

Institution: Newcastle University		
Unit of Assessment: UoA4		
Title of case study: Optimising thrombectomy services to improve patient outcomes from stroke		
Period when the underpinning research was undertaken: 2017-2019		
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:
Prof Philip White	Professor of Neuroradiology and PEARS Strand 2 lead	1/10/12 to present
Prof Gary Ford	Honorary NU Status and programme grant lead	1/8/92 to present
Prof Christopher Price	PEARS2 interface and assistance with paramedic and modelling work	2/11/06 to present
Dr Peter McMeekin	Lead for all PEARS modelling and Health Economics	1/10/05 to 30/6/14
Dr Darren Flynn	Senior RA & Qualitative research lead	1/10/09 to 31/1/19
Dr Kristoffer Halvorsrud	RA. Surveys/PPE & decision tree analyses	4/1/16 to 8/5/17
Mr Kai Lee	RA modelling service provision	27/1/16 to 6/4/17
Dr Diarmuid Coughlan	Senior RA modelling service provision & cost effectiveness components	18/9/17 to present
Ms Hannah Lumley	RA for modelling & cost effectiveness components	15/1/18 to present
Prof Luke Vale	Supervisory role for health economics components	1/2/11 to present
Prof Dawn Craig	Health economics & systematic review analysis	21/7/14 to present
Dr Anand Dixit	Clinical Research Associate	1/12/03 to 31/1/21
Mr David Burgess	PCPEI rep	1/2/13 to 31/1/14
Dr Adela Cora	PhD student (Prof White)	2014 to 2017
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 <p>The most severe type of stroke, large arterial occlusion, accounts for a disproportionately large amount of the stroke disability burden. Newcastle confirmed the high effectiveness of endovascular mechanical thrombectomy (MT) via randomised trial, systematic literature review and meta-analysis. In addition, Newcastle identified that 8,000 stroke patients in England are eligible for MT annually. Finally, the work modelled optimum service configuration for MT units in comprehensive stroke centres (CSCs). Together, this research informed national commissioning of MT services, underpinned planned changes in the numbers of CSCs and increased the number of MTs performed from just over 150 in 2015 to around 1,600 in England in 2019-20, though the number of thrombectomy referrals was reduced by ~28% during COVID-19 pandemic peaks (EV6).</p>		
2. Underpinning research <p><u>The burden of stroke and the potential value of mechanical thrombectomy</u> Ischaemic stroke (caused by blockage of arteries supplying the brain) is a huge societal burden and the largest single cause of acquired adult disability in the UK. Large arterial occlusion (LAO) accounts for around 40% of ischaemic strokes and a disproportionately large amount of the disability burden because many LAOs are moderate or severe. At the outset of research, the main treatment for LAO was intravenous thrombolysis (IVT, the dissolution of blood clots using</p>		

enzymes). However, IVT has low efficacy in LAO stroke and many patients are ineligible due to existing medical problems, recent surgery or other contraindication.

The most effective method for treating LAO is intra-arterial extraction of the clots blocking major brain arteries, known as mechanical thrombectomy (MT). MT can be provided to many of these patients but was only given in <1% of ischaemic stroke cases¹ because the required evidence, equipment or expertise was not yet available.

PISTE

To address this unmet need, the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE, R1) randomised controlled clinical trial started in 2013 (ClinicalTrials.gov ID - NCT01745692) and was partly coordinated by Newcastle University (Prof White, Co-Cl and Prof Ford, Trial Steering Committee Chair). PISTE compared MT in combination with IVT against IVT alone (best medical care at the time) in patients with LAO. Administering MT as fast as possible following LAO was found to be safe and improved clinical outcomes, including improving disability-free survival (R1). Overall, one in three patients had reduced disability after 90 days as a result. Evidence from this trial and others (R1, R2) showed such a clear benefit of MT that the PISTE trial was stopped early as it was no longer ethical to randomise patients into the control arm (R1).

PEARS 2

In 2015, fewer than 150 thrombectomies were performed across the whole of the UK, as stroke services were not configured to facilitate routine MT. The Promoting Effective and Rapid Stroke Services (PEARS) project, led by Newcastle, was started in 2014 to model the reconfiguration of stroke services required for MT to be provided quickly and effectively. The overall aim of PEARS was to improve the effectiveness, efficiency and speed of early management of stroke patients. PEARS 2, the second strand of the project, aimed specifically to model the effectiveness of MT treatment in a restructured service, and to plan and promote its implementation for acute ischaemic stroke patients. This was achieved using a combination of an in-depth review process (R3), professional engagement (R4), and service modelling (R3, R5, R6). PEARS 2 modelling identified that between 9,000 and 10,000 patients per annum in the UK (~10% of stroke admissions) would benefit from accessing a MT service (R3). It also identified that MT could be provided 80 minutes sooner if patients were directed to treatment at comprehensive stroke service centres (CSCs, R5).

Newcastle research formed the evidence basis for the reconfiguration of England's stroke services, not only showing the effectiveness of MT but identifying how stroke services could be reconfigured to implement MT. The ultimate impact is that more patients benefit from MT and subsequently have improved recovery outcomes, as described below.

3. References to the research

SciVal field-weighted citation impact (FWCI) as of December 2020. Newcastle researchers in **bold**.

- R1. Muir KW, **Ford GA**, Messow C-M, Ford I, Murray A, Clifton A, Brown MM, Madigan J, Lenthall R, Robertson F, **Dixit A**, Cloud GC, Wardlaw J, Freeman J, **White P**, on behalf of the PISTE Investigators. (2017) Endovascular therapy for acute ischaemic stroke: the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial. *J Neurol Neurosurg Psychiatry*. 88:38–44. DOI: 10.1136/jnnp-2016-314117. FWCI: 17.38.
- R2. **White PM**, Bhalla A, Dinsmore J, James M, McConachie N, Roffe C, Young G, on behalf of British Association of Stroke Physicians, British Society of Neuroradiologists, Intercollegiate Stroke Working Party, Neuroanaesthesia and Neurocritical Care Society of GB & Ireland, UK Neurointerventional Group, 2015. (2017) Standards for providing safe acute ischaemic stroke thrombectomy. *Clinical Radiology*. 72 (2):75.e1–175.e9. DOI: 10.1016/j.crad.2016.11.008. FWCI: 2.75.

¹ Sentinel Stroke National Audit report Royal Coll. Phys. London 2016/17 pages 34 & 36.
www.strokeaudit.org/Documents/AnnualReport/2016-17-SSNAP-Annual-Report.aspx

- R3. **McMeekin P, White P, James MA, Price CI, Flynn D, Ford GA.** (2017) Estimating the number of UK stroke patients eligible for endovascular thrombectomy. *Eur Stroke J.* 2(4):319-326, DOI: 10.1177/2396987317733343. FWCI: 4.32.
- R4. **Halvorsrud K, Flynn D, Ford GA, McMeekin P, Bhalla A, Balami J, Craig D, White P.** (2018) A Delphi study and ranking exercise to support commissioning services: future delivery of Thrombectomy services in England. *BMC Health Services Research.* 18(1):135. DOI: 10.1186/s12913-018-2922-3. FWCI: 1.05.
- R5. Allen M, Pearn K, James M, **Ford G, White P**, Rudd A, **McMeekin P**, Stein K. (2019) Maximising access to thrombectomy services for stroke in England: a modelling study. *Eur Stroke J.* 4(1):39-49. DOI: 10.1177/2396987318785421 FWCI: 3.
- R6. **McMeekin P, Flynn D, Allen M, Coughlan D, Ford GA, Lumley H, Balami JS, James MA, Stein K, Burgess D, White P.** (2019) Estimating the effectiveness and cost-effectiveness of establishing additional endovascular Thrombectomy stroke Centres in England: A discrete event simulation. *BMC Health Services Research.* 19(1). DOI: 10.1186/s12913-019-4678-9. FWCI: 2.27.

4. Details of the impact

Impact on guidance and policy

Newcastle research (PISTE and PEARS 2) has directly informed national guidance and commissioning policy for the provision of stroke services and implementation of MT. Preliminary PEARS 2 work informed recommendations in the 2016 National Clinical Guideline for Stroke (NCGS, EV1). This is a highly influential publication with a proven track record of influencing stroke service provision in the UK for more than 15 years. On page 41 (section 3.5) the guidelines state “*mechanical thrombectomy (MT) is an effective acute stroke treatment for selected patients with proximal large artery occlusions as an adjunct to IVT ... Centres that provide endovascular treatment should meet the professional standards set out by the joint societies’ working group (National Institute for Health and Care Excellence, 2015b, [R2])*”. Furthermore the joint editor of the guidelines confirms that as well as R2, the committee “*had information on the time metrics of MT performance from PISTE, a UK based trial, that matched international comparator trials*”, referring to R1 data (EV2a).

The 2018 NICE guideline (NG128, EV3) explicitly references R3 when considering the cost effectiveness of MT on ischaemic stroke treatment. It states “*The committee was informed by a published modelling study [R3]... [which] indicates that 40% of people ... are potentially eligible for thrombectomy [MT]*”. The guidance also says “*The committee was confident that the economic evidence accurately demonstrates that offering thrombectomy alongside intravenous thrombolysis ... is cost-effective compared with current practice... and would therefore be a good use of NHS resources*”, and recommends that MT be offered to ischaemic stroke patients as soon as possible after the onset of symptoms (EV3).

Impacts on stroke service provision, stroke specialists and healthcare providers

Following the 2016 NCGS policy decision to commission MT, NHS England published service specifications in 2017 (EV4, EV5). Newcastle research (R2) is one of only 3 national standards informing this document. One of the others is NICE guidance IPG548, which is directly informed by the 2018 NICE guidance (EV3) referenced above and underpinned by Newcastle research.

This MT service specification was rolled out across NHS England in April 2018 and led to substantial changes in the national provision of MT services. The primary change was an increase in the number of large CSCs to implement hyperacute thrombectomy services (EV5). This change is indicated as larger units have better performance metrics for patient outcomes in national audit data (SSNAP) and can provide all treatments including MT. There are currently 24 centres in the UK that provide MT (EV6).

Impacts on patients

Restructuring stroke services and commissioning MT services have directly increased the number of patients receiving MTs as part of routine stroke care. Before PEARS research, figures voluntarily submitted to SSNAP showed that just over 150 MTs were carried out in 2015 (EV2b).

Following restructuring, this number has grown annually with approximately 800 MTs carried out in 2017 and >1,200 in 2018 (EV7). As of July 31st 2020, MT numbers had increased markedly in England to an annual rate of >1,600 (EV5, EV7) or from <5% of those eligible to ~20% (EV2a). This was expected to be 1,800-2,000 (EV2a), but due to the COVID-19 pandemic, the number of referrals dropped by 27.7% compared to the first 3 months of 2020 (EV6).

MT has a very powerful treatment effect, as shown in PISTE and other clinical trials (R1, EV8). Given the median age of stroke is around 70 years, functional independence has been the focus of investigation in most studies. A 2019 NHS England Clinical Priorities Advisory Group recognised the benefits of MT, stating that “63% of patients treated with thrombectomy [MT] will be independent or mobile without assistance; with usual care this would be only 43%”. Additionally, “20% more stroke patients treated with thrombectomy will be independent after stroke than those treated using current standard care” (EV9). This Advisory Group was supported by an additional NHS service specification (EV10), itself informed by R2 and NICE guidance NG128 (EV3). The specification has been available online since 2019 through public consultation, although due to the COVID-19 pandemic, it was not published until January 2021.

As stroke is the UK's leading cause of acquired disability, it has major repercussions amongst families of stroke patients and wider society. LAO stroke is disproportionately responsible for poor outcomes after stroke. Given that 8,000 English patients per annum are eligible for MT treatment, an estimated 1,600 patients per annum will make a good recovery after stroke with a further 1,300 left less disabled than they would have been without MT. Reducing long-term disability in these 3,000 people per annum will have clear societal gains (R6).

In summary

Newcastle research identified that 10% of LAO stroke patients are eligible for MT treatment and modelled the changes required to stroke service centres to optimise care. This led to optimal implementation of thrombectomy care in England and approximately 1,600 MTs performed in 2019-20, quadruple the number in 2016 before PISTE/PEARS, subsequently improving patient recovery and reducing disability.

5. Sources to corroborate the impact

- EV1. 2016 National Clinical Guideline for Stroke (NCGS) 5th edition. Section 3.5
- EV2. Evidence from the Joint Editor of the 2016 National Clinical Guidelines for Stroke and Clinical Director of the Sentinel Stroke National Audit Programme
 - EV2a. Letter of support as the Joint Editor of the 2016 National Clinical Guidelines for Stroke. PDF
 - EV2b. Confirmation available on request from Clinical Director of the Sentinel Stroke National Audit Programme. Refer to Corroborator 1 details.
- EV3. NICE Guideline “Stroke and transient ischaemic attack in over 16s: diagnosis and initial management”, (Guideline NG128) [D] Evidence review for thrombectomy, NICE, Intervention evidence review, May 2019, Section 1.9.2, page 28. PDF.
<https://www.nice.org.uk/guidance/ng128/evidence/d-thrombectomy-pdf-6777399569>
- EV4. 2018 NHS England Service Specification (170034S), “Neurointerventional Services for Acute Ischaemic & Haemorrhagic Stroke”
- EV5. Letter of support from Senior Manager, National Programme of Care, NHS England evidencing restructure of stroke services based on PEARS2 modelling. PDF available on request
- EV6. McConachie et al. (2020) – Mechanical thrombectomy for acute ischaemic stroke during the COVID-19 pandemic: changes to UK practise and lessons learned. *Clinical Radiology*. 75(10):795.e7e795.e13. DOI: <https://doi.org/10.1016/j.crad.2020.07.001>
- EV7. SSNAP 2019-2020 annual report. “Number of patients receiving thrombectomies”, Page 34. PDF.
<https://www.strokeaudit.org/Documents/National/Clinical/Apr2019Mar2020/Apr2019Mar2020-AnnualReport.aspx>
- EV8. Flynn et al. (2017) Intra-arterial mechanical thrombectomy stent retrievers and aspiration devices in the treatment of acute ischaemic stroke: A systematic review

and meta-analysis with trial sequential analysis. *European Stroke Journal*. 2(4):308–318. DOI: 10.1177/2396987317719362

- EV9. NHS England Clinical Priorities Advisory Group - “Stroke Thrombectomy Service for Acute Ischaemic Stroke”, (URN=1868). PDF.

<https://www.engage.england.nhs.uk/consultation/stroke-thrombectomy-service/>

- EV10. NHS Service Specification “Stroke Thrombectomy Service for Acute Ischaemic Stroke”, Spec No. 1868, which supports EV10. PDF.

<https://www.engage.england.nhs.uk/consultation/stroke-thrombectomy-service/>