

# Systematic Review of the Cost and Cost-Effectiveness of Rapid Endovascular Therapy for Acute Ischemic Stroke

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**Background and Purpose**—Rapid endovascular therapy (EVT) is an emerging treatment option for acute ischemic stroke. Several economic evaluations have been published examining the cost-effectiveness of EVT, and many international bodies are currently making adoption decisions. The objective of this study was to establish the cost-effectiveness of EVT for ischemic stroke patients and to synthesize all the publicly available economic literature.

**Methods**—A systematic review of the published literature was conducted to identify economic evaluations and cost analyses of EVT for acute ischemic stroke patients. Systematic review best practices were followed, and study quality was assessed.

**Results**—Four-hundred sixty-three articles were identified from electronic databases. After deduplication, abstract review, and full-text review, 17 studies were included. Seven of the studies were cost analyses, and 10 were cost-effectiveness studies. Generally, the cost analyses reported on the cost of the approach/procedure or the hospitalization costs associated with EVT. All of the cost-effectiveness studies reported a cost per quality-adjusted life year as the primary outcomes. Studies varied in regards to the costs considered, the perspective adopted, and the time horizon used. All the studies reported a cost per quality-adjusted life year of <\$50 000 as the primary outcome.

**Conclusions**—There is a robust body of evidence for the cost and cost-effectiveness of EVT. The cost analyses suggested that although EVT was associated with higher costs, it also resulted in improved patient outcomes. From the cost-effectiveness studies, EVT seems to be good value for money when a threshold of \$50 000 per quality-adjusted life year gained is adopted. (*Stroke*. 2017;48:2519-2526. DOI: 10.1161/STROKEAHA.117.017199.)

**Key Words:** brain ■ hospital costs ■ hospitalization ■ odds ratio ■ stroke

The incidence of ischemic stroke globally was estimated to be 11.6 million events in 2010.<sup>1</sup> In 2013, stroke (ischemic and hemorrhagic) was determined to be the second leading cause of death internationally, resulting in ≈6.5 million deaths.<sup>2</sup> In the United States, stroke remains the leading cause of long-term disability.<sup>3</sup> Along with the impactful physical burden, stroke also carries a large economic burden. Recent estimates from the United States show that the direct and indirect cost of stroke is ≈\$33.0 billion annually (2011 USD).<sup>4</sup> When stratifying by stroke type, another recent study estimated that the average annual costs of ischemic stroke in Canada was \$2.8 billion.<sup>5</sup> This study further estimated that the average annual cost per ischemic stroke patient was \$75 353, and that the annual cost of caring for a patient with a disabling stroke is double that of a patient with a nondisabling stroke.<sup>5</sup>

Previous guidelines have recommended treating ischemic stroke with intravenous alteplase (tPA [tissue-type plasminogen activator]); however, rapid endovascular therapy (EVT)

is an emerging treatment option. A series of five 2015 randomized control trials demonstrated that for patients with an ischemic stroke caused by a blockage in a large intracranial artery, a favorable baseline brain and neurovascular imaging profile, and time from onset within the required timeframe, EVT significantly improved functional outcomes compared with standard care.<sup>6–10</sup> Furthermore, an international meta-analysis of 5 trials suggests that EVT significantly improves functional outcomes at 90-day poststroke compared with standard care (adjusted odds ratio, 2.49; confidence interval, 1.76–3.53).<sup>11</sup>

Although studies have shown that EVT is an effective treatment option for eligible ischemic stroke patients, the associated financial costs should be considered before implementation. Several economic evaluations have been published, and many international bodies are currently making adoption decisions. The objective of this study was to establish the cost-effectiveness of EVT for ischemic stroke patients and to synthesize all the publicly available economic literature.

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## Methods

### Search Strategy

MEDLINE, EMBASE (Excerpta Medica Database), Health Technology Assessment Database, the UK National Health Services Economic Evaluation Database, and EconLit were all searched from inception until October 17, 2016. A detailed search strategy was developed by an academic librarian. For all databases, terms relevant to EVT (thrombectomy, clot retrieval, stent-assisted, clot disruption) were combined using the Boolean operator AND, with terms reflecting the health state (ischemia, brain, cerebral, stroke) and economic evaluations (cost, economic, cost-effectiveness). The initial search strategy was developed for use in MEDLINE and then adapted for the other databases. Studies were limited to human studies published in English or French. The reference lists of included studies were also searched to identify additional studies of relevance to this review.

### Study Selection

Titles and abstracts were reviewed independently and in duplicate by study investigators (L.K.S. and S.G.). Studies proceeded to full-text review if they were economic evaluations (including cost-effectiveness [calculates an incremental cost-effectiveness ratio], cost-utility [a cost-effectiveness study that reports a cost per quality-adjusted life year (QALY)], cost minimization (examines cost reductions), and cost-benefit analyses (cost and benefits in dollars), cost analysis (only examines cost, does not include clinical benefit), or business cases of EVT for ischemic stroke patients. The initial screen was kept intentionally broad, and all abstracts included by either reviewer were included in the full-text review.

Full-text articles were retrieved and reviewed independently by the same 2 trial investigators (L.K.S. and S.G.). Articles were excluded if they were published in abstract form only, not a peer-reviewed journal article, in any language other than English or French, not an economic evaluation, cost analysis, or business case, did not examine patients with ischemic stroke, or because the intervention was not EVT. Discrepancy between reviewers was resolved through consensus, and agreement was measured ( $\kappa$  statistic).

### Data Extraction and Analysis

The primary outcomes of interest were the cost-effectiveness, cost-utility, cost-benefit, and costs associated with the use of EVT for ischemic stroke. Data were extracted independently and in duplicate by study investigators (L.K.S. and S.G.). 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 were then resolved through consensus and review of source documents.

To assess the quality of the economic evaluations, the Consensus on Health Economic Criteria list was applied.<sup>12</sup> Quality assessment was completed independently and in duplicate with discrepancies being resolved through discussion and review of source documents. Using this checklist, each study was assessed based on whether they reported on the 19 recommended criteria (eg, appropriate valuation of outcomes, sensitivity analysis, and appropriate economic study design). For each criterion, a study was assigned 1 point for appropriately addressing the criterion, and zero points if it did not. As per the tool instructions, all criteria are weighted equally.<sup>12</sup> Where appropriate, some criteria were deemed to be Not Applicable for cost analyses, as the Consensus on Health Economic Criteria list is designed for economic evaluations. A final tally out of a possible 19 (modified for cost analyses) points was calculated for each study.

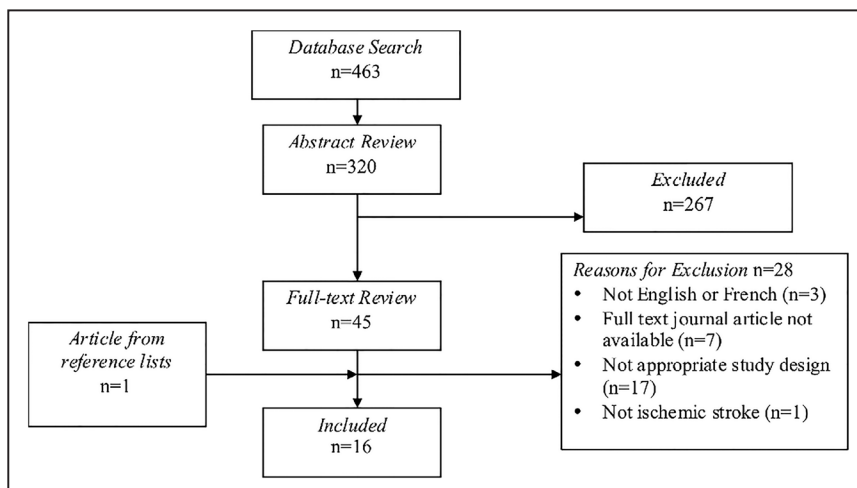
A component-based analysis was used to describe and synthesize the included studies. For the identified cost-utility studies, all incremental cost-effectiveness ratios estimating the cost per QALY, and varying by perspective and time horizon, were extracted. This includes the primary outcome, as well as secondary outcomes, reported in the sensitivity analysis. To synthesize the results, all estimates were converted and inflated to 2016 Canadian dollars.

## Results

A total of 463 abstracts were identified through the literature search, and reviewers screened 320 unique citations after deduplication. Of those abstracts, 277 were excluded and 45 proceeded to full-text review (Figure 1). The reference lists of all identified articles were hand searched, and 1 additional study was identified. Ultimately, 17 studies were included,<sup>13–29</sup> and there was almost perfect agreement between reviewers ( $\kappa=0.856$ ).<sup>30</sup>

### Included Studies

Overall, 7 cost analyses<sup>16,18–22,25</sup> and 10 cost-utility studies<sup>13–15,17,23,24,26–29</sup> were identified. All the studies were in English. Using the Consensus on Health Economic Criteria list, quality scores ranged from 8 to 15 for the cost analyses and 17 to 19 for the cost-utility studies. All the studies appropriately described the study population and the competing alternatives, while also identifying all the important and relevant costs for each alternative. However, very few of the studies appropriately discussed ethical and distributional issues associated with EVT.



**Figure 1.** Flowchart of study selection and inclusion process.

Of the cost analyses, 6 are from the United States,<sup>16,18–21,25</sup> and 1 is from Sweden.<sup>22</sup> All were published between 2011 and 2015. Generally, the studies reported on the cost of the approach/procedure or the hospitalization costs associated with EVT.

For the cost–utility studies, 5 are from the United States,<sup>13–15,24,27</sup> 2 are from the United Kingdom,<sup>23,28</sup> 1 is from the Netherlands,<sup>17</sup> 1 is from Sweden,<sup>26</sup> and 1 is from Canada.<sup>29</sup> All studies were published between 2009 and 2016, and all reported an incremental cost-effectiveness ratio of the cost per QALY gained as the primary outcome. Clinical effectiveness and life expectancy were estimated from a variety of sources and literature.<sup>31–41</sup> The Table provides a summary of all the included studies.

### Cost Analyses

Seven studies performed cost analyses and reported different costs for providing EVT. The studies are grouped into 2 broad categories.

#### Cost of Procedure/Approach

Four studies reported on the cost of the devices and the costs of the different approaches for performing EVT.<sup>18,21,22,25</sup> Kass-Hout et al<sup>18</sup> calculated the total procedural cost of EVT using the list prices for the devices used (catheters, thrombectomy devices); however, consumable goods, staff, and imaging equipment costs were not included. In comparison to previous technologies, procedural cost using Solitaire or Trevo stent retrievers for EVT was significantly higher than performing thrombectomy with a non-stent retriever. Although cost of EVT was \$13 419 (2014 USD) compared with \$9308 (2014 USD), the use of the stent retrievers provided better outcomes.<sup>18</sup> Comai et al<sup>22</sup> included cost inputs for all angiographic devices used to perform EVT 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 €–2747.82 (2013 Euros), with an estimated cost saving of €32226 (2013 Euros).<sup>22</sup> Turk et al<sup>21</sup> (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 a differential cost of \$4862.91 (2012 USD) for the stent retriever compared with Penumbra.<sup>21</sup> Last, Turk et al<sup>25</sup> (2015) reported the average total cost for 3 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 \$47673, stent retriever was \$46735, and ADAPT was \$31 716 (2013 USD).<sup>25</sup> 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 with 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.

#### Hospitalization Costs of EVT

Three studies reported the hospitalization costs for patients treated with EVT.<sup>16,19,20</sup> All studies were from the United

States. The costs in this analysis included cost of discharge location, hospital charges, and cost of EVT therapies. The study by Brinjikji et al<sup>16</sup> compared the cost of EVT with the average Medicare reimbursement payment (\$36 999 versus \$22 075 [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 result in decreases in long-term costs. Simpson et al<sup>19</sup> compared costs for patients treated with EVT and patients treated with intravenous tPA alone, and found that EVT patients incurred \$9500 (2012 USD) more in costs than tPA patients. Last, Rai et al<sup>20</sup> found a net financial gain of \$476 (2008 USD) associated with EVT, compared with the net financial loss of \$1752 (2008 USD) associated with tPA; however, results were not significant.

### Cost–Utility Studies

To summarize the results of the cost–utility studies, all cost-effectiveness ratios varying by perspective and time horizon were extracted and plotted as a cost per QALY (Figure 2). This includes estimates that varied by time horizon or study perspective in a secondary analysis or in the sensitivity analysis. Overall, 2 studies determined EVT to be a dominant treatment strategy resulting in cost savings,<sup>26,28</sup> whereas the remaining 8 studies all reported incremental cost-effectiveness ratios within the generally acceptable cost-effectiveness range.<sup>13–15,17,23,24,27,29</sup> Only 1 estimate was outside this range.<sup>29</sup>

### Discussion

In summary, this review identified 17 studies that reported on the costs or cost-effectiveness of EVT for acute ischemic stroke. Seven of the studies were cost analyses that either reported on the cost of procedure/EVT approach or on total hospitalization costs associated with EVT.<sup>16,18–22,25</sup> The other 10 studies were cost–utility studies and reported a cost per QALY gained as the primary outcome.<sup>13–15,17,23,24,26–29</sup> Quality scores ranged from 8 to 19 using the Consensus on Health Economic Criteria list.

Previous systematic reviews and meta-analyses on this topic have reported on the clinical effectiveness of EVT. For instance, a systematic review and meta-analysis by Balami et al<sup>42</sup> identified 8 RCTs on this topic and reported an odds ratio of 1.71 (confidence interval, 1.18–2.48) for being functionally independent (modified Rankin Scale score of 0–2) at 90 days poststroke. This result becomes more pronounced when one examines only the 2015 literature (odds ratio, 2.23; confidence interval, 1.77–2.81).<sup>42</sup> Authors also identified a nonsignificant difference in the incidence of spontaneous intracerebral hemorrhage between the EVT and control groups, and although they identified a possible decrease in all-cause mortality in favor of the EVT group, this result was also not significant. The HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) collaboration pooled patient-level data from the five 2015 trials (as opposed to the aggregate data pooled Balami et al<sup>42</sup>). The HERMES study reported an adjusted odds ratio of 2.49 (confidence interval, 1.76–3.53) for functional independence (modified Rankin Scale score of 0–2) at 90 days and nonsignificant findings

**Table. Summary of Included Studies by Year**

Author, Year, Country (Currency)	States Included	Source of Clinical Effectiveness	Long-Term Survival	Costs Included	Primary Outcome	CHEC	Conclusion
Patil et al, <sup>13</sup> 2009, United States	Independent (mRS score of $\leq 2$ ), dependent (mRS score of 3–5), or dead	MERCI study <sup>31</sup>	Annual probability of dying based on age-related mortality rate and the risk of recurrent stroke	Cost of hospitalization for acute stroke, cost of rehabilitation after stroke, cost of long-term care associated with independent and dependent health states	\$12 120 per QALY (USD 2008) Time horizon: 20 y Perspective: Societal	17/19	Cost-effective
Kim et al, <sup>14</sup> 2011, United States	Independent (mRS score of $\leq 2$ ), dependent (mRS score of 3–5), or dead	Multi-MERCI study <sup>32</sup>	Age-specific all-cause mortality rates from the 2006 US Centers for Disease Control and Prevention life tables	Initial procedural and hospitalization costs, physician costs, cost of long-term care associated with independent and dependent health states	\$16 001 per QALY (USD 2009) Time horizon: Lifetime Perspective: Societal	17/19	Cost-effective
Nguyen-Huynh et al, <sup>15</sup> 2011, United States	Independent (mRS score of $\leq 2$ ), dependent (mRS score of 3–5), or dead	Multi-MERCI study <sup>32</sup>	Age- and sex-specific all-cause mortality rates from 2005 US mortality data	National average payment rates for mechanical embolectomy and best medical therapy	\$9386 per QALY (USD 2009) Time horizon: Lifetime Perspective: Societal	17/19	Cost-effective
Brinjikji et al, <sup>16</sup> 2011, United States	...	...	...	Hospitalization costs	The 2006–2008 median cost of hospitalization for patients treated with EVT with a good outcome is \$36 999 (USD 2008). This is higher than the average 2008 Medicare payment	8/15	Medicare payments had not been sufficient in reimbursing EVT hospitalizations
Bouvy et al, <sup>17</sup> 2013, the Netherlands	Good outcome (mRS score of 0–1, mRS score of 2–3), Poor outcome (mRS score of 4, mRS score of 5, Death)	Brekenfeld et al <sup>33</sup> and expert opinion	Survival probabilities from concurrent Dutch follow-up studies <sup>34</sup>	Cost of hospital care, rehabilitation, nursing home, and home care differentiated by mRS	€31 687 per QALY gained at 6 mo and €1922 per QALY gained over a lifetime (Euros 2010) Perspective: Not specified (assumed societal)	17/19	Cost-effective
Kass-Hout et al, <sup>18</sup> 2015, United States	...	...	...	Costs of thrombectomy devices, microcatheter/microwire systems, access catheters and wires, and support catheters and balloon guide catheters	Procedural cost using Solitaire or Trevo stent retrievers was significantly higher than thrombectomy with a nonstent retriever (\$13 419 vs \$9308 [USD 2010])	9/16	Solitaire and Trevo retrievers have better outcomes, but larger studies are needed to show cost-effectiveness
Simpson et al, <sup>19</sup> 2014, United States	...	...	...	Cost of initial hospital admission, IV tPA, free devices, and hospital requested device replacements	EVT patients incurred costs of \$35 130 compared with \$25 630 incurred by tPA alone ( $P < 0.0001$ ; USD 2012).		EVT was associated with greater costs per subject when compared with subjects treated with tPA alone

(Continued)

Table. Continued

Author, Year, Country (Currency)	States Included	Source of Clinical Effectiveness	Long-Term Survival	Costs Included	Primary Outcome	CHEC	Conclusion
Rai and Evans, <sup>20</sup> 2015, United States	...	...	...	Hospital costs (including direct and total costs)	Hospital had net financial gain of \$476 with EVT and a net financial loss of \$1752 with tPA (USD 2008)	15/17	Among patients with indicators of financial recovery, EVT showed a net financial benefit compared with tPA alone
Turk et al, <sup>21</sup> 2014, United States	...	...	...	Cost of all devices used in the procedure (femoral sheaths, IA tPA, guidewires, and catheters) and cost of devices used to treat complication	The average cost of treating a patient with the Penumbra aspiration system was \$11 158.62. Average cost of stent retriever was \$16 021.53 (USD 2012)	12/16	Stent retrievers had higher rates of complete recanalization, were more expensive, had a higher complication rate, but improved overall outcomes
Comai et al, <sup>22</sup> 2015, Sweden	...	...	...	Costs of all angiographic devices used in standardized procedures (femoral sheath, diagnostic catheter, guide catheter/ microcatheter, guidewires, reperfusion catheter, and stent retriever)	Total cost of aspiration thrombectomy was €2585.93, 2-step thrombectomy, including reperfusion catheter, and stent retriever was €6329.93. Total cost of stent retriever without aspiration catheter was €5333.75. Differential cost between ADAPT technique and stent-assisted thrombectomy is -€2747.82 (Euros 2013)	11/16	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 et al, <sup>23</sup> 2015, United Kingdom	Independent (mRS score of ≤2), dependent (mRS score of 3–5), or dead	MR CLEAN, ESCAPE, EXTEND IA, SWIFT-PRIME, REVASCAT	Davis et al <sup>35</sup> and Morris et al <sup>36</sup> (UK specific reports)	Cost of IV tPA, EVT, acute management of patients in first 3 mo, and ongoing annual costs	\$11 651 per QALY (USD 2013) Time horizon: 20 y Perspective: Healthcare payer	17/19	Cost-effective
Leppert et al, <sup>24</sup> 2015, United States	mRS score of 1, mRS score of 2, mRS score of 3, mRS score of 4, mRS score of 5, death	MR CLEAN	Age-specific mortality rates from 2006 U S Life Tables multiplied by relative death hazard ratios from Samsa et al <sup>37</sup>	Cost of index stroke by mRS, tPA, EVT, recurrent stroke hospitalizations, and annual posthospitalization costs	\$14 137 per QALY (USD 2012) Time horizon: 30 y Perspective: Societal	18/19	Cost-effective
Turk et al, <sup>25</sup> 2015, United States	...	...	...	Cost of all devices used in the procedure (femoral sheaths, IA tPA, guidewires, and catheters), cost of devices used to treat complication and direct and indirect hospital costs associated with patient's admission	Average total cost associated with the Penumbra system was \$47 673, \$46 735 for a stent retriever, and \$31 716 using the ADAPT technique (USD 2013)	14/16	ADAPT was the least costly method. The addition of the stent retriever improves recanalization, but increases costs of care

(Continued)



Table. Continued

Author, Year, Country (Currency)	States Included	Source of Clinical Effectiveness	Long-Term Survival	Costs Included	Primary Outcome	CHEC	Conclusion
Aronsson et al, <sup>26</sup> 2016, Sweden	mRS score of 1, mRS score of 2, mRS score of 3, mRS score of 4, mRS score of 5, death	MR CLEAN, ESCAPE, EXTEND IA, SWIFT-PRIME, REVASCAT	2014 Statistics Sweden Life Tables and hazard ratios from Fang et al <sup>38</sup> and Hankey et al <sup>39</sup>	Costs of first year after initial stroke and restroke (including acute care, rehabilitation, follow-up, drugs, home assistance, residential housing) by mRS, long-term costs (including health care, home assistance, residential housing) by mRS, cost of EVT	Dominant (\$–223 per QALY; USD 2015) Time horizon: Lifetime Perspective: Healthcare payer	18/19	Cost savings
Kunz et al, <sup>27</sup> 2016, United States	mRS score of 1, mRS score of 2, mRS score of 3, mRS score of 4, mRS score of 5, death	HERMES	Age-specific death rate from 2011 US Life Table multiplied by relative death hazard ratios from Samsa et al <sup>37</sup>	Costs of index stroke, cost of acute and long-term care costs (pulled from Leppert et al <sup>24</sup> )	\$3096 per QALY (US 2015) Time horizon: 30 y Perspective: Healthcare payer	18/19	Cost-effective
Lobotesis et al, <sup>28</sup> 2016, United Kingdom	mRS score of 1, mRS score of 2, mRS score of 3, mRS score of 4, mRS score of 5, death	SWIFT-PRIME	2011–2013 UK National Statistics Life Tables and relative risk of dying by mRS from Slot et al <sup>40</sup>	Treatment costs (including physician, nursing, diagnostics, and device cost), and acute and long-term care costs by mRS	Dominant (£–14 368 per QALY) Time horizon: Lifetime Perspective: Healthcare payer	19/19	Cost savings
Xie et al, <sup>29</sup> 2016, Canada	Independent (mRS score of ≤2), dependent (mRS score of 3–5), or dead	MR CLEAN, ESCAPE, EXTEND IA, SWIFT-PRIME, REVASCAT	Oxford Vascular Study <sup>41</sup>	Direct costs associated with stroke by functional independence (including emergency services, hospitalization, rehabilitation, physician services, diagnostics, medications), additional cost of EVT	\$11 990 per QALY (CND 2015) Time horizon: 5 y Perspective: Healthcare payer	18/19	Cost-effective

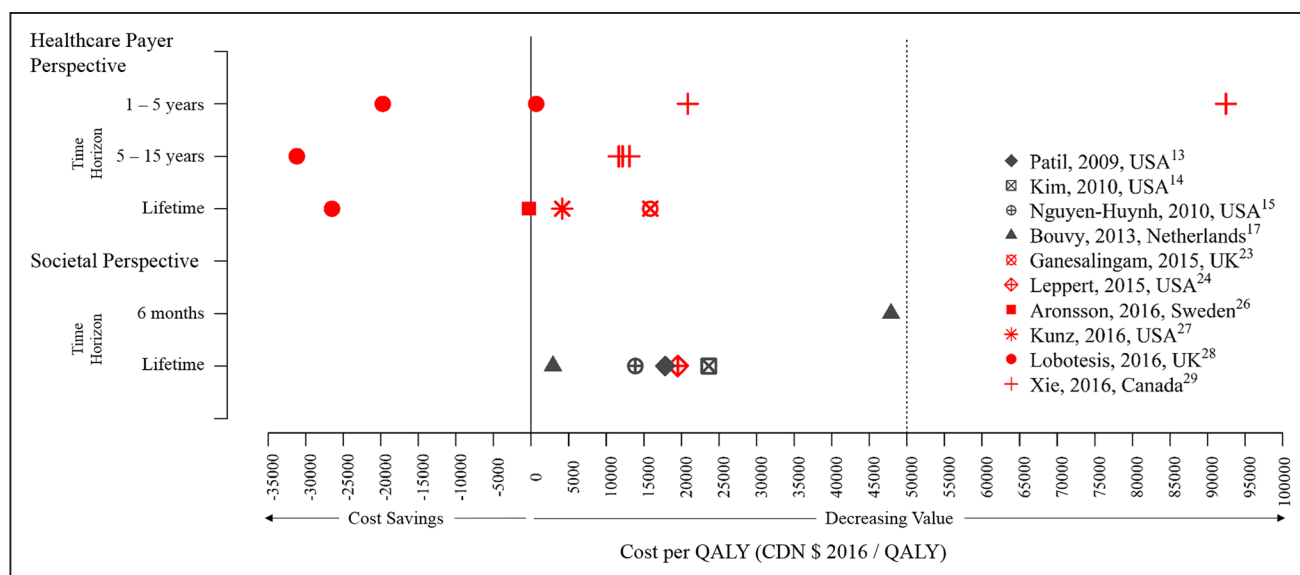
CHEC indicates Consensus on Health Economic Criteria; ESCAPE, Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times; EVT, endovascular therapy; EXTEND IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits—Intra-Arterial; HERMES, Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials; IV, intravenous; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; mRS, modified Rankin Scale; QALY, quality-adjusted life year; REVASCAT, Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke due to Anterior Circulation Large Vessel Occlusion Presenting Within Eight Hours of Symptom Onset; SWIFT-PRIME, Solitaire™ FR With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke; and tPA, tissue-type plasminogen activator.

for incidence of sICH and mortality.<sup>11</sup> Overall, these studies established that EVT is a clinically effective treatment option for eligible ischemic stroke patients.

Of the cost analyses identified in this review, most varied in terms of their primary objective and costs considered. Four studies had the primary objective of determining the cost of EVT procedure/approach.<sup>18,21,22,25</sup> To achieve this objective, the 4 studies considered the costs of all devices used during the EVT procedure, generally including thrombectomy devices, microcatheter/microwire systems, access catheters and wires, and support catheters and balloon guide catheters). The other 3 cost analyses had the primary objective of determining the

cost of the incident hospitalization for EVT patients.<sup>16,19,20</sup> The studies considered both procedure costs and other direct hospitalization costs. General conclusions from all the cost analyses were that although EVT with a stent retriever improves outcomes, it may be more expensive than other alternatives.

Like the cost analyses, cost–utility studies varied in terms of the costs considered, which were largely defined by the study perspective adopted and the time horizon considered. When a threshold of \$50 000 per QALY (CDN) is adopted, all the studies showed good value for money. Although this threshold is debated, it remains the most commonly referenced in Canada, the United States, and Australia. Some studies have



**Figure 2.** Summary of cost per quality-adjusted life year (QALY) results from included cost-effectiveness studies.

suggested that a higher threshold would be more appropriate. Nevertheless, only 1 estimate from the Canadian study by Xie et al<sup>29</sup> remained outside the generally acceptable \$50 000 cost-effectiveness range at \$91 080 per QALY gained (CND 2015). This estimate was based on a 1-year time horizon and a healthcare payer perspective. Other cost per QALY estimates from this study, including the primary outcome, was all within the generally accepted cost-effectiveness range. Authors also noted that with a threshold of \$50 000 per QALY, EVT had a probability of 89.7% of being cost-effective.<sup>29</sup>

When analyzing only the cost-utility studies using recent clinical effectiveness (2015 current), 2 of the 6 studies identified a potential cost savings associated with EVT, suggesting that EVT is both less expensive and more effective than tPA alone.<sup>26,28</sup> Both studies are from Europe and used a healthcare payer perspective, meaning that the cost savings would be completely recouped by the healthcare system. It remains unclear whether other countries and healthcare systems would experience a similar cost savings. Moreover, depending on how healthcare systems break down their budgets, it is uncertain which sectors and departments would benefit from these cost savings. The lifetime time horizon used in both studies also suggests that systems will face opportunity costs whereby spending more in the first year of stroke will lead to long-term cost savings.

One limitation of this review is that none of the studies considered the cost of patient transportation. On the basis of the high level of expertise required to perform EVT and appropriately care for the patient in hospital, it can be assumed that some patient transport to a specialized center would be required. Furthermore, none of the studies used randomized patient level costing to determine the hospital costs associated with EVT. This costing technique could provide a more accurate estimate of EVT patient hospitalization costs. Finally, very few of the studies appropriately discussed ethical and distributional issues associated with EVT. Because of the time constraints and expertise required, future studies should consider the ethics around patient access to EVT. Another limitation is that this review was limited to studies published in

English or French. The inclusion of studies published in other languages may have yielded different results.

## 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 results in the highest hospitalization and procedural costs; however, these devices were also associated with improved patient outcomes. All reported cost-effectiveness ratios were <\$50 000 per QALY except when a time horizon of 1 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. EVT seems to be good value for money when a threshold of \$50 000 per QALY gained is adopted.

## Disclosures

None.

## References

- Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the global burden of disease study 2010. *Lancet Glob Health*. 2013;1:e259–e281.
- Owens DK. Interpretation of cost-effectiveness analyses. *J Gen Inter Med*. 1998;13:716–717.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al; Writing Group Members; American Heart Association Statistics Committee; Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation*. 2016;133:e38–e360. doi: 10.1161/CIR.0000000000000350.
- Tables. MEPSHCS. Table 4: Total Expenses and Percent Distribution for Selected Conditions by Source of Payment: United States, 2011. Agency for Healthcare Research and Quality Website. [http://meps.ahrq.gov/mepsweb/data\\_stats/tables\\_compendia\\_hh\\_interactive.jsp?\\_SERVICE=MEPSSocket0&\\_PROGRAM=MEPSPGM.TC.SAS&File=HCFY2011&Table=HCFY2011\\_CNDXP\\_D&\\_Debug=.](http://meps.ahrq.gov/mepsweb/data_stats/tables_compendia_hh_interactive.jsp?_SERVICE=MEPSSocket0&_PROGRAM=MEPSPGM.TC.SAS&File=HCFY2011&Table=HCFY2011_CNDXP_D&_Debug=.) 2011.

5. Mittmann N, Seung SJ, Hill MD, Phillips SJ, Hachinski V, Coté R, et al. Impact of disability status on ischemic stroke costs in Canada in the first year. *Can J Neurol Sci*. 2012;39:793–800.
6. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, et al; MR RESCUE Investigators. A trial of imaging selection and endovascular treatment for ischemic stroke. *N Engl J Med*. 2013;368:914–923. doi: 10.1056/NEJMoa1212793.
7. Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, et al; SYNTAXIS Expansion Investigators. Endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2013;368:904–913. doi: 10.1056/NEJMoa1213701.
8. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030. doi: 10.1056/NEJMoa1414905.
9. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792.
10. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi: 10.1056/NEJMoa1411587.
11. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X.
12. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: consensus on Health Economic Criteria. *Int J Technol Assess Health Care*. 2005;21:240–245.
13. Patil CG, Long EF, Lansberg MG. Cost-effectiveness analysis of mechanical thrombectomy in acute ischemic stroke. *J Neurosurg*. 2009;110:508–513. doi: 10.3171/2008.8.JNS08133.
14. Kim AS, Nguyen-Huynh M, Johnston SC. A cost-utility analysis of mechanical thrombectomy as an adjunct to intravenous tissue-type plasminogen activator for acute large-vessel ischemic stroke. *Stroke*. 2011;42:2013–2018. doi: 10.1161/STROKEAHA.110.606889.
15. Nguyen-Huynh MN, Johnston SC. Is mechanical clot removal or disruption a cost-effective treatment for acute stroke? *AJNR Am J Neuroradiol*. 2011;32:244–249. doi: 10.3174/ajnr.A2329.
16. Brinjikji W, Kallmes DF, Rabinstein AA, Lanzino G, Cloft HJ. Hospitalization costs for patients with acute ischemic stroke treated with endovascular embolectomy in the United States. *Stroke*. 2011;42:3271–3273. doi: 10.1161/STROKEAHA.111.618405.
17. Bouvy JC, Fransen PS, Baeten SA, Koopmanschap MA, Niessen LW, Dippel DW. Cost-effectiveness of two endovascular treatment strategies vs intravenous thrombolysis. *Acta Neurol Scand*. 2013;127:351–359. doi: 10.1111/ane.12065.
18. Kass-Hout T, Kass-Hout O, Sun CH, Kass-Hout T, Belagaje SR, Anderson AM, et al. Periprocedural cost-effectiveness analysis of mechanical thrombectomy for acute ischemic stroke in the stent retriever era. *Interv Neurol*. 2015;3:107–113. doi: 10.1159/000371729.
19. Simpson KN, Simpson AN, Mauldin PD, Hill MD, Yeatts SD, Spilker JA, et al; IMS III Investigators. Drivers of costs associated with reperfusion therapy in acute stroke: the Interventional Management of Stroke III Trial. *Stroke*. 2014;45:1791–1798. doi: 10.1161/STROKEAHA.113.003874.
20. Rai AT, Evans K. Hospital-based financial analysis of endovascular therapy and intravenous thrombolysis for large vessel acute ischemic strokes: the 'bottom line'. *J Neurointerv Surg*. 2015;7:150–156. doi: 10.1136/neurintsurg-2013-011085.
21. Turk AS III, Campbell JM, Spiotta A, Vargas J, Turner RD, Chaudry MI, et al. An investigation of the cost and benefit of mechanical thrombectomy for endovascular treatment of acute ischemic stroke. *J Neurointerv Surg*. 2014;6:77–80. doi: 10.1136/neurintsurg-2012-010616.
22. Comai A, Haglmüller T, Ferro F, Dall'Orta E, Currò Dossi R, Bonatti G. Sequential endovascular thrombectomy approach (SETA) to acute ischemic stroke: preliminary single-centre results and cost analysis. *Radiol Med*. 2015;120:655–661. doi: 10.1007/s11547-015-0501-9.
23. Ganesalingam J, Pizzo E, Morris S, Sunderland T, Ames D, Lobotesis K. Cost-utility analysis of mechanical thrombectomy using stent retrievers in acute ischemic stroke. *Stroke*. 2015;46:2591–2598. doi: 10.1161/STROKEAHA.115.009396.
24. Leppert MH, Campbell JD, Simpson JR, Burke JF. Cost-effectiveness of intra-arterial treatment as an adjunct to intravenous tissue-type plasminogen activator for acute ischemic stroke. *Stroke*. 2015;46:1870–1876. doi: 10.1161/STROKEAHA.115.009779.
25. Turk AS, Turner R, Spiotta A, Vargas J, Holmstedt C, Ozark S, et al. Comparison of endovascular treatment approaches for acute ischemic stroke: cost effectiveness, technical success, and clinical outcomes. *J Neurointerv Surg*. 2015;7:666–670. doi: 10.1136/neurintsurg-2014-011282.
26. Aronsson M, Persson J, Blomstrand C, Wester P, Levin LÅ. Cost-effectiveness of endovascular thrombectomy in patients with acute ischemic stroke. *Neurology*. 2016;86:1053–1059. doi: 10.1212/WNL.0000000000002439.
27. Kunz WG, Hunink MG, Sommer WH, Beyer SE, Meinel FG, Dorn F, et al. Cost-effectiveness of endovascular stroke therapy: a patient subgroup analysis from a US healthcare perspective. *Stroke*. 2016;47:2797–2804. doi: 10.1161/STROKEAHA.116.014147.
28. Lobotesis K, Veltkamp R, Carpenter IH, Claxton LM, Saver JL, Hodgson R. Cost-effectiveness of stent-retriever thrombectomy in combination with IV t-PA compared with IV t-PA alone for acute ischemic stroke in the UK. *J Med Econ*. 2016;19:785–794. doi: 10.1080/13696998.2016.1174868.
29. Xie X, Lambrinos A, Chan B, Dhalla IA, Krings T, Casaubon LK, et al. Mechanical thrombectomy in patients with acute ischemic stroke: a cost-utility analysis. *CMAJ Open*. 2016;4:E316–E325. doi: 10.9778/cmajo.20150088.
30. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960;20:37–46.
31. Smith WS, Sung G, Starkman S, Saver JL, Kidwell CS, Gobin YP, et al; MERCI Trial Investigators. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. *Stroke*. 2005;36:1432–1438. doi: 10.1161/01.STR.0000171066.25248.1d.
32. Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS, et al; Multi MERCI Investigators. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. *Stroke*. 2008;39:1205–1212. doi: 10.1161/STROKEAHA.107.497115.
33. Brekenfeld C, Remonda L, Nedeltchev K, Arnold M, Mattle HP, Fischer U, et al. Symptomatic intracranial haemorrhage after intra-arterial thrombolysis in acute ischaemic stroke: assessment of 294 patients treated with urokinase. *J Neurol Neurosurg Psychiatry*. 2007;78:280–285. doi: 10.1136/jnnp.2005.078840.
34. Baeten SA, van Exel NJ, Dirks M, Koopmanschap MA, Dippel DW, Niessen LW. Lifetime health effects and medical costs of integrated stroke services - a non-randomized controlled cluster-trial based life table approach. *Cost Eff Resour Alloc*. 2010;8:21. doi: 10.1186/1478-7547-8-21.
35. Davis S, Holmes M, Simpson E, Sutton A. Alteplase for the treatment of acute ischaemic stroke (review of technology appraisal 122). 2012: 1–110. <https://www.nice.org.uk/guidance/ta264/documents/stroke-acute-ischaemic-alteplase-review-of-ta122-evidence-review-group-report2>.
36. Morris S, Hunter R, Davie C, Thompson A, Walker H, Thompson N, et al. *Cost-Effectiveness Analysis of the London Stroke Service*. London, United Kingdom: University College London Report; 2011:1–62.
37. Samsa GP, Reutter RA, Parnigiani G, Ancukiewicz M, Abrahamse P, Lipscomb J, et al. Performing cost-effectiveness analysis by integrating randomized trial data with a comprehensive decision model: application to treatment of acute ischemic stroke. *J Clin Epidemiol*. 1999;52:259–271.
38. Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, et al. Long-term survival after ischemic stroke in patients with atrial fibrillation. *Neurology*. 2014;82:1033–1037. doi: 10.1212/WNL.0000000000000248.
39. Hankey GJ, Jamrozik K, Broadhurst RJ, Forbes S, Burvill PW, Anderson CS, et al. Five-year survival after first-ever stroke and related prognostic factors in the Perth Community Stroke Study. *Stroke*. 2000;31:2080–2086.
40. Slot KB, Berge E, Sandercock P, Lewis SC, Dorman P, Dennis M; Oxfordshire Community Stroke Project; Lothian Stroke Register; International Stroke Trial (UK). Causes of death by level of dependency at 6 months after ischemic stroke in 3 large cohorts. *Stroke*. 2009;40:1585–1589. doi: 10.1161/STROKEAHA.108.531533.
41. Luengo-Fernandez R, Paul NL, Gray AM, Pendlebury ST, Bull LM, Welch SJ, et al; Oxford Vascular Study. Population-based study of disability and institutionalization after transient ischemic attack and stroke: 10-year results of the Oxford Vascular Study. *Stroke*. 2013;44:2854–2861. doi: 10.1161/STROKEAHA.113.001584.
42. Balami JS, Sutherland BA, Edmunds LD, Grunwald IQ, Neuhaus AA, Hadley G, et al. A systematic review and meta-analysis of randomized controlled trials of endovascular thrombectomy compared with best medical treatment for acute ischemic stroke. *Int J Stroke*. 2015;10:1168–1178. doi: 10.1111/ijs.12618.



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