NICE advice

Mechanical thrombectomy devices for acute ischaemic stroke

Medtech innovation briefing
Published: 30 July 2018

www.nice.org.uk/guidance/mib153

Summary

- The **technologies** described in this briefing are 21 mechanical thrombectomy devices of 2 types: stent retrievers and aspiration catheters. They are used to remove blood clots from a main cerebral artery to restore blood flow after acute ischaemic stroke.
- The **innovative aspects** are that the devices restore blood flow in people who are not able to have pharmacological treatment. They can also be used in people for whom pharmacological treatment has not worked effectively.
- The intended **place in therapy** would be in patients with confirmed acute ischaemic stroke caused by a blockage in 1 or more large artery in the brain.

- The **main points from the evidence** summarised in this briefing are from 8 clinical studies (1 systematic review and 7 randomised controlled trials) including a total of 2,718 adults in secondary and tertiary care. Overall, the studies show that mechanical thrombectomy devices used with thrombolysis are more effective than thrombolysis alone in patients with acute ischaemic stroke. Overall, the evidence base is greater for stent retrievers.
- **Key uncertainties** around the evidence or technology are that there is little comparative evidence between the devices. The evidence that does exist does not take into account underlying differences in patient populations or care pathways, which may be different to the NHS.
- The **cost** of mechanical thrombectomy devices ranges from £550 to £1,349 for aspiration catheters and £1,500 to £5,000 for stent retrievers per unit (excluding VAT). Current evidence suggests the **resource impact** in the UK is higher because of the cost of the mechanical thrombectomy procedure. Twelve cost-effectiveness studies were also identified, including 2 from a UK payer perspective. The resource impact may be lower if effective treatment results in a reduction in long-term care.

This briefing describes technologies that fulfil a similar purpose. During development, every effort was made to identify and include relevant technologies but devices may not have been identified, or key information may have been unavailable.

The technology

This briefing describes 21 technologies for delivering mechanical thrombectomy (MT) for acute ischaemic stroke. Further background information on the condition and the intervention is in the NHS England clinical commissioning policy on mechanical thrombectomy for acute ischaemic stroke (all ages).

There are 2 types of MT devices:

- Aspiration catheters are flexible with a large inner distal diameter. A guide wire is inserted into the patient, followed by a small access catheter. The access catheter is then used to guide the aspiration catheter to the right place. When the clot is reached, it is broken into smaller pieces that can be aspirated through the catheter using a pump or manual suction.

- Stent retrievers have an expanding wire mesh tube and are intended to remove the clot in 1 piece. The retriever is placed using a delivery catheter, and once in place the mesh expands. The clot is trapped in the expanding mesh and is then withdrawn into the catheter.

In some cases, both types of devices may be used to remove the clot.

All the devices in this briefing have a Class III CE mark and their key features are summarised in table 1 for aspiration catheters and table 2 for stent retrievers.

Table 1 Summary of key features of included aspiration catheters

Device (Company)	Aspiration method	Available models	Distal inner diameter in inches	Working length in cm
ARC ARC Mini (Medtronic)	Manual	ARCA-132 ARCA-160	0.061 0.035	132 160
Navien (Medtronic)	Manual	RFXA058 RFXA072	0.058 0.072	125 or 130
Sofia (MicroVention)	Manual	DA5115ST DA5125ST DA6115ST	0.055 0.070	115 125 115
Sofia Plus (MicroVention)	Manual	DA6125ST DA6131ST	0.070	125 131
ACE reperfusion catheter (Penumbra)	External pump	ACE60 ACE64 ACE68	0.060 0.064 0.068	132
MAX reperfusion catheter (Penumbra)		3MAX 4MAX 5MAX	0.035 0.041 0.054	153 139 132

AXS Catalyst Distal Access Catheter (Stryker)	Manual	AXS Catalyst 5 AXS Catalyst 5 AXS Catalyst 6	0.058 0.058 0.060	115 132 132

Table 2 Summary of key features of included stent retrievers

Device (Company)	Available models	Stent diameter and length in mm	Delivery catheter: minimum inner diameter in inches
Aperio (Acandis; UK supplier: Neurologic)	01-000700 01-000701 01-000702 01-000703	3.5×28 4.5×30 4.5×40 6×40	0.0165 to 0.021 0.0165 to 0.021 0.021 to 0.027 0.021 to 0.027
Catch + (Balt; UK supplier Sela Medical)	Catch+ Mini Catch+ Catch+ Maxi	3×15 4×20 6×30	0.017 0.021 0.024
EmboTrap II (Cerenovus Johnson and Johnson)	ET-007-521 ET-007-533	5×21 5×33	0.021 0.021
ReVive SE (Cerenovus Johnson and Johnson)	ReVive SE	4.5×30	0.021 to 0.027
Solitaire 2 (Medtronic)	SFR2-4-15 SFR2-4-20 SFR2-4-40 SFR2-6-20 SFR2-6-30	4×15 4×20 4×40 6×20 6×30	0.021 0.021 0.021 0.027 0.027

Solitaire Platinum (Medtronic)	SRD3-4-20-05 SRD3-4-20-10 SRD3-4-40-10 SRD3-6-20-10 SRD3-6-24-06 SRD3-6-40-10	4×20 4×20 4×40 6×20 6×24 6×40	0.021 0.021 0.021 0.027 0.027 0.027
ERIC (MicroVention)	ERIC 3 ERIC 3 ERIC 4 ERIC 4 ERIC 6	3×15 3×20 4×24 4×30 6×44	0.017 0.017 0.021 0.021 0.027
3D Revascularization (Penumbra)	PSR3D	4.5×20	0.024
pREset (Phenox)	PRE-4-20 PRE-6-30	4×20 6×30	0.021 0.021
pREset LITE (Phenox)	PRE-LT-3-20 PRE-LT-4-20	3×20 4×20	0.0165 0.0165
Tigertriever (Rapid Medical; UK supplier: Neurologic)	TRPP3166 TRPP3155	3×23 6×32	0.017 0.021
Trevo ProVue (Stryker)	90184	4×20	0.021
Trevo XP ProVue (Stryker)	90182 90183 90185 90186	4×20 3×20 4×30 6×25	0.021 0.017 0.021 0.027

Innovations

MT devices offer an additional or alternative option for restoring blood flow compared with current care. They can be used in people for whom pharmacological treatments such as

thrombolysis are likely to be ineffective (for example, because the clot is too large) or inappropriate (for example, because of recent surgery or in people who are taking oral anticoagulants). Thrombolysis (pharmacological treatments to dissolve the clot) must be given within 4.5 hours of stroke onset. Clot retrieval should be done within 6 hours.

Current NHS pathway

People with suspected acute stroke should be admitted to the nearest accident and emergency department with a hyperacute stroke unit or a specialist stroke unit for immediate brain imaging (usually within 1 hour). If imaging confirms a diagnosis of acute ischaemic stroke then urgent thrombolysis should be given to try to restore blood flow in the brain.

Other forms of pharmacological therapy are often used, whether or not thrombolysis has been attempted. This usually consists of short-term antiplatelet treatment (such as aspirin for 2 weeks), followed by an antithrombotic treatment that the patient will generally have for the rest of their life.

As well as pharmacological therapy, people with acute ischaemic stroke will also have therapy intended to minimise brain damage, such as oxygen therapy, blood pressure control and blood sugar control.

The following NICE guidance has been identified as relevant to this care pathway:

- Stroke and transient ischaemic attack in over 16s: diagnosis and initial management
- Stroke rehabilitation in adults
- Mechanical clot retrieval for treating acute ischaemic stroke

Population, setting and intended user

MT is indicated for people with confirmed acute ischaemic stroke caused by a blockage in 1 or more large artery in the brain. This includes people already treated with intravenous thrombolysis that has not been effective, as well as people who have not had this treatment. MT should be done within 6 hours of the onset of symptoms, but this may be extended to between 12 and 24 hours if advanced brain imaging shows that there is substantial brain tissue that can be salvaged. It is not indicated for transient ischaemic

attacks.

The procedure must be done in designated specialised stroke centres. These centres must give the Sentinel Stroke National Audit Programme databases information for all patients admitted with stroke.

Costs

Technology costs

The list prices and associated procedural accessories are shown in table 3. Additional resources are needed for each procedure, including: theatre time, staff time, imaging tests and surgical equipment. It has been estimated that the average total cost of MT is £8,365, which includes the cost of the device and the surgical procedure (Ganesalingham 2015).

Table 3 Cost of included MT devices

Company	Device	List price (excluding VAT)*	Procedural accessories
Acandis; UK supplier: Neurologic	† Aperio	£2,700	NeuroSlider micro catheters £495
Balt; UK supplier: Sela Medical	† Catch+ Mini	£3,000	VASCO delivery catheters £435; hybrid guide wires £290
	† Catch+	£1,900	
	† Catch+ Maxi	£1,900	
Cerenovus Johnson and Johnson	† EmboTrap II	£3,500	ReVive intermediate access catheters £648.90
	† ReVive SE	£4,936	
Medtronic	‡ ARC	£1,349	Information not supplied
	‡ ARC Mini	£1,249	
	‡ Navien	£613	

	† MindFrame Capture LP	£3,190	
	† Solitaire 2	£3,190	
	† Solitaire Platinum	£3,349	
Microvention	‡ Sofia/Sofia Plus	£550	Headway micro delivery catheter £440
	† ERIC	£2,500	
Penumbra	‡ ACE60, ACE64, ACE68 reperfusion catheters	£1,275	MAX Pump £7,500; Velocity micro delivery catheter £700; Neuron access catheters £300; MAX canister £190; devices are also available as part of reperfusion kits
	‡ 3MAX, 4MAX, 5MAX reperfusion catheters	£1,090	
	† 3D Revascularization device	£5,000	
Phenox	† pREset/pREset LITE	£1,995	Information not supplied
Rapid Medical; UK supplier: Neurologic	† Tigertriever	£3,000	NeuroSlider micro catheters £495
Stryker	‡ AXS Catalyst DAC	£900	Trevo Pro 14/18 microcatheter £300; Flowgate balloon guide catheter £750; Infinity access catheter £350; devices are also available as part of kits and multipacks
	† Trevo ProVue	£3,250	
	† Trevo XP ProVue	£3,250	

† Stent retriever.

‡ Aspiration catheter.

* Individual companies may offer commercial terms including lower acquisition costs depending on purchase quantity.

Costs of standard care

NICE's clinical guideline on the diagnosis and management of stroke recommends thrombolysis (alteplase) for the treatment of acute ischaemic stroke. The Sentinel Stroke National Audit Programme estimated the unit costs of thrombolysis to be £875 (2016). The NHS England commissioning policy suggests that around 12% of all people with stroke are eligible for treatment with thrombolysis. This amounts to around 9,600 people admitted with stroke.

Resource consequences

Adopting MT devices will increase treatment costs compared with current standard care. However, if the devices led to improvement in treatment outcomes such as a reduction in long-term disabilities, then this could lead to cost savings.

Changes in facilities and 24-hour infrastructure would be needed if MT devices become used more widely. This would be to ensure standards for providing safe acute ischaemic stroke thrombectomy services. This is likely to result in substantial upfront costs for training interventional neuroradiologists and other staff such as anaesthetists and stroke nurses involved in providing care. Substantial system-wide reorganisation of acute stroke services will be needed.

Two economic studies with a UK perspective were also identified, with the results from these studies summarised in table 5. One study (Lobotesis 2016) found that using stent retrievers (Solitaire) with intravenous thrombolysis was more cost effective than intravenous thrombolysis alone for treating acute ischaemic stroke, based on the results of the SWIFT-PRIME trial. The second study (Ganesalingham 2015) did not focus on a specific stent retriever but looked at MT devices in general, based on the results of 5 RCTs (SWIFT-PRIME, MR CLEAN, ESCAPE, REVASCAT, EXTEND-IA), and found the devices were more cost effective when used together with intravenous thrombolysis compared with intravenous thrombolysis alone. The authors estimated that MT devices would lead to increased costs of £7,431 per patient over 20 years when compared with thrombolysis

(using intravenous tissue plasminogen activator). These additional costs were because of the cost of the MT procedure. MT would be cost effective because of improved patient outcomes with an estimated incremental cost-effectiveness ratio of £7,061.

A further 10 economic studies were identified from a non-UK perspective (Achit 2016, Aronsson 2016, Carlsson 2017, de Andres-Nogales 2017, HQA 2016, Kunz 2016, Leppert 2015, MSAC 2016, Shireman 2017, Xie 2016). Two of the studies (de Andres-Nogales 2016, Shireman 2017) focused on stent retrievers (Solitaire) using the results of the SWIFT-PRIME trial and found the device was more cost effective compared with intravenous thrombolysis alone. Therefore, using the device led to an improvement in patient quality of life and less cost. The remaining studies considered MT devices in general compared with intravenous thrombolysis alone. Most of the results came from the 5 RCTs above, although this was often supported by data from other sources such as local registries. In all studies, MT was found to be cost effective. There were no relevant economic studies focusing specifically on aspiration catheters.

MT is used in some specialist stroke centres in the UK. The NHS England commissioning policy estimates that 8,000 people per year in England are eligible for treatment with MT.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

The risk of stroke increases with age and the risk is also higher in men and black and Asian people. As thrombolysis is contraindicated during pregnancy, this treatment provides an alternative in the absence of access to standard of care. Age, gender and race are protected under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technologies. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Eight studies reporting on the clinical effectiveness of the devices are summarised in this briefing. Many systematic reviews were identified and there was substantial overlap in the trials summarised. As a result, only the most recent, highest-quality systematic reviews (that is, systematic reviews with multiple reviewers, quality assessment of studies, searches in multiple databases and reporting according to PRISMA guidelines) with meta-analyses were selected. Randomised controlled trials (RCTs) were selected only if they were not included in any of the systematic reviews and if they were recent and focused on the devices listed in the technology section. There is also other observational and registry based data on mechanical thrombectomy (MT) devices that has not been included in the MIB.

One systematic review with a meta-analysis and 7 RCTs (with a total of 2,718 patients) are summarised in this briefing. The systematic review included RCTs using mainly stent retriever devices. Six of the included RCTs compared MT devices with medical management against medical management alone. Of these, 3 mainly used stent retriever devices, 1 used only the Trevo stent retriever, 1 mainly used aspiration devices, and 1 did not report the type of devices used. Notably, 3 of these RCTs, as well as 1 of the trials included in the systematic review by Bush et al. (2016), were stopped early because of evidence showing that MT with medical management gave better clinical outcomes than medical management alone. A further RCT was a direct comparison of stent retrievers against aspiration devices with a superiority trial design.

Table 4 summarises the clinical evidence and its strengths and limitations. The main clinical outcomes assessed in the included studies are outlined below.

Functional independence

Functional independence was a primary outcome in all studies and was measured using modified Rankin Scale (mRS) score at 90 days of follow-up. In general, MT devices used with medical management gave substantially better mRS scores than medical management alone. However, 1 study comparing aspiration devices plus intravenous thrombolysis with intravenous thrombolysis alone did not find a statistically significant difference in mRS scores at 90 days (although the study may have been underpowered because of enrolment being stopped early). All of the studies comparing stent retriever, or mainly stent retriever, devices with medical management showed statistically significant improvements in mRS scores at 90 days.

When stent retrievers and aspiration devices were compared, they performed similarly with no significant differences in mRS scores. However, it is important to note that the study comparing the 2 types of device (Lapergue et al. 2017) did not have a non-inferiority design and so results from this trial cannot be taken to show equivalence.

Successful revascularisation

Revascularisation, measured using modified Thrombolysis in Cerebral Infarction (mTICI) scores, was reported in 9 of the 10 clinical studies. Using MT devices led to successful revascularisation rates of around 70% or higher. No difference was found in the studies that looked at a direct comparison between stent retrievers and aspiration devices.

Mortality and adverse events

Overall, there was very little difference in reported mortality rates between the intervention and control arms of the included studies. However, 1 study that compared MT devices (predominantly stent retrievers) with medical management alone found a significantly higher risk of mortality in the control group (Albers et al. 2018). Another study that compared predominantly aspiration devices used together with thrombolysis with thrombolysis alone reported a mortality rate more than 2 times greater in the thrombolysis-only group (Mocco et al. 2017).

There was little difference in the risk of intracerebral haemorrhage adverse events, when comparing stent retrievers and aspiration catheters against medical management alone or one another.

Overall assessment of the evidence

Several prospective RCTs and systematic reviews were identified. Stent retrievers were compared with other treatments commonly used for acute ischaemic stroke, including medical management alone (mainly thrombolysis with alteplase) and MT using aspiration catheters. A number of these studies focused on the Solitaire and Trevo stent retriever devices. Several studies also included a number of other stent retriever devices used in a few of the included patients, although no evidence was identified that explicitly assessed other stent retriever devices included in this briefing.

The evidence base for aspiration catheters is less well developed. One RCT made a direct comparison between aspiration devices and stent retrievers, while another compared aspiration devices used together with thrombolysis against thrombolysis alone. The studies included a number of the aspiration devices listed in this briefing, including Penumbra reperfusion catheters (90% in ASTER aspiration arm and in 96% of Therapy IAT arm) and a more limited number of Sofia and ARC devices.

A limitation of all of these studies was that, because of the nature of the intervention, participants and users could not be blinded and this presents some potential risk of bias. However, this risk was judged to be relatively low.

A large number of economic studies were identified and all compared MT with thrombolysis, which is a relevant comparison, and used appropriate sources for the data that informed the economic models (for example, pivotal phase III RCTs for effectiveness data). Only 2 of the studies were from the UK, which limits the generalisability of the evidence. Furthermore, the 3 studies that focused on the Solitaire device were funded by the company.

Table 4 Summary of selected clinical studies

Albers et al. (2018)	
Study design and population	A randomised, open-label trial with blinded outcome assessment. Conducted in 38 centres in the US. 182 patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion were randomised before the trial was stopped early because of the efficacy of the endovascular therapy.

Interventions	**Intervention:** Endovascular therapy plus standard medical therapy (n=92). Devices used were stent retrievers (n=74) and aspiration devices (n=25). Specific devices used were not specified. A small number of patients also had cervical angioplasty and/or stent placement (n=13), intra-arterial thrombolysis (n=2), intracranial angioplasty or stent placement (n=3), or no endovascular therapy (n=2). **Comparator:** Standard medical therapy alone, based on American Heart Association guidelines (n=90).

Results	**Successful revascularisation (mTICI):** TICI scores in the intervention arm: 10 (11%) patients had a TICI score of 0; 12 (13%) had a score of 2a; 52 (57%) had a score of 2b; 17 (19%) had a score of 3. **Functional independence (mRS):** Distribution of mRS scores at 90 days was more favourable in the intervention arm: adjusted OR=3.36 (95% CI 1.96 to 5.77). Percentage of patients who were functionally independent (mRS score of 0 to 2) at 90 days: 45% in the intervention arm compared to 17% in the control arm (risk ratio: 2.67, 95% CI 1.60 to 4.48). **Mortality:** Mortality at 90 days: 14% in the intervention arm compared to 26% in the control arm. **ICH:** Rates of S-ICH (increase ≥4 points on NIHSS) were 7% and 4%, with 5 and 2 resultant deaths, in the intervention and control arms respectively. **NIHSS Score:** Reported in relation to specific adverse events (S-ICH and thrombectomy-related complications). **ASPECTS Score:** Not reported post-intervention. **Other** *Adverse events:* Serious adverse events were reported in 43% and 53% of patients in the intervention and control groups respectively. Parenchymal haematoma type 2 occurred in 9% and 3% of patients in the intervention and control groups respectively. Thrombectomy-related complications occurred in 2 patients, 1 of which led to neurological worsening (3-point increase on NIHSS). *Imaging outcomes:* Median growth of the volume of the infarct region was 23 ml in the intervention arm and 33 ml in the control arm. Reperfusion of >90% at 24 hours was 79% in the intervention arm and 18% in the control arm. Percentage of patients with complete recanalisation of the primary arterial occlusive lesion at 24 hours was 78% in the intervention group and 18% in the controls.
Strengths and limitations	**Strengths:** A multicentre RCT. **Limitations:** none.
Bracard et al. (2016)	

Study design and population	RCT in 26 centres in France. 412 patients with AIS and proximal cerebral artery occlusion were randomised before the trial was stopped early because results showed superiority of intravenous thrombolysis plus MT over thrombolysis alone.
Interventions	**Intervention:** Intravenous thrombolysis plus MT (n=204) MT was performed using stent retrievers (n=108), including Solitaire, Trevo, pREset, and ReVive; aspiration alone (n=13), including the Penumbra System; or multiple systems (n=19). 59 patients randomised to the intervention did not have MT because of significant clinical improvement, partial/complete recanalisation, or violation of exclusion criteria. **Comparator:** Intravenous thrombolysis alone (n=208) 8 (4%) patients randomised to the control arm eventually had MT.

Results	**Successful revascularisation (mTICI):** 95 (69%) patients in the intervention arm achieved an mTICI score of 2b or 3. **Functional independence (mRS):** Percentage of patients with functional independence (mRS score 0 to 2) at 90 days: 53% (106/200) and 42% (85/202) in the intervention and control groups respectively (OR=1.55, 95% CI 1.05 to 2.30). No difference was found between the 2 groups when mRS score at 90 days was considered as an ordinal variable in a regression model (OR=1.39, 95% CI 0.99 to 1.97). **Mortality:** No significant differences were seen: 24 (12%) patients in the intervention arm and 27 (13%) patients in the control arm. **ICH:** S-ICH at 24 hours: 4 (2%) patients in the intervention arm and 3 (2%) patients in the control arm. **NIHSS Score:** Median NIHSS score at discharge/7-days post-intervention: 4 (IQR: 1 to 14) in the intervention arm; 8 (IQR: 2 to 16) in the control arm. **ASPECTS Score:** Only reported at baseline and as a prognostic factor for acute stroke. **Other:** *Adverse events:* Thrombectomy-associated complications occurred in 9 (6%) of patients. No significant differences seen in the proportion of patients with adverse events at 3 months (31% and 27% in the intervention and control groups, respectively). *Activities of daily living:* A higher proportion of patients in the intervention group had a Barthel index score of 95 to 100 at 3 months (61% versus 49%), although no significant difference was seen when the EQ-5D questionnaire was used.
Strengths and limitations	**Strengths:** A multicentre RCT with large number of patients. **Limitations:** The vast majority of patients had anterior circulation strokes, so findings are only applicable in this group; protocol changes occurred during the trial; clinicians estimating mRS score were not blinded to treatment allocation.
Bush et al. (2016)	

Study design and population	A systematic review and meta-analysis, incorporating results from 5 RCTs (NTR1804, NCT01778335, NCT01492725, NCT01657461 and NCT01692379) in various settings worldwide, including the UK, USA, Australia and several European countries. 1,287 patients with AIS. 634 patients (50.7%) were in the intervention group and 653 in the control group.
Interventions	**Intervention:** Stent retrievers used in 536 (85%) patients. Three of the included RCTs used Solitaire only, while 2 included a number of different devices (unnamed). 526 patients (83%) received IV t-PA in addition to thrombectomy. **Comparator:** Medical management alone. 573 (88%) patients received IV t-PA.

Results	**Successful revascularisation (mTICI):** 373 patients (80.4%) in the intervention arm had mTICI scores of 2b or 3 and were reported as having achieved good reperfusion. **Functional independence (mRS):** Patients in the intervention groups from all 5 RCTs had a pooled OR of 2.22 (95% CI 1.66 to 2.98) for improved mRS score at 90 days post-stroke compared to the control group (p<0.0001) with modest statistical heterogeneity across trials (I^2=46.38%). **Mortality:** Patients in the intervention groups from all 5 RCTs had a pooled OR=0.78 (95% CI 0.54 to 1.12) for mortality compared to the control group (p=0.1056) with no statistically significant heterogeneity across trials. **ICH:** Patients in the intervention groups from all 5 RCTs had a pooled OR=1.19 (95% CI 0.69 to 2.05) for symptomatic ICH compared to the control group (p=0.5348) with no statistically significant heterogeneity across trials. **NIHSS Score:** Patients in the intervention groups from 4 of the RCTs had a pooled OR=2.23 (95% CI 1.58 to 3.15) for NIHSS scores ≥17 at 90 days post-stroke compared to the control group (p<0.0001) with no statistically significant heterogeneity across trials. **ASPECTS Score:** Patients in the intervention groups from 4 of the RCTs had a pooled OR=2.19 (95% CI 1.61 to 2.98) for high ASPECTS scores (≥8) at 90 days post-stroke compared to the control group (p<0.0001) with no statistically significant heterogeneity across trials.
Strengths and limitations	**Strengths:** High-quality systematic review and meta-analysis (multiple reviewers, quality assessment of included studies, statistical analysis, use of PRISMA guidelines). **Limitations:** Includes 2 studies that do not specify the devices used.
Khoury et al. (2017)	
Study design and population	Randomised care trial conducted in a single hospital in Canada. 77 patients with AIS were randomised. Randomised allocation was interrupted when results from other trials were published that showed the benefits of endovascular therapy.

Interventions	**Intervention:** Standard care plus MT (n=40). Of the 30 patients in whom MT was attempted, a stent retriever was used in 29. Specific devices used were not reported. **Comparator:** Standard care alone (n=37), including intravenous thrombolysis when appropriate.
Results	**Successful revascularisation (mTICI):** Of the patients who had MT, 23 (76.7%) achieved TICI scores of 2b or 3. **Functional independence (mRS):** mRS 0 to 2 at 90 days: 20 (50%) patients and 14 (37.8%) patients in the intervention and control arms respectively. **Mortality:** Mortality at 3 months: 11 (27.5%) patients in the intervention arm and 9 (24.3%) patients in the control arm. **ICH:** S-ICH occurred in 3 (7.5%) and 2 (5.7%) patients in the intervention and control arms respectively. **NIHSS Score:** Of the patients with mRS scores of 0 to 2 at 90 days: 87.5% (14/16) and 62.5% (10/16) had NIHSS ≤16 and 25% (6/24) and 19% (4/21) had NIHSS >16 in the intervention and control arms, respectively. **ASPECTS Score:** Not reported post-intervention.
Strengths and limitations	**Strengths:** Randomised trial design. **Limitations:** Single-centre trial; relatively low number of patients because of trial interruption.
Lapergue et al. (2017)	
Study design and population	A randomised, open-label, blinded endpoint clinical trial in 8 stroke centres in France. 381 adults were randomised. Patients were admitted with suspected ischaemic stroke secondary to occlusion of the anterior circulation.
Interventions	**Intervention:** Contact aspiration (n=192). Penumbra ACE and MAX reperfusion catheters were used in 90% of 'aspiration first' patients. Sofia and ARC devices were used in 17 patients and 1 patient respectively. **Comparator:** Stent retrievers (n=189). Various devices were used, including Solitaire, Trevo, ReVive, ERIC and EmboTrap.

Results	**Successful revascularisation (mTICI):** Percentage of patients with successful revascularisation defined as mTICI score of 2b or 3 after all endovascular treatments: for the ITT analysis, 85.4% for the intervention group and 83.1% for the controls (OR 1.20; 95% CI 0.68 to 2.10); for the per protocol analysis, 91.5% for the intervention group and 84.9% for the controls (OR=1.91, 95% CI 0.93 to 3.91). **Functional independence (mRS):** 45.3% patients in the intervention group achieved independence at 3 months, compared to 50% in the control group (OR=0.83, 95% CI 0.54 to 1.26). The median mRS score at 3 months was 3 for the intervention group and 2.5 for the controls (OR=0.76, 95% CI 0.53 to 1.10). **Mortality:** Overall all-cause mortality at 3 months was 19.3% the intervention (35/181) and 19.2% (35/182) for the controls. **ICH:** ICH at 24 hours was 46.3% (87/188) in the contact aspiration group and 46.2% (85/188) in the stent retriever group. S-ICH at 24 hours was 5.3% (10/188) and 6.5% (12/188) for the intervention and control groups respectively. **NIHSS Score:** The mean change in NIHSS score at 24 hours was −4.8 (95% CI −6.1 to −3.6) for the intervention compared to −5.2 (95% CI −6.5 to −3.9) for the control group. **ASPECTS Score:** The median score (at baseline) was 7 for both study arms. **Other:** Procedure-related adverse events were 16.2% (31/192) and 15.9% (30/189) for the intervention and controls respectively.
Strengths and limitations	**Strengths:** RCT with a large number of patients; comparison of stent retrievers and contact aspiration. **Limitations:** Trial was not designed to establish non-inferiority between aspiration devices and stent retrievers as first-line strategies; primary outcome was technical (successful revascularisation) rather than clinical (for example, mRS score); authors report that participating centres were highly experienced in the techniques, thus generalisability to stroke centres with less experience may be limited.
Mocco et al. (2017)	

Study design and population	A multicentre, randomised concurrent controlled trial, conducted in 36 centres in the US and Germany. A total of 108 patients were randomised. Patients were adults presenting with large-vessel ischaemic stroke.
Interventions	**Intervention:** Thrombolysis (intravenous alteplase) plus thrombectomy (IAT; n=55). Devices used were predominantly Penumbra aspiration catheters (n=43). A small number of patients received Solitaire or Trevo stent retrievers. **Comparator:** Thrombolysis (intravenous alteplase) alone (IA; n=53).
Results	**Successful revascularisation (mTICI):** 73% (95% CI 58 to 85) patients achieved successful reperfusion, with mTICI scores of 2b or 3. For patients treated with the Penumbra system alone, this figure was 70%. **Functional independence (mRS):** Patients achieving mRS scores of 0 to 2 at day 90: 38% in the IAT group compared to 30% in the IA group (OR=1.4, 95% CI 0.60 to 3.3). These figures were 41% and 29% respectively for IAT and IA in the per protocol analysis (OR=1.6, 95% CI 0.64 to 4.2). **Mortality:** 12% and 24% in the IAT and IA groups respectively (OR=2.3, 95% CI 0.8 to 6.8). These figures were 7.3% and 24% respectively for IAT and IA in the per protocol analysis (OR=4.1, 95% CI 1.0 to 16.0). **ICH:** The S-ICH (as treated) rates were 9.3% and 9.7% for the IAT and IA groups respectively (OR=1.0, 95% CI 0.3 to 3.9). **NIHSS Score**: Not reported. **ASPECTS Score:** 24-hour median ASPECTS score was 6 for IAT and 5 for the IA group (OR=1.9, 95% CI 0.93 to 1.7). ASPECTS worsening at 24 hours was 1 for IAT and 2 for the IA group (OR=2.4, 95% CI 1.2 to 4.9). In the per protocol analysis, 24-hour median ASPECTS score was 7 for IAT and 5 for the IA group (OR=2.5, 95% CI 1.1 to 5.5). ASPECTS worsening at 24 hours was 1 for IAT and 2.5 for the IA group (OR=2.5, 95% CI 1.1 to 5.4).

Strengths and limitations	**Strengths:** A multicentre RCT. **Limitations:** Small numbers of patients; trial was halted following external evidence of the added benefit of endovascular therapy to IA alone.
Muir et al. (2017)	
Study design and population,	A multicentre randomised, controlled, parallel group clinical trial with blinded endpoint evaluation, conducted in 10 centres in the UK. A total of 65 patients were randomised. Patients were adults presenting with acute supratentorial ischaemic stroke.
Interventions	**Intervention:** IVT+MT (IVT+MT) (n=33). MT Devices used were not specified Stent retrievers were used first in 68% procedures and aspiration devices in 32%. **Comparator:** Intravenous thrombolysis alone (IVT; n=32).
Results	**Successful revascularisation (mTICI):** TICI 2b or 3 reperfusion at the end of MT procedure was achieved in 26 (87%) of 30 assessable immediate post-procedure angiograms. **Functional independence (mRS):** Percentage of patients achieving mRS scores 0-2 at day 90: 51% in the intervention arm compared to 40% in the controls (OR=2.12, 95% CI 0.65 to 6.94). After adjustment for minimisation variables these figures were 57% and 35%, respectively (OR=4.92, 95% CI 1.23 to 19.7). Complete functional recovery at day 90 (mRS 0-1): OR=7.63 (95% CI 1.56 to 37.22) in favour of IVT+MT. **Mortality:** 7 deaths in the IVT+MT group compared to 4 in the IVT group (OR=1.56, 95% CI 0.29 to 8.40). **ICH:** 3 cases of ICH were reported in each study arm. No S-ICH occurred. **NIHSS Score:** No significant difference was found in early neurological improvement (improvement of ≥8 points on the NIHSS or an NIHSS of 0 or 1 24 hours after stroke) between groups. **ASPECTS Score:** Not reported. **Other:** The overall serious adverse events (including deaths) were 15 (45%) in the IVT+MT group and 11 (34%) in the IVT group.

Strengths and limitations	**Strengths:** A multicentre RCT conducted in the UK. **Limitations:** Relatively low number of patients.
Nogueira et al. (2018)	
Study design and population	A randomised controlled trial in 26 centres in the USA, Canada, Europe and Australia. Patients were included who had acute stroke with a mismatch between salvageable brain tissue and volume of infarcted tissue. 107 patients were randomly assigned to the thrombectomy group and 99 to the control group.
Interventions	**Intervention:** MT using the Trevo device, plus standard medical care (n=107). **Comparator:** Standard medical care alone (n=99).
Results	**Successful revascularisation (mTICI):** 90 (84%) patients in the thrombectomy group had mTICI scores of 2b or 3. Recanalisation was achieved in 82 (77%) patients in the thrombectomy group and 39 (39%) in the control group at 24 hours. **Functional independence (mRS):** The utility-weighted mRS was 5.5 for the thrombectomy group compared to 3.4 for the control group at 90 days. Patients with functional independence at 90 days was 52 (49%) for the thrombectomy group and 13 (13%) for the controls. **Mortality:** All-cause mortality at 90 days was 20 (19%) for the thrombectomy group and 18 (18%) for the control group (risk ratio: 1, 95% CI 1 to 2); stroke-related deaths at 90 days were 17 (16%) and 18 (18%) for the thrombectomy and control groups, respectively (95% CI 1 to 2). **ICH:** Patients with symptomatic ICH at 24 hours was 6 (6%) and 3 (3%) (risk ratio: 2, 95% CI 1 to 7) for the thrombectomy and control groups respectively. **NIHSS Score:** Patients classified as having an early response (a decrease in NIHSS Score of 10 points or more from baseline or an NIHSS Score of 0 or 1 on day 5, 6 or 7 post-intervention). **ASPECTS Score**: Not assessed.

Strengths and limitations	**Strengths:** Multicentre RCT. **Limitations:** Study was sponsored by device manufacturer (Stryker).

Abbreviations: AIS, acute ischaemic stroke; ASPECTS, Alberta stroke program early CT score; CI, confidence interval; IA, intravenous alteplase; IAT, intravenous alteplase plus thrombectomy; ICH, intracerebral haemorrhage; IQR, interquartile range; ITT, intention to treat; IVT, intravenous thrombolysis; IV t-PA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PST, primary suction thrombectomy; RCT, randomised controlled trial; S-ICH, symptomatic intracerebral haemorrhage; SRT, stent retriever thrombectomy; TICI, treatment in cerebral infarction.

Table 5 Summary of the cost-effectiveness studies

Ganesalingham 2015			
Outcome	**IV t-PA + SR[1]**	**IV t-PA**	**Difference**
Total costs	£39,274[2]	£31,815[2]	£7,432[2]
QALYs	4.84	3.79	1.05
ICER	N/A	N/A	£7,065
Lobotesis 2017			
Outcome	**IV t-PA + SR (Solitaire)**	**IV t-PA**	**Difference**
Total costs	£110,322	£143,512	−£33,190
Total QALYs	7.01	4.70	2.31
ICER	N/A	N/A	Dominant

Abbreviations: ICER, incremental cost-effectiveness ratio, IV t-PA, intravenous tissue plasminogen activator; SR, stent retriever; QALY, quality-adjusted life year.

[1]Pooled data from 5 trials: ESCAPE, EXTEND-IA, MR CLEAN, REVASCAT and SWIFT-PRIME.

[2]Values in the paper reported in US dollars and converted using an exchange rate of 0.61 (given in the paper).

Recent and ongoing studies

Five ongoing (currently recruiting) RCTs were identified:

- SWIFT DIRECT: Bridging thrombolysis versus direct mechanical thrombectomy in acute ischemic stroke. ClinicalTrials.gov identifier: NCT03192332. Status: Currently recruiting. Indication: acute ischaemic stroke. Devices: Solitaire, Medtronic.
- RESILIENT: Endovascular treatment with stent-retriever and/or thromboaspiration vs. best medical therapy in acute ischemic stroke. ClinicalTrials.gov identifier: NCT02216643. Status: Currently recruiting. Indication: acute ischaemic stroke due to large-vessel occlusion. Devices: Stentriever Solitaire or Penumbra System.
- Endovascular therapy in acute ischaemic stroke due to large vessel occlusion. ClinicalTrials.gov identifier: NCT03328403. Status: Currently recruiting. Indication: acute ischaemic stroke due to large-vessel occlusion. Devices: Trevo, Solitaire, Penumbra System.
- ASTER 2: Combined Use of Contact Aspiration and the Stent Retriever Technique Versus Stent Retriever Alone for Recanalisation in Acute Cerebral Infarction. ClinicalTrials.gov identifier: NCT03290885. Status: Currently recruiting. Indication: acute ischaemic stroke. Devices: Stent Retriever, Penumbra System.
- REDIRECT: RECO Flow Restoration Device Versus Solitaire FR With the Intention for Thrombectomy Study. ClinicalTrials.gov identifier: NCT01983644. Status: Currently recruiting. Indication: acute ischaemic stroke caused by large-vessel occlusion. Devices: Solitaire FR, RECO.

Two completed RCTs were identified:

- COMPASS Trial: a Direct Aspiration First Pass Technique. ClinicalTrials.gov identifier: NCT02466893. Status: Recruitment completed. Indication: acute ischaemic stroke. Devices: aspiration catheters, stent retrievers.
- A Randomised, Concurrent Controlled Trial to Assess the Safety and Effectiveness of the Separator 3D as a Component of the Penumbra System in the Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke. ClinicalTrials.gov identifier: NCT0 1584609. Status: NCT01584609. Status: Completed, has results. Indication: acute ischaemic stroke, large-vessel occlusion. Devices: Penumbra.

In addition to these RCTs, 1 single-arm study was identified:

- ARISEII: Analysis of revascularization in ischemic stroke with EmboTrap. ClinicalTrials.gov identifier: NCT02488915. Status: Currently recruiting. Indication: cerebrovascular infarction involving large-vessel occlusion. Devices: EmboTrap.

4 observational studies were identified:

- RAPID: Revive AIS Patients ImmeDiately. ClinicalTrials.gov identifier: NCT03007082. Status: Currently ongoing. Indication: acute ischaemic stroke. Devices: Revive SE.
- ARISE: Analysis of Revascularisation in Ischemic Stroke With EmboTrap. ClinicalTrials.gov identifier: NCT02190552. Status: Completed. Devices: EmboTrap.
- Re-Act: Evaluation of the ReVive SE Device for Intra-Arterial Thrombectomy in Acute Ischemic Stroke. ClinicalTrials.gov identifier: NCT02169492. Status: Completed. Devices: ReVive SE.
- European Registry on the ACE Reperfusion Catheters and the Penumbra System in the Treatment of Acute Ischemic Stroke (PROMISE). ClinicalTrials.gov identifier: NCT01584609. Status: Registry. Indication: acute ischaemic stroke. Devices: Penumbra, ACE Reperfusion catheters.

There are 7 other ongoing studies involving MT listed in which the device has not been specified: 3 RCTs, 3 observational and 1 non-randomised interventional study.

Specialist commentator comments

Comments on this technology were invited from clinical specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 7 clinical specialists were familiar with or had used the technology before. One specialist had been involved in developing and testing the devices. Currently the devices are only being used in commissioned UK neuroscience centres.

Level of innovation

The specialists thought that the devices were highly innovative and a novel concept, with 1

describing the technologies as a 'paradigm shift' in the treatment of acute ischaemic stroke. Two others highlighted that mechanical thrombectomy (MT) was partly a redevelopment of existing technologies used in neuro-intervention, but acknowledged that the concept was highly novel.

One specialist stated that the technique is arguably now the standard care for intracranial large-vessel occlusion; however, another suggested that uptake of MT techniques in the UK had been slow, and that the devices were still relatively new in this setting. One specialist commentator disagreed with this statement, and said that although the numbers of procedures are low compared with international standards (because of delays in commissioning of services), there has been a higher level of uptake of these techniques in centres with the right resources.

One specialist noted that stent retriever type devices are used most commonly in the UK, while a further 2 specialists highlighted that the current evidence base favours stent retrievers.

Potential patient impact

The specialists remarked that using the technology could lead to substantial patient benefits, particularly in post-stroke morbidity and disability. Improvements in functional outcomes, including functional independence; short- and long-term disability; recovery times and length of hospital stay; complications; and carer burden were all cited as potential benefits of MT. One specialist added that the likelihood of functional recovery for patients having the treatment was 50% to 70%, compared with about 10% for conventional medical treatment. Another specialist noted this level of functional recovery will only happen when an excellent technical thrombectomy result is achieved within 4.5 hours of the stroke onset.

The specialists stated that MT devices could be particularly beneficial in: patients with confirmed large proximal acute ischaemic stroke or large-vessel occlusion (who make up around 10% of all stroke patients); patients with no significant established infarct; people presenting 4 to 6 hours after the onset of symptoms; patients on warfarin or a direct-acting oral anticoagulant; patients who cannot have intravenous thrombolysis; patients who have already had intravenous thrombolysis; and those presenting past 4.5 hours, with or without perfusion scanning.

The figure of about 10% of stroke patients having large-vessel occlusion was disputed by 1

specialist who suggested the figure, based on prospective studies and RCTs, was between 39 and 56% of acute ischaemic stroke. The specialist suggested that 10% represents those patients with large-vessel occlusions presenting in time for MT with no additional contraindications.

Potential system impact

Specialists proposed that the devices could have a positive effect on NHS and social services by reducing length of hospital stay and longer-term care costs post-stroke. One specialist remarked that it is anticipated that care for stroke patients treated with MT would move from a long inpatient stay to a short stay with subsequent outpatient follow-up.

The specialists commented that there would be a large upfront cost to the healthcare system associated with uptake of the devices. But they felt that this would be off-set by long-term savings because of the reduced long-term care burden for patients with stroke, as shown in published cost-effectiveness studies. The costs of purchasing the devices, training large numbers of interventional neuroradiologists and other clinical and support staff, and providing additional staffing and facilities for 24-hour services were all cited as sources of additional costs to the NHS.

Several specialists thought that more widespread use of MT devices would need substantial changes to facilities and infrastructure. One suggested that stroke services would need to be centralised into fewer larger units that can deliver MT. The specialist thought that this could lead to destabilisation of smaller stroke units and those that were unable to provide thrombectomy. Specialists also suggested that the effect on ambulance services would be significant because more inter-hospital transfers would be needed. One noted that transport may be a problem in areas that are far from existing neuroscience centres, but noted that 85% of the population is within 1 hour of a centre. Two specialists noted that access to neuro-optimised angiographic facilities would be needed to offer a complete thrombectomy service, and 1 added that a back-up angiography machine on site would also be needed. One commentator noted that having a back-up angiography machine is in line with NHS England service specifications.

Specialists identified problems with staffing (providing and training staff to offer 24-hour thrombectomy services) as the most likely problem that could prevent the technology from being adopted in the NHS. For instance, 2 specialists referred to the British Society of Neuroradiologists' training guidance for mechanical thrombectomy, which noted that the

numbers of fully trained interventional neuroradiologists in the UK would have to double to meet the demands of a 24/7 MT service. One specialist noted that to provide efficient care in hyperacute stroke units and comprehensive stroke centres care, further centralisation of stroke services would be needed. One specialist commented (and another agreed) that imaging protocols at hyperacute stroke units would also need to be upgraded to enable rapid access to CT or magnetic resonance (MR) angiography. If this didn't happen, the thrombectomy pathway would not be activated early enough for clinical benefit to be realised in many patients.

General comments

A number of specialists emphasised that MT is a complex and technical intervention. Because of this it is important that clinicians doing the procedure are highly trained to avoid substantial patient morbidity and mortality. One specialist added that training plans would need to ensure that clinicians were sufficiently skilled to achieve the same efficacy and safety profile when delivering the procedure in practice as had been seen in clinical trials. Without this measure, the benefits of MT would likely to be lost. Another stated that adopting the procedure in non-neuroscience centres, without ensuring that operators had the right credentials and adequate training, would likely to be unsafe. One specialist also stated the procedure should be completed as early as possible to improve outcomes.

Specialists also remarked that only 1 or 2 stroke centres in the UK currently operate 24 hours a day, 7 days a week. They thought that 24-hour services would be needed at all centres in order to deliver a complete thrombectomy service. Specialists stated that the devices are currently used in the NHS in commissioned neuroscience centres and that about 500 procedures are performed annually. This need is expected to increase in future years, with current forecasts suggesting that up to 8,000 patients per year could be eligible for the procedure. One specialist suggested that, once 24-hour services are provided across England, a large thrombectomy centre would expect to perform about 5 or 6 MT procedures per week.

A number of specialists thought that further research was needed in the field of MT with the following topics highlighted: head-to-head comparisons of stent retriever and aspiration type devices; the benefits of using MT for more distal occlusions (such as M2 segment occlusions); the relative risks of using general anaesthesia or conscious sedation for the procedure; comparing MT alone against MT with tissue plasminogen activator; and comparing direct transfer of patients to thrombectomy centres compared with a model in which patients are transferred from local hyperacute stroke units.

Patient organisation comments

A representative of the Stroke Association commented on the technology.

The representative noted that a 2015 survey done by the Stroke Association found that people who had treatment with mechanical thrombectomy (MT) following a stroke reported a strong positive response to the treatment. Some of the benefits reported included avoiding severe disability, survival and quick recovery. The representative noted that patients with large-vessel occlusions (about 1 in 10 stroke patients) would benefit in particular from this treatment, as well as those unable to have thrombolysis. As MT can be used for longer than some other treatments (for instance, thrombolysis), patients could have access to life-saving treatment for longer. It was also reported that this treatment could prevent and reduce long-term disability in people with severe stroke, thereby reducing dependency on others, as well as increasing quality of life in stroke survivors. Disability following stroke may not only lead to physical and social isolation, but may also lead to people experiencing prejudice.

Some negative aspects of MT were also mentioned, including pain and discomfort, as well as the risk of bleeding during the procedure, and uncertainty about whether disability was caused by the treatment or the stroke.

The representative noted that people from black and minority ethnic groups are at a greater risk of stroke and of experiencing a stroke at a younger age compared to other ethnic backgrounds, as are people from economically deprived areas of the UK. Access to this treatment could, the representative noted, reduce the effect of stroke, reduce disability and help to reduce overall health inequality.

The representative stated that MT cannot happen without the correct clinical pathway being in place and currently a sub-optimal pathway is the norm for a lot of people. For example, many people do not have access to a hyperacute stroke unit and face long delays for vital diagnostic procedures. It was also noted that too many people eligible for thrombolysis are not getting the treatment.

Specialist commentators

The following clinicians contributed to this briefing:

- Ms Maria Fitzpatrick, lead consultant nurse, King's College Hospital, London. Did not declare any interests.
- Dr Ajay Bhalla, consultant physician, Guy's and St Thomas' Hospital, London. Did not declare any interests.
- Professor Philip White, honorary consultant neuroradiologist, Royal Victoria Infirmary, Newcastle upon Tyne. Professor White does paid work on behalf of Stryker and Microvention, and is involved in a phase 2 mechanical thrombectomy device trial cofunded by Microvention.
- Dr Robert Crossley, consultant neuroradiologist, North Bristol NHS Foundation Trust. Dr Crossley has previously received industry financial sponsorship to attend conferences relevant to the topic of this briefing and has a consultancy contract with Microvention.
- Professor Anthony Rudd, national clinical director for stroke, NHS England; stroke consultant, Guy's and St Thomas' Hospital; professor of stroke medicine, King's College London. Professor Rudd is the honorary vice chair of the Stroke Association and chairs the intercollegiate stroke working party at the Royal College of Physicians.
- Dr Trevor Cleveland, consultant vascular radiologist, Sheffield Teaching Hospitals NHS Foundation Trust. Did not declare any interests.
- Dr Victoria Young, consultant interventional neuroradiologist, Oxford University Hospitals NHS Foundation Trust. Did not declare any interests.

Development of this briefing

This briefing was developed Newcastle and York External Assessment Centre. The UK analysis from the Lobotesis 2016 publication was conducted by members of the External Assessment Centre but none of those members were involved in the production of this briefing. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

ISBN: 978-1-4731-3047-0