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Cost-effectiveness analysis of mechanical thrombectomy plus tissue-type plasminogen activator compared with tissue-type plasminogen activator alone for acute ischemic stroke in France.

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Abstract

Background and purpose. Recent studies demonstrated the benefit of mechanical thrombectomy (MT) plus intravenous tissue-type plasminogen activator (IV-tPA) (MT-IV-tPA) in acute ischemic stroke. This study aimed to estimate the cost-utility of MT-IV-tPA compared with IV-tPA alone from the perspective of the French National Health Insurance.

Methods. We developed a decision tree for the first 3 months after stroke onset and a Markov model until 10 years post-stroke. The health states of the Markov model were according to the modified Rankin Scale (mRS): independent (mRS=0-2), dependent (mRS=3-5), dead (mRS=6). Recurrent stroke was the fourth health stage of our model. We conducted systematic literature reviews and meta-analyses to estimate the cost and utility of each health state, and the transition probabilities between health states. A microcosting study was conducted to estimate the cost of MT. We estimated the incremental cost-effectiveness ratio of MT-IV-tPA and conducted a probabilistic analysis in order to estimate the probability that MT-IV-tPA is cost-effective compared to IV-tPA, the expected value of perfect information (EVPI), and the expected value of partial perfect information (EVPPI), given the uncertainty surrounding the value of our model's parameters.

Results. The total mean (standard deviation (SD) cost of MT was $\in 6708.9$ (2357.0). The incremental cost-effectiveness ratio (ICER) of the strategy using IV-tPA combined to MT costs was $\in 14$ 715 per QALY gained as compared to a strategy using IV-tPA alone. The probabilistic analysis showed that the probability of MT-IV-TPA being cost-effective was 85.4% at threshold willingness-to-pay of $\in 30,000$ per QALY gained, reaching 98% at $\in 50,000$ per QALY gained.

Conclusion. Although there is no universally accepted willingness-to-pay threshold in France, our analysis suggest that MT combined to IV-tPA can be considered a cost-effective treatment compared with IV-tPA alone.

Keywords: acute ischemic stroke; mechanical thrombectomy; cost-utility; costeffectiveness; expected value of perfect information, expected value of partial perfect information

Introduction

Stroke is a leading cause of death and long-term disability that affects more than 130,000 patients each year in France [1]. Its economic burden was estimated around \notin 5.3 billion in France in 2007 [1]. This cost is for some part related to the management of the acute phase but most of it depends on the management of post-stroke residual handicap and loss of productivity for those who were still professionally active at the time of symptom onset [2]. About 80% of strokes are ischemic of which 25 to 35% are caused by large-vessel occlusion [3].

From more than 10 years, intravenous tissue-type plasminogen activator (IV-tPA) is the standard of care for treating patients with acute ischemic stroke (IS) admitted less than 4.5 hours after symptom onset. Since 2014, several randomized controlled trials (RCT) have demonstrated that, using new generation devices, mechanical thrombectomy, in addition to IV-tPA, dramatically improves the functional outcome of IS patients with proximal intracranial artery occlusion and allows to extend the therapeutic window up to 6 hours after stroke symptom onset, and even later in highly selected patients [4-9].

Mechanical thrombectomy (MT) in addition to IV-tPA, or alone in some circumstances, is now considered as the new standard of care for patients admitted for an IS related to an intracranial proximal occlusion [10].

Effectiveness and economic data are major inputs in the reimbursement decision process and market access. Recent studies have demonstrated the short-term cost-effectiveness of MT performed in addition to IV-thrombolysis compared to IV-tPA alone [11-15]. According to these observations MT is reimbursed by the French National Health Insurance since July 6th 2017.

However, none of these studies has investigated the long-term cost-effectiveness of this procedure taking into account the overall yearly cost of post-stroke sequels management. The aim of this study was to elaborate a Markov decision model to assess the 10-year costutility of MT combined with IV-tPA, as compared to IV-tPA alone, in acute IS caused by large-artery occlusion from the French National Health Insurance perspective. We also estimated the real cost of MT through a complete microcosting analysis. This manuscript was prepared according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines [16].

The results of this work have been transmitted to the French National Authority for Health and to French National Health Insurance at the beginning of 2017.

Methods

Target population

Our target population was patients suffering from an acute IS related to a large intracranial artery occlusion and eligible for MT according to recent recommendations [10].

Settings and comparators

MT combined to IV-tPA was the evaluated strategy.

IV-tPA alone administered within the first 4.5 hours after IS onset was considered as the reference strategy in our analysis.

Because rehabilitation is a critical determinant of management of post-stroke recovery, we considered in our model that the strategy of care following the acute phase differs according to the severity of post-stroke disabilities (which define the health states of our model), but not according to compared interventions.

Model structure

Our model structure was based on those proposed in previous studies [12, 15]. It combined a decision tree for the first 3 months after acute IS and a Markov decision model beyond these first 3 months using three-month cycles, over a 10-year time horizon. This time horizon is sufficient to capture the relevant consequences and cost of each strategy. Mutually exclusive health states were defined according to the modified Rankin Scale (mRS): independent (mRS=0-2), dependent (mRS=3-5), dead (mRS=6). Recurrent stroke was the fourth health stage of our model (figure 1). A panel of multidisciplinary experts (vascular neurologists, neuro-radiologists, epidemiologists and economists) validated the structure of the model.

Main assumptions of the model

We assumed that patients' health state was consolidated after one year. For example, a disabled patient could not recover or an independent patient could not become disabled after this time point, unless a new stroke occurred which is taken into account through a specific health state. Patients could then transit from dependent to independent or from independent to dependent only during the first year after stroke onset.

We did not take into account symptomatic intracerebral hemorrhages within 3 months after stroke because the two strategies have a similar risk [4-9].

We considered that beyond 3 months after stroke onset, patients could transit between the different health states with the same probabilities independently from acute treatment strategies.

We assumed that deaths occurring during the acute stroke phase have a significant cost due to reanimation and palliative care that may be needed. This cost was taken into account in our model.

Model input parameters

Probabilities

For probabilities of the first 3 months after stroke, we performed a systematic literature search using PubMed-MEDLINE, on July 31st 2016. This literature search focused on RCT that compared IV-tPA and MT using stent retrievers or thromboaspiration devices (see the literature search algorithm in the appendix 1).

For probabilities beyond 3 months, we performed a systematic literature search using PubMed-MEDLINE, interrogated on July 31st 2016 (see the literature search algorithm in the appendix 1). We searched for cohort studies in which results were presented in subgroups defined by the mRS.

We used a two-step selection process, firstly on titles and abstracts, and then on full texts. At each step, two reviewers (AB and NK) independently reviewed references. Selected articles where those where results were stratified according to the mRS, and where data needed for probability calculation were available: mean duration of follow-up in years (Y), the number of individuals (n), the number of incident cases (corresponding to health states) (O), and the number of individual at risk (S).

After data extraction, we calculated, for each selected article, the duration of follow-up in person-years (*nY*), and the yearly incidence rate (YI=O/nY). Yearly incidence rates were transformed into quarterly transition probabilities (*QT*) as follows: QT=1 - exp (-YI/4).

When needed, random-effects meta-analyses were conducted using MetaXL® Version 5.2.

Costs

All costs are reported in euro 2015 (\in).

Common costs for both interventions

As IV-tPA is used in both compared interventions in our model, its cost has been systematically taken into account. As stated earlier, the strategy of care after the acute phase is similar in both interventions, and is specific to each health state (level of dependency). Thus, the common costs for both interventions include the costs of hospitalization and IV-tPA in the acute phase and the cost of rehabilitation. These costs are based on data from the literature. We searched for studies conducted in France in which costs results were reported in subgroups defined by the modified Rankin scale.

In our model, the cost of MT comes as an additional cost in the IV-tPA + MT intervention.

Costs of mechanical thrombectomy

We conducted a microcosting study to estimate the cost of MT. Throughout the year 2015, we systematically gathered all medical consumables (device, guide catheter, guidewire, microcatheter, stent thrombectomy, aspiration catheter) used per patient and the start time of the imaging in the hospital emergency room, the start time of puncture by the neuroradiologist in the intervention room, the end-time of MT, and the type of MT (stent retrievers, thromboaspiration or mixed).

Staff cost

We calculated the average staff time. The neurologist time corresponded to the start time of puncture minus the start time of the imaging, the neuroradiologist and radiologist times being the end-time of MT minus the start time of the imaging. The anesthetist and nurse anesthetist times were determined by the end-time of MT minus the start-time of puncture. The hourly costs per health professional were based on the fee guidelines of Bordeaux University Hospital [17] assuming 1664 annual working hours for the physicians (neurologist, neuroradiologist, and anesthetist). Staff time costs were estimated, multiplying the average time of each health professional by each corresponding hourly cost assuming that 50% of MT are performed during on-call service.

Medical devices cost

The unit costs were those applied at the Bordeaux University Hospital for each medical consumable used, including MT procedure (stent retrievers, thromboaspiration and mixed).

Operating room

In collaboration with the financial department of the Bordeaux University Hospital, we estimated the operating room cost assuming that 55% of the interventional neuroradiology activity will be dedicated to MT and that there will be 650 acts per year. The amount of investments to adapt the operating room to the MT activity has been taken into account over an 8 years' time horizon corresponding to depreciation period of biomedical equipment. Structural costs were taken into account by applying a systematic structure rate of 16.8%.

Health utilities

Modified Rankin Scale is a commonly used scale for measuring the functional dependence of individuals who suffered a stroke [18]. Utility values for use in health economics can be

derived from the disease-specific scale. We translated the mRS into EuroQol five dimensions questionnaire (EQ-5D-3L) utility values using a mapping algorithm [19].

This mapping algorithm has been developed for categories 0 to 5 of the mRS (the utility of death being 0), and for time points of 1, 6, 12, and 24 months after stroke onset.

The utility of states independent and dependent of the first cycle of our model (first 3 months after stroke onset) was the average of utility scores given by the mapping algorithm for mRS categories 0 to 2 and 3 to 5, respectively, at month-1 after stroke, and weighted for the proportion of individuals being in these mRS categories in the randomized clinical trials included in our systematic review.

The utility of states independent and dependent beyond the first 3 months of our model was the average of utility scores given by the mapping algorithm for mRS categories 0 to 2 and 3 to 5, respectively, beyond 6 months after stroke onset.

The utility of recurrent stroke was given by the average scores of mRS categories 0 to 2 and 3 to 5 given by the mapping algorithm, weighted by the probability of being dependent or independent after a recurrent stroke.

Discounting

All costs and outcomes after the first year were discounted at an annual rate of 4% as recommended by the French National Authority for Health [20].

Probability distributions of the parameters

Gamma distributions were used for costs, Dirichlet distribution was used for the probabilities of the first 3 months after stroke, and beta distributions were used for utility values and transition probabilities beyond the first 3 months. The method of moments was used to derive distribution parameters from means and standard deviations issued from the literature [21].

Analysis of the model

Because cycles' duration was 3 months, we had to proceed to a half-cycle correction for which we used the life table method [22].

Parameter uncertainty was handled through a probabilistic analysis (1000 Monte Carlo simulations) using the probability distributions described above.

The following results were produced using Microsoft Excel 2010: cost-utility ratio and its probabilistic distribution on a cost-effectiveness plan; incremental net monetary benefit (INMB); cost-effectiveness acceptability curve; and the expected opportunity loss associated with the uncertainty surrounding the decision to be made with the information provided by our model.

This expected opportunity loss can be quantified in a monetary value and is known as the expected value of perfect information (EVPI) because it is the amount the decision maker should be willing to pay to eliminate all uncertainty in the decision. These concepts were developed within Bayesian statistical decision theory [23].

Expected value of perfect partial information (EVPPI), that is, EVPI for a single or a group of parameters, was computed using the Sheffield Accelerated Value of Information online tool (http://savi.shef.ac.uk/SAVI/) [24].

Values of information analyses were carried out based on a hypothetical size of the target population of 8000 individuals per year during 10 years, and on a cost-effectiveness threshold of \notin 30,000 per QALY gained, which is approximately the gross domestic product per capita per year in France.

Results

All the parameters of our model with their distribution parameters, resulting from our systematic reviews and meta-analyses, are presented in table 1.

Real cost of mechanical thrombectomy

The results of the microcosting study are presented in table 1. The total mean (standard deviation (SD) cost of MT was €6708.9 (2357.0). Indetails, a total of 87 MTs were conducted from January 2015 to December 2015. The cost per hour of work (except on-duty service) was €62.6 for physicians (neurologists, neuroradiobgists, and anesthetists), €29.5 for radiology technicians, and €38.8 for operating room nurses. The mean (standard deviation (SD) duration of work per MT were 132 (58) minutes for neuroradiologists and radiology technicians, 87 (48) minutes for neurologists, and 45 (25) minutes for anesthetists and operating room nurses. The additional cost related to on-duty service was €107.8 for physicians, €11.4 for operating room nurses, and €78 for radiology technicians. After application of a 16.8% structure rate, the total mean (SD) cost of health professionals (including two radiology technicians per procedure) involved in MT at our center in 2015 was €653.46 (188.8).

Out of the 87 MTs performed in 2015, 36% used a stent retriever, 18% used thromboaspiration and 46% were mixed procedures. After application of a 16.8% structure rate, the mean (SD) cost of medical devices was €5873.9 (2356.9).

The fixed cost of operating room utilization was €179.9 per MT.

Cost of stroke (hospitalization, IV-tPA, and rehabilitation)

Costs of stroke were based on the lone study in which costs' results were stratified on mRS in France [2]. This study reported the cost of acute care, rehabilitation, ambulatory care, drugs, ortheses, nursing home and long-term institutionalization. In this study, acute care could have been delivered in stroke units or not, depending on the distribution of stroke units over the French territory at that time. Costs were estimated in the perspective of the French National Health Insurance, in \notin 1997.

Cost of death occurring during the first 3 months after stroke onset were extracted from a study where costs were estimated in the perspective the French National Health Insurance, in \notin 2007 [1].

For all these costs we applied an inflation rate until December 2015 using the Consumer Prices Index provided by the French National Institute of Statistics and Economic Studies (https://www.insee.fr/fr/statistiques/2122401#tableau-Donnes, consulted on January 16th 2017).

Transition probabilities

A random effect meta-analysis of the six randomized clinical trials of last generation MT [4-9] was conducted to value the probabilities of the first 3 months after stroke. The French THRACE trial, published after July 31st 2016, was added afterwards to our systematic review. When there was more than one reference, a random effect meta-analysis was conducted (table 1).

Cost-effectiveness results

Base case analysis

For a fictive cohort of 1000 individuals admitted for an acute IS related to a proximal intracranial artery occlusion, and for a period of 10 years after stroke onset (4% discount rate), the strategy using IV-tPA alone costs \leq 35,198,650 and generates 1462 QALY while the strategy using IV-tPA combined to MT costs \leq 40,195893 and generates 2584 QALY. The incremental cost-effectiveness ratio (ICER) of the strategy using IV-tPA combined with MT costs was \leq 14 715 per QALY gained as compared to a strategy using IV-tPA alone, from the perspective of the French National Health Insurance.

Probabilistic analysis

The 1000 ICER resulting from Monte Carlo Simulations are represented in Figure 2. Nine hundred and fifty of these ICER are located in the north-east quadrant of the cost-effectiveness plane, meaning that MT in addition to IV-tPA is more costly and more effective than IV-tPA alone, with a probability of 95%.

The black line in Figure 2 represents a ceiling ICER (or ceiling monetary value of a QALY) of €30000/QALY. Eight hundred and fifty-four ICERs out of the 1000 resulting from Monte Carlo Simulations are situated below this line, meaning that the cost-effectiveness probability of MT plus IV-tPA as compared to IV-tPA alone is 85.4%.

The cost-effectiveness probability of MT plus IV-tPA depends on the chosen ceiling ICER. The ceiling ICER may vary from 0 to $+\infty \notin$ /QALY, corresponding to an angle between the abscise axis and the ceiling ICER from 0 to 90°. For each ceiling ICER, the proportion of ICER resulting from Monte Carlo Simulations situated below it will vary. This can be represented on a cost-effectiveness acceptability curve (figure 3). For ceiling ICERs from 0 to 100 000€/QALY, the cost-effectiveness probability of mechanical thrombectomy plus IV-tPA as compared to IV-tPA ranges from 4.8% to 98.5%.

Value of information analysis

The total expected value of perfect information (EVPI) was €31.98 million and the EVPI per patient was €473.93.

When estimating the expected value of perfect information per parameter (EVPPI), two parameters explain the vast majority of the uncertainty regarding the value of our model's parameters: the utility score of individuals who are independent three months after stroke onset (population EVPPI: ≤ 11.80 million), and the staff cost entering the cost of mechanical thrombectomy (population EVPPI: ≤ 4.91 million).

Discussion

While MT has revolutionized the functional prognosis of patients admitted for an IS and proximal large-artery occlusion the increased cost related to this procedure has shed doubt on its cost-effectiveness. The main result of this 10-year cost-effectiveness study is that MT combined with IV-tPA compared to IV-tPA alone generated an additional QALY at a cost of €14,715. Although there is no universally accepted willingness-to-pay threshold in France, our analysis suggests that at a ceiling cost-effectiveness ratio of €30,000, MT combined with IV-tPA can be considered a cost-effective treatment compared with IV-tPA alone. Our finding is in line with recently published cost-effectiveness studies, including decision-models and clinical trials, of MT conducted in Canada [15], France [11], the United Kingdom [12], and the USA [13, 14] that identified the short-term cost-effectiveness of MT for IS patients with proximal-artery occlusion.

There are always some limitations in model-based cost-effectiveness analyses that are inherently a simplification of reality. In France, MT must be performed by trained senior interventional neuroradiologist, in hospitals with a stroke unit and interventional radiologists. Some patients are transported by helicopter to stroke units to carry out MT. We ignored the cost of helicopter transportation because of lack of data, and because this cost may vary dramatically between areas in France. Another possible limitation comes from the data used to populate our model. On one hand, RCTs provided valid and detailed data but the follow-up was systematically limited to 3 months after stroke onset. On the other hand, data from cohort studies used to model long-term outcomes may present selection or measurement biases. However, we only selected cohort studies where results were sufficiently informative so that we could get the data required to calculate transition probabilities (follow-up in person-years, number of events, number of individuals at risk), which is a fair guarantee of methodological quality. Except data from the THRACE trial, our parameter estimates came from studies conducted outside France, but for the vast majority from countries where health-care services are comparable to the offer in France. Costs of stroke in France beyond 3 months after stroke were based on a unique study published in 2004, 13 years ago [2]. Recent data would have been more accurate but after actualization to get 2015 costs, we come close to current inpatient costs for instance.

Our value of information analysis indicates that the uncertainty surrounding the decision that could be taken based on the results of our model is mainly driven by the value of two parameters: the staff cost during MT intervention, and the utility score of individuals being independent three months after stroke onset. For this latter parameter, our systematic literature review revealed a major lack of data concerning the fate of individuals who recover and are independent following a stroke. Registries and cohort studies should focus on this subgroup to inform scientists and decision makers. The uncertainty regarding the staff cost during MT intervention is now erased as a conventional tariff within the French Health System has been attributed to MT performed for proximal intracranial occlusion. This decision, to which this study has probably contributed, will afford the development and spreading of MT in several French centers. However new questions already arise such as the cost-effectiveness of drip and ship vs mothership strategies or of late MT alone according to the DAWN trial [30]. MT is just starting to change the acute care of IS and modeling studies such as our might help

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Declarations of interest

The authors declare that they have no conflict of interest.

taking appropriate decisions in providing efficient care pathways in IS.

References

1. Chevreul K, Durand-Zaleski I, Gouépo A, Fery-Lemonnier E, Hommel M, Woimant F. Cost of stroke in France. European journal of neurology. 20 (2013) 1094-1100.

2. Spieler J-F, Lanoë J-L, Amarenco P. Costs of stroke care according to handicap levels and stroke subtypes. Cerebrovascular Diseases (Basel, Switzerland). 17 (2004) 134-142.

3. Mattioni A, Cenciarelli S, Biessels G, van Seeters T, Algra A, Ricci S. Prevalence of intracranial large artery stenosis and occlusion in patients with acute ischaemic stroke or TIA. Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology. 35 (2014) 349-355.

4. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. The New England journal of medicine. 372 (2015) 11-20.

5. Bracard S, Ducrocq X, Mas JL, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. The Lancet Neurology. 15 (2016) 1138-1147.

6. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. The New England journal of medicine. 372 (2015) 1009-1018.

7. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. The New England journal of medicine. 372 (2015) 1019-1030.

8. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. The New England journal of medicine. 372 (2015) 2296-2306.

9. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. The New England journal of medicine. 372 (2015) 2285-2295.

10. Wahlgren N, Moreira T, Michel P, et al. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. International journal of stroke : official journal of the International Stroke Society. 11 (2016) 134-147.

11. Achit H, Soudant M, Hosseini K, et al. Cost-Effectiveness of Thrombectomy in Patients With Acute Ischemic Stroke: The THRACE Randomized Controlled Trial. Stroke. 48 (2017) 2843-2847.

12. 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. 46 (2015) 2591-2598.

13. 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. 42 (2011) 2013-2018.

14. Shireman TI, Wang K, Saver JL, et al. Cost-Effectiveness of Solitaire Stent Retriever Thrombectomy for Acute Ischemic Stroke: Results From the SWIFT-PRIME Trial (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke). Stroke. 48 (2017) 379-387.

15. Xie X, Lambrinos A, Chan B, et al. Mechanical thrombectomy in patients with acute ischemic stroke: a cost-utility analysis. CMAJ open. 4 (2016) E316-325.

16. Husereau D, Drummond M, Petrou S, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. International journal of technology assessment in health care. 29 (2013) 117-122.

17. Guide de la tarification - CHU de Bordeaux. 2017 [updated 2017-10-09 21:28:42].

18. Sulter G, Steen C, De Keyser J. Use of the Barthel index and modified Rankin scale in acute stroke trials. Stroke. 30 (1999) 1538-1541.

19. Rivero-Arias O, Ouellet M, Gray A, Wolstenholme J, Rothwell PM, Luengo-Fernandez R. Mapping the modified Rankin scale (mRS) measurement into the generic EuroQol (EQ-5D) health

outcome. Medical Decision Making: An International Journal of the Society for Medical Decision Making. 30 (2010) 341-354.

20. Santé. HAd. Choix méthodologiques pour l'évaluation économique à la HAS. . 2011.

21. Briggs A, Claxton K, Sculpher M. Decision modelling for health economic evaluation. Oxford: Oxford University Press; 2006.

22. Barendregt JJ. The half-cycle correction: banish rather than explain it. Medical Decision Making: An International Journal of the Society for Medical Decision Making. 29 (2009) 500-502.

23. Ades AE, Lu G, Claxton K. Expected value of sample information calculations in medical decision modeling. Medical decision making : an international journal of the Society for Medical Decision Making. 24 (2004) 207-227.

24. Strong M, Oakley JE, Brennan A, Breeze P. Estimating the Expected Value of Sample Information Using the Probabilistic Sensitivity Analysis Sample: A Fast, Nonparametric Regression-Based Method. Medical decision making : an international journal of the Society for Medical Decision Making. 35 (2015) 570-583.

25. Hankey GJ, Spiesser J, Hakimi Z, Bego G, Carita P, Gabriel S. Rate, degree, and predictors of recovery from disability following ischemic stroke. Neurology. 68 (2007) 1583-1587.

26. Hankey GJ, Spiesser J, Hakimi Z, Carita P, Gabriel S. Time frame and predictors of recovery from disability following recurrent ischemic stroke. Neurology. 68 (2007) 202-205.

27. Luengo-Fernandez R, Paul NLM, Gray AM, et al. A population-based study of disability and institutionalisation after TIA and stroke: 10-year results of the Oxford Vascular Study. Stroke; a journal of cerebral circulation. 44 (2013) 2854-2861.

28. Magalhães R, Abreu P, Correia M, Whiteley W, Silva MC, Sandercock P. Functional status three months after the first ischemic stroke is associated with long-term outcome: data from a community-based cohort. Cerebrovascular Diseases (Basel, Switzerland). 38 (2014) 46-54.

29. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. Stroke. 29 (1998) 2491-2500.

30. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. The New England journal of medicine. 378 (2018) 11-21.



Figure 1. Model structure. Cost-effectiveness of mechanical thrombectomy plus tissue-type plasminogen activator (IV-tPA) as compared to IV-tPA alone in the 6 hours after ischemic stroke onset, France 2015.



Figure 2. Cost-effectiveness plane of mechanical thrombectomy (MT) plus tissue-type plasminogen activator (IV-tPA) as compared to IV-tPA alone in acute ischemic stroke, France 2015



Figure 3. Cost-effectiveness acceptability curve of mechanical thrombectomy (MT) plus tissue-type plasminogen activator (IV-tPA) as compared to IV-tPA alone in acute ischemic stroke, France 2015.

Table 1. Model inputs

	Base-Case Value	Distribution (α , β) for PSA	Standard deviation	Reference
Probabilities				
IVT alone				
Independent (mRS 0-2)	0.317	Dir (268.205 , 578.795)		[4-9]
Dependent (mRS 3-5)	0.513	Dir (434.272 , 412.728)		[4-9]
Dead (mRS 6)	0.171	Dir (144.523 , 702.477)		[4-9]
Thrombectomy + IVT				
Independent (mRS 0-2)	0.516	Dir (429.495 , 403.505)		[4-9]
Dependent (mRS 3-5)	0.352	Dir (293.002 , 539.998)		[4-9]
Dead (mRS 6)	0.133	Dir (110.503 , 722.497)		[4-9]
Transition probabilities				
From 3 mo to 12 mo				
From Independent (mRS 0-2) to				
Independent (mRS 0-2)	0.900	β (288.071 , 31.929)		[25-28]
Dependent (mRS 3-5)	0.044	-		
Recurrent stroke	0.026	β (16.717 , 616.283)		[29]
Dead (mRS 6)	0.030	β (5.202 , 170.798)		[28]
From Dependent (mRS 3-5) to				
Independent (mRS 0-2)	0.082	β (98.002 , 1103.319)		[25-28]
Dependent (mRS 3-5)	0.777	-		
Recurrent stroke	0.026	β (9.058 , 333.942)		[29]
Dead (mRS 6)	0.115	β (20.221 , 155.779)		[28]
From 1 year to 2 years				
From Independent (mRS 0-2) to				
Independent (mRS 0-2)	0.932	-		
Dependent (mRS 3-5)	0	-		Hypothesis
Recurrent stroke	0.003	β (0.529 , 210.471)		[29]
Dead (mRS 6)	0.065	β (11.064 , 158.936)		[28]
From Dependent (mRS 3-5) to				
Independent (mRS 0-2)	0	-		Hypothesis
Dependent (mRS 3-5)	0.891	-		
Recurrent stroke	0.003	β (0.529 , 210.471)		[29]
Dead (mRS 6)	0.106	β (18.064 , 151.936)		[28]
From 2 years to 3 years				
From Independent (mRS 0-2) to				
Independent (mRS 0-2)	0.960	-		
Dependent (mRS 3-5)	0	-		Hypothesis
Recurrent stroke	0.012	β (2.634 , 208.366)		[29]
Dead (mRS 6)	0.028	β (4.339 , 152.661)		[28]
From 2 years to 3 years				
From Dependent (mRS 3-5) to				
Independent (mRS 0-2)	0	-		Hypothesis
Dependent (mRS 3-5)	0.881	-		
Recurrent stroke	0.012	β (2.634 , 208.366)		[29]
Dead (mRS 6)	0.106	β (16.683 , 140.317)		[28]
From 3 years to 4 years				
From Independent (mRS 0-2) to				

Independent (mRS 0-2)	0.939	-		
Dependent (mRS 3-5)	0	-		Hypothesis
Recurrent stroke	0.010	β (1.900 , 190.1)		[29]
Dead (mRS 6)	0.051	β (7.717 , 144.283)		[28]
From Dependent (mRS 3-5) to				
Independent (mRS 0-2)	0	-		Hypothesis
Dependent (mRS 3-5)	0.860	-		
Recurrent stroke	0.010	β (1.643 , 164.357)		[29]
Dead (mRS 6)	0.130	β (19.793 , 132.207)		[28]
Over than 4 years				
From Independent (mRS 0-2) to				
Independent (mRS 0-2)	0.891	-		
Dependent (mRS 3-5)	0	-		Hypothesis
Recurrent stroke	0.010	β (1.336 , 133.664)		[29]
Dead (mRS 6)	0.099	β (14.204 . 128.796)		[28]
From Dependent (mRS 3-5) to	0.000	p (1) 1		[=0]
Independent (mRS 0-2)	0	-		Hypothesis
Dependent (mRS 3-5)	0.860	-		,potricolo
Becurrent stroke	0.010	ß (1 336 133 664)		[29]
Dead (mRS 6)	0.130	β (18 621 124 379)		[28]
From Recurrent stroke to	0.150	p (10.021) 12 1.57 5)		[20]
Independent (mRS 0-2)	0 849	_		
Dependent (mRS 3-5)	0.116	ß (73 814 563 186)		[26]
Dead (mRS 6)	0.035	β (12 141 332 859)		[26]
Health utility	0.000	p (12.111) 332.033)		[20]
For < 3 mo after stroke				
Independent (mRS 0-2)	0 788	B (1 935 0 522)		[10]
Dependent (mRS 2 5)	0.700	β (1.333, 0.322)		[10]
Eq. > 2 mo after stroke	0.299	p (0.392 , 0.920)		[19]
For ≥ 5 find after stroke	0.915	Q (2 124 0 492)		[10]
Dependent (mRS 0-2)	0.242	p (2.124 , 0.483)		[19]
Dependent (IIIKS 3-5)	0.343	p (0.338 , 0.048)		[19]
Recurrent stroke	0.703	p (0.917 , 0.387)		
Dead	0	-		
Aguta stroke initial bespitalization secto				
Acute stroke mitial hospitalization costs	0251 007	(4000 872 - 1 008)	124.050	[2]
Den en dent (mRS 0-2)	9251.607	γ (4699.873, 1.968)	134.950	[2]
Dependent (mRS 3-5)	10216.427	γ (397.916, 25.675)	512.157	[2]
Recurrent From Independent (mRS 0-2) Recurrent From Dependent (mRS 3-5)	9251.607 10216.427	γ (4699.873 , 1.968) γ (397.916 , 25.675)	134.950 512.157	[2] [2]
Ongoing costs every 3 mo				
Independent (mRS 0-2)	989.089	γ (124.666, 7.934)	88.585	[2]
Dependent (mRS 3-5)	5973.648	γ (6.660, 896.912)	2314.700	[2]
Dead (< 3 mo after acute stroke)	5661.710	-		[1]
Thrombectomy additional cost				
-			2256 04 4	Microcosti
Device	5873.86	γ (6.211,945.723)	2356.914	WIICIOCOSLI
Device Staff cost	5873.86 653.460	γ (6.211 , 945.723) γ (11.983 , 54.534)	2356.914 188.775	Microcostir