis of stroke at 1 of 2 hospitals (primary stroke center (PSC) and rural community hospital (RCH)).	Alert and able to follow simple commands. Patients had to be able to provide reliable yes/no answers. Able to provide informed consent.	None reported	**53 patients included:** 15 from RCH, 38 from PSC, 50% <59 years old, 54% Caucasian, 52% female, 63% >High School education.	Stroke patients prefer to have their initial rehabilitation at home. 85% preferred to be discharged home. 94% preferred to not have inpatient rehabilitation.
Maniva, 2013, Brazil (46)	Rev Esc Enferm USP	Qualitative study based on symbolic interactionism. Recorded open interviews.	Stroke patients in specialist unit of tertiary public hospital.	None reported	None reported	**10 patients included:** Acute stroke patients who were in hospital with preserved cognitive and verbalization status.	Subjects experienced feelings of sadness when faced with a period of hospitalization. Some experienced such a strong dislike that they compared a hospital to a prison and patients to prisoners. Patients also expressed longing for family.

Table 12 Results of the CASP Qualitative Research Checklist by study year

	Was there a clear statement of aims?	Is a qualitative methodology appropriate	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?
Gregory, 2010, USA (45)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Maniva, 2013, Brazil (46)	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes

Gregory et al. assessed the association between stroke patients' preferences during the hospitalization and their actual discharge destination(45). Fifty-three patients were recruited from two hospitals in North Carolina. Included patients were medically stable, and were able to provide informed consent and to participate in a 45-minute questionnaire. Patients were asked about their preference for initial rehabilitation therapy setting with four options: patient's home, family's home, skilled nursing facility, and inpatient rehabilitation unit. In addition, the distance each patient was willing to travel to an inpatient facility was also assessed. Overall, 85% of patients preferred to be discharged home and only 6% preferred inpatient rehabilitation(45). This preference was strongly associated with an actual discharge destination of home. Further, 63% reported a willingness to travel less than 30 miles for rehabilitation(45).

Maniva et al. reported a qualitative study based on symbolic interactionism that evaluated the illness experience of the acute stroke patients during the hospitalization period(46). The study included ten acute stroke patients, with preserved cognitive and verbalization status, hospitalized in a tertiary public hospital in Ceara, Brazil. Participants were asked generally about their hospitalization due to the stroke and the data collection was done from those recorded open interviews. Patients experienced a feeling of sadness as they were in a foreign place away from their home and family members, and expressed a strong dislike for hospitals. Most of the subjects talked about the distance to the family members and showed a longing to be with them. "Here I'm different [crying], I'm far from my family, my home, it is very sad,"(46).

9.1.5 Conclusions

Two studies of moderate quality were identified. Participants in both studies reported a strong preference to be home as opposed to in the hospital. Maniva et al. characterized these feelings as sorrow due to the distance from one's home and loved ones (46).

9.2 Focus Groups: Patient Voices Network

9.2.1 Purpose

To explore the experiences of BC patients travelling from a rural or remote area to a major centre for critical care to identify considerations for care pathway development and implementation.

9.2.2 Methods

The University of Calgary HTA team worked closely with the BC Patient Voices Network to recruit patients living in rural or remote areas, who had experience with obtaining critical care far from their home community to participate in a focus group. An emphasis was placed on obtaining patient insights into how transitions to and from large centers can be optimally handled.

Two 1.5-hour teleconference focus groups were conducted the week of July 18, 2016. Detailed notes were taken, and the discussion was audio-taped with the consent of the participants. A consent form was circulated prior to the focus group, and all participants provided either written or verbal consent. An opening question and a number of follow-up probing questions were developed to guide the focus group discussion. A draft of the interview guide and the consent form can be found in the Appendix D. The opening question was:

> Could you talk about any experience you have had travelling to a major centre for critical care (e.g., stroke, heart condition, severe trauma, other) or any experience that required hospitalization in such a centre? If you've not had this kind of experience, could you talk more generally about experiences with having to seek out specialized care in a major city far from home?

9.2.3 Findings and Key Themes

There were six participants – two in the first interview and four in the second. Five of the participants were currently living, or had lived for a long period of time, in a remote area of the province. One participant was currently living in Vancouver, but had a life-threatening health event occur while she was in a remote area of the province. One participant lived in a northern First Nation community and worked as a Licensed Practical Nurse, along with having her own healthcare experiences. Five of the participants were women, and ranged in age from middle-aged to elderly. Three of the six participants were still working. It is important to note that these are the opinions of a sub-set of patients, and are not representative of all patient voices.

Several key themes emerged through the focus group discussions. Each of the key themes are briefly described below.

9.2.3.1 Transition to Major Centre

Timely transportation to a major centre was identified as a possible problem. One family member described a lack of communication within the hospital that contributed to the delay in getting her husband, who had a major stroke, transported from a remote setting in time to be eligible for treatment. Patients for whom their acute condition resulted in ongoing care needs described learning to have a bag packed that included a change of clothes, medications and a phone, so that when EMS arrived they can simply ask them to grab their bag.

9.2.3.2 Costs of Travel

Often people are required to stay in a major centre for a period of time after the procedure. This requires paying for accommodation and food for their loved one, in addition to themselves, as well as additional transportation costs. One family member suggested their travel costs for each year being more than $10,000 as they dealt with ongoing chronic care needs. Travel costs were described as a significant burden to those who cannot afford it.

9.2.3.3 Transitioning Home (Repatriation)

Early and effective discharge planning was described by many patients as lacking. One participant stated: *"Discharge is difficult to plan because often there isn't a lot of time in between the time they tell you and the time you are released. To coordinate someone to come pick you up might take longer than that. It would be nice if the hospitals were more transparent about when you will be discharged."*

Effective discharge planning was described by patients as: making the effort to ask if the patient has somewhere to go, getting contact information to call ahead, and ensuring that all the preparations for the patient's arrival can happen. In some communities, where there is a lot of transport out, there is likely someone responsible for facilitating transport to the treatment facility, ensuring you have a change of clothes, etc. Patients said that it would be helpful to have someone with the same expertise at the "other end", that is responsible for ensuring that you get home well.

Patients described having written information for them to take home and refer to. Support with transition to rehabilitation centres, where needed, was also identified as an important factor. One patient asked: "Who gets to decide who is eligible for rehab and how is that communicated with

patients and families?" Transparency around decision-making criteria, including who gets to be involved in these decisions, was identified as very important.

9.2.3.4 Communication & Information Exchange

Information exchange was described as essential throughout the treatment process and particularly critical at transitions. Some participants described having difficulty "tracking down" family members that had been transported by air to major centres; *"patients get lost in the computer system"*. It was also described as important to educate the families about the entire treatment process, and including the likely time of discharge.

Patients experienced information being given in a rushed manor when they are not well-suited to absorb the information (i.e. emotionally stressed and scared). In addition to ensuring that this information is also provided to family, one participant noted that it would be good to have a hospital social worker come and review the information when the patient is in a less heightened state. The timing and presentation of information by specialists is important.

Participants also identified a lack of communication and information exchange between different groups involved in care. For instance, exchange of medical information between major centres and local physicians was not optimal, and communication across professional groups during hospital and rehabilitation centre stays was lacking. One participant voiced this as *"Communication between doctors exists, between nurses, between therapists, between family, but not in between those groups*." Simple solutions were identified such as a white board in the room to mitigate asynchronies in communication.

9.2.3.5 Access to Medical Records, including Test Results

Patients living with chronic health issues end up being very involved in the coordination and management of their own care; however, participants describe needing to be very persistent to get copies of medical records, test results, etc. One patient living with a complex cardiac condition spoke about needing to: *"take control of her health, and having to play a big role in her own healthcare"*.

Participants noted that it would be great to have *"a large provincial database that would allow healthcare professionals to have access to records"*, and many patients living with chronic conditions would want access as well. It is important for patients to have easy access to

important information that they need to share with their local physicians and other healthcare providers.

Some patients described carrying copies of specialty consult letters back from major centres, so as to be able to share them in a timely fashion with local physicians. They also obtained copies of local test results to be able to share them back with specialists in major centres. Others talked about paying to get medical information copied so that they could take them to their family physician.

9.2.3.7 Access to and Communication with Family

Often there is no room for family on air ambulances, so families are required to find their own transportation to a major centre. Family members described experiences with being allowed to travel on ground ambulance with patient, which was deeply appreciated.

Although families were described as being welcome in big city hospitals, communication with family was lacking, with some describing family as being afraid to leave the bedside in case they missed receiving important information (e.g., what kinds of tests had been done, so they would know to ask about the results). As one patient noted: "*they were often kept out of the loop*".

9.2.3.8 Flexibility of Protocols

Ensuring that there is enough flexibility inherent in system policies and protocols to enable care to be provided in a patient-centred way, was described by a number of patients and families as being important. For example, if a patient chooses to obtain care in a major centre outside of their health region, there should be support. There needs to be awareness that not every stroke patient is the same, and it's important to work with patients to identify goals that are important to them. This was described as being particularly important in a rehabilitation context.

9.2.4 Conclusions and Final Words of Advice from Patients

Overall, several key themes were identified from the Patient Focus Groups. Importantly, as with all qualitative research, the findings are not intended to be representative of the entire patient population but rather identify considerations that affect the patient experience. In planning implementation of new, highly specialized treatments such as EVT that will require travel to a major centre, patients felt it was critical to think about transitions in and out of the hospital, as well as ongoing follow up care. Currently there are barriers in place that make accessing time

sensitive treatments such as EVT within the required time window impossible; *"There is time being wasted"*. The process needs to be streamlined, with communication throughout admission and discharge with the patient/family and local health professionals who will be supporting the patient once they return to their home community. As patients often rely on family members to help with care management and coordination, families not only need to be welcome, but also included in communication. Lastly, there needs to be enough flexibility built into protocols to be able to respond to the needs of individual patients. *"One size will never fit all"*.

10.0 Budget Impact Analysis

Summary

- A budget impact analysis of four identified implementation scenario was completed
- Implementation scenario I (No support of EVT) was the least costly while scenario III (VGH, RCH and VicGH operating with increased catchment due to coordinated transport system) was the most costly

10.1 Purpose

To estimate the budgetary impact of EVT adoption for four implementation scenarios.

10.2 Methods

Four implementation scenarios were developed to demonstrate a breadth of implementation possibilities. The four scenarios considered were as follows:

1. No EVT
2. VGH, RCH and VicGH continue to operate "as is" without patient transport coordination
3. VGH, RCH and VicGH operating with increased catchment due to coordinated transport system
4. VGH, RCH, VicGH and Kelowna General Hospital (KGH) operating with increased catchment due to coordinated transport system

For all of the scenarios, only costs directly attributable to EVT compared to current care were included. Due to this, all costs are reflective of an increase in costs due to the addition of EVT on top of current care. All costs are in 2016 CAD dollars.

10.2.1 Cost Inputs

To calculate the additional transportation costs associated with EVT, it was assumed that there would be no additional ground transportation (ambulance) costs. Specifically, stroke patients are

currently being transported to the nearest hospital for care, thus there is assumed to be no increase in the number of patients transported by ground that is directly attributable to EVT. The costs for air ambulances (helicopters and planes) were provided by the BC Emergency Health Services (Table 15). These costs are service estimates based on the direct billing to persons without a valid BC Care Card; the actual cost and billing for BC residents was unavailable.

For stent retrievers, all patients were assumed to be treated with Solitaire 2 stent retriever. This retriever is currently being used throughout BC and across Canada. Costs for the retriever were taken from the ESCAPE trial, confirmed with the stent manufacturer, and are reflective of current Canadian prices (Table 15).

In comparison to current care, the only additional physician billing code associated with EVT was assumed to be the cost of the interventionist performing the procedure. Billing codes were identified by a BC neuro-radiologist and the cost was provided in the BC Medical Services Commission Payment Schedule. On-call and alternative payment mechanisms were not considered.

In order to capture healthcare resource use, the average 3-month increase in hospitalization costs was also taken from ESCAPE trial data. Specifically, Alberta Health Services microcosting data was obtained for ESCAPE trial patients treated at Foothills Medical Centre. Microcosting is the gold standard for costing estimates as all costs incurred by the patient within the hospitalization are captured and directly allocated to the patient. Included in these costing data are total direct costs (nursing, drugs, diagnostics, etc.) and total indirect costs (overhead, transportation, electrical, etc.). The initial hospitalization due to stroke was costed as well as all subsequent hospitalization re-admissions within 3 months of the incident stroke. An average 3-month cost was calculated for the control and EVT (intervention) groups by functional status (mRS 0-2, 3-5, 6). The difference between the average cost by functional status was then calculated to show the estimated increase in 3-month hospitalization costs.

To estimate the annual costs (4-12 months) by functional status, costs from the Economic Burden of Ischemic Stroke Study (BURST) were incorporated(47). This study is the only study to report long-term costs of stroke survivors, including all healthcare, patient and rehabilitation costs from a Canadian perspective. The estimates include societal costs such as lost patient productivity and unpaid care giver time, direct health care costs including: hospitalization,

rehabilitation, physician services, diagnostics, medications, allied health professional services, homecare, medical/assistive devices, changes to residence and paid caregiver time(47). The study estimates by disability status for 4-6 months, and 7-12 months were totalled and inflated to 2016 CDN dollars (Table 15).

Table 13 Cost Inputs (2016 $CDN)

		EVT ($)	Current Care ($)
Transportation	Helicopter	4,119.00	-
	Plane	7 per 1.6 Km	-
Treatment	Stent	4,985.00	-
	Cost of interventionist	1,273.79	-
3-month hospitalization	Independent	30,313.17	26,929.44
	Dependent	84,404.79	47,990.18
	Dead	28,507.56	18,803.14
4-12 month societal costs	Independent	24,904.32	24,904.32
	Dependent	55,636.00	55,636.00

10.2.2 Number of Patients Treated

The number of patients transported was modelled in the implementation scenarios. A one-year timeframe was adopted. Specifically, the number of patients being transported either by helicopter or plane after having a CT scan at a local hospital was computed. For helicopters and fixed wing transport, it was assumed that 80% of patients would have a diagnosis of ischemic stroke. Of those, only 10% would be eligible for EVT which is the expert opinion estimate of Canadian neurologists. This 10% represents the maximum possibly treated with EVT. Finally, for patients presenting with symptoms suggesting EVT eligibility, a 20% false activation rate was assumed; an additional 20% of patients would be transported and subsequently not undergo EVT due to ineligibility or time delays. As previously mentioned, it was assumed that there would be no additional ground transportation costs attributable to EVT as all stroke patients are currently being transported by ambulance. Table 16 summarizes the number of patients captured in each scenario by health authority.

Table 14 Number of patients captured in each scenario by health authority

		Interior Health	Fraser Health	Vancouver Coastal Health	Vancouver Island Health Authority	Northern Health
Number of Strokes		1145	1921	1154	1017	325
Potential number eligible for EVT*		92	154	92	81	26
Number of patients captured in timeframe	Scenario I	0	0	0	0	0
	Scenario II	39	1921	1056	869	0
	Scenario III	1145	1921	1154	1017	321
	Scenario IV	1145	1921	1154	1017	321

For costs that vary depending on the patient's functional status (3-month hospitalization and 4-12 month societal costs), the total number of patients treated was calculated (80% of stokes are ischemic and 10% of those are EVT eligible). This number was then multiplied by pooled estimates of effect (using only the 2015 trials) from the meta-analysis for mRS 0-2. Mortality was not considered as it the trend of a mortality benefit was not statistically significant.

Table 17 provides the total number of patients captured, the assumed number that would be transported by helicopter, the number of patients treated, and the number of patients in each functional group. In implementation scenario I, there are no costs and no estimated effects. There would be no additional costs with EVT, no one would be transported after imaging with the intent of providing EVT and no one would possibly benefit from EVT. An estimate of the total number of patients transported by plane was not calculated, as costs were provided based on travel distance. Instead a total cost was calculated and then subjected to the same assumptions as the helicopter travel.

Table 15 Patient Transport, Treatment and Functional Status Estimations

Implementation Scenario	I*		II		III		IV	
Number of strokes captured for evaluation of eligibility for EVT (% captured)**	0		3885 (70)		5558 (99.9)		5558 (99.9)	
Number transported by helicopter after imaging	0		0		152		78	
Number of strokes treated with EVT	0		311		445		445	
*Outcomes of those eligible for EVT treatment (N=445)****	*EVT*	*Current Care*	*EVT*	*Current Care*	*EVT*	*Current Care*	*EVT*	*Current Care*
Independent	-	-	135	81	194	115	194	115
Dependent	-	-	127	170	182	244	182	244

*Only additional patients and outcomes attributable to EVT are captured. If EVT were no longer supported, no patients would be evaluated for EVT eligibility. Additionally, as we do not have current treatment and outcomes of those who are EVT eligible, we do not present the outcomes in the absence of EVT.

** Total number of strokes in 2014-2015 provided by the BC Ministry 5562

* **Deaths are not presented as the mortality benefit was not statistically significant

10.3 Results

Table 18 provides a detailed budget impact analysis. Implementation scenario I (no EVT) has the lowest budget impact directly attributable to EVT due to non-adoption, while implementation scenario III (VGH, RCH and VicGH operating with increased catchment due to coordinated transport system) has the highest budget impact due to the increase in transportation costs. Of note, program costs for Kelowna are not included in implementation scenario IV; the additional costs may include recruitment costs for neurologists and neuro-interventional radiologists, modifications to existing interventional suites and possibly the training of dedicated stroke nurses. However, the physician costs, stent costs and hospitalization costs would all remain the same as implementation scenario III as patients are simply being shifted from one of the existing three sites to Kelowna.

Table 16 Results of Budget Impact Analysis (2016 $CDN)

		I	II	III	IV
Transportation	Helicopter	-	-	624,374	322,665
	Plane	-	-	2,096,172	2,088,180
Total Transportation costs		**-**	**-**	**2,720,546**	**2,410,836**
Treatment	Stent	-	1,549,338	2,216,530	2,216,530
	Cost of interventionist	-	396,148	566,836	566,836
3-month hospitalization	Independent	-	1,937,266	2,771,972	2,771,972
	Dependent	-	2,561,077	3,602,977	3,602,977
	Dead	-	263,509	377,046	377,046
Total 3-month healthcare costs			**6,707,338**	**9,535,361**	**9,535,361**
4-12 month societal costs	Independent	-	1,344,833	1,967,441	1,967,441
	Dependent	-	(2,392,348)	(3,505,068)	(3,505,068)
Total:		**0**	**5,659,825**	**10,718,283**	**10,408,583**

The avoided costs due to increased outcomes of functional independence are significant; approximately $2.4M in scenario II, $3.5M in scenario III and IV. This cost avoidance is comprised of lower rehabilitation intensity, less rehabilitation demand and fewer long-term care admissions among other costs borne by both the system and the patients. However, within one year, the avoided costs do not offset the entire required investment as the costs of helicopter and plane transportation are significant.

There are differences in cost estimates between this report and the *Provincial Planning of EVT for Acute Ischemic Stroke* report produced by Stroke Services BC(48). The budget impact analysis presented here includes: physician costs, indirect hospital costs (overhead and hoteling), societal costs, and transportation costs. The assumptions made by the Stroke Services BC report did not include these costs. The inclusion here is a strength as it represents the costs borne to the entire system and families.

11.0 Conclusions

Overall, EVT appears to be safe and effective with approximately 50% more patients being functionally independent at 90-days post stroke. Furthermore, EVT appears to reduce 90-day mortality; however, this result was not significant. Results of a systematic review suggest that EVT is good value for money. Of the five recent cost-effectiveness studies, 2 suggested that EVT is cost savings, while the other 3 reported incremental cost-effectiveness ratios below the commonly accepted $50,000 per QALY threshold. Only one data point was greater than this threshold with a public payer perspective and a time horizon of 1 year. EVT is currently being used internationally and across Canada. In addition, EVT is considered best practice as stated in the Canadian stroke guidelines. Within BC, three hospitals are currently offering EVT (VGH, RCH, and VicGH). As transport to a major centre will be required for EVT, it is important to consider transitions, communication, and discharge plans from a patients' perspective.

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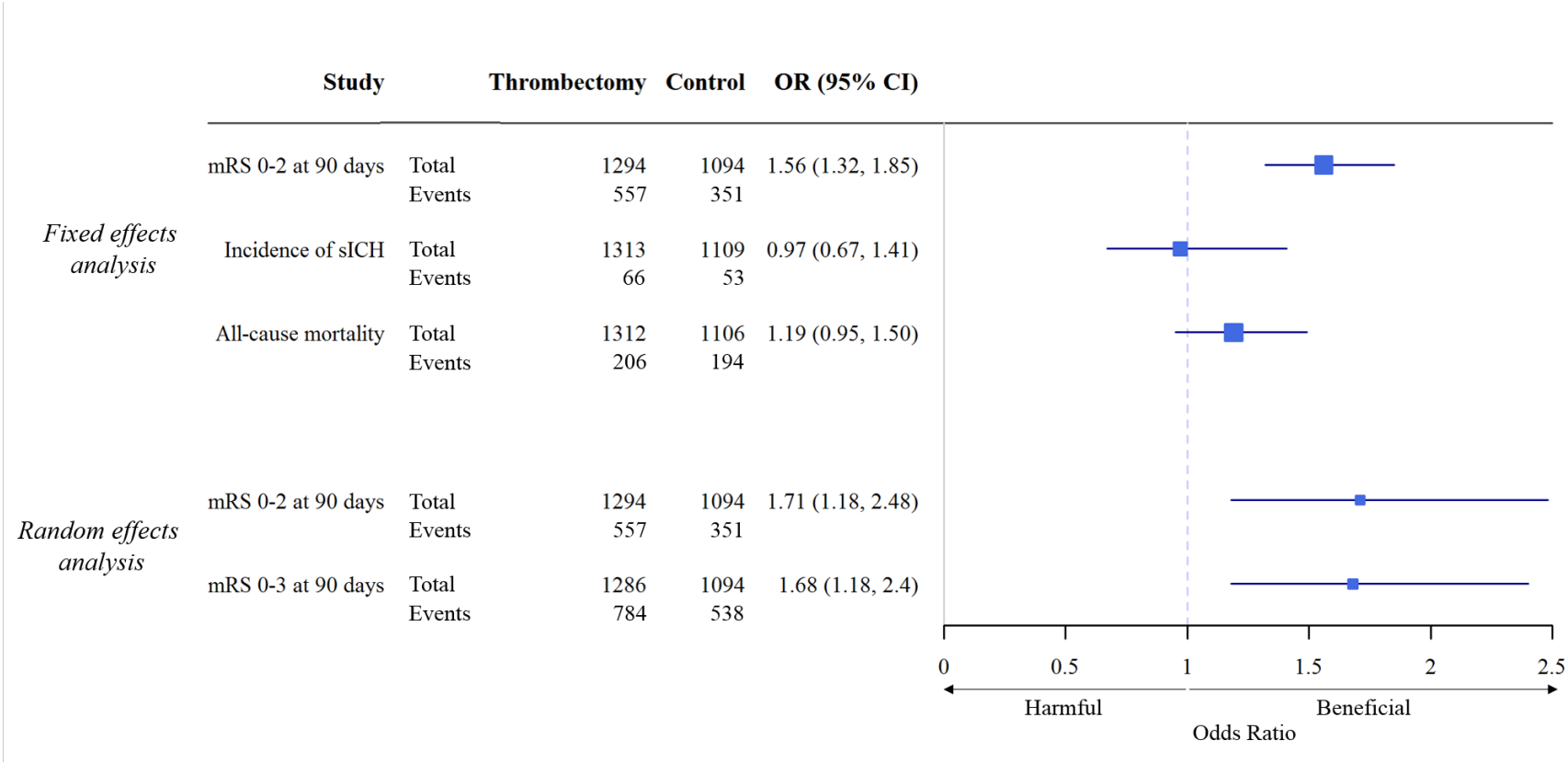
Appendix A: Clinical Effectiveness of EVT for Ischemic Stroke

Figure 1 Results of Primary and Secondary Outcomes of the Meta-Analysis (all 8 RCTs)



Appendix B: Cost-Effectiveness of EVT for Ischemic Stroke

Search Strategy

MEDLINE:

1. exp Brain Ischemia/
2. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw
3. exp stroke/
4. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
5. intracranial arteriosclerosis/
6. "intracranial embolism and thrombosis"/
7. carotid artery thrombosis/
8. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw.
9. transient isch?emi* attack.tw,kw.
10. carotid artery thrombosis.tw,kw.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp thrombectomy/
13. embolectomy/
14. ((mechanical adj3 (thromb* or embol* or clot disruption* or clot retrieval*)) or ((clot* or thromb* or embol*) adj3 (retriev* or disruption* or fragmentation)) or ((stent* or stent-assisted) adj3 retriev*) or stentriever*).tw,kw.
15. ((intravenous or intra?arterial or intra arterial or endovascular) adj3 (thromb* or interven* or therap* or treatment or embolect*)).tw,kw.
16. ((catch or merci or trevo or penumbra or phenox clot or solitaire) adj3 (retriever* or system* or device*)).tw,kw.
17. 12 or 13 or 14 or 15 or 16
18. 11 and 17
19. limit 18 to animals
20. limit 18 to (animals and humans)
21. 19 not 20
22. 18 not 21
23. limit 22 to (comment or editorial or letter)
24. 22 not 23
25. limit 24 to "review"
26. ((critical or systematic or scoping or realist or evidence-based) adj (review or synthesis)).tw.
27. 24 and 26
28. 24 not 25
29. 27 or 28
30. exp "Costs and Cost Analysis"/
31. exp Economics/
32. (cost or costs or economic*).tw.
33. economics.fs.
34. 30 or 31 or 32 or 33
35. 29 and 34

Total: 132 abstracts

EMBASE:

1. exp brain ischemia/
2. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw.
3. exp cerebrovascular accident/
4. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
5. brain atherosclerosis/
6. brain embolism/
7. exp occlusive cerebrovascular disease/
8. carotid artery thrombosis/
9. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw.
10. transient isch?emi* attack.tw,kw.
11. carotid artery thrombosis.tw,kw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. exp thrombectomy/
14. exp thrombectomy device/
15. exp embolectomy/
16. embolectomy system/
17. ((mechanical adj3 (thromb* or embol* or clot disruption* or clot retrieval*)) or ((clot* or thromb* or embol*) adj3 (retriev* or disruption* or fragmentation)) or ((stent* or stent-assisted) adj3 retriev*) or stentriever*).tw,kw.
18. ((intravenous or intra?arterial or intra arterial or endovascular) adj3 (thromb* or interven* or therap* or treatment or embolect*)).tw,kw.
19. ((catch or merci or trevo or penumbra or phenox clot or solitaire) adj3 (retriever* or system* or device*)).tw,kw.
20. 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 12 and 2
22. limit 21 to animal studies
23. limit 21 to (human and animal studies)
24. 22 not 23
25. 21 not 24
26. limit 25 to (conference abstract or conference proceeding or editorial or letter)
27. 25 not 26
28. limit 27 to "review"
29. 27 not 28
30. limit 27 to (meta analysis or "systematic review")
31. ((critical or systematic or scoping or realist or evidence-based) adj (review or synthesis)).tw.
32. 27 and 31
33. 29 or 30 or 32
34. exp economic aspect/
35. (cost or costs or economic*).tw.
36. 34 or 35
37. 33 and 36

Total: 252 abstracts

HTA database 2nd Q 2016
Total: 17 abstracts

NHSEED
Total: 17 abstracts

EconLit

1. ((((isch?emi* N3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS)) OR ((stroke* N3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*))) OR (((occlus* or hypoxi* or block* or infarct* or clot* or termination) N6 (carotid or cerebr* or MCA or ACA))) OR transient isch?emi* attack OR carotid artery thrombosis)[All Fields]
2. ((((mechanical N3 (thromb* or embol* or clot disruption* or clot retrieval*)) or ((clot* or thromb* or embol*) N3 (retriev* or disruption* or fragmentation)) or ((stent* or stent-assisted) N3 retriev*) or stentriever*)) OR (((intravenous or intra?arterial or intra arterial or endovascular) N3 (thromb* or interven* or therap* or treatment or embolect*))) OR (((catch or merci or trevo or phenox clot or penumbra or solitaire) N3 (retriever* or system* or device*))))[All Fields]
3. 1 and 2
4. Results 0

Total: 0 abstracts

Table 1 Quality Assessment of Included Cost-Analysis and Cost-Effectiveness Studies Using CHEC

	Patil, 2009, USA	Kim, 2010, USA	Nguyen-Huynh, 2010, USA	Brinjikji, 2011, USA	Bouvy, 2013, Netherlands	Kass-Hout, 2014, USA	Simpson, 2014, USA	Rai, 2014, USA	Turk, 2014, USA	Comai, 2015, Sweden	Ganesalingam, 2015, UK	Leppert, 2015, USA	Turk, 2015, USA	Aronsson, 2016, Sweden	Lobotesis, 2016, UK	Xie, 2016, Canada
(1) Is the study population clearly described?	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
(2) Are competing alternatives clearly described?	1	1	1	N/A	1	1	1	1	1	1	1	1	1	1	1	1
(3) Is a well-defined research question posed in answerable form?	1	1	1	0	1	1	1	0	0	1	1	1	0	1	1	1
(4) Is the economic study design appropriate to the stated objective?	1	1	1	1	1	0	1	1	0	0	1	1	0	1	1	1
(5) Is the chosen time horizon appropriate in order to include relevant costs and consequences?	1	1	1	N/A	1	N/A	N/A	N/A	N/A	N/A	1	1	N/A	1	1	1
(6) Is the actual perspective chosen appropriate?	1	1	1	N/A	0	N/A	1	1	N/A	N/A	1	1	N/A	1	1	1
(7) Are all important and relevant costs for each alternative identified?	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1

(8) Are all costs measured appropriately in physical units?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
(9) Are costs valued appropriately?	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
(10) Are all important and relevant outcomes for each alternative identified?	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
(11) Are all outcomes measured appropriately?	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
(12) Are outcomes valued appropriately?	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1
(13) Is an incremental analysis of costs and outcomes of alternatives performed?	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1
(14) Are all future costs and outcomes discounted appropriately?	1	1	1	N/A	1	N/A	N/A	N/A	N/A	N/A	1	1	N/A	1	1	1
(15) Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	1	1	1	0	1	1	0	0	0	0	1	1	1	1	1	1
(16) Do the conclusions follow from the data reported?	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1

(17) Does the study discuss the generalizability of the results to other settings and patient/client groups?	0	0	1	0	1	0	1	1	0	0	1	1	1	1	1	1
(18) Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1
(19) Are ethical and distributional issues discussed appropriately?	0	0	0	0	0	0	0	1	1	1	0	0	1	0	1	0
Total:	17/19	17/19	17/19	8/15	17/19	9/16	15/17	15/17	12/16	11/16	17/19	18/19	14/16	18/19	19/19	18/19

Table 2 Summary of Included Studies in Cost-Effectiveness Systematic Review

Author, Year, Country	Population	Model	Perspective	Compators	Time Horizon	Discount Rate (%)	Outcome	Clinical Inputs	Source of Clinical Inputs	Preference measurement	Included Cost Inputs	Assessment of Uncertainty	Currency (Year)	Primary Result	General Conclusions
Patil, 2009, USA (24)	67-year-old patient with large-vessel ischemic stroke	Cost utility analysis, decision tree with Markov state-transition model	US societal perspective	Standard of care including tPA	Lifetime (20 years)	3	Cost per QALY	Rates of morbidity and mortality, recanalization, annual mortality	PROACT II Study, MERCI trial, NINDS tPA trial	Quality of life factors for each health state based on previously published work	Cost of hospitalization for acute stroke with average professional fees, cost of rehabilitation after stroke, and cost of long-term care. Costs from Medicare	Deterministic sensitivity analysis, univariate sensitivity analysis	USD (2008)	12,120 per QALY. Borderline cost effective for patients older than 82 years of age	EVT performed within 8 hrs of stroke onset appears to be cost-effective. Estimates should be reassessed once data from RCTs becomes available.
Kim, 2010, USA (3)	68 year old patient with large-vessel ischemic stroke	Cost-utility, decision tree with Markov model	Societal	IV tPA	Lifetime	3	Cost per QALY	Recanalization rates within 1hr, symptomatic intracerebral hemorrhage, mortality	Patient level data from Multi-MERCI trial, CLOT-BURST study, and meta-analysis, USCDC life tables	Utility scores (0-1), assumed median utility for mild strokes and average for moderate to major strokes	Reimbursement data from the Centers for Medicare and Medicaid – procedural and hospitalization, physician costs, diagnostic angiography, long-term disability	Univariate sensitivity analysis using input distributions, multivariable sensitivity analysis using beta distribution for inputs based on a proportion, probabilistic sensitivity analysis	USD (2009)	16,001 per QALY	EVT with tPA is cost effective when compared to tPA alone. 97.6% of 10,000 simulated iterations were cost-effective.

Nguyen-Huynh, 2010, USA (25)	Hypothetical cohort of 65-year-old patients with acute ischemic stroke of a major intracranial artery beyond the 3-hour window for IV tPA.	Cost-utility analysis, decision tree with Markov model	Societal	Best medical therapy for acute ischemic stroke outside 3hr window for IV tPA	Lifetime	3	Cost per QALY	Recanalization and rated of hemorrhagic conversion, mRS score at 90 days	Multi-MERCI trial, PROACT II, other literature, US mortality data	Utility scores by mRS from prior cost effectiveness in patients with intracerebral hemorrhage	Cost data from the Centers for Medicare and Medicaid	Univariate sensitivity analysis, multivariable sensitivity analysis	USD (2009)	9,386 per QALY	EVT may be highly cost-effective. Additional evidence of stent retriever performance required.

Brinjikji, 2011, USA (26)	1649 patients were ≥65 years old and 2205 patients were <65 years old. Patients who experienced an ischemic stroke and those undergoing EVT were identified.	Cost-analysis	-	-	To discharge from hospitalization (2006-2008)	-	Hospital costs	Data for: age, gender, discharge status, length of stay, intracranial hemorrhage, gastrointestinal bleeding, mechanical ventilation, gastrostomy, and tracheostomy	NIS - Hospital discharge database	-	Database hospitalization costs, and discharge location costs	Completed multivariate analysis	USD (2008)	Median cost of hospitalization for patients treated with EVT is 36,999, which does not compare favorably with Medicare payment of 22,075. The median hospital costs of $50,628 for patients with morbidity and $35,109 for patients with mortality do not compare favorably with the average 2008 Medicare payment of $26639 with major complication.	Hospitalization costs for ischemic stroke patients treated with EVT are quite high, Medicare payments have not been adequate in reimbursing these hospitalizations. EVT is associated with reduced death and higher percentage with little or no disability, so it is quite possible that costs associated with hospitalization will be compensated later by decreases in long-term costs.

Bouvy, 2013, Netherlands (27)	Patients with ischemic stroke, admitted within 4.5 hrs from onset, without contraindications for IVT or intra-arterial treatment (IAT) – EVT only for patients with intracranial arterial occlusion	Cost-utility, decision tree	-	Conservative treatment for all, tPA for all, EVT for some and tPA for others, tPA for all followed by EVT as appropriate	Lifetime and 6 months	3	Cost per QALY	mRS at 6 months	Recanalization rates from literature, lifetime effects from epidemiological estimates used to create multistate life table	Functional outcome into health utility measure using PRACTISE trial. Dutch general public EQ5D health states used to assign utility values to the different health states.	0-6 month costs from PRACTISE, 7-12 month costs from EDISSE trial – patient-level cost data differentiated by functional outcome at 6 months, treatment costs from hospital	Probabilistic sensitivity analysis	Euros (2010)	(EVT with tPA vs tPA) 1922 per QALY at lifetime; 31,687 per QALY at 6 months	Cost effective using €50,000 per QALY threshold, but highly sensitive
Kass-Hout, 2015, USA (28)	Retrospective review of consecutive patients treated with EVT	Cost analysis with logistic regression	-	MERCI and Penumbra stent retrievers	-	-	Total procedural cost	Patient characteristics, LOS, procedure time, rate of successful perfusion, rate of good functional outcome (mRS at 90 days)	Cohort data	-	List prices for thrombectomy devices - excluding consumable goods	-	USD (2014)	Procedural cost using Solitaire or Trevo stent retrievers was significantly higher than thrombectomy with a non-stent retriever (13,419 vs. 9,308)	Solitaire and Trevo retrievers have better outcomes, but larger studies are needed to show cost effectiveness.

Simpson, 2014, USA (29)	Patients from the IMS III trial	Prospective cost-analysis	Societal perspective	tPA alone	-	-	Hospitalization costs associated with EVT and tPA	-	-	-	The cost of the endovascular devices used to administer intra-arterial tPA or to perform thrombectomy, cost of therapies using UB04 billing forms	Multivariable analysis	USD (2012)	EVT patients incurred costs of 35,130 compared to 25,630 incurred by tPA alone (P<0.0001)	EVT was associated with greater costs per subject when compared to subjects treated with tPA alone.
Rai, 2014, USA (30)	Consecutive patients with large vessel occlusions who had undergone either IV thrombolysis with r-tPA, or EV therapy	Cost-analysis	Academic hospital's financial perspective	IV thrombolysis (rtPA or tPA)	-	-	Hospital costs of EVT vs tPA patients	LOS, discharge destination, in-hospital mortality, mRS at 90 days	Retrospective data from various health sources	-	Hospital cost, hospital charges	-	USD (2008)	Hospital had net financial gain of $476 with EVT and a net financial loss of $1,752 with tPA	Among patients with indicators of financial recovery, EVT showed a net financial benefit.
Turk, 2014, USA (31)	Retrospective review of all stroke patients treated with EVT at one hospital over a 4-year period (171 patients)	Cost-analysis of devices used in recanalization	-	Penumbra aspiration catheters	-	-	Total cost of procedure including complication costs	Restored flow post procedure and occurrence of intraprocedural complications, mRS at 90 days	Chart review	-	All devices used in the procedure, and device cost to treat complication	-	USD (2012)	Average cost of Penumbra was 11,158.62. Average cost of stent retriever was 16,021.53.	Stent retrievers had higher rates of complete recanalization, were more expensive, had a higher complication rate, but improved overall outcomes

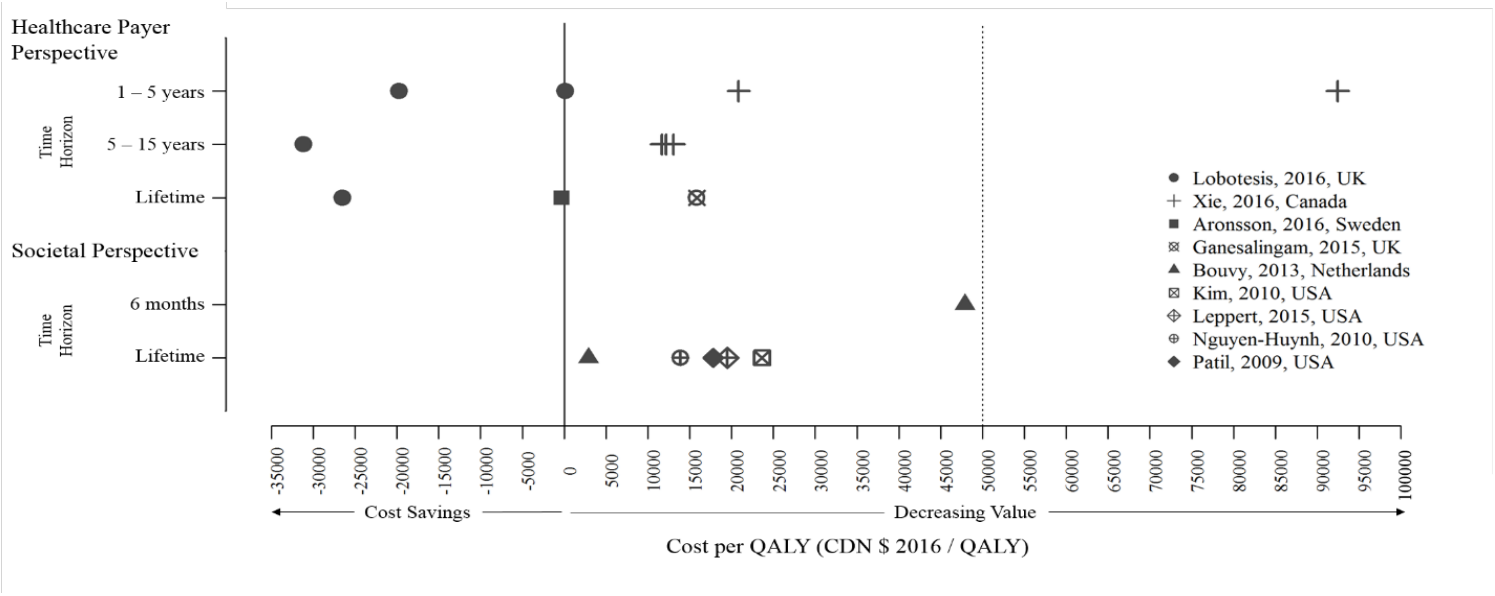
Comai, 2015, Sweden (32)	Patients with moderate to severe ischemic stroke, and a time window of less than 6hrs for anterior circulation and 12hrs for posterior circulation, and no poor neurologic response to IV tPA.	Cost-analysis	-	-	3 months	-	3 month costs for patients treated with EVT	Recanalization of the target vessel as assessed by two radiologists	Prospective database of consecutive patients from July 2013. Patients followed for three months	-	Cost of all angiographic devices from Bursar office – excluding consumable goods	-	Euros (2013)	Total cost of aspiration thrombectomy was $2,585.93, two-step thrombectomy including reperfusion catheter and stent retriever was $6,329.93. Total cost of stent retriever was $5,333.75. Differential cost between ADAPT technique and stent-assisted thrombectomy is −$2,747.82. We can estimate a savings of $32,226	The most expensive devices are reperfusion catheter and stent retriever. Sequential endovascular approach (SETA) with first-line direct aspiration could be useful to optimize EVT of stroke in terms of efficacy, safety and cost-effectiveness

Ganesalingam, 2015, UK (33)	Theoretical cohort of 1000 patients	Cost-utility analysis, short run decision tree with long run Markov model	UK National Health Service and Personal Social Services	IV tPA	Lifetime (20 years)	3.5	Cost per QALY and cost per death avoided	mRS score at 90 days	Pooled data from ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT, SWIFT PRIME	Utility score from Dorman et al, Sandercock et al, and Morris et al	Cost of IV tPA, cost of EVT, cost of the acute management of patients in the first 3 months after stroke, cost of recurrent stroke	One-way sensitivity varying probabilities, utilities and costs. Probabilistic sensitivity analysis	USD (2013)	Cost per QALY gained: $11,651. 71 deaths avoided over 20 years. CE acceptability curves showed 100% probability of being CE	EVT saves 1 life for every 14 therapies performed. Use of stent retrievers for EVT is cost effective in the UK.
Leppert, 2015, USA (34)	65-year-old patients meeting the inclusion criteria of the MR CLEAN trial	Cost-utility analysis, decision analytic model with Markov state transition model	Societal	Standard of care (tPA)	Lifetime	3	Cost per QALY	Mortality and mRS at 90 days, stroke recurrence, relative death hazard ratios	MR CLEAN trial data, literature sources	Quality of life estimates for stroke survivors from published literature	Cost of index stroke, cost of tPA, recurrent stroke hospitalization costs, annual post hospitalization cost	Deterministic one-way sensitivity, scenario analysis representing most unfavourable scenario	USD (2012)	Cost per QALY gained of $14,137.	Using a threshold of $50,000 per QALY, EVT was cost effective within the 6-hour window in addition to standard medical therapy and held up to significant variation in modelling assumptions

Turk, 2015, USA (35)	Retrospective review of all stroke patients treated with EVT at one hospital over a 4-year period (222 patients).	Cost analysis of thrombectomy device(s) used.	-	Penumbra aspiration and A Direct Aspiration first Past Technique (ADAPT)	-	-	Average total cost of treatment group	mRS at 90 days, rate of revascularization	Chart review	-	All devices used during the procedure, direct and indirect hospital costs associated with patients' admission from hospital financial database	-	USD (2013)	Average cost for Penumbra was $47,673. Average cost for stent retriever was $46,735. Average cost for ADAPT was $31,716. Not significant.	ADAPT was the least costly method. The addition of the stent retriever improves recanalization, but increases costs of care.
Aronsson, 2016, Sweden (36)	Simulated cohort of ischemic stroke patients, matched the population of the 5 RCTs	Cost-utility, decision analytic Markov model	Health care payer	Standard of care from trials	Lifetime	3	Cost per QALY	mRS at 90 days and hazard ratio	Pooled data from ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT, SWIFT PRIME	Age dependent utility weights based on population data	First year after stroke, long term costs (including: rehabilitation, follow-up, drugs, home assistance and residential housing), cost of EVT	Two-way sensitivity analyses; probabilistic Monte Carlo simulation	USD (2015)	Dominated (-223 per QALY)	EVT with up-to-date stent retrievers, short door-to-groin puncture time and neuroimaging criteria appears cost effective.
Lobotesis, 2016, UK (37)	Based on population in the SWIFT PRIME trial. Base case age 66 years	Cost-utility analysis with Markov state transition model	UK health provider perspective	IV tPA alone	Lifetime, 1, 2 and 5 years	3.5	Cost per QALY	mRS score at 90 days, relative risk of dying, probability of recurrent stroke	SWIFT PRIME Clinical trial, Slot et al, Mohan et al	Utilities based on patients in the Oxford Vascular Study	Device and drug costs, costs of administering treatment management of adverse events, hospitalization costs, and long-term care costs.	Deterministic sensitivity analysis, probabilistic sensitivity analysis	Pound (£) (2013)	Lifetime: dominant (-£14,368), 1yr: 62 per QALY, 2yr: Dominant (-£10,700), 5yr: Dominant (-£16,904)	EVT is a highly effective treatment for acute ischemic stroke and results in long term cost saving.

Xie, 2016, Canada (38)	Patients with proximal occlusions and contraindications to intravenous tissue plasminogen activator, representing 25% of the trial participants and the group of patients who may obtain the most benefit from mechanical thrombectomy treatment.	Cost utility analysis, decision analytic model and Markov model	Public payer perspective	IV tPA alone	5-year time horizon in base case. 1, 3, 10 and 15 in sensitivity	5	Cost per QALY	mRS at 90 days, long term survival	Meta-analysis of ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT, SWIFT PRIME, Oxford Vascular Study	Pooled estimate of utility scores from 5 RCTs at 90 days, and EQ-5D utilities from Dorman et al (The Oxford Vascular Study).	Annual costs form Economic Burden of Ischemic Stroke study. Assumed additional cost of EVT was $15,000 from literature	Scenario analysis of ESCAPE only, and IMS III with MR CLEAN only. One way and multiway sensitivity conducted. Probabilistic sensitivity.	CAD (2015)	Base case: cost per QALT was $11,990. 1yr: $91,090, 3yr: $20,540, 10yr: $11,491, and 15yr: $12,877	Treatment with EVT is cost effective compared to tPA alone. In Canada, EVT is likely to represent good value for money and should be supported.

Figure 1 Summary of Cost per QALY Findings (all 9 identified studies)



Organization, Year, Country	Type of Report	Search Dates	Device(s) Evaluated	Patient Selection	Evidence	Conclusions
AHTA, Australia, 2010 (39)	Horizon Scanning Technology Prioritizing Summary	Not reported	Penumbra System	Not reported	• 1 single-arm study • 2 case series	"The low-level of available evidence makes the wider clinical impact of the Penumbra system uncertain at this stage. The technology has already begun to diffuse into the Australian health care system and has potential benefit to those patients who have ready access to the technology in term of their proximity. The device is substantially more expensive than existing treatments."
BlueCross BlueShield, 2015, USA (42)	Technology Assessment	1 January 2002 to 29 September 2014	MERCI retriever, Penumbra System, Solitaire Neurovascular Remodeling Device, TREVO stent retriever	Adults with acute ischemic stroke treated with EVT	• 5 RCTs	"For acute ischemic stroke, RCTs have not demonstrated a health benefit – usually defined as a reduction in disability at 90 days – for endovascular therapy compared with IV tPA. The Solitaire and TREVO devices appear to produce better outcomes than the Merci device; how the 2 newer devices compare with each other is not known. Trials are under way to provide more information on the value of endovascular treatments and possibly on the patient groups for whom they may be most effective."

Appendix C: Environmental Scan (reports without 2015 evidence)

Appendix D: Patient Perspectives

Search Strategy for Stroke Travel Perspectives

MEDLINE

1. exp Brain Ischemia/
2. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw
3. exp stroke/
4. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
5. intracranial arteriosclerosis/
6. "intracranial embolism and thrombosis"/
7. carotid artery thrombosis/
8. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw.
9. transient isch?emi* attack.tw,kw.
10. carotid artery thrombosis.tw,kw.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. (care or healthcare or management or rehabilitation or therapy or treatment).tw.
13. (drug therapy or prevention control or rehabilitation or therapy).fs.
14. exp patient care management/ or exp patient care/
15. 12 or 13 or 14
16. 11 and 15
17. travel/ or medical tourism/
18. Patient Transfer/
19. (patient* adj5 (transfer* or transport*)).tw.
20. (distance or travel*).tw.
21. medical tourism.tw.
22. 17 or 18 or 19 or 20 or 21
23. 16 and 22
24. exp Attitude/
25. Choice Behavior/
26. Decision Making/
27. Consumer Behavior/
28. "patient acceptance of health care"/ or patient satisfaction/ or patient preference/
29. (accept* or attitude* or behavior* or behaviour* or belief* or choice or perspective* or preference* or satisfaction or view or views).tw.
30. exp qualitative research/
31. Grounded Theory/
32. interview/
33. qualitative.tw.
34. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 33
35. 23 and 34
36. limit 35 to animals
37. limit 35 to (animals and humans)

38. 36 not 37
39. 35 not 38

Total: 160 abstracts

Cochrane CENTRAL Register

1. exp Brain Ischemia/
2. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw.
3. exp stroke/
4. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
5. intracranial arteriosclerosis/
6. "intracranial embolism and thrombosis"/
7. carotid artery thrombosis/
8. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw.
9. transient isch?emi* attack.tw,kw.
10. carotid artery thrombosis.tw,kw.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. (care or healthcare or management or rehabilitation or therapy or treatment).tw.
13. (drug therapy or prevention control or rehabilitation or therapy).fs.
14. exp patient care management/ or exp patient care/
15. 12 or 13 or 14
16. 11 and 15
17. travel/ or medical tourism/
18. Patient Transfer/
19. (patient* adj5 (transfer* or transport*)).tw.
20. (distance or travel*).tw.
21. medical tourism.tw.
22. 17 or 18 or 19 or 20 or 21
23. 16 and 22
24. exp Attitude/
25. Choice Behavior/
26. Decision Making/
27. Consumer Behavior/
28. "patient acceptance of health care"/ or patient satisfaction/ or patient preference/
29. (accept* or attitude* or behavior* or behaviour* or belief* or choice or perspective* or preference* or satisfaction or view or views).tw.
30. exp qualitative research/
31. Grounded Theory/
32. interview/
33. qualitative.tw.
34. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 33
35. 23 and 34
36. limit 35 to animals
37. limit 35 to (animals and humans)
38. 36 not 37

39. 35 not 38

Total: 14 abstracts

Cochrane Database of Systematic Reviews

1. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw.
2. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
3. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw
4. transient isch?emi* attack.tw,kw
5. carotid artery thrombosis.tw,kw.
6. 1 or 2 or 3 or 4 or 5
7. (care or healthcare or management or rehabilitation or therapy or treatment).tw
8. 6 and 7
9. (patient* adj5 (transfer* or transport*)).tw
10. (distance or travel*).tw
11. medical tourism.tw
12. 9 or 10 or 11
13. 8 and 12
14. (accept* or attitude* or behavior* or behaviour* or belief* or choice or perspective* or preference* or satisfaction or view or views).tw
15. 13 and 14

Total: 115 abstracts

HTA database

1. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw.
2. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
3. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw
4. transient isch?emi* attack.tw,kw
5. carotid artery thrombosis.tw,kw.
6. 1 or 2 or 3 or 4 or 5
7. (care or healthcare or management or rehabilitation or therapy or treatment).tw
8. 6 and 7
9. (patient* adj5 (transfer* or transport*)).tw
10. (distance or travel*).tw
11. medical tourism.tw
12. 9 or 10 or 11
13. 8 and 12
14. (accept* or attitude* or behavior* or behaviour* or belief* or choice or perspective* or preference* or satisfaction or view or views).tw

15. 13 and 14

Total: 2 abstracts

EMBASE

1. exp brain ischemia/
2. ((isch?emi* adj3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA)) or AIS).tw,kw.
3. exp cerebrovascular accident/
4. (stroke* adj3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)).tw,kw.
5. brain atherosclerosis/
6. brain embolism/
7. exp occlusive cerebrovascular disease/
8. carotid artery thrombosis/
9. ((occlus* or hypoxi* or block* or infarct* or clot* or termination) adj6 (carotid or cerebr* or MCA or ACA)).tw,kw.
10. transient isch?emi* attack.tw,kw.
11. carotid artery thrombosis.tw,kw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. limit 12 to animal studies
14. limit 12 to (human and animal studies)
15. 13 not 14
16. 12 not 15
17. limit 16 to (conference abstract or conference proceeding or editorial or letter)
18. 16 not 17
19. limit 18 to "review"
20. 18 not 19
21. limit 18 to (meta analysis or "systematic review")
22. ((critical or systematic or scoping or realist or evidence-based) adj (review or synthesis)).tw.
23. 18 and 22
24. 20 or 21 or 23
25. patient care/ or case management/
26. therapy/ or exp drug therapy/
27. health care delivery/
28. disease management/
29. (prevention or treatment or management or care or therapy).tw.
30. (drug therapy or rehabilitation or therapy).fs.
31. intervention*.tw.
32. 25 or 26 or 27 or 28 or 29 or 30 or 31
33. 24 and 32
34. exp patient transport/
35. (patient* adj5 (transfer* or transport*)).tw.
36. travel/
37. medical tourism/
38. (distance or travel*).tw.

39. medical tourism.tw.
40. 34 or 35 or 36 or 37 or 38 or 39
41. 33 and 40
42. attitude/ or attitude to health/ or attitude to illness/ or consumer attitude/ or exp family attitude/ or exp patient attitude/
43. decision making/
44. qualitative.tw.
45. exp qualitative analysis/ or exp qualitative research/
46. (accept* or attitude* or behavior* or behaviour* or belief* or choice or experience* or perspective* or preference* or satisfaction or view or views).tw.
47. 42 or 43 or 44 or 45 or 46
48. 41 and 47

Total: 235 abstracts

CINAHL

1. ((MH "Stroke") OR (MH "Stroke Patients") OR (MH "Cerebral Ischemia+") OR (MH "Intracranial Arteriosclerosis") OR (MH "Intracranial Embolism and Thrombosis+") OR (MH "Carotid Artery Thrombosis")) OR TI ((ischemi* or ischaemi*) N3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA or AIS)) OR AB ((ischemi* or ischaemi*) N3 (stroke* or apoplex* or cerebr* or brain or encephalopath* or neur* or CVA or AIS)) OR TI (stroke* N3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)) OR AB (stroke* N3 (acute or cerebr* or attack* or accident* or lacunar* or cardioembol*)) OR TI (((occlus* or hypoxi* or block* or infarct* or clot* or termination) N6 (carotid or cerebr* or MCA or ACA))) OR AB (((occlus* or hypoxi* or block* or infarct* or clot* or termination) N6 (carotid or cerebr* or MCA or ACA))) OR TI (transient ischemi* attack or transient ischaemi* attack) OR AB (transient ischemi* attack or transient ischaemi* attack) OR TI carotid artery thrombosis OR AB carotid artery thrombosis)
2. (care or healthcare or management or rehabilitation or therapy or treatment)) OR (drug therapy or prevention control or rehabilitation or therapy)
3. ((MH "Travel Health") OR (MH "Travel+") OR (MH "Medical Tourism")) OR TI (distance or travel*) OR AB (distance or travel*)
4. ((MH "Patient Attitudes") OR (MH "Consumer Attitudes") OR (MH "Patient Satisfaction") OR TI ((accept* or attitude* or behavior* or behaviour* or belief* or choice or experience* or perspective* or preference* or satisfaction or view or views)) OR AB ((accept* or attitude* or behavior* or behaviour* or belief* or choice or experience* or perspective* or preference* or satisfaction or view or views)))
5. 1 and 2 and 3 and 4

Total: 66 abstracts

Focus Group Consent Form

Travelling to Obtain Critical Care: Rural and Remote Perspectives Focus Group

Focus group consent

What is the background for this project?

The Health Technology Review (HTR) is a joint BC Ministry of Health and Health Authority process used to provide evidence-informed recommendations about which new non-drug health technologies should be publicly provided in the province. Additional information on the Health Technology Review process is available online at www.health.gov.bc.ca/htr.

The B.C. Ministry of Health has contracted the University of Calgary's Health Technology Assessment (HTA) unit to conduct a review of the evidence on a new stroke treatment called endovascular therapy (EVT). This 'clot retrieval' treatment shows promise for improving outcomes for people who experience a certain kind of stroke (i.e., an acute ischemic stroke caused by a larger clot).

EVT technology is currently only available in larger city centres, however, meaning that patients in rural and remote areas would need to travel away from their home communities to receive care.

What does your participation involve?

Your participation in this 1.5-hour long teleconference focus group will involve a discussion about your experiences obtaining critical care away from your home community, and your insights on how this transitions to and from large centers can optimally be handled. A toll-free phone number will be provided for the teleconference.

Your participation in this focus group is voluntary. You may decline to answer any questions you do not wish to answer, and withdraw from participation in the focus group at any time. We are asking for your permission to record the discussion; this will help ensure that we have a complete record of everything discussed in the focus group.

How will the information you share be kept confidential?

The Ministry of Health is collecting your personal information under section 26 (c) of the Freedom of Information and Protection of Privacy Act. We ask that you do not provide any third party information (i.e. talk about others by name) during the focus group discussion. The information you share will be used to generate a report. Once the report has been completed the recorded information, including any personal information collected, will be destroyed. If you have any questions about the collection of your personal information please contact Kevin Samra, Director, Health Technology Review at 250-952-6213, PO BOX 9637 STN PROV GOVT.

We also ask that you do not share what you heard from the other participants outside of this focus group. Having said that, the U of C team cannot control what participants choose to discuss

outside of the meeting. Please keep this in mind when you are deciding what information you feel comfortable sharing.

The U of C team will keep the information that you provide through this discussion confidential. Although anonymous quotes may be included in the report to illustrate important points, no names or identifying information will be used in any reporting.

Do you understand what your participation entails?

Your signature on this form, or your verbal consent, confirms your willingness to participate in this focus group discussion. It also means that you understand and agree to what has been outlined above. If you have questions about this focus group please contact: Gail MacKean, Health Technology Assessment Unit, University of Calgary at: 403-830-2580 or gail.mackean@gmail.com.

_____ _____

Your name printed Your signature

_____

Date

Focus Group Interview Guide

Travelling to Obtain Critical Care: Rural and Remote Perspectives Focus Group

Go over project background in the consent form re why we are interested in people experience with having to access care in a major centre far from home.

Thank you again for taking the time to share your experience with us.

Any questions before we get started?

Questions to guide the conversation

Introductory

1) **Roundtable introductions:** I am just going to go around our virtual table here and ask you to share your name (no need to say your last name, unless you want to), where you are currently living, and why you were interested in participating in this focus group discussion.
2) **Could you talk about any experience you have had travelling to a major centre** for critical care (e.g., stroke, heart condition, severe trauma, other) or any experience that required hospitalization in such a centre? If you've not had this kind of experience, could you talk more generally about experiences with having to seek out specialized care in a major city far from home?

Transition in

3) How did the transport/travel into the major centre go? What went well? What didn't go quite so well?
   Probe around:

   - Emergency transport to a major centre (e.g., ground ambulance, air transport)… Was someone (family/friend) able to accompany you? If not, why not?
   - Other kinds of transportation to a major centre…
   - Communication with you/family about what was happening…
   - Obtaining important information from you/family…
   - How you/your family were treated…(e.g., kindness, dignity, respect, welcomed)…
   - Anything else?

4) How about the arrival at the major centre? What went well? What didn't go quite so well?
   Probe around:

   - Communication with you/family about what was happening…
   - Obtaining important information from you/family/friend…
   - How you/your family were treated…(e.g., kindness, dignity, respect, welcomed)…
   - Informed consent process…
   - Experience with the actual treatment (e.g., cardiac catheterization, stroke Tx, other)…
   - Anything else?

Hospital stay in the major centre

5) How did the hospital stay in the major centre go? What went well? What didn't go quite so well?
   Probe around:

   - Length of stay
   - Rehabilitation
   - Access to family/friends
   - Hardship for family/friends
   - Discharge planning
   - Anything else?

Transition out

6) Where were you 'discharged to' from the large hospital (e.g., rehab centre, hospital closer to home, home)?
7) How did the travel/transport back go? What went well? What didn't go quite so well?
   Probe around:

   - Emergency transport to a major centre (e.g., ground ambulance, air transport)… Was someone (family/friend) able to accompany you? If not, why not?
   - Other kinds of transportation to a major centre…
   - Communication with you/family about what was happening…
   - How you/your family were treated…(e.g., kindness, dignity, respect, welcomed)…
   - Anything else?
8) How about the arrival at another hospital or rehab centre (if applicable)?
   Probe around:

   - Communication with you/family about what was happening…
   - Sharing of information between the major centre and the local hospital or rehab centre…
   - How you/your family were treated…(e.g., kindness, dignity, respect, welcomed)…
   - Anything else?
9) Arrival home and any follow-up care required?
   Probe around:

   - Communication with you/family, including the sharing of the information you needed at home…
   - Sharing of information between the major centre and your family doctor, nurse practitioner, physiotherapist or others…
   - Anything else?

Closing

10) Reflecting on your experiences - what is the most important advice you would give to someone planning to introduce a new treatment like EVT in BC, which will require emergency transport to a major centre?

Is there anything else you'd like to say?