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Economic evaluation of endovascular treatment for acute ischaemic stroke in Thailand

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ABSTRACT

Objectives Endovascular therapy (EVT) has proven to be clinically effective in treating large vessel occlusion acute ischaemic stroke (AIS), either alone or in combination with intravenous alteplase. Despite this, there is a limited evidence on the cost-effectiveness of EVT in Thailand and other low-income and middle-income countries. This study aims to assess whether EVT is a cost-effective therapy for AIS, and to estimate the fiscal burden to the Thai government through budget impact analysis.

Methods An economic evaluation was performed to compare AIS therapy with and without EVT from a societal perspective. The primary outcome was incremental cost-effectiveness per quality-adjusted life year (QALY) gained. Clinical parameters were derived from both national and international literature, while cost and utility data were collected locally. The analysis applied a cost-effectiveness threshold of 160 000 Baht (~$5000) per QALY, as set by the Thai government.

Results Both EVT alone and EVT combined with intravenous alteplase, among patients who are ineligible and eligible for intravenous alteplase, respectively, improved health outcomes but incurred additional cost. The combination of EVT and intravenous alteplase was associated with an incremental cost-effectiveness ratio (ICER) of 146 800 THB per QALY gained compared with intravenous alteplase alone, and the ICER of EVT alone compared with supportive care among patients ineligible for intravenous alteplase was estimated at 115 000 THB per QALY gained. Sensitivity analysis showed that the price of EVT has the greatest impact on model outcomes. Over a time horizon of 5 years, the introduction of EVT into the Thai health benefit package would require an additional budget of 887 million THB, assuming 2000 new cases per year.

Conclusions EVT represents good value for money in the Thai context, both when provided to patients eligible for intravenous alteplase, and when provided alone to those who are ineligible for intravenous alteplase.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a model-based health economic evaluation that followed the national methodological guideline for health technology assessment in Thailand.
⇒ The intervention effectiveness was retrieved from high-quality international literature, while costs and utilities were collected from local sources.
⇒ This study did not include the initial fixed capital costs for establishing a comprehensive stroke unit, including capital investment and staff training, which might be necessary for hospitals without such a stroke unit.
⇒ The budget impact estimate may be an underestimate since free provision of endovascular therapy recommended by this study may increase the service demand.

INTRODUCTION

Although stroke is preventable, it represents one of the leading causes of disability and death worldwide, with more than 80% of the burden (in terms of disability adjusted life years) occurring in low/middle-income countries (LMICs).[1] Since 1995, the standard of care for patients with acute ischaemic stroke (AIS) has been to provide thrombolytic therapy with intravenous alteplase during early onset of the disease.[2] Although this can significantly reduce morbidity and mortality, only patients meeting eligibility recommendations[3] receive intravenous alteplase treatment. For large vessel occlusion AIS, endovascular therapy (EVT), has shown promising outcomes in clinical trials, whether or not the patient is eligible to receive adjunctive intravenous alteplase.[4]

With the global commitment to universal health coverage, economic evaluation, especially cost–utility analysis, is increasingly being employed to assess value for money of interventions and to inform decisions around their introduction into national essential health service packages.[5] In Thailand, value for money is one of the main criteria determining whether an intervention is included under the publicly financed health insurance scheme.[6] Although EVT has shown clinical efficacy, evidence on its value for money is scarce in LMICs.

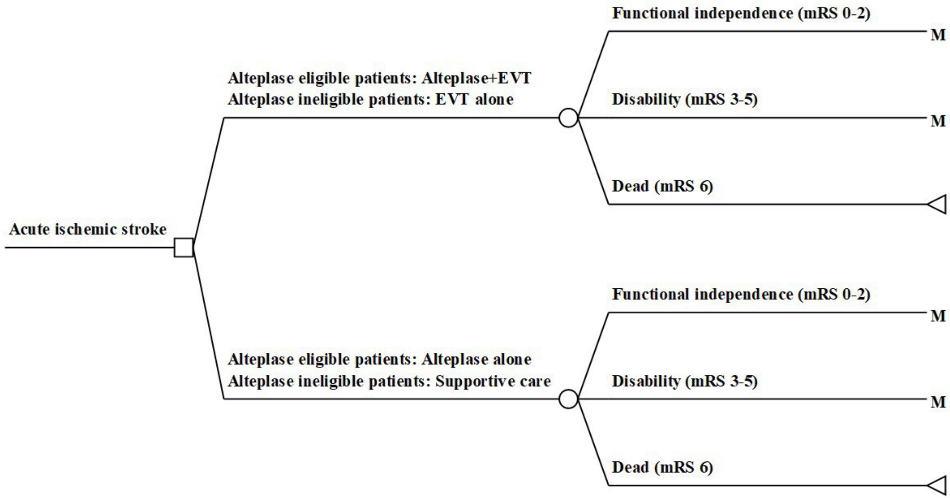

Figure 1 Decision tree model showing the policy options for treating patients with acute large-artery ischaemic stroke. EVT, endovascular therapy; mRS, modified Rankin scale.

This study aims to assess whether EVT is cost-effective for the treatment of large vessel occlusion AIS in Thailand, and to report the results of a budget impact analysis to estimate the fiscal burden of introducing EVT to the Thai government.

METHODS

A model-based economic evaluation was performed from a societal perspective. For each policy option (detailed below), we computed expected costs and expected outcomes in terms of quality-adjusted life years (QALYs), to account for both expectancy and quality of life. Costs and outcomes were calculated over the lifetime of stroke patients, based on an average age of 65 years.[7] This study adhered to the Thai methodological and process guidelines for conducting health technology assessment including health economic evaluation.[8 9]

Population and policy options

This study evaluates EVT combined with current practice for the treatment of acute large-artery AIS, against a comparator of current practice alone. Following Thai clinical practice guidelines,[10 11] this results in two populations in our model. For patients eligible to receive intravenous alteplase, the intervention is EVT plus intravenous alteplase, and the comparator is intravenous alteplase alone. For patients not eligible to receive intravenous alteplase, the intervention is EVT alone, and the comparator is supportive care.

Model structure

A hybrid model, with decision tree and Markov elements, was constructed using Microsoft Excel with the Plant-A-Tree add-in.[12] The decision tree model (figure 1) represents the acute phase pathway, until 90 days after stroke onset. The main outcome measure after receiving treatment was the degree of disability on modified Rankin scale (mRS) at 90 days postonset.

Additionally, a Markov model (see figure 2) was developed from 90 days poststroke to follow the natural history of disease progression over time. Patients remain in each health state for a cycle length of 3 months. After each cycle, the model allows patients to stay in the same health state, to move between health states, or to transition to dead (either from stroke or other causes), as shown in figure 2. The Markov model was run repeatedly until the end of the cohort lifetime, following which the accumulated costs and health outcomes were computed.

Model input parameters

All input parameters for the model are listed in online supplemental tables 1 and 2. The clinical efficacy, in terms of the distribution of mRS scores at 90 days by treatment population, is based on pooled data from the MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME and EXTEND IA trials.[4] The transitional probabilities and assumptions applied in the Markov model are based on a literature review of patients receiving alteplase treatment.[13–15] The probability of experiencing recurrent

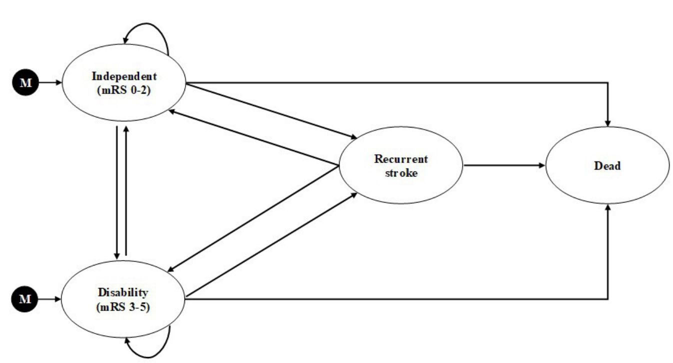

Figure 2 Markov model representing the health states that could occur for patients after treatment with or without endovascular therapy. It is possible to transit to another health state, as shown by the arrows. mRS, modified Rankin scale.

stroke was assumed to be the same regardless of mRS score. Transition between the disability (high mRS score) and independent (low mRS score) states was not allowed after 1 year. Those who were in the disability and independent states at 12 months were assumed to remain in that state thereafter, unless they experienced another stroke. These assumptions are consistent with existing literature. Transitional probabilities in the Markov model for the alteplase ineligible group were adopted from the data used for alteplase eligible patients. Age-adjusted mortality of the Thai population was derived from the Thai Burden of Disease and Injury Study.[16]

Since we employed a societal perspective, direct medical and direct non-medical costs were taken into account (see online supplemental table 2). The cost of thrombectomy devices and equipment for the EVT procedure is based on price estimates from the manufacturers offered to the government. The lowest submitted price across any type of thrombectomy devices (aspiration manual, aspiration pump or stent retriever) was adopted as the base case price. The cost of alteplase is a fixed payment per case under the Universal Coverage Scheme.

Direct non-medical costs include travel and food, accommodation and opportunity costs incurred by patients and caregivers. The stroke-related direct non-medical costs incurred for an acute phase hospital visit, rehabilitation and follow-up outpatient visits were collected from patients at Siriraj Stroke Center from 2015 to 2021 (N=86). Because of the lack of primary data, direct non-medical costs for recurrent stroke hospitalisation were based on another Thai study.[17] The medical records of stroke patients at Siriraj Stroke Center and Neurological Institute of Thailand were reviewed to identify length of stay (N=327) and average number of outpatient visits (N=362); total direct non-medical costs were estimated using average unit (direct non-medical) costs from a previous study.[18]

Cost data from other studies were converted to 2021 values using the Thai consumer price index[19] and presented in Thai Baht (THB) (approximately THB 33=US$1 in 2021). Future costs predicted by the model were shown as net-present values using a discounting rate of 3% with 0%–4% discounting rate used in one-way sensitivity analysis.

Utility scores for the independent and disability states were gathered from 82 patients at the Neurological Institute of Thailand. For recurrent strokes, we applied utility scores from Morris *et al*.[15] QALYs were then calculated by combining length of life and utility scores. All future QALYs gained beyond the first year were discounted by 3% each year with 0%–2% discounting rate used in one-way sensitivity analysis.

Cost and utility data were collected from patients meeting treatment criteria for EVT: 18–80 years of age, AIS with large vessel occlusion, preadmission mRS score between 0 and 2, initial National Institute of Health Stroke Scale and Alberta Stroke Programme Early CT Score ≥6, and able to receive alteplase within 4.5 hours of stroke onset, if eligible.

Cost-effectiveness analysis and sensitivity analysis

The cost-effectiveness was assessed in terms of incremental cost and incremental QALYs. An incremental cost-effectiveness ratio (ICER) was compared against the official cost-effectiveness threshold (CET) in Thailand, which is set at 160 000 THB per QALY.[20]

Sensitivity analyses were undertaken to determine whether the results are robust to parameter uncertainty. A probabilistic sensitivity analysis (PSA) simulation was run 1000 times to generate results, which were presented in cost-effectiveness acceptability curves (CEAC). Beyond PSA, one-way sensitivity analysis was employed, in which parameters for age, utilities, costs and discount rate were varied one at a time while other parameters were held constant (see ranges listed in online supplemental tables 1 and 2).

Budget impact analysis

The budget impact analysis follows the recommendations from the Thai guidelines.[9] The annual direct medical cost was calculated using an incidence-based approach, assuming a new cohort of 2000 patients per year, as recommended during an expert consultation meeting.[21] Budget impact was reported over a period of 5 years from the government payer perspective. No discounting was applied.

Model validation

Face and internal validation were performed through two rounds of stakeholder consultation meetings, attended by relevant policy makers, health professionals, academicians and industry representatives. The first meeting was performed on 17 February 2021[11] to define the research questions and study scope, as well as to identify potential data sources to populate the model. The second meeting was conducted on 8 February 2022[21] to verify model structure, preliminary results and to endorse policy recommendations. In addition, the incremental QALY estimates from our model were compared with the results from other studies included in a systematic review of economic evaluations published by Waqas *et al*.[22]

Patient and public involvement

None.

RESULTS

The comparison of total costs and QALYs from PSA are described in table 1. Among all patients, EVT costs more but yields greater health benefit over a lifetime horizon than providing intravenous alteplase alone to patients eligible to receive alteplase and supportive care to other patients. The incremental QALYs estimated from this study are in the midrange of the published QALYs gained from EVT in the previous studies which reported QALYs gained between 0.11 in the Netherlands and 3.5 in New

Table 1 Lifetime costs and health outcomes of each policy option using societal perspective

	Patients eligible for intravenous alteplase		Patients not eligible for intravenous alteplase	
	Alteplase	**Alteplase and EVT**	**Supportive care**	**EVT**
Costs (THB)	637 600	848 700	547 000	721 300
Life years (years)	5.76	6.81	5.36	6.17
QALYs (years)	2.48	3.92	2.13	3.65
Incremental costs (THB)		211 100		174 300
Incremental QALYs (years)		1.44		1.52
ICER per QALY gained (95% CI)		146 800 (146 300 to 147 300)		115 000 (114 200 to 116 000)

EVT, endovascular treatment; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year(s); THB, Thai Baht.

Zealand.[22] EVT plus intravenous alteplase was associated with an ICER of 146 800 THB per QALY gained (95% CI 146 300 to 147 300) for alteplase eligible patients, while the ICER of EVT compared with supportive care for alteplase ineligible patients was estimated at 115 000 THB per QALY gained (95% CI of 114 200 to 116 000).

The results of the PSA are presented as CEAC, which show the probability of each policy option being cost-effective at different CET. As illustrated by figures 3 and 4, EVT has a 68% and 89% probability of being cost-effective, for alteplase eligible and alteplase ineligible patients respectively, at the Thai threshold of 160,000 THB per QALY gained.

The one-way sensitivity analyses show that the most influential parameter is price of thrombectomy devices. Increasing the device price from 73 800 THB (base-case analysis) to 114 300 THB (maximum price among the three types of thrombectomy device) results in a 26% higher ICER for alteplase eligible patients and a 31% higher ICER for alteplase ineligible patients. A threshold analysis identified 88 100 THB as the maximum thrombectomy device price (including all auxiliary devices for the procedure) for which EVT is cost-effective for treating both patient groups. Other parameters with a high impact on results are shown in figures 5 and 6.

A budget impact analysis was performed to estimate the financial consequences of introducing EVT. Public payer expenditures for the current practice scenario without EVT are estimated at 1024 billion THB (intravenous alteplase alone) and 710 million THB (supportive care) over 5 years. The expected budget for including EVT is 1494 billion THB (EVT plus intravenous alteplase) and 1127 billion THB (EVT alone). As a result, the implementation of EVT would result in an overall budget increase of 887 million THB over 5 years.

DISCUSSION

This study found that introducing EVT incurs higher total costs and results in greater health benefits compared with intravenous alteplase alone or supportive care over a lifetime horizon for all large vessel occlusion AIS patients.

Our findings are consistent with two published systematic reviews of economic evaluations of EVT.[22 23] Most

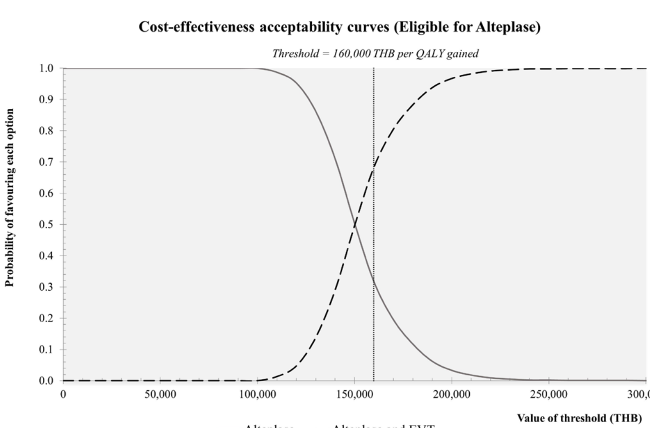

Figure 3 Acceptability curves of the cost-effectiveness at different thresholds of two treatment strategies for acute ischaemic stroke in alteplase eligible patients. EVT, endovascular treatment; QALY, quality-adjusted life year(s); THB, Thai Baht.

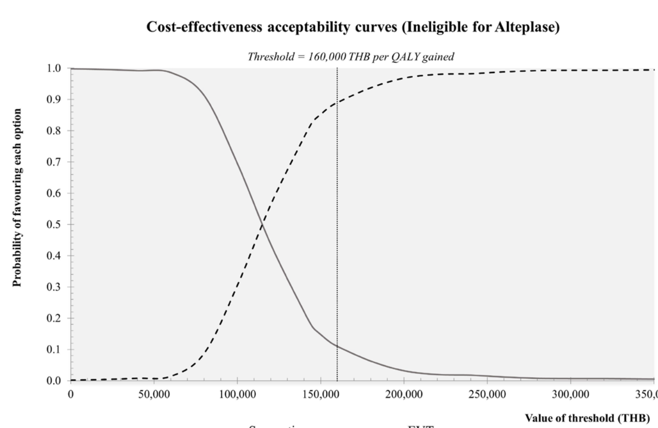

Figure 4 Acceptability curves of the cost-effectiveness at different thresholds of two treatment strategies for acute ischaemic stroke in alteplase ineligible patients. EVT, endovascular treatment; QALY, quality-adjusted life year(s); THB, Thai Baht.

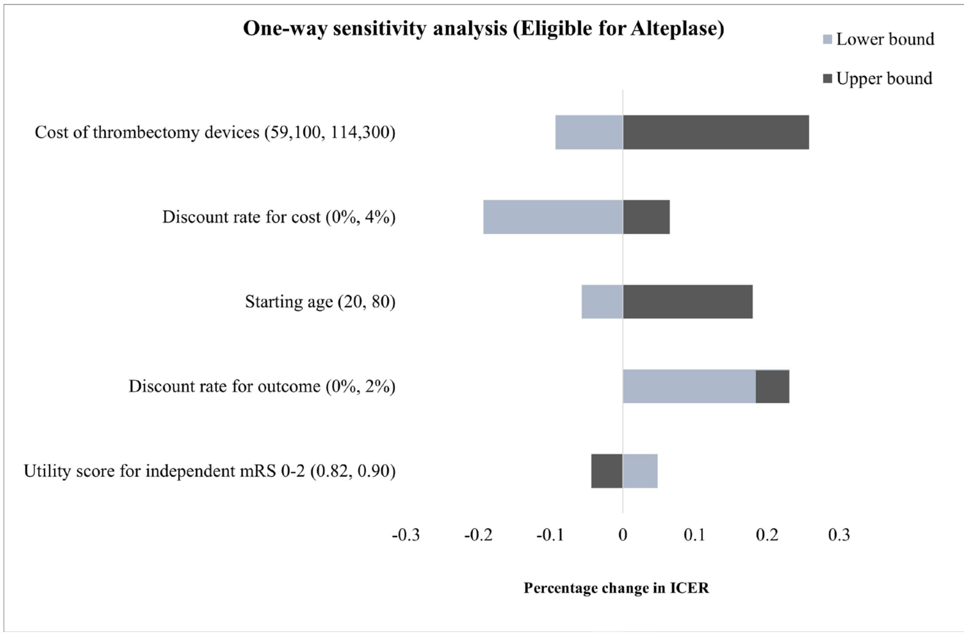

Figure 5 Results of one-way sensitivity analysis for alteplase eligible patients. ICER, incremental cost-effectiveness ratio.

studies in the reviews, conducted across different countries and perspectives, reported EVT to be cost-effective for stroke treatment. Notably, the two studies conducted in Asia (China[24] and Korea[25]) illustrated good value for money, despite applying different perspectives and time horizons to our study. If we applied the same study perspective to these previous two studies, offering EVT will be even more cost-effective under the government's viewpoint. ICERs of EVT in Thailand reduced approximately 20% for both alteplase eligible and alteplase ineligible patients.

These findings support the Thai clinical practice guidelines which recommend intravenous alteplase combined with EVT for treating AIS.[10] The financial resources required to add EVT to the reimbursement list, at around 177 million THB per year, appear to be feasible, given that the annual budget increase of the universal health coverage scheme in Thailand equates to around 4–5 billion Baht annually.[26] This means that the inclusion of EVT in the Thai health benefit package should not affect to the availability of other interventions in the same benefit package.

To address the significant burden of stroke in LMICs, it is critical to make effective interventions accessible. Berkowitz *et al*[27] showed a clear link between national healthcare expenditure per capita and reported use of intravenous alteplase,

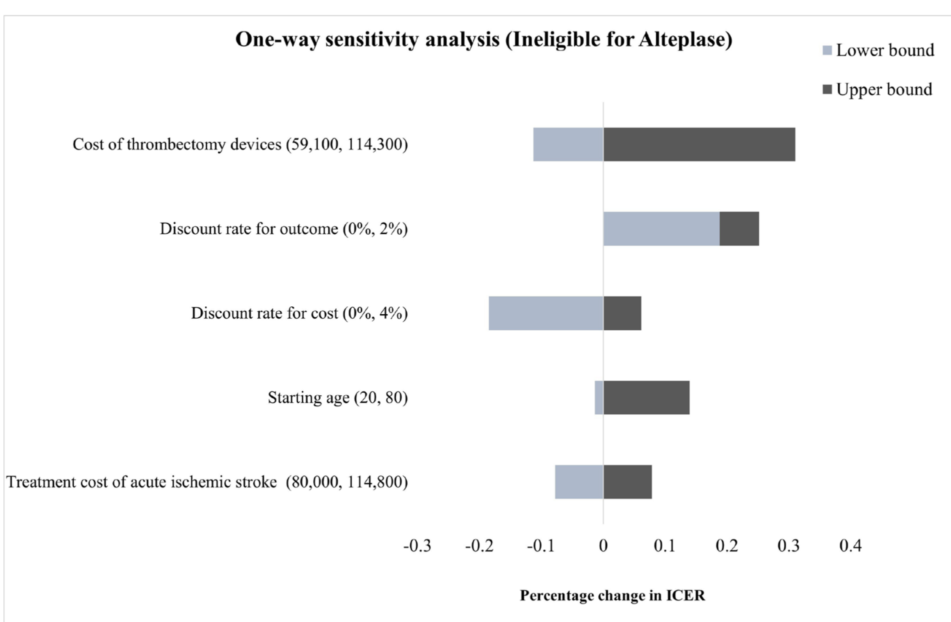

Figure 6 Results of one-way sensitivity analysis for alteplase ineligible patients. ICER, incremental cost-effectiveness ratio.

suggesting poor accessibility to treatments for AIS in LMICs, where the greatest need exists.

Beyond adequate financing, service availability is likely to be a key factor for successful implementation. Currently, there are 52 public and private facilities that provide EVT for stroke patients in Thailand, although the majority (40 centres) are concentrated in the central part of the country. However, if EVT were to be introduced as part of the reimbursement policy, it is likely that service availability would increase due to greater demand. A second important factor for successful implementation is local capacity to provide radio-intervention and neuro-intervention. This should be part of a long-term plan for professional associations and the Ministry of Public Health, which are jointly responsible for human resource planning and distribution in Thailand. Finally, it should be noted that our budget impact estimate may be an underestimate in the intermediate to long term, since free provision of EVT may increase demand, as has been the case with previous interventions added into the benefit package.

To the best of our knowledge, there is no published economic evaluation of EVT for both alteplase eligible and alteplase ineligible patients in LMICs. An advantage of this study over others is that it confirms even greater value for money of EVT for patients ineligible for intravenous alteplase, as compared with EVT for alteplase eligible patients. This is because EVT is the only treatment option for alteplase ineligible patients, and therefore affords greater benefit than when provided after intravenous alteplase treatment.

There are a number of limitations to our study. First, this study assessed the cost-effectiveness of EVT based on the data from patients who met treatment criteria for EVT. Although this is in line with the clinical guideline,[10] in practice health professionals may be faced with patients who do not exclusively meet the criteria for EVT treatment. Evidence on value for money of EVT treatment in this patient group remains limited. Furthermore, this study did not include the initial fixed capital costs for establishing a comprehensive stroke unit, including capital investment and staff training, which might be necessary for hospitals without such a stroke unit. In Thailand, the Ministry of Public Health manages a separate budget for capital investment, thus this study did not include such costs in the budget impact analysis. However, the capital investment budget can be significant, which should be noted when using the results of this study to inform policy in other settings. Finally, we used intervention effectiveness data from clinical trials in other settings, which may not be reflective of the Thai context. It will therefore be important to put in place a monitoring system after introduction of EVT, particularly to collect real-world effectiveness data for different mRS scores including probability of experiencing recurrent stroke across mRS scores.

CONCLUSION

In conclusion, using the Thai CET, adding EVT to intravenous alteplase for alteplase eligible patients or provided alone for alteplase ineligible patients is cost-effective in treating patients with acute large-artery ischaemic stroke. We recommend that EVT be publicly funded in the Thai healthcare system.

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Contributors All authors attest they meet the ICMJE criteria for authorship. YT, WR, WI, TW and YN contributed to conception and design of the study. WR constructed the model. WR, BS and VL conducted the review of model input parameters and analysis of economic evaluation. MK, TW and YN collected the data on cost and utility. YT and WR prepared the manuscript. All authors revised the manuscript and approved the final version. YT and WR are guarantors of this work.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethical approvals were sought from the Siriraj Institutional Review Board and the ethics committee of the Neurological Institute of Thailand with the reference number Si 762/2021 and 037/2564, respectively.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The data are not publicly available due to privacy or ethical restrictions according to the data sharing agreement with Siriraj hospital and Neurological Institute of Thailand.

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