Institution: Imperial College London

Unit of Assessment: 04 Psychology, Psychiatry and Neuroscience

Title of case study: Mechanical thrombectomy for acute ischaemic stroke: transforming stroke care

Period when the underpinning research was undertaken: 2015 - 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Kyriakos Lobotesis	Consultant Neuroradiologist Head of Specialty Professor of Practice	2016 - present

Period when the claimed impact occurred: 2016 - present

Is this case study continued from a case study submitted in 2014? No

1. Summary of the impact (indicative maximum 100 words)

A lack of evidence on the cost-effectiveness of mechanical thrombectomy (MT) has limited its clinical commissioning and utilisation in acute ischaemic stroke (AIS). Research at Imperial College established that MT is a highly cost-effective treatment for AIS, singularly underpinning the UK's National Institute for Health and Care Excellence (NICE) policy recommendations supporting MT as a treatment for patients with AIS. This has had a significant impact on outcomes for patients with severe stroke deficits: between April 2019 and March 2020, 1,607 patients were treated by MT in England, Wales and Northern Ireland, with 70.3% experiencing improvement in their clinical outcome.

2. Underpinning research (indicative maximum 500 words)

Since 2012, thrombolysis with intravenous tissue plasminogen activator (IV t-PA) has been the standard treatment for acute ischemic stroke (AIS) in the UK. Subsequently, for patients with disabling strokes secondary to large vessel occlusion, mechanical thrombectomy (MT) has emerged as a powerful new intervention.

Based on clinical trials, a 2014/2015 consensus statement by the European Stroke Organisation (ESO), European Society of Minimally Invasive Neurological Therapy (ESMINT), European Society of Neuroradiology (ESNR) and European Academy of Neurology (EAN) stated MT was "recommended to treat acute stroke patients with large artery occlusions in the anterior circulation up to 6 hours after symptom onset". Despite the clinical case supporting the use of MT for AIS, a lack of economic evidence to support its use, restricted the ability of individual hospital Trusts to invest in this service, and significantly delayed the national commissioning of MT for AIS in the UK.

To address this, Lobotesis led cost-utility analyses of MT for AIS from a UK payer perspective (1). The cost-effectiveness of MT for AIS was investigated using a Markov model developed to simulate health outcomes of competing therapies over short and lifetime time horizons. For stroke with symptom onset under 6 hours, Lobotesis found that combined MT (carried out predominantly with stent retrievers) and IV t-PA was associated with improved quality-of-life and increased life expectancy compared to IV t-PA alone (1, 2). The higher treatment costs associated with the use of stent-retriever thrombectomy were offset by substantial long-term savings due to improved health outcomes with reduced hospital stays and long-term care costs, leading to an estimated mean cost saving of £33,190 per patient treated. This translates to a saving of £39,800,000 in England, Wales and Northern Ireland for thrombectomies conducted between April 2018 and

March 2019. NHSE estimates that 10,140 patients per year may be clinically eligible for MT once national implementation is complete. Over seven lifetime quality-adjusted life years (QALYs) were estimated to be gained by using stent-retriever MT with a net monetary benefit of £79,402 per QALY (3, 4).

In a continuation of this research, Lobotesis found that performing MT up to 24 hours following acute stroke symptom onset was also cost-effective. Over a 20-year period, the incremental cost per QALY of MT was £1,219 when performed after 12 hours from stroke onset, £4,096 after 16 hours and £2,894 after 24 hours. Probabilistic sensitivity analysis indicated that MT had a 99.9% probability of being cost-effective based on the maximum cost the UK is commonly willing to pay per QALY (5).

In further work, based on systematic review and meta-analysis of the published literature (6), Lobotesis's research has also had an impact on the development of practice guidelines for MT for AIS and treatment modality recommendations (addressing Population, Intervention, Comparator, Outcome (PICO) questions: PICO 3, PICO 11 and PICO 12). These are for use by hospitals in the UK and Europe based on the standard operating procedures (SOPs) of the European Stroke Organisation (using the Grading of Recommendations, Assessment, Development, and Evaluation [GRADE] approach), and cover pre-hospital management and patient selection based on clinical and imaging criteria and MT treatment modality options.

3. References to the research (indicative maximum of six references)

(1) Ganesalingam, J., Pizzo, E., Morris, S., Sunderland, T., Ames, D., Lobotesis, K. (2015). Cost-utility analysis of mechanical thrombectomy using stent retrievers in acute ischaemic stroke. *Stroke*; 46(9): 2591-2598. DOI.

(2) Lobotesis, K., Veltkamp, R., Carpenter, I.H., Claxton, L.M., Saver, J.L., Hodgson, R. (2016).Cost-effectiveness of stent-retriever thrombectomy in combination with IV t-PA compared with IV t-PA alone for acute ischemic stroke in the UK. *Journal of Medical Economics*; 19(8): 785-794. DOI.

(3) Arora, N., Makino, K., Tilden, D., Lobotesis, K., Mitchell, P., Gillespie, J. (2018). Cost-effectiveness of mechanical thrombectomy for acute ischemic stroke: an Australian payer perspective*. Journal of Medical Economics;* 21(8): 799-809. DOI.

(4) Ruggeri, M., Basile, M., Zini, A., Mangiafico, S., Agostoni, C., Lobotesis, K., Saver, J., Coretti, S., Drago, C., Cicchetti, A. (2018). Cost-effectiveness analysis of mechanical thrombectomy with stent retriever in the treatment of acute ischemic stroke in Italy. *Journal of Medical Economics*; 21(9): 902-911. DOI.

(5) Pizzo, E., Dumba, M., Lobotesis, K. (2020). Cost-utility analysis of mechanical thrombectomy between 6 and 24 hours in acute ischemic stroke. *International Journal of Stroke*; 15(1): 75-84. DOI.

(6) Turc, G., Bhogal, P., Fischer, U., Khatri, P., Lobotesis, K., Mazighi, M., Schellinger, P.D., Toni, D., de Vries, J., White, P., Fiehler, J. (2019). European Stroke Organisation (ESO) – European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischaemic Stroke Endorsed by Stroke Alliance for Europe (SAFE). *European Stroke Journal*; 4(1): 6-12. DOI.

4. Details of the impact (indicative maximum 750 words)

In the UK each year, approximately 113,000 individuals suffer a stroke, 87% of which are of an ischaemic aetiology. There are around 1,000,000 stroke survivors who live with chronic stroke-related disability, the repercussions of which can be severe and widespread for both patients and carers. The current UK annual societal cost of stroke is £25.6 billion. Owing to the UK's ageing

population, these figures, based on retrospective data, are likely underestimates, as both the incidence of stroke and its economic burden from the needs for extensive hospitalisation and long-term care are rising each year. Currently, between 10,140 and 11,530 stroke patients per year in the UK could be eligible for MT, which approximates to 10% of all stroke admissions.

Despite the substantial evidence for the clinical effectiveness of MT for AIS, its use in routine practice in the UK had been limited by the lack of cost effectiveness data, especially given the significant costs of the procedure and its implementation. The latter challenges are related to high-level upfront investment required for an acute therapy like MT as well as the need for workforce training and service reconfiguration/integration in stroke and neuroscience centres nationwide.

Key to addressing this practical economic barrier to adoption in routine clinical practice was the demonstration that the associated long-term health benefits significantly outweighed the additional costs of the procedure. Research from Lobotesis at Imperial provided the first evidence of the substantial long-term cost savings that offset the higher treatment costs. These analyses, which are still the only UK-based cost-utility analyses of MT for AIS, singularly underpinned NICE policy recommendations in 2016, 2018 and 2019 that MT is a cost-effective treatment for patients with AIS in the UK [**A, B, C**].

The analyses also led to MT being commissioned at Imperial College Healthcare NHS Trust (ICHT) in 2017 as a new flagship clinical service, and nationally by NHS England (NHSE) in 2019 [**D**]. This national Clinical Commissioning Policy [**D**] was based on the NICE Medtech innovation briefing, 'Mechanical thrombectomy devices for acute ischaemic stroke' [**B**], which looked into the cost of MT devices and the subsequent resource impact in England, Wales and Northern Ireland, of the cost of the procedure. Overall, 12 cost-effectiveness studies were analysed, including 2 from a UK payer perspective, both of which were led by Dr Lobotesis and his team at Imperial.

Prior to 2017 and the policy recommendations underpinned by Lobotesis' research, only 424 patients were treated with MT in England, Wales and Northern Ireland in the period 2015-2016 (2016 Acute Organisational Audit data). Between April 2019 and March 2020 (Sentinel Stroke National Audit Programme [SSNAP] data), 1,607 patients were treated with MT by 26 teams across England, Wales and Northern Ireland [**E**]. Nationally, 70.3% of treated patients who had a National Institutes of Health Stroke Scale score fully recorded on arrival and again 24 hours after thrombectomy, showed neurologic improvements. The research findings and clinical experience underpinned the development of guidelines for implementation of MT for AIS in the UK including business case development sponsored by the UK Stroke Association, NIHR and the Oxford Academic Health Sciences Network [**F**].

Subsequent to establishing one of the first 24/7 comprehensive MT services, ICHT currently continues to be the largest MT service in the UK, receiving patients from across South West England. In 2020, a total of 201 stroke patients were treated with MT at ICHT. In the same period, an average of 56 MT procedures were performed in other neuroscience centres nationally. This adoption has also had a significant impact on outcomes for patients with severe deficits at ICHT. Of the 201 MT patients, 43% had Rankin scores 0-2 ("alive and independent") and 81.6% achieved TICI2B/3 ("complete cerebral reperfusion") angiographic outcomes [**E**]. Subsequently the Stroke/Thrombectomy service at ICHT was awarded, in 2020, the Imperial Chair's Award for its outstanding performance and excellent clinical outcomes.

The peer-reviewed published recommendations (detailed above) arising from these findings have been successfully endorsed and incorporated into local (ICHT), national (NICE, NHSE) and international (Stroke Alliance for Europe [SAFE], ESMINT) policy documents [**G**].

5. Sources to corroborate the impact (indicative maximum of 10 references)

[**A**] NICE interventional procedures guideline 2016:
NICE mechanical clot retrieval for treating acute ischaemic stroke
(https://www.nice.org.uk/guidance/ipg548). This guidance made recommendations relating to the

clinical effectiveness of MT for AIS but contained no guidance on cost effectiveness, and highlighted practice uncertainties relating to best type of imaging to guide patient selection, best kind of retrieval device and effectiveness of MT in patients with strokes in different parts of the brain. Archived here.

[**B**] NICE technology briefing 2018:
NICE Medtech innovation briefing on mechanical thrombectomy devices for acute ischaemic stroke (https://www.nice.org.uk/advice/mib153/chapter/Summary). The guidance cites Lobotesis research that MT for AIS is cost effective in the UK for stroke with symptom onset within 6 hours with cost savings over 20 years when compared to thrombolysis alone (text and Table 5 in the 2018 briefing). Archived here.

[**C**] NICE guidelines for stroke and TIA 2019:
NICE stroke and transient ischaemic attack in over 16s: diagnosis and initial management (https://www.nice.org.uk/guidance/ng128). Page 25; the committee looked at the results of the published cost–utility analyses with a UK NHS by Lobotesis. The second of these studies demonstrated the cost effectiveness of thrombectomy therapy when performed 6 to 24 hours after stroke onset. "Therefore, the committee agreed to recommend thrombectomy up to 24 hours after stroke onset, for people with appropriate clinical and radiological characteristics". Archived here.

[**D**] NHS England Clinical Commissioning Policy: Mechanical Thrombectomy for acute ischaemic stroke (Reference 170033P). First published January 2018, Updated 29/0/2019. NHSE document concluding there is sufficient evidence to support the routine commissioning of mechanical thrombectomy for acute ischaemic stroke. Archived here.

[**E**] The Sentinel Stroke National Audit Programme (SSNAP) (https://www.strokeaudit.org). This is a national audit programme collecting data on the implementation of thrombectomy in the UK to ensure treatment is provided safely and effectively. ICHT submits data on all patients treated to the SSNAP. Archived here.

[**F**]
https://bsnr.org.uk/_userfiles/pages/files/standards_and_guidelines/implementation_of_stroke_thrombectomy_guide_v1_29_april_2019.pdf (Archived here).

[**G**] International standards/guidance 2019:
European stroke organisation Guideline Directory (https://eso-stroke.org/eso-guideline-directory/). European Stroke Organisation (ESO) and European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischaemic Stroke endorsed by Stroke Alliance for Europe (SAFE). Published in European Stroke Journal February 2019 and co-published in Journal of Neurointerventional Surgery in February 2019. DOI.