Cost-Effectiveness of Endovascular Stroke Therapy
A Patient Subgroup Analysis From a US Healthcare Perspective

Wolfgang G. Kunz, MD; M.G. Myriam Hunink, MD, PhD; Wieland H. Sommer, MD, MPH; Sebastian E. Beyer, MD; Felix G. Meinel, MD; Franziska Dorn, MD; Stefan Wirth, MD, MBA, MSc; Maximilian F. Reiser, MD; Birgit Ertl-Wagner, MD, MHBA; Kolja M. Thierfelder, MD, MSc

Background and Purpose—Endovascular therapy in addition to standard care (EVT+SC) has been demonstrated to be more effective than SC in acute ischemic large vessel occlusion stroke. Our aim was to determine the cost-effectiveness of EVT+SC depending on patients’ initial National Institutes of Health Stroke Scale (NIHSS) score, time from symptom onset, Alberta Stroke Program Early CT Score (ASPECTS), and occlusion location.

Methods—A decision model based on Markov simulations estimated lifetime costs and quality-adjusted life years (QALYs) associated with both strategies applied in a US setting. Model input parameters were obtained from the literature, including recently pooled outcome data of 5 randomized controlled trials (ESCAPE [Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke], EXTEND-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial], MR CLEAN [Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands], 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 8 Hours of Symptom Onset], and SWIFT PRIME [Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment]). Probabilistic sensitivity analysis was performed to estimate uncertainty of the model results. Net monetary benefits, incremental costs, incremental effectiveness, and incremental cost-effectiveness ratios were derived from the probabilistic sensitivity analysis. The willingness-to-pay was set to $50,000/QALY.

Results—Overall, EVT+SC was cost-effective compared with SC (incremental cost: $4,938; incremental effectiveness: 1.59 QALYs, and incremental cost-effectiveness ratio: $3,110/QALY) in 100% of simulations. In all patient subgroups, EVT+SC led to gained QALYs (range: 0.47–2.12), and mean incremental cost-effectiveness ratios were considered cost-effective. However, subgroups with ASPECTS ≤5 or with M2 occlusions showed considerably higher incremental cost-effectiveness ratios ($14,273/QALY and $28,812/QALY, respectively) and only reached suboptimal acceptability in the probabilistic sensitivity analysis (75.5% and 59.4%, respectively). All other subgroups had acceptability rates of 90% to 100%.

Conclusions—EVT+SC is cost-effective in most subgroups. In patients with ASPECTS ≤5 or with M2 occlusions, cost-effectiveness remains uncertain based on current data. (Stroke. 2016;47:2797-2804. DOI: 10.1161/STROKEAHA.116.014147.)

Key Words: cost-effectiveness ■ economics ■ stroke ■ thrombectomy ■ thrombolysis

The currently estimated direct and indirect annual costs of stroke in the United States are $33 billion.1 Improved therapy is an urgent need not only from a medical perspective but also from an economic point of view. Five randomized controlled trials (RCTs) using latest generation endovascular therapy (EVT) devices (ESCAPE [Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke],2 EXTEND-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial],3 MR CLEAN [Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands],4 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 8 Hours of Symptom Onset],5 and SWIFT PRIME [Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment]6 conducted between 2010 and 2014 have demonstrated significant

Received May 24, 2016; final revision received August 16, 2016; accepted August 24, 2016.
From the Institute for Clinical Radiology (W.G.K., W.H.S., S.E.B., F.G.M., S.W., M.F.R., B.E.-W., K.M.T.) and Department of Neuroradiology (F.D.), LMU Munich, Munich, Germany; Departments of Radiology (M.G.M.H.) and Epidemiology (M.G.M.H.), Erasmus University Medical Center, Rotterdam, The Netherlands; and Center for Health Decision Sciences, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA (M.G.M.H.).

The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.116.014147/-/DC1.
Correspondence to Wolfgang G. Kunz, MD, Institute for Clinical Radiology, LMU Munich, Marchioninistr. 15, 81377 Munich, Germany. E-mail wolfgang.kunz@med.lmu.de
© 2016 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org
DOI: 10.1161/STROKEAHA.116.014147
benefits of EVT in addition to standard care (EVT+SC), which includes intravenous thrombolysis where applicable, over SC alone in terms of reperfusion, functional outcome, and mortality.

Recent cost-effectiveness analyses based on these trials have shown EVT+SC to be generally cost-effective in large vessel occlusions in the United States, the United Kingdom, and the Swedish healthcare systems7–10 (Table 1).

While both proven therapy efficacy and cost-effectiveness of latest generation EVT are rightly considered an important milestone in ischemic stroke treatment, a significant number of patients with large vessel occlusions still do not benefit from this therapy. Although it is important to leave room for the interventionalist to make a decision that is tailored to the individual patient presentation and history, recent trials show associations that can be exploited in a systematic way to support the individual therapy decision.

Recent meta-analyses building on the entire data of the 5 large RCTs allow for subgroup analyses,11 thereby creating a solid base for more detailed cost-effectiveness analyses. In particular, the therapy effect has been demonstrated to largely depend on the clinical presentation of the patient in terms of the National Institutes of Health Stroke Scale (NIHSS) score, the time from symptom onset (TFSO), and imaging characteristics, such as the Alberta Stroke Program Early CT Score (ASSPECTS) and the localization of vessel occlusion.

Our aim was to determine the cost-effectiveness of EVT+SC compared with SC taking into account recent data on the influence of NIHSS score, TFSO, ASSPECTS, and occlusion location.

Methods

Model Structure

We developed a decision model using decision-analytic software (TreeAge Pro 2016, version 16.1.1.0; TreeAge, Williamstown, MA)
Initial and Transition Probabilities

The initial probabilities (ie, the probability of entering a specific mRS health state at the end of the initial 3 months) for the total study population and patient subgroups were extracted from a recent meta-analysis by Goyal et al.11 (Table I and Figure I in the online-only Data Supplement). To account for patients who did not receive intravenous thrombolysis, the acute treatment costs implied in both strategies were adjusted by the percentage of patients receiving intravenous thrombolysis. Patients were considered to be 68 years of age, which is the median age in the meta-analysis.

The transition probabilities consisted of the recurrent stroke rate, the age-specific death rate, the probability of staying in the same health state, and the probabilities of reentering the same or a lower health state after recurrent stroke. The recurrent stroke rate is known to decrease over time after the index stroke, which we took into account using a long-term study providing corresponding rates based on the data from 1995 to 2008.13 The age-specific death rate was drawn from the US Life Table14 and adjusted to hazard rate ratios for each mRS health state.15 The probabilities to reenter the specific mRS health states after a recurrent stroke were approximated for both treatment groups using the initial probabilities of the overall population receiving SC in the meta-analysis. This modeled the recurrent stroke event to share the same features as the index stroke (ischemic large vessel occlusion stroke), a conservative assumption based on literature review.13,19–21

Costs

The costs were based on a recent cost-effectiveness analysis in the US setting by Leppert et al17 and adjusted to 2015 US Dollars according to the medical care component of the Consumer Price Index. In brief, the costs of the index stroke were taken from previous literature using US nationwide estimates of Medicare Costs for EVT and intravenous thrombolysis. Because of the lack of more detailed data, acute and long-term costs adjusted for mRS scores had to be obtained from a study that calculated cost for 3 groups of mRS scores (mRS score, 0–3: discharge to home or home health services; mRS score, 4–5: discharge to skilled nursing facility; mRS score, 6: dead at discharge).18 Nevertheless, we used a model with health states for each mRS score to integrate as much of the available evidence for the other model input parameters. The costs of recurrent stroke hospitalization were based on Chambers et al.17 All costs were discounted by 3% each year.29

Model Input Parameters

Input parameters for the model were based on recently published literature (Table 2).11,13–14

Initial and Transition Probabilities

The initial probabilities (ie, the probability of entering a specific mRS health state at the end of the initial 3 months) for the total study population and patient subgroups were extracted from a recent meta-analysis by Goyal et al11 (Table I and Figure I in the online-only Data Supplement). To account for patients who did not receive intravenous thrombolysis, the acute treatment costs implied in both strategies were adjusted by the percentage of patients receiving intravenous thrombolysis. Patients were considered to be 68 years of age, which is the median age in the meta-analysis.

The transition probabilities consisted of the recurrent stroke rate, the age-specific death rate, the probability of staying in the same health state, and the probabilities of reentering the same or a lower health state after recurrent stroke. The recurrent stroke rate is known to decrease over time after the index stroke, which we took into account using a long-term study providing corresponding rates based on the data from 1995 to 2008.13 The age-specific death rate was drawn from the US Life Table14 and adjusted to hazard rate ratios for each mRS health state.15 The probabilities to reenter the specific mRS health states after a recurrent stroke were approximated for both treatment groups using the initial probabilities of the overall population receiving SC in the meta-analysis. This modeled the recurrent stroke event to share the same features as the index stroke (ischemic large vessel occlusion stroke), a conservative assumption based on literature review.13,19–21

Costs

The costs were based on a recent cost-effectiveness analysis in the US setting by Leppert et al17 and adjusted to 2015 US Dollars according to the medical care component of the Consumer Price Index. In brief, the costs of the index stroke were taken from previous literature using US nationwide estimates of Medicare Costs for EVT and intravenous thrombolysis. Because of the lack of more detailed data, acute and long-term costs adjusted for mRS scores had to be obtained from a study that calculated cost for 3 groups of mRS scores (mRS score, 0–3: discharge to home or home health services; mRS score, 4–5: discharge to skilled nursing facility; mRS score, 6: dead at discharge).18 Nevertheless, we used a model with health states for each mRS score to integrate as much of the available evidence for the other model input parameters. The costs of recurrent stroke hospitalization were based on Chambers et al.17 All costs were discounted by 3% each year.29

Table 2. Base-Case Values and References of Model Input Parameters

<table>
<thead>
<tr>
<th>Model Input</th>
<th>Expected Value</th>
<th>Distribution</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial probabilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For each mRS state</td>
<td>Table I/Figure I in online-only Data Supplement</td>
<td>Dirichlet</td>
<td>Goyal et al11</td>
</tr>
<tr>
<td>Transition probabilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent stroke rate</td>
<td>0.059 (in first year)</td>
<td>β</td>
<td>Pennlert et al13</td>
</tr>
<tr>
<td>Age-specific death rate</td>
<td>0.016 (eg, 68 y/o)</td>
<td>β</td>
<td>Arias et al14</td>
</tr>
<tr>
<td>Death hazard rate ratios for mRS score, 0–5</td>
<td>1.00/1.00/1.11/1.27/1.71/2.37</td>
<td>Log normal</td>
<td>Samsa et al19</td>
</tr>
<tr>
<td>Costs—Acute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute stroke mRS score, 0–3</td>
<td>$7979</td>
<td>γ</td>
<td>Earnshaw et al16</td>
</tr>
<tr>
<td>Acute stroke mRS score, 4–5</td>
<td>$12153</td>
<td>γ</td>
<td>Earnshaw et al16</td>
</tr>
<tr>
<td>Acute stroke mRS score, 6</td>
<td>$14170</td>
<td>γ</td>
<td>Earnshaw et al16</td>
</tr>
<tr>
<td>Additional cost of IVT</td>
<td>$7421</td>
<td>γ</td>
<td>National Inpatient Sample 2012</td>
</tr>
<tr>
<td>IVT-eligible patients</td>
<td>0.830 (EVT+SC) 0.870 (SC)</td>
<td>β</td>
<td>Goyal et al11</td>
</tr>
<tr>
<td>Additional cost of EVT</td>
<td>$15510</td>
<td>γ</td>
<td>National Inpatient Sample 2012</td>
</tr>
<tr>
<td>Costs—Long term</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posthospitalization mRS score, 0–3, annual</td>
<td>$7023</td>
<td>γ</td>
<td>Earnshaw et al16</td>
</tr>
<tr>
<td>Posthospitalization mRS score, 4–5, annual</td>
<td>$19062</td>
<td>γ</td>
<td>Earnshaw et al16</td>
</tr>
<tr>
<td>Recurrent stroke hospitalization</td>
<td>$21648</td>
<td>γ</td>
<td>Chambers et al17</td>
</tr>
<tr>
<td>Utilities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS score, 0–6</td>
<td>1.00/0.91/0.76/0.65/0.33/0.00</td>
<td>β</td>
<td>Chaisinanunkul et al18</td>
</tr>
</tbody>
</table>

All costs were converted to 2015 USD using the medical care component of the Consumer Price Index. EVT indicates endovascular therapy; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; and SC, standard care.
Utilities

Therapy effectiveness was measured by quality-adjusted life years (QALYs), calculated by multiplying years spent in mRS health states by assigned utility weights. Utility weights were derived from a recent study by Chaisinanunkul et al. combining assessments by patients of the OXVASC trial (Oxford Vascular Study) and by stroke experts of the World Health Organization (WHO) global burden of disease project. Values range from 0.0 to 1.0, with 0.0 representing no and 1.0 representing perfect quality of life. All QALYs were discounted by 3% each year.

Cost-Effectiveness Analysis

Treatment strategies were compared in terms of net monetary benefits, incremental costs, incremental effectiveness, and incremental cost-effectiveness ratios (ICERs). The willingness-to-pay was set to $50,000 per QALY as in recent studies. Net monetary benefits combine costs and effectiveness in 1 measure: net monetary benefit = (QALYs × willingness-to-pay) – costs.

Sensitivity Analysis

We used comprehensive deterministic and probabilistic sensitivity analysis (PSA) to test the robustness of the model. Deterministic 1-way sensitivity analysis was performed to identify variables that significantly influence the model outcomes. The ranges for deterministic sensitivity analysis were determined by the 95% confidence interval of the initial probabilities, by previous expert panel-based values for hazard rate ratios and by ±30% for costs. The utility value ranged between the mean values of the OXVASC trial patient assessment and the WHO global burden of disease project’s stroke expert assessment.

Moreover, PSA allows simultaneous alteration of multiple model input parameters using distributions according to probability density functions for second order Monte Carlo simulation runs (n=100000).

Results

Base-Case Analysis

In the base-case analysis of the total study population using a time horizon of 30 years, EVT+SC led to increased effectiveness of 1.59 QALYs at increased costs of $4919 compared with SC. The ICER was determined at $3096/QALY.

Deterministic Sensitivity Analysis

The results of the deterministic 1-way sensitivity analysis are presented in Figure 2, grouped by the categories of model input parameters. Concerning initial probabilities, model outcomes were particularly sensitive to varying the probabilities of the mRS health states 4, 5, and 6. With respect to the strategy EVT+SC, an increase of the probabilities for the mRS health states 4 and 5 led to unfavorable ICER values, whereas an increase of the probability to die due to the index stroke (ie, mRS health state 6) lead to favorable ICER values. These effects were reversed for the strategy SC.

Probabilistic Sensitivity Analysis

Overall, EVT+SC was cost-effective with an ICER of $3110/QALY in 100% of Monte Carlo simulation runs, indicating robustness of the model.

In all patient subgroups, the mean incremental effectiveness was positive, meaning that EVT+SC led to increased QALYs.
in all scenarios. Moreover, the mean values for the ICERs were below the willingness-to-pay threshold in all patient subgroups. In patients presenting with a TFSO of more than 300 minutes and in patients presenting with an ASPECTS of 9 to 10 on imaging, EVT+SC was the dominant strategy, meaning that it provided better outcomes at lower costs. The highest mean incremental cost was observed in patients presenting with M2 occlusions ($13,545). The highest mean incremental effectiveness was achieved in patients presenting with internal carotid artery occlusions (2.12 QALYs).

The patient subgroups presenting with an ASPECTS of 0 to 5 or presenting with M2 occlusions yielded the least favorable mean ICERs with $14,273/QALY and $28,812/QALY, as well as the lowest acceptability rates of 75.5% and 59.4% at a willingness-to-pay of $50,000/QALY. All other patient subgroups achieved an acceptability rate >90%. The detailed results of the PSA are shown in Table 3 and Figure 3.

### Discussion

This study investigated the cost-effectiveness of EVT in different subgroups of patients with acute ischemic stroke. In accordance with previous cost-effectiveness analyses, EVT+SC was generally cost-effective compared with SC. While different NIHSS scores and TFSO are not likely to compromise cost-effectiveness, cases with an ASPECTS of ≤5 or an M2 occlusion show considerably higher ICERs and only reach suboptimal acceptability rates in the PSA.

Our results are in line with and extend the current literature on cost-effectiveness of EVT in large vessel occlusions. Similar to our study, Leppert et al7 performed an analysis in a US setting and found an overall ICER for EVT+SC of $14,137/QALY, which is considerably higher compared with the overall ICER determined by our analysis ($3,110/QALY). This can be partially explained by the fact that Leppert et al performed their analysis on the MR CLEAN data, which compared with the other RCTs had shown below-average outcomes compared with the other published RCTs. The other recent studies on cost-effectiveness of EVT in large vessel occlusion had been performed in British or Swedish settings and had also shown EVT+SC to be cost-effective.

Patient subgroup analyses taking different patient characteristics into account have not yet been addressed in latest generation EVT. Ganesalingam et al8 and Aronsson et al9 used the pooled data from all 5 RCTs, but did not perform subgroup analyses extending beyond the classification of patients depending on the respective underlying RCT.

The NIHSS is a well-recognized measure for the level of the acute neurological deficit. Our analysis showed that EVT+SC is highly likely to be cost-effective in patients with an NIHSS score of 11 and higher (acceptability of PSA >99.9%). In the subgroup of patients with a mild neurological deficit (NIHSS score, 0–10), the acceptability of PSA was slightly lower (91.5%), probably reflecting the fact that patients in this subgroup have a considerable chance to reach a favorable outcome with SC.

With respect to TFSO, the absolute risk difference for a good outcome for EVT patients has recently been demonstrated to be reduced by 6% per hour. According to our analysis based on TFSO to randomization, however, EVT is highly likely to be cost-effective even in patients presenting more than 5 hours after symptom onset (acceptability rate in PSA: 91.2%). This might be partially explained by the poor outcome of the competing therapy, SC, in this subgroup.

Patients with extensive early signs of infarction (ie, low ASPECTS) are likely to have a poor functional outcome. For this reason, 3 of the 5 RCTs excluded patients with
an ASPECTS of \( \leq 5 \) on initial imaging. A recent meta-analysis\(^{11}\) showed only a nonsignificant trend to favor EVT+SC in this subgroup, and the guidelines by the American Stroke Association only reported a Class IIb, Level of Evidence B recommendation for EVT+SC in patients with an ASPECTS of \( \leq 5 \).\(^{31}\) Our cost-effectiveness analysis supports this approach because cases with an ASPECTS of \( \leq 5 \) have a lower probability of being cost-effective (acceptability rate in PSA: 75.5%). However, it should be noted that small sample sizes (EVT+SC: \( n=57 \); SC: \( n=64 \)) affect the PSA significantly. Therefore, larger studies are needed for the evaluation of this subgroup.

The combination of EVT and SC has originally been only applied in patients with internal carotid artery and M1 occlusions. However, technical feasibility and potential benefits have recently been demonstrated in more peripherally located M2 occlusions,\(^{32,33}\) which have only received a Class IIb, Level of Evidence C recommendation by the 2015 guidelines of the American Stroke Association.\(^{31}\) The pooled data of the 5 RCTs show a considerably lower success rate of EVT in M2 occlusions when compared with more proximal internal carotid artery and M1 occlusions.\(^{11}\) In our study, this is reflected by a relatively high ICER of over $28,000/QALY and an acceptability in the PSA of only 59.4% in patients with M2 occlusions. However, to date only relatively small sample sizes (EVT+SC: \( n=51 \); SC: \( n=43 \)) are available. Further research on this patient subgroup is warranted to identify factors influencing clinical outcome and cost-effectiveness.

Interestingly, although the adjusted treatment effects of EVT+SC using the outcome measure common odds ratio (cOR) are more favorable in patients presenting within 5 hours compared to later (TFSO \( \leq 300 \) minutes: \( \text{cOR}=2.66 \); TFSO \( >300 \) minutes: \( \text{cOR}=1.76 \)), cost-effectiveness is considered superior in patients presenting later than 5 hours (TFSO \( \leq 300 \) minutes: \( \text{ICER}=$4377/QALY \); TFSO \( >300 \) minutes: EVT+SC dominant). A similar relationship was present when comparing patients with internal carotid artery occlusions (cOR=3.96; ICER=$3465/QALY) to patients with M1 occlusions (cOR=2.29; ICER=$2459/QALY).

While these results might be surprising at first sight, they can be explained by the results of the deterministic sensitivity analysis. These highlight the importance of the percentage of patients with severe disabilities (mRS scores 4–5), which are
affecting the ICERs considerably because of the generation of higher lifetime costs. If EVT+SC manages to decrease the amount of patients with mRS scores of 4 to 5 compared with SC, this will largely benefit its cost-effectiveness. Therefore, the distribution across every level of the mRS in addition to the adjusted treatment effects should be considered in medical decision-making. These initially counterintuitive and subtle effects are difficult to consider when making decisions without explicit modeling. Decision modeling synthesizes all the evidence and provides insights that may otherwise have been too complex to consider.

Patient age is another relevant aspect contributing to clinical decision-making. Modeling the influence of age on cost-effectiveness, however, is challenging and requires a more diverse and stratified analysis. Because many relevant model input parameters about age-specific costs, utilities, or transition probabilities are not available and would have to be modeled based on expert opinion, this aspect would have been beyond the scope of this study.

There are some limitations in our study that need to be taken into account when interpreting the results. First, the sample sizes in the subgroups of ASPECTS of ≤5 and of M2 occlusions are relatively small and might affect the results of the cost-effectiveness analysis considerably. This patient sample, however, by now constitutes the largest completely documented cohort of patients in these subgroups.

Second, the acute and long-term treatment costs used by Earnshaw et al16 were based on the stroke treatment economic model by Caro et al15 using unit costs from the United Kingdom in 1996. Luengo-Fernandez et al36 reported cost data based on the Oxford Vascular Study between 2002 and 2007, which are overall comparable but at a maximum 2-fold higher than the costs reported by Caro et al.35 Because this evaluation was solely based on atrial fibrillation stroke, which only represents a third of the population in the meta-analysis by Goyal et al11 and is known to be associated with higher costs,37 we decided against using these data. Because of the lack of more current cost data, the estimates from Earnshaw et al16 were used and inflated to 2015 US dollars.

Third, the cost data used in our study needed to be grouped and assigned to the mRS score of 0 to 3, 4 to 5, and 6 as more detailed data are not available at this time. This affects the analysis on the part of cost estimation to some extent and must be considered when interpreting our results. Modeling each individual mRS level as health states, however, allowed us to take into account when interpreting the results. First, the cost data used in our study needed to be grouped and assigned to the mRS score of 0 to 3, 4 to 5, and 6 as more detailed data are not available at this time. This affects the analysis on the part of cost estimation to some extent and must be considered when interpreting our results. Modeling each individual mRS level as health states, however, allowed us to take into account when interpreting the results.

Fourth, there is no general consensus on the definition of an M2 occlusion. In a strictly anatomical sense, the M2 segment begins after its turn from its transverse to the longitudinal direction.32,33 Many clinicians, however, consider the first bifurcation of the MCA as the beginning of the M2 segment. Because we used a meta-analysis as the basis for costs and effectiveness, there is a certain amount of imprecision on the occlusion location.

Fifth, the analysis was performed from a US healthcare system perspective. A wider perspective, such as a societal one, would also include impacts on the rest of society, including indirect costs caused by the loss of productivity.

In conclusion, our study based on the pooled data of 5 large RCTs confirms that latest generation EVT+SC is generally cost-effective. Particular caution is required in patients with a low ASPECTS and M2 occlusions. Larger prospective studies with more strictly defined inclusion criteria are necessary to further characterize the cost-effectiveness of EVT+SC in these patient groups.

Disclosures
None.

References
Cost-Effectiveness of Endovascular Stroke Therapy: A Patient Subgroup Analysis From a US Healthcare Perspective


*Stroke*. 2016;47:2797-2804; originally published online October 6, 2016; doi: 10.1161/STROKEAHA.116.014147

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2016 American Heart Association, Inc. All rights reserved.

Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://stroke.ahajournals.org/content/47/11/2797

Data Supplement (unedited) at:

http://stroke.ahajournals.org/content/suppl/2016/10/06/STROKEAHA.116.014147.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:

http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:

http://stroke.ahajournals.org//subscriptions/
ONLINE SUPPLEMENT

Cost-Effectiveness of Endovascular Stroke Therapy:
A Patient Subgroup Analysis from a U.S. Health Care Perspective

Wolfgang G. Kunz, MD
M.G. Myriam Hunink, MD, PhD
Wieland H. Sommer, MD, MPH
Sebastian E. Beyer
Felix G. Meinel, MD
Franziska Dorn, MD
Stefan Wirth, MD, MBA, MSc
Maximilian F. Reiser, MD
Birgit Ertl-Wagner, MD, MHBA
Kolja M. Thierfelder, MD, MSc

aInstitute for Clinical Radiology, LMU Munich, Munich, Germany

bDepartment of Radiology and Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands; and Center for Health Decision Sciences, Harvard T.H. Chan School of Public Health, Harvard University, Boston/MA, USA

cDepartment of Neuroradiology, LMU Munich, Munich, Germany
### Table I. Model Input Parameters for Initial Probabilities of Patient Subgroups

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Strategy (Sample Size)</th>
<th>Initial Probabilities for Health States (in %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>mRS 0</td>
</tr>
<tr>
<td>Total</td>
<td>EVT+SC (N=653)</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>SC (N=634)</td>
<td>5.0</td>
</tr>
<tr>
<td>NIHSS 0-10</td>
<td>EVT+SC (n=77)</td>
<td>20.3</td>
</tr>
<tr>
<td></td>
<td>SC (n=100)</td>
<td>14.3</td>
</tr>
<tr>
<td>NIHSS 11-15</td>
<td>EVT+SC (n=167)</td>
<td>9.0</td>
</tr>
<tr>
<td></td>
<td>SC (n=140)</td>
<td>5.7</td>
</tr>
<tr>
<td>NIHSS 16-20</td>
<td>EVT+SC (n=237)</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>SC (n=236)</td>
<td>3.4</td>
</tr>
<tr>
<td>NIHSS 21-42</td>
<td>EVT+SC (n=152)</td>
<td>8.6</td>
</tr>
<tr>
<td></td>
<td>SC (n=169)</td>
<td>1.2</td>
</tr>
<tr>
<td>TFSO ≤ 300 min</td>
<td>EVT+SC (n=528)</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>SC (n=542)</td>
<td>4.8</td>
</tr>
<tr>
<td>TFSO &gt; 300 min</td>
<td>EVT+SC (n=105)</td>
<td>9.5</td>
</tr>
<tr>
<td>ASPECTS 9-10</td>
<td>EVT+SC (n=324)</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>SC (n=358)</td>
<td>5.9</td>
</tr>
<tr>
<td>ASPECTS 6-8</td>
<td>EVT+SC (n=252)</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>SC (n=223)</td>
<td>4.0</td>
</tr>
<tr>
<td>ASPECTS 0-5</td>
<td>EVT+SC (n=57)</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>SC (n=64)</td>
<td>1.8</td>
</tr>
<tr>
<td>Occlusion ICA</td>
<td>EVT+SC (n=133)</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>SC (n=141)</td>
<td>2.1</td>
</tr>
<tr>
<td>Occlusion M1</td>
<td>EVT+SC (n=438)</td>
<td>9.8</td>
</tr>
<tr>
<td></td>
<td>SC (n=449)</td>
<td>5.1</td>
</tr>
<tr>
<td>Occlusion M2</td>
<td>EVT+SC (n=51)</td>
<td>19.6</td>
</tr>
<tr>
<td></td>
<td>SC (n=43)</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Note – All values were drawn from a meta-analysis of five randomized controlled trials of EVT+SC vs. SC by Goyal et al. [Lancet 2016]. mRS, modified Rankin Score; EVT, Endovascular Therapy; SC, Standard Care; NIHSS, National Institutes of Health Stroke Scale; TFSO, Time From Symptom Onset; ASPECTS, Alberta Stroke Program Early CT Score.
All values were drawn from a meta-analysis of five randomized controlled trials of EVT+SC vs. SC by Goyal et al. [Lancet 2016]. mRS, modified Rankin Score; EVT, Endovascular Therapy; SC, Standard Care; NIHSS, National Institutes of Health Stroke Scale; TFSO, Time From Symptom Onset; ASPECTS, Alberta Stroke Program Early CT Score.