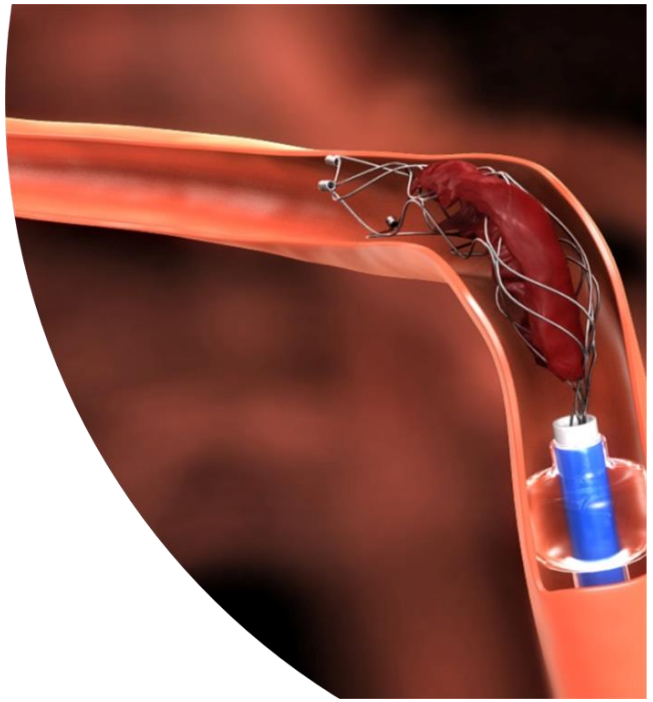
GP Symposium:

Hyperacute Treatment of Ischaemic Stroke: Thrombolysis & Mechanical Thrombectomy

Soma Banerjee

Stroke Consultant
Head of Speciality
Imperial College Healthcare NHS Trust



What will be covered?

01

CASE PRESENTATION &

CONCEPT OF ISCHAEMIC PENUMBRA

02

EVIDENCE FOR IV THROMBOLYSIS

03

WHAT IS MECHANICAL THROMBECTOMY?

IS MT A MAGIC BULLET FOR ISCHAEMIC STROKE?

04

MT: FUTURE DIRECTIONS

05

PUBLIC AWARENESS & PRE-HOSPITAL ASSESSMENT

06

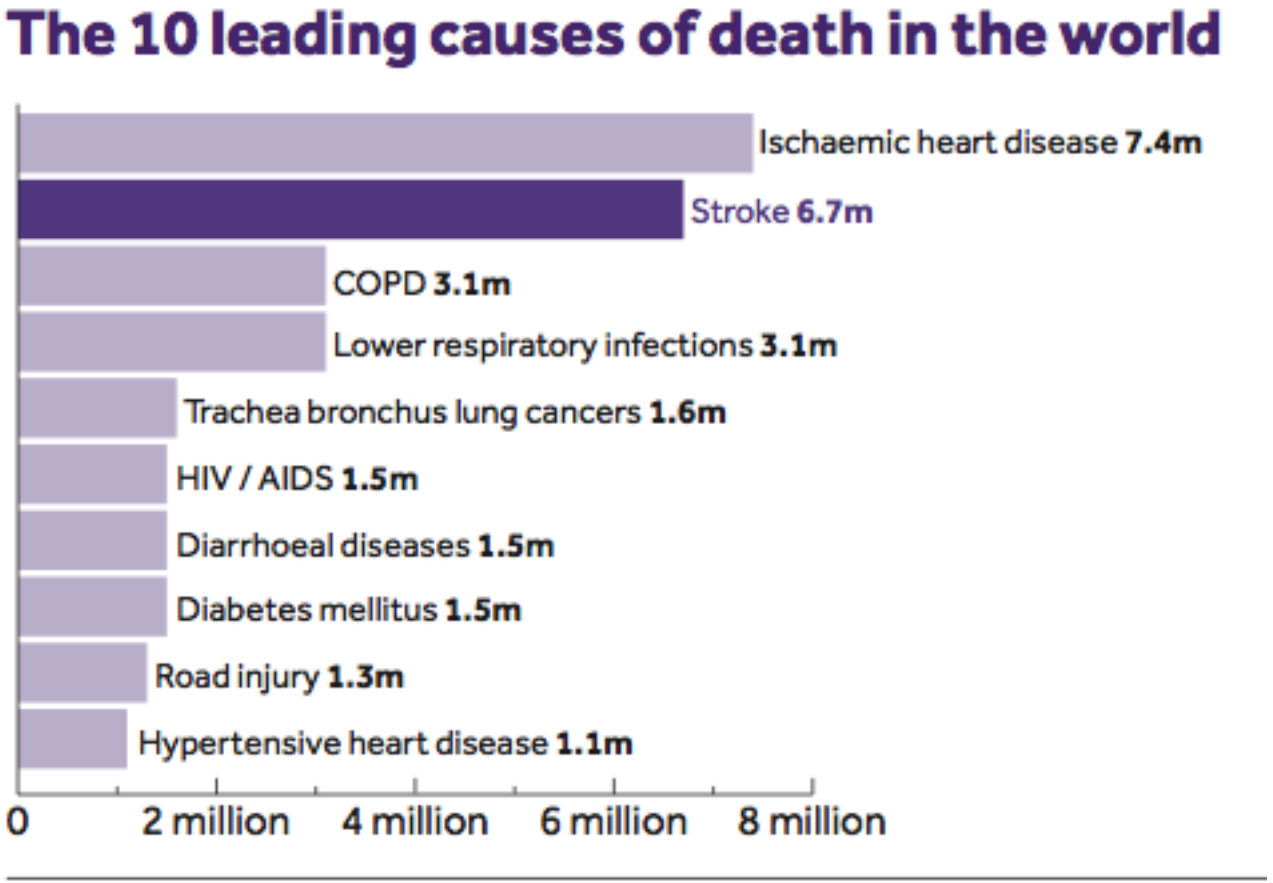
IMPORTANCE OF ORGANISATION OF SERVICES: THE LONDON STROKE MODEL

Epidemiology and Burden of Stroke

Stroke Association UK

- Stroke is the second commonest cause of death in the World
- Largest single cause of severe disability
- 130,000 people will suffer a stroke in England each year
- Incidence increases with age
- Cost to NHS : £2.8bn
- Stroke patients occupy ~20% of all acute hospital beds and ~25% of long term beds

Leading causes of Death Worldwide



Case Presentation

- 65 year old lady
- Previously fit and well
- Blue call to Stroke Team
- FAST positive

On arrival

- Severe expressive dysphasia
- Dense right hemiparesis (0/5 power)
- Hemianopia
- Rest of examination normal

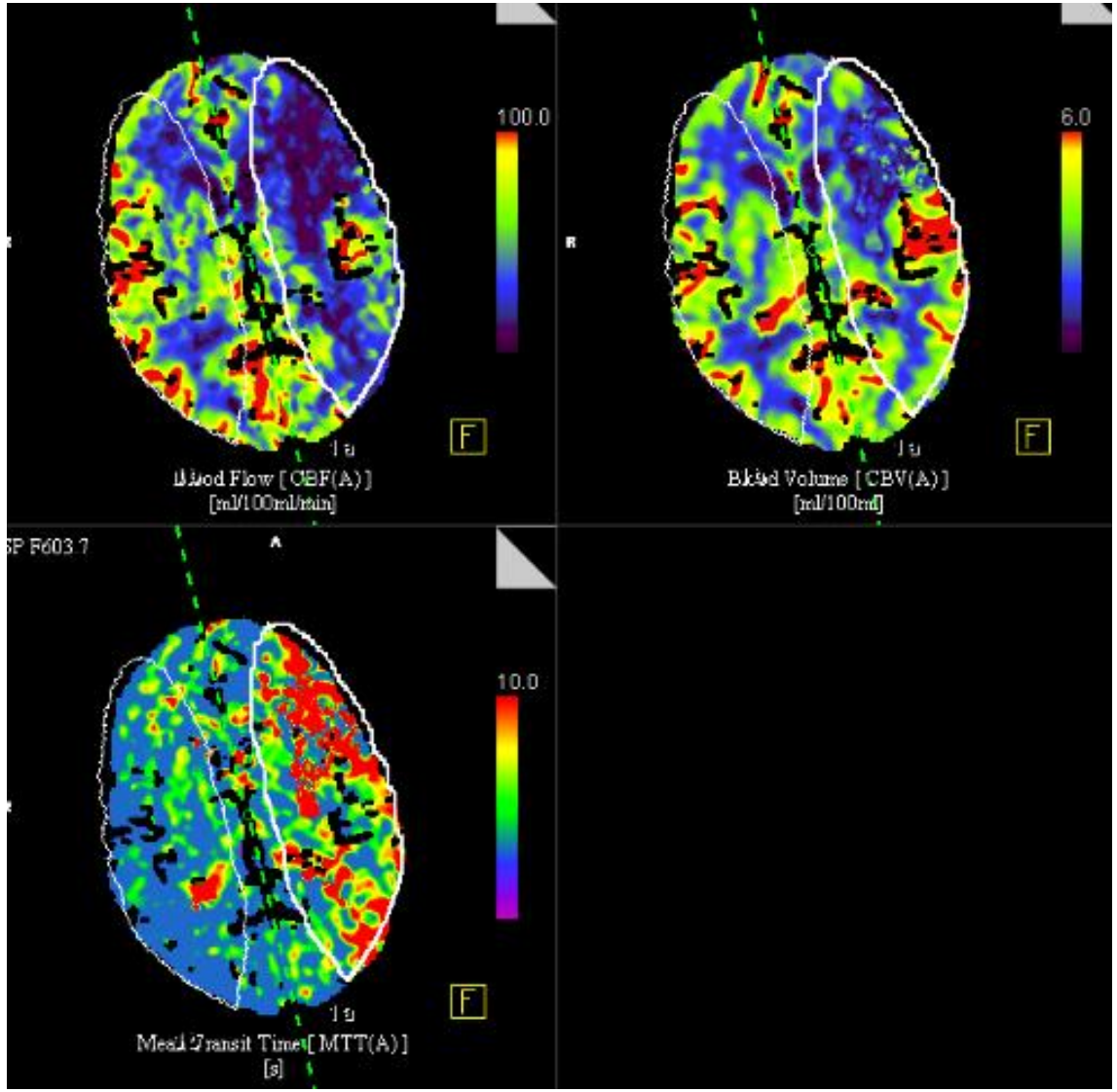
- Patient transferred straight to CT

(patient examined in entrance to resus)

CT/ CT Angiogram

Filling defect in Left middle cerebral artery

CT perfusion of anterior circulation

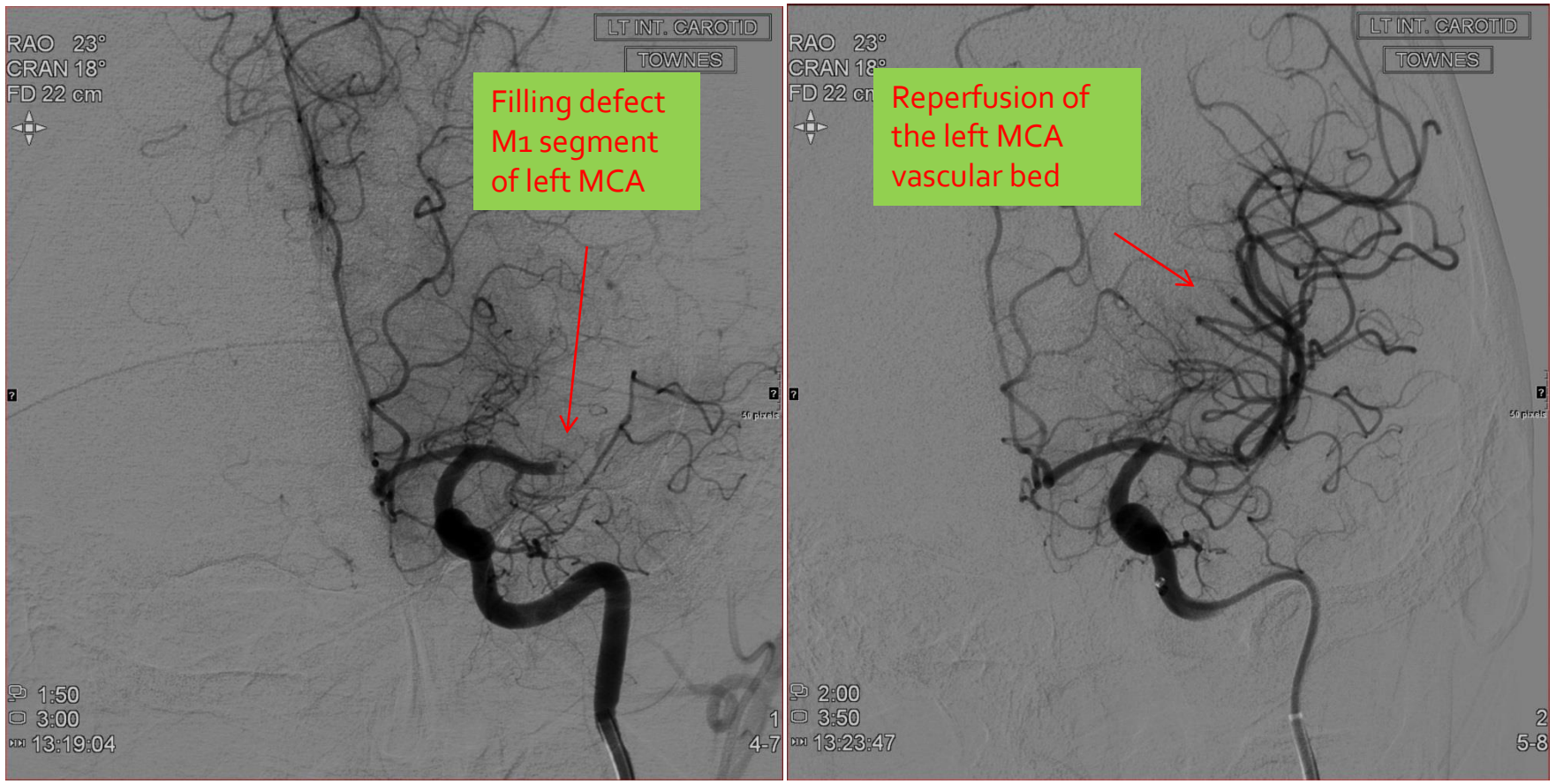


Small ischaemic core with large non-matched penumbra

Treatment

- Immediate iv thrombolysis
- Decision made to proceed with thrombectomy under LA
- Transferred to interventional radiology suite

Digital subtraction angiography




Aspirated thrombus

Post procedure progress

- Door to Groin time of 1hour
- Immediate on table neurological improvement post aspiration
- Mild dysarthria and mild expressive dysphasia

Treatment Concepts in Ischaemic Stroke

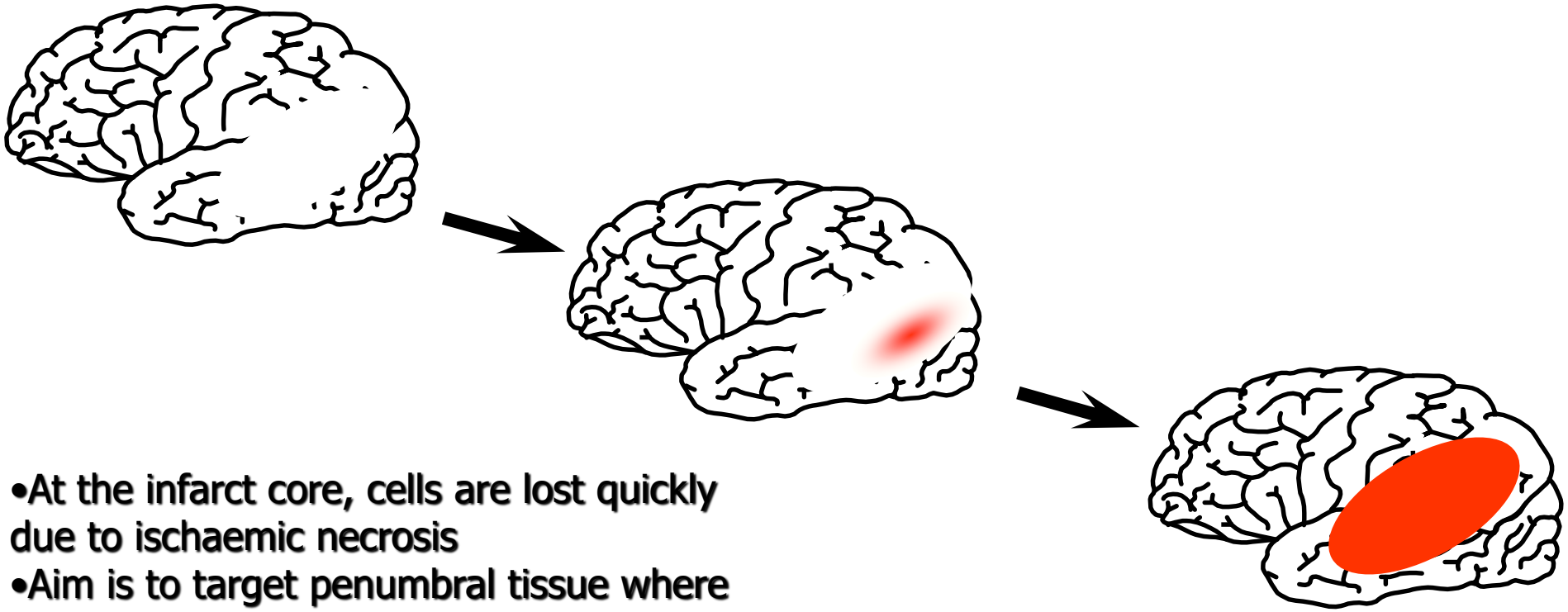
'The Ischaemic Penumbra'

- Ischaemic Stroke occurs due to an interruption of blood supply to the brain, with subsequent death of the neurons in that area

- Ischaemic Penumbra refers to the neurons at the periphery of the damaged area which may either go on to die or may survive if re-perfused in time

- Therefore the aim of acute treatment of stroke is to reperfuse the ischaemic penumbra

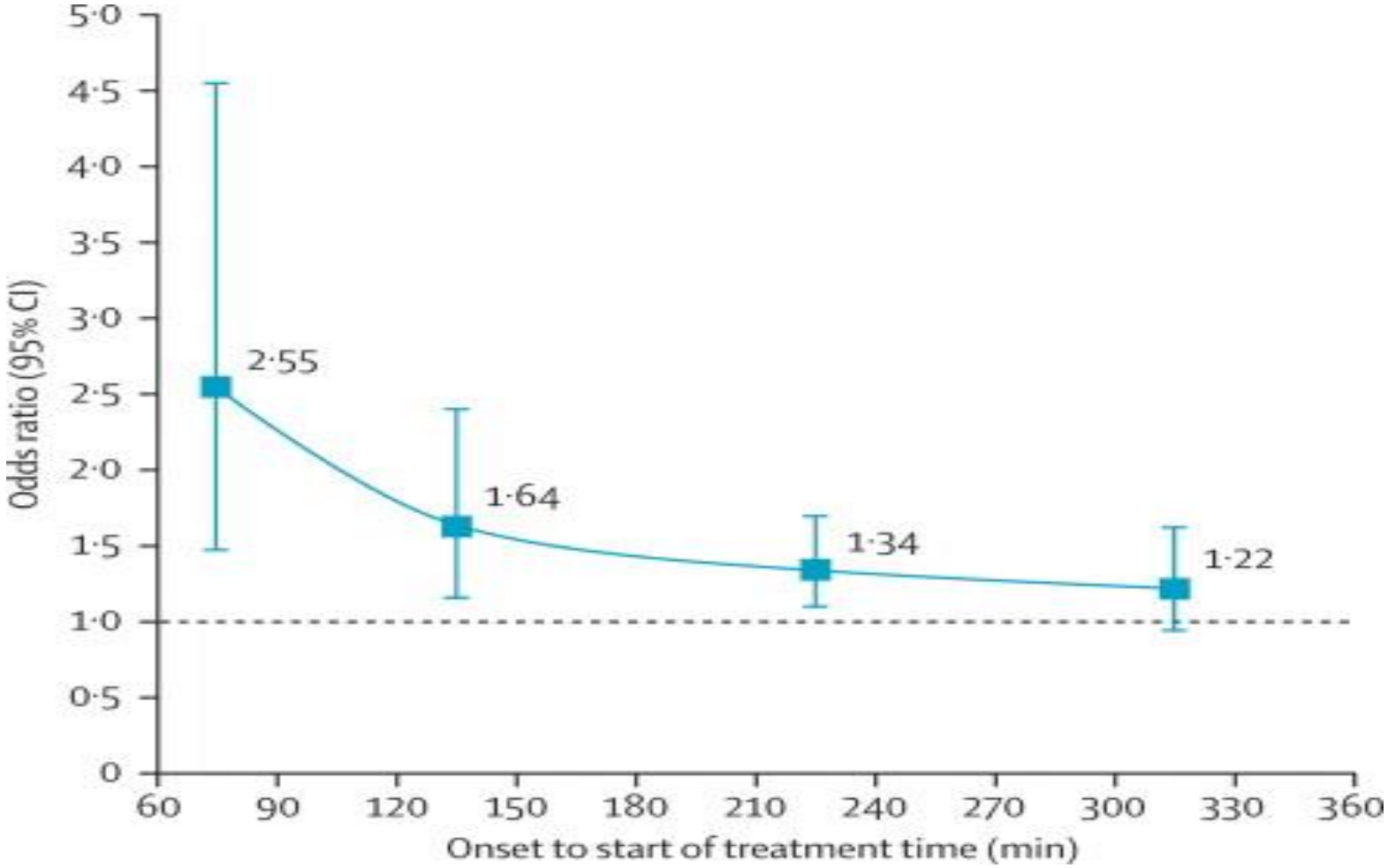
The Ischaemic Penumbra & Underlying Core Infarct



- At the infarct core, cells are lost quickly due to ischaemic necrosis
- Aim is to target penumbral tissue where neurones die by a mixture of necrosis and apoptosis

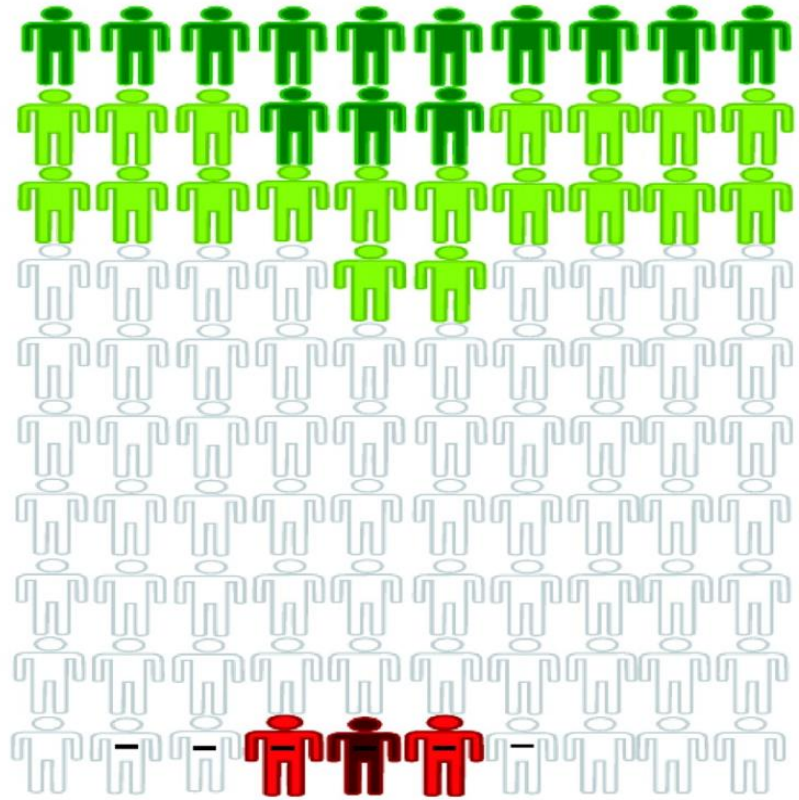
The objective is to avoid lesion enlargement

Intravenous Thrombolysis:
Time is Brain



Odds of excellent outcome after Thrombolysis (mRS 0-1)

TPA for Cerebral Ischemia within 3 Hours of Onset-Changes in Outcome Due to Treatment



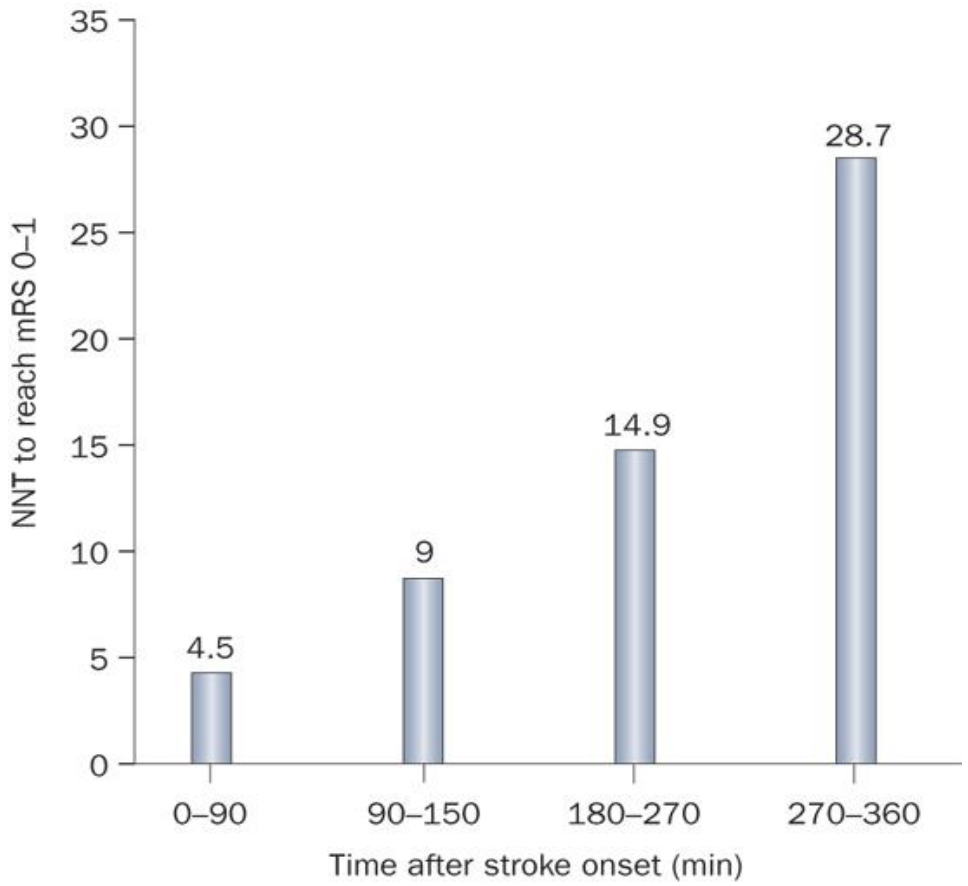
Changes in final outcome as a result of treatment:

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

Number needed to treat



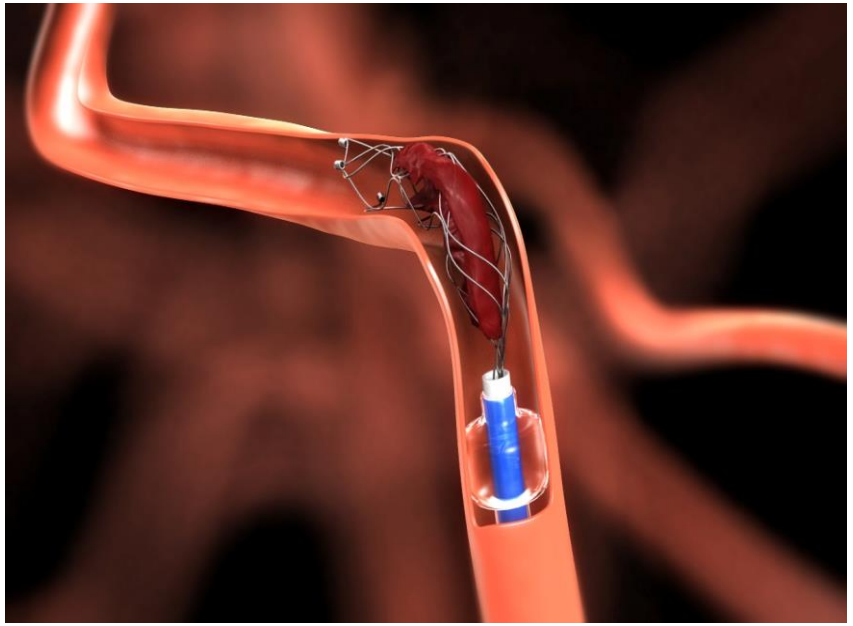
Intravenous Thrombolysis

Indications and Licensing

- Acute ischaemic stroke
- Imaging has excluded haemorrhage
- Indicated within 3hours, including over 80’s and for 3-4.5hrs, below 80 years
- Can extent treatment to 6 hours
- For 3-6 hours, consider on a case by case basis

Thrombectomy……is this the future?

- Exciting new RCT data published in 2015; 6 trials
- Level 1 evidence for improved patient outcome compared with standard care.
- Most patients underwent thrombectomy in addition to thrombolysis with intravenous alteplase
- Significant improvement in functional outcome compared to iv thrombolysis
- No difference in mortality or symptomatic intracerebral haemorrhage



Solitaire Stent – Clot retrieval device

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2015 VOL. 372 NO. 1

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.F. Lingsma, A.J. Yoo, W.J. Schonewille, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J. Staals, J. Hofmeijer, J.A. van Oostayen, G.J. Lycklama à Nijeholt, J. Boiten, P.A. Brouwer, B.J. Emmer, S.F. de Bruijn, L.C. van Dijk, L.J. Kappelle, R.H. Lo, E.J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. van den Berg, B.A.A.M. van Hasselt, L.A.M. Aerden, R.J. Dallinga, M.C. Visser, J.C.J. Bot, P.C. Vroomen, O. Eshghi, T.H.C.M.L. Schreuder, R.J.J. Heijboer, K. Keizer, A.V. Tielbeek, H.M. den Hertog, D.G. Gerrits, R.M. van den Berg-Vos, G.B. Karas, E.W. Steyerberg, H.Z. Flach, H.A. Marquering, M.E.S. Sprengers, S.F.M. Jenniskens, L.F.M. Beenen, R. van den Berg, P.J. Koudstaal, W.H. van Zwam, Y.B.W.E.M. Roos, A. van der Lugt, R.J. van Oostenbrugge, C.B.L.M. Majoie, and D.W.J. Dippel, for the MR CLEAN Investigators*

ABSTRACT

BACKGROUND

In patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion, intraarterial treatment is highly effective for emergency revascularization. However, proof of a beneficial effect on functional outcome is lacking.

METHODS

We randomly assigned eligible patients to either intraarterial treatment plus usual care or usual care alone. Eligible patients had a proximal arterial occlusion in the anterior cerebral circulation that was confirmed on vessel imaging and that could be treated intraarterially within 6 hours after symptom onset. The primary outcome was the modified Rankin scale score at 90 days; this categorical scale measures functional outcome, with scores ranging from 0 (no symptoms) to 6 (death). The treatment effect was estimated with ordinal logistic regression as a common odds ratio, adjusted for prespecified prognostic factors. The adjusted common odds ratio measured the likelihood that intraarterial treatment would lead to lower modified Rankin scores, as compared with usual care alone (shift analysis).

RESULTS

We enrolled 500 patients at 16 medical centers in the Netherlands (233 assigned to intraarterial treatment and 267 to usual care alone). The mean age was 65 years (range, 23 to 96), and 445 patients (89.0%) were treated with intravenous alteplase before randomization. Retrievable stents were used in 190 of the 233 patients (81.5%) assigned to intraarterial treatment. The adjusted common odds ratio was 1.67 (95% confidence interval [CI], 1.21 to 2.30). There was an absolute difference of 13.5 percentage points (95% CI, 5.9 to 21.2) in the rate of functional independence (modified Rankin score, 0 to 2) in favor of the intervention (32.6% vs. 19.1%). There were no significant differences in mortality or the occurrence of symptomatic intracerebral hemorrhage.

CONCLUSIONS

In patients with acute ischemic stroke caused by a proximal intracranial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe. (Funded by the Dutch Heart Foundation and

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Dippel at the Department of Neurology H643, Erasmus MC University Medical Center, PO Box 2040, Rotterdam 3000 CA, the Netherlands, or at d.dippel@erasmusmc.nl.

Drs. Berkhemer, Fransen, and Beumer and Drs. van Zwam, Roos, van der Lugt, van Oostenbrugge, Majoie, and Dippel contributed equally to this article.

*A complete list of investigators in the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) is provided in the Supplementary Appendix, available at NEJM.org.

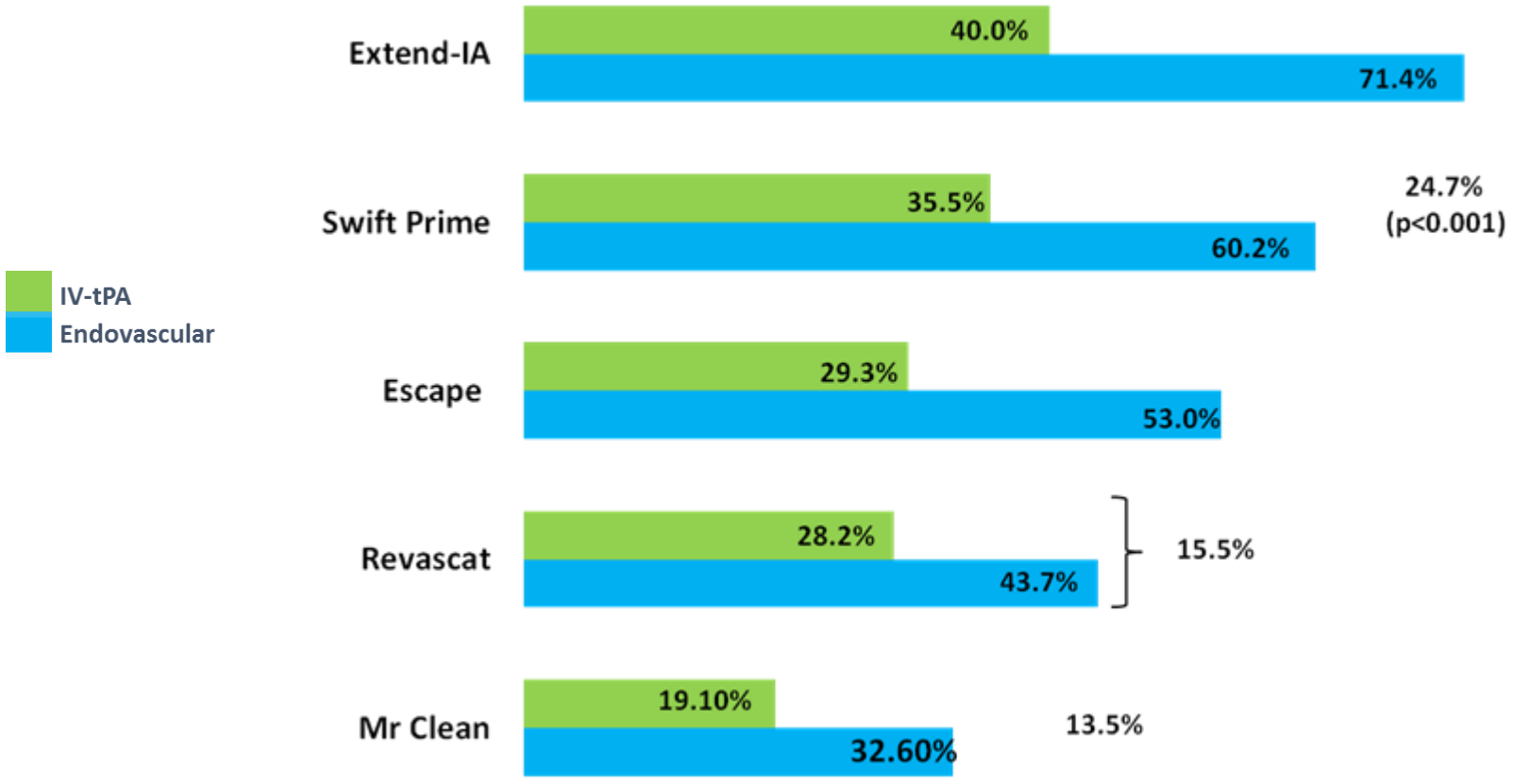
This article was published on December 17, 2014, and updated on January 1, 2015, at NEJM.org.

N Engl J Med 2015;372:11-20.
DOI: 10.1056/NEJMoa1411587

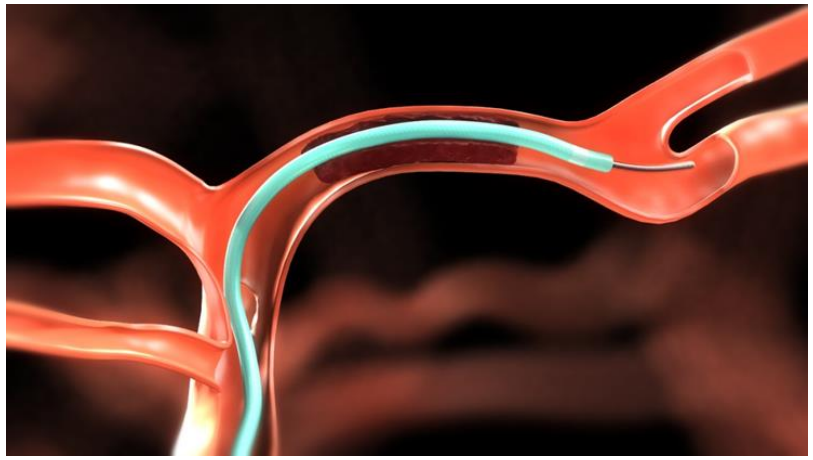
MR CLEAN

A Multicenter Randomized CLinical trial of Endovascular treatment for Acute Ischemic stroke in the Netherlands

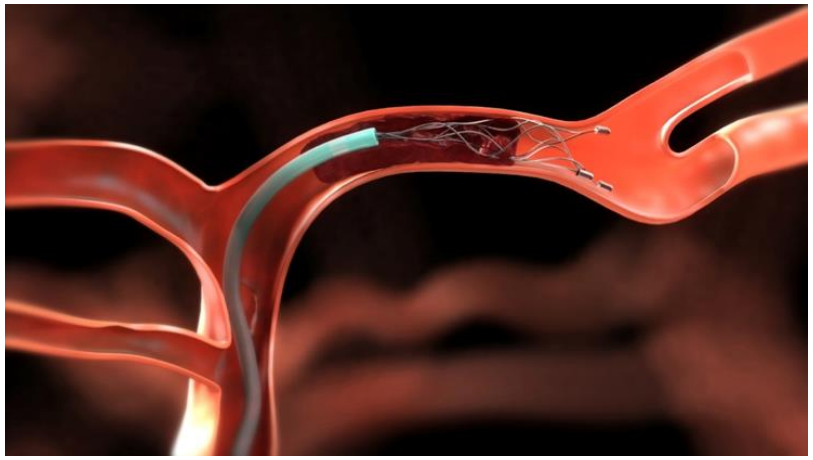
What is the evidence?



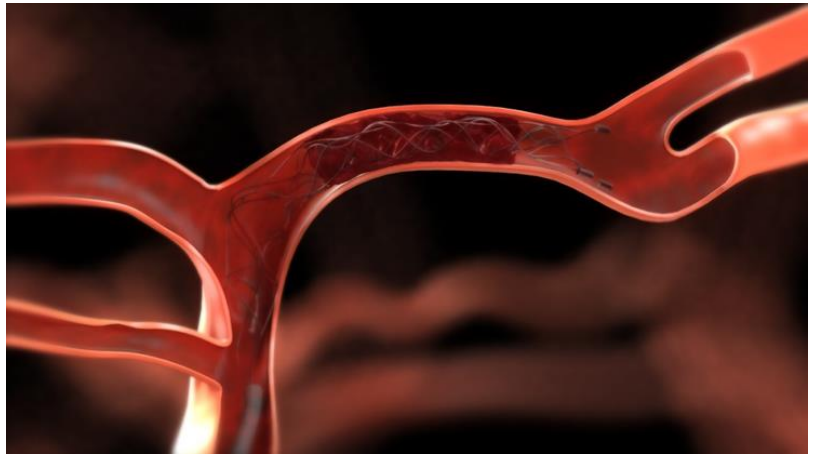
Stentrievers



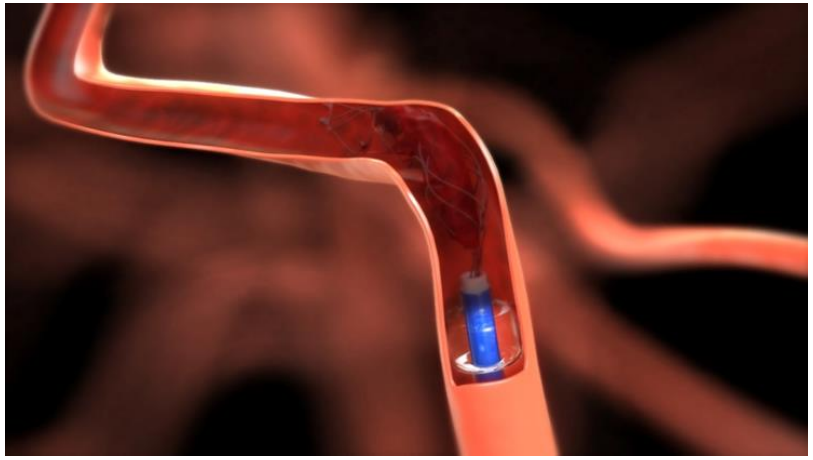
1



2



3



4

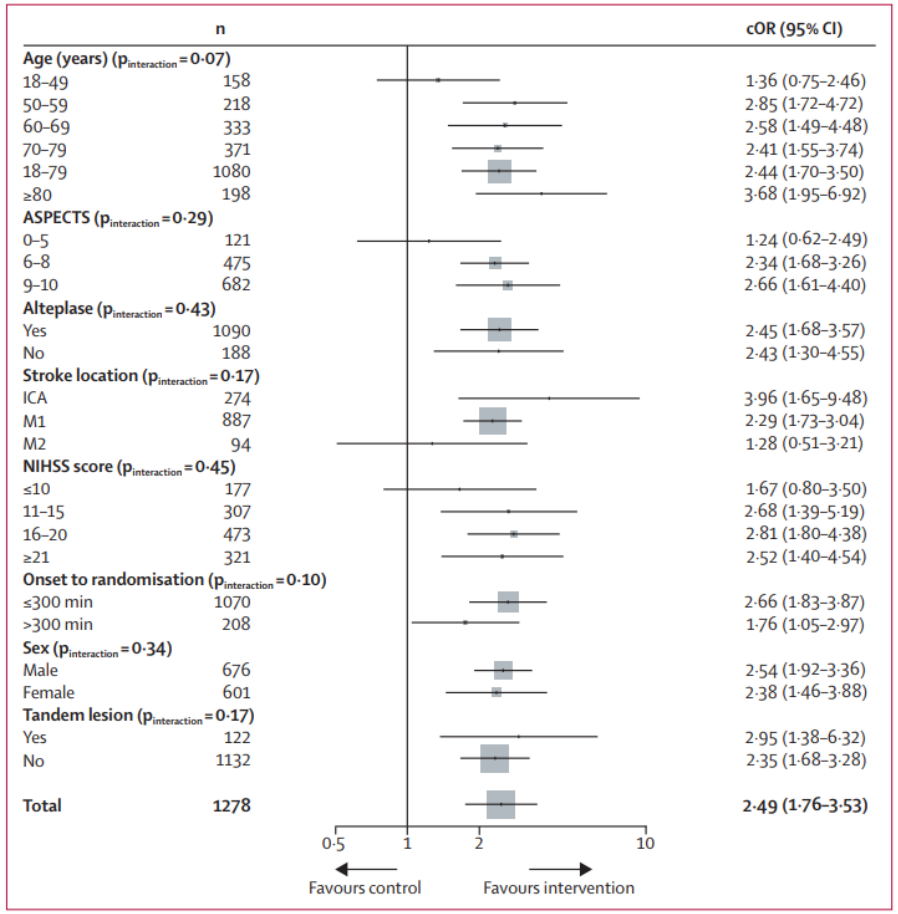
Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Peter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majoie, Aad van der Lugt, Maria A de Miquel, Geoffrey A Donnan, Yvo B W E M Roos, Alain Bonafe, Reza Jahan, Hans-Christoph Diener, Lucie A van den Berg, Elad I Levy, Olvert A Berkhemer, Vitor M Pereira, Jeremy Rempel, Mònica Millán, Stephen M Davis, Daniel Roy, John Thornton, Luis San Román, Marc Ribó, Debbie Beumer, Bruce Stouch, Scott Brown, Bruce C V Campbell, Robert J van Oostenbrugge, Jeffrey L Saver, Michael D Hill, Tudor G Jovin, for the HERMES collaborators

	Intervention population (n=634)	Control population (n=653)
Demographic characteristics		
Median age (years)	68 (57–77)	68 (59–76)*
Men	330 (52%)	352 (54%)
Women	304 (48%)	301 (46%)
Past medical history		
Hypertension	352 (56%)	388 (59%)
Diabetes mellitus	82 (13%)	88 (13%)
Atrial fibrillation	209 (33%)	215 (33%)
Smoking (recent or current)	194 (31%)	210 (32%)
Clinical characteristics		
Baseline NIHSS score	17 (14–20))†	17 (13–21)‡
Baseline blood glucose (mmol/L)	6·6 (5·9–7·8)§	6·7 (5·9–7·8)¶
Imaging characteristics		
ASPECTS on baseline CT	9 (7–10)§	9 (8–10)¶
Intracranial occlusion location		
Internal carotid artery	133 (21%)	144 (22%)
M1 segment middle cerebral artery	439 (69%)	452 (69%)
M2 segment middle cerebral artery	51 (8%)	44 (7%)
Other	11 (2%)	13 (2%)
Treatment details and process times		
Treatment with intravenous alteplase	526 (83%)	569 (87%)
Treatment with intravenous alteplase documented within 180 min	442 (70%)	462 (71%)
Process times (min)		
Onset to randomisation	195·5 (142–260)‖	196 (142–270)*
Onset to intravenous alteplase	100 (75–133)**	100 (74–140)††
Onset to reperfusion	285 (210–362)	NA

Data are median (IQR), n (%), or mean (SD). NIHSS=National Institutes of Health Stroke Scale. ASPECTS=Alberta Stroke Program Early CT Score. *n=650. †n=631. ‡n=648. §n=620. ¶n=644. ‖n=632. **n=598. ††n=618.

Table 1: Baseline characteristics in the pooled data



Endovascular Therapy for Stroke — It's about Time

Anthony J. Furlan, M.D.

June 11, 2015
N Engl J Med 2015; 372:2347-2349

Evidence

Trials:

MR CLEAN, ESCAPE, SWIFT-PRIME, EXTEND-IA, REVASCAT, THRACE, THERAPY

Hermes Metanalysis:

(Lancet 2016, Goyal et al)

NNT for one additional person to have reduced disability of at least one mRS point was 2.6

Guidelines

- ESO-ESMINT 2014 and 2015 update
- AHA 2015
- BASP 2015
- NICE 2016
- EROICAS 2016
- RCP 2016

- Level 1 evidence for improved patient outcome compared with current gold standard treatment (iv thrombolysis)
- Eligible patients with evidence of large vessel anterior circulation occlusion: This is key
- Significant improvement in functional outcome compared to iv thrombolysis
- No difference in mortality or symptomatic intracerebral haemorrhage
- NNT 2.6

Thrombectomy – Where next?……

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

ABSTRACT

BACKGROUND

The effect of endovascular thrombectomy that is performed more than 6 hours after the onset of ischemic stroke is uncertain. Patients with a clinical deficit that is disproportionately severe relative to the infarct volume may benefit from late thrombectomy.

METHODS

We enrolled patients with occlusion of the intracranial internal carotid artery or proximal middle cerebral artery who had last been known to be well 6 to 24 hours earlier and who had a mismatch between the severity of the clinical deficit and the infarct volume, with mismatch criteria defined according to age (<80 years or ≥80 years). Patients were randomly assigned to thrombectomy plus standard care (the thrombectomy group) or to standard care alone (the control group). The coprimary end points were the mean score for disability on the utility-weighted modified Rankin scale (which ranges from 0 [death] to 10 [no symptoms or disability]) and the rate of functional independence (a score of 0, 1, or 2 on the modified Rankin scale, which ranges from 0 to 6, with higher scores indicating more severe disability) at 90 days.

RESULTS

A total of 206 patients were enrolled; 107 were assigned to the thrombectomy group and 99 to the control group. At 31 months, enrollment in the trial was stopped because of the results of a prespecified interim analysis. The mean score on the utility-weighted modified Rankin scale at 90 days was 5.5 in the thrombectomy group as compared with 3.4 in the control group (adjusted difference [Bayesian analysis], 2.0 points; 95% credible interval, 1.1 to 3.0; posterior probability of superiority, >0.999), and the rate of functional independence at 90 days was 49% in the thrombectomy group as compared with 13% in the control group (adjusted difference, 33 percentage points; 95% credible interval, 24 to 44; posterior probability of superiority, >0.999). The rate of symptomatic intracranial hemorrhage did not differ significantly between the two groups (6% in the thrombectomy group and 3% in the control group, P=0.50), nor did

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Jovin at the University of Pittsburgh Medical Center Stroke Institute, Department of Neurology, Presbyterian University Hospital, 200 Lothrop St., C-400, Pittsburgh, PA 15217, or at jovintg@upmc.edu.

*A complete list of sites and investigators in the DAWN trial is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Nogueira and Jovin contributed equally to this article.

This article was published on November 11, 2017, at NEJM.org.

DOI: 10.1056/NEJMoa1706442

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*

ABSTRACT

BACKGROUND

Thrombectomy is currently recommended for eligible patients with stroke who are treated within 6 hours after the onset of symptoms.

METHODS

We conducted a multicenter, randomized, open-label trial, with blinded outcome assessment, of thrombectomy in patients 6 to 16 hours after they were last known to be well and who had remaining ischemic brain tissue that was not yet infarcted. Patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion, an initial infarct size of less than 70 ml, and a ratio of the volume of ischemic tissue on perfusion imaging to infarct volume of 1.8 or more were randomly assigned to endovascular therapy (thrombectomy) plus standard medical therapy (endovascular-therapy group) or standard medical therapy alone (medical-therapy group). The primary outcome was the ordinal score on the modified Rankin scale (range, 0 to 6, with higher scores indicating greater disability) at day 90.

RESULTS

The trial was conducted at 38 U.S. centers and terminated early for efficacy after 182 patients had undergone randomization (92 to the endovascular-therapy group and 90 to the medical-therapy group). Endovascular therapy plus medical therapy, as compared with medical therapy alone, was associated with a favorable shift in the distribution of functional outcomes on the modified Rankin scale at 90 days (odds ratio, 2.77; P<0.001) and a higher percentage of patients who were functionally independent, defined as a score on the modified Rankin scale of 0 to 2 (45% vs. 17%, P<0.001). The 90-day mortality rate was 14% in the endovascular-therapy group and 26% in the medical-therapy group (P=0.05), and there was no significant between-group difference in the frequency of symptomatic intracranial hemorrhage (7% and 4%, respectively; P=0.75) or of serious adverse events (43% and 53%, respectively; P=0.18).

CONCLUSIONS

Endovascular thrombectomy for ischemic stroke 6 to 16 hours after a patient was last known to be well plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion and a region of tissue

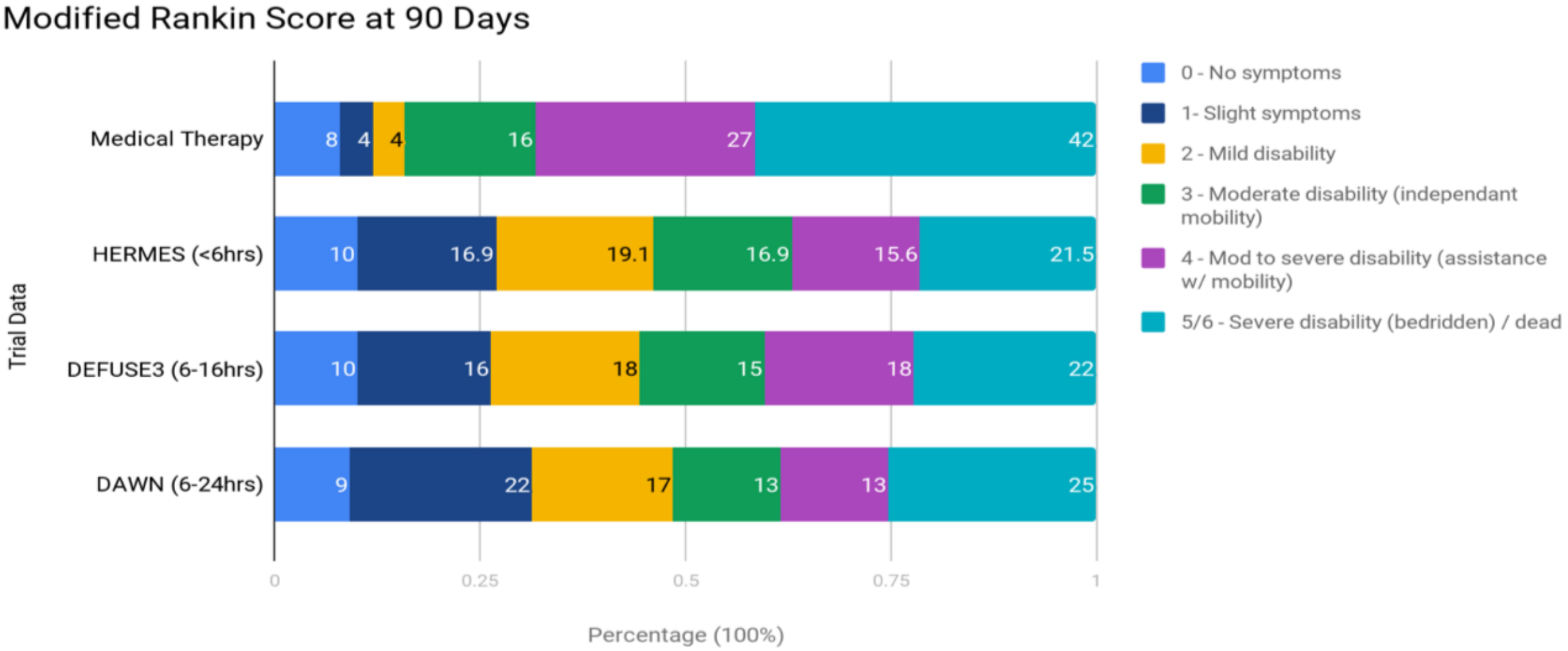
The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Albers at the Stanford Stroke Center, 780 Welch Rd., Suite 350, Palo Alto, CA 94304-5778, or at albers@stanford.edu.

*A complete list of the DEFUSE 3 investigators is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on January 24, 2018, and updated on February 16, 2018, at NEJM.org.

N Engl J Med 2018;378:708-18.
DOI: 10.1056/NEJMoa1713973

Trials in Context



Public Awareness and Organisation of Services

- FAST campaign
- London Stroke Model

FAST Campaign

- Better public awareness is key
- Now targeting ethnic minorities

London Stroke Model

- Hub and Spoke model
- 8 Hyperacute stroke units / 24 Acute stroke units
- LAS will bring patients to the nearest HASU if FAST positive
- Hugely successful to date

London Stroke Model

- Improved thrombolysis rates
- ~5% nationwide vs ~15% in London
- 30 day mortality ~ 17% nationwide versus ~7%
- Shorter hospital stays; more patients discharged straight home
- Significant cost savings: £5.2 million/year (at 90 days post-event) PLoS One 2013

Stroke Treatments in Perspective

Intervention	NNT
Stroke Units	18
Thrombolysis	4.5 – 14
Thrombectomy	3 - 7
Aspirin	83
Clopidogrel	62
Warfarin	33
Anti-Hypertensives	17
Statin	59
Carotid surgery	26

Conclusions

- Acute Stroke: Time is Brain
- Good organisation of services is imperative
- Thrombectomy is a ‘game-changer’ for stroke treatments
- Immediate priority is the delivery of 24/7 Thrombectomy service for all of London
- North West London now has comprehensive cover, with CXH currently being the largest volume thrombectomy centre in the UK
- Extension of thrombectomy time-window has significant implications

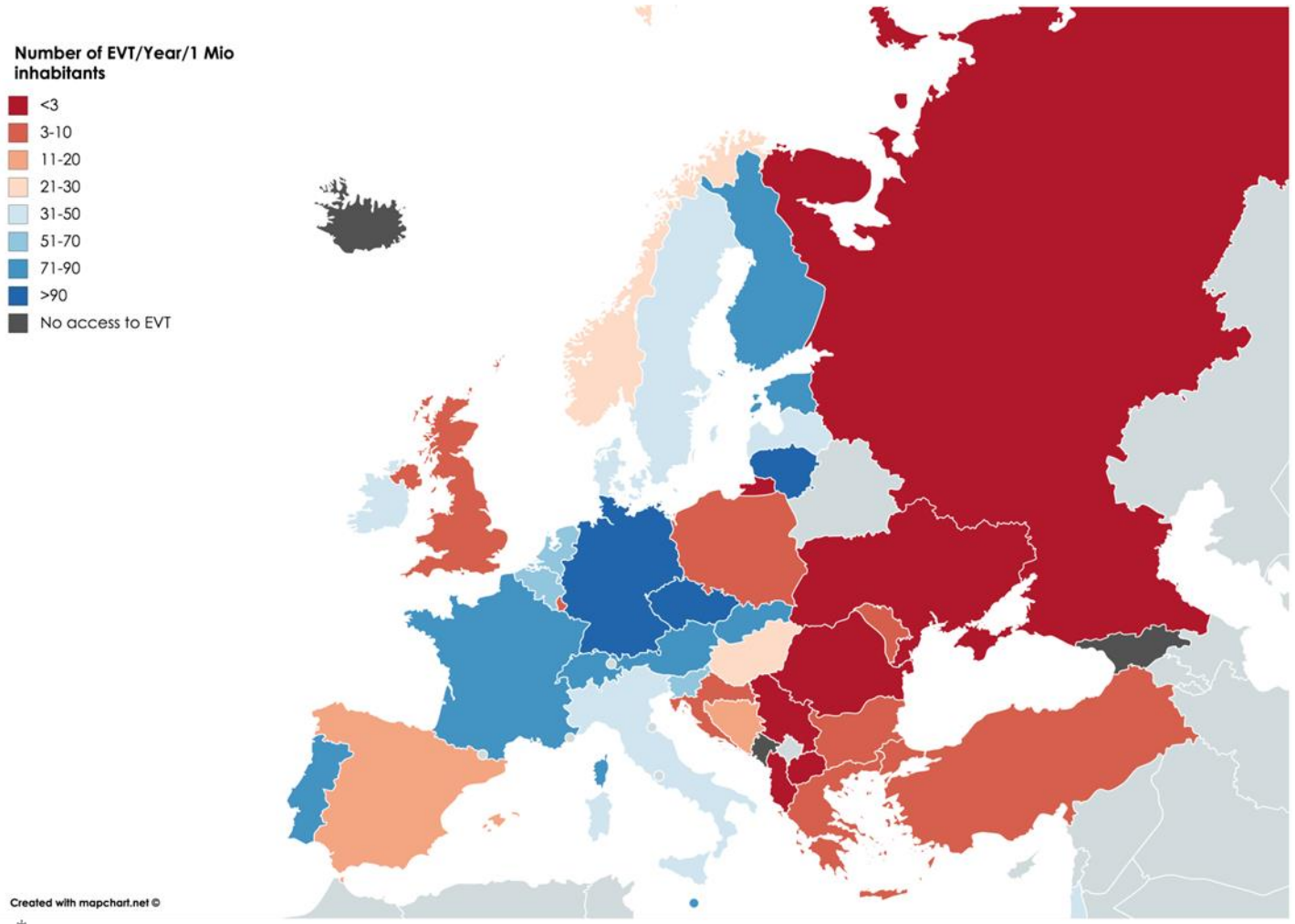

CHARING CROSS HOSPITAL
© Matt Writtle


ST MARY'S HOSPITAL
www.londonphotoproject.co.uk

Questions?


Imperial College
London
← Imperial Centre for
Translational &
Experimental Medicine

Thrombectomy in Europe



*2015