

Outcomes that matter



Gates Vascular Institute

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Disclosures

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- **National Steering Committees/PI:** Penumbra: 3D Separator Trial, COMPASS Trial, INVEST Trial; Medtronic: SWIFT DIRECT Trial; MicroVention: FRED Trial, CONFIDENCE Study; POSITIVE Trial,
- No consulting salary arrangements. All consulting is per project and/or per hour.

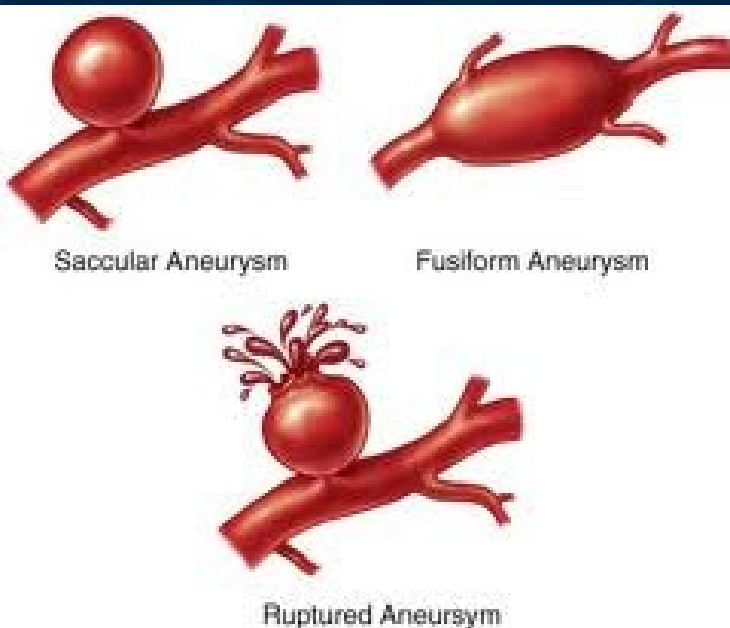
Goals of MEDCAC

- Implications of approving devices without well established evidence
- Intermediate and surrogate outcomes rather than longer term data
- Clinically meaningful health outcomes measurement instruments and follow-up durations in IDE analyses and National coverage analyses (NCAs)
- Stroke status and recurrence, hospitalization and health care resource utilization, clinician reported patient outcome and patient reported outcome measures (PROM)

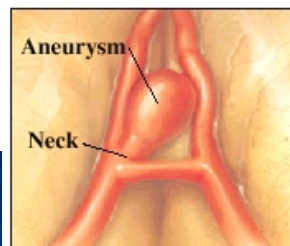
The MEDCAC panel will examine what health outcomes should be of interest to CMS in studies for cerebrovascular disease treatment with a focus on new technologies.

Food and Drug Administration (FDA) questions on safety and efficacy vs CMS focus is on health outcomes associated with the technologies

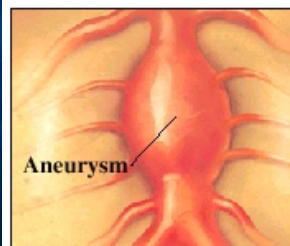
Intracranial Aneurysms



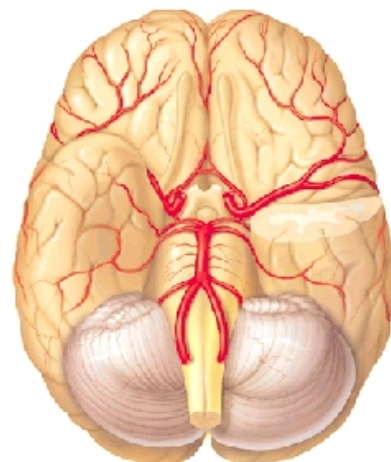
Ruptured Aneurysms
50% MORTALITY
30% SEVERE DISABILITY
20% GOOD OUTCOME at 2 years



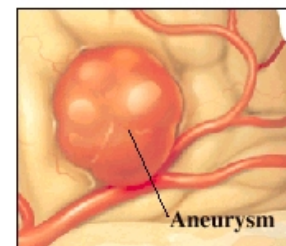
A **saccular (berry) aneurysm** bulges from one side of an artery. A neck leads to it.



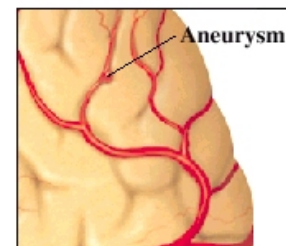
A **fusiform aneurysm** bulges from all sides of an artery. It rarely has a neck.



Using this picture, the surgeon may mark the site of the aneurysm.

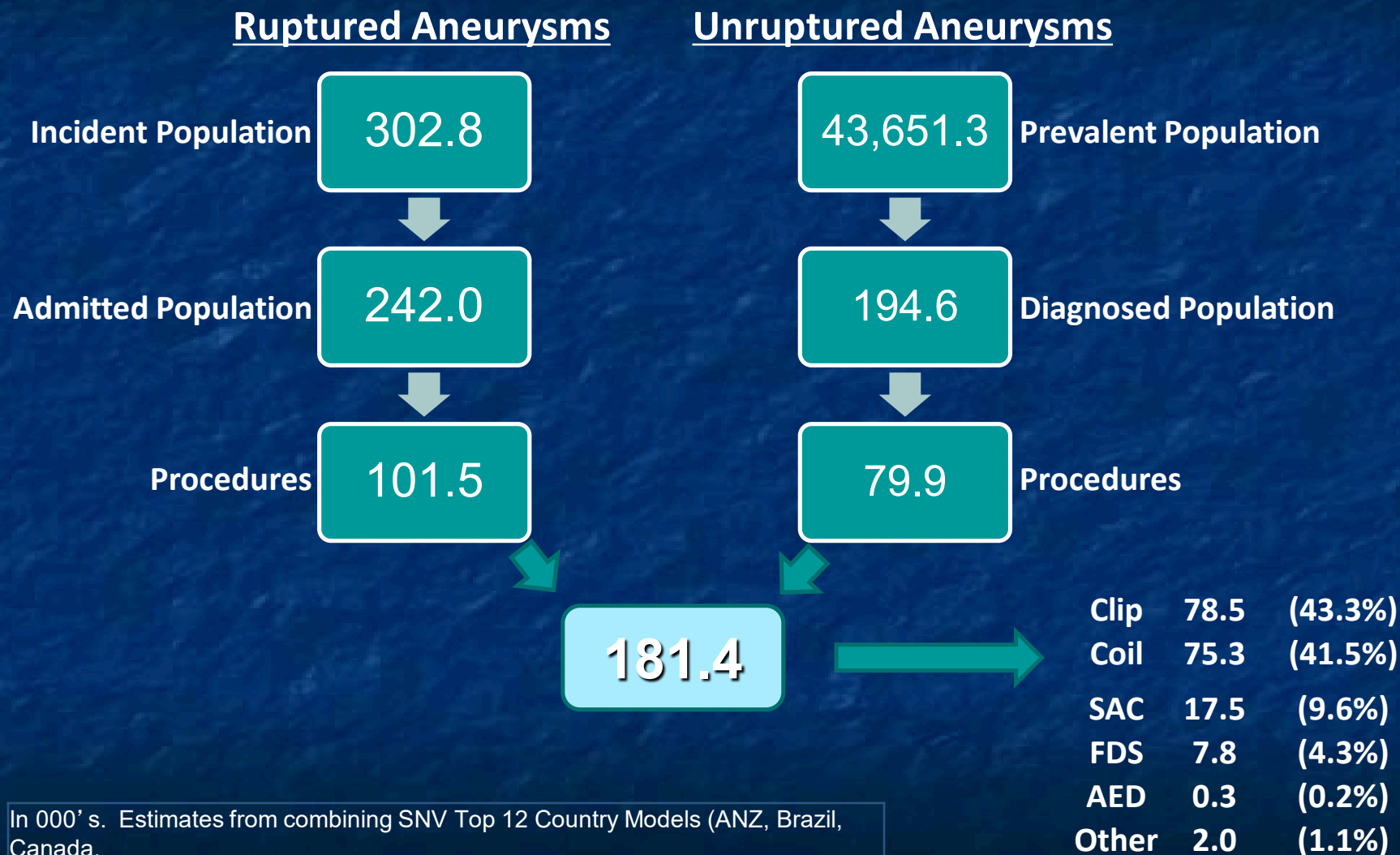


A **giant aneurysm** can involve more than one artery. It is over 2.5 centimeters (cm) wide.



A **mycotic aneurysm** is caused by an infected artery wall. This type of aneurysm is fairly rare.

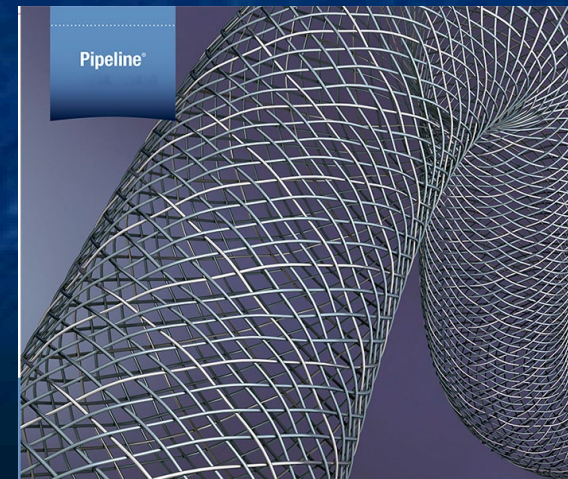
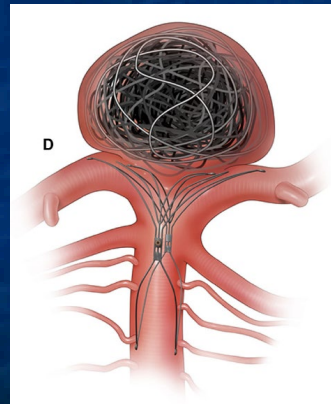
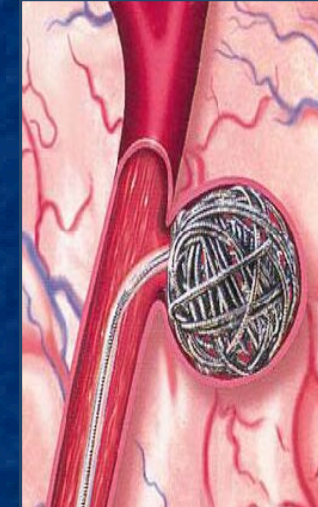
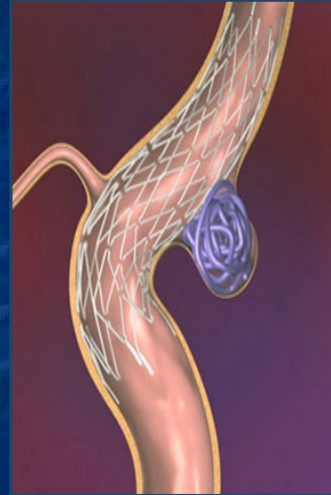
WW Aneurysm Treatment Population



In 000' s. Estimates from combining SNV Top 12 Country Models (ANZ, Brazil, Canada, China, Japan, Korea, France, Germany, Italy, Spain, US and UK, as of May, 2015)

Conventional Therapy

- Open Surgical Techniques
 - Clipping seals aneurysm to exclude it
 - Bypass/parent artery exclusion
- Endovascular
 - Bare metal and bioactive coils
 - Aneurysm bridging stent
 - Liquid embolics
 - Parent artery occlusion
 - Stent assisted Coiling
 - Flow Diversion
 - Endosaccular Devices



WEB (Sequent) Concept

- ✦ Intrasaccular
- ✦ Microcatheters 0.027 for device ≤ 7 mm to 0.032 compatible for device > 7 mm
- ✦ Two layers of Nitinol mesh (216 or 288 wires)
- ✦ 3 platinum markers
- ✦ Retrieval and detachable
- ✦ CE marked



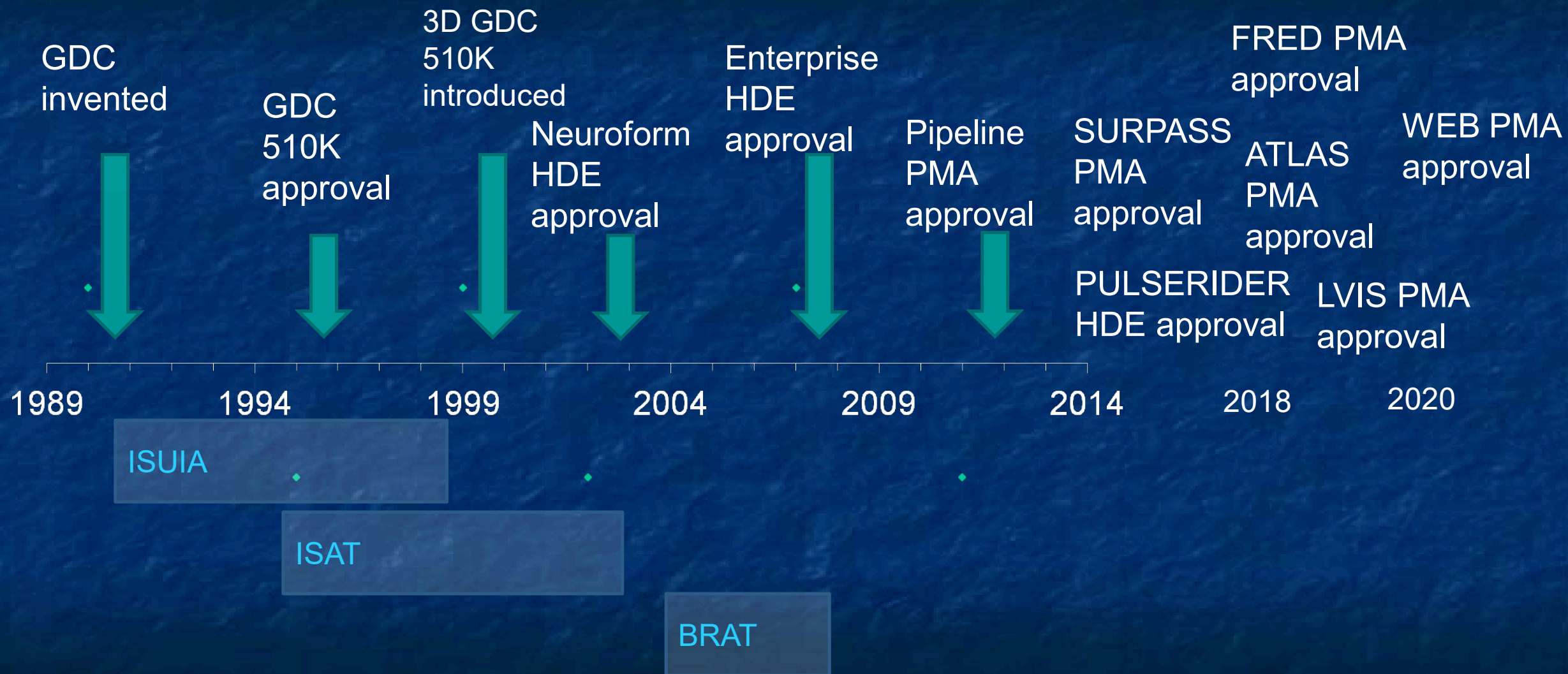
Aneurysm endovascular technology timeline

COILS

STENTS

FLOW DIVERSION

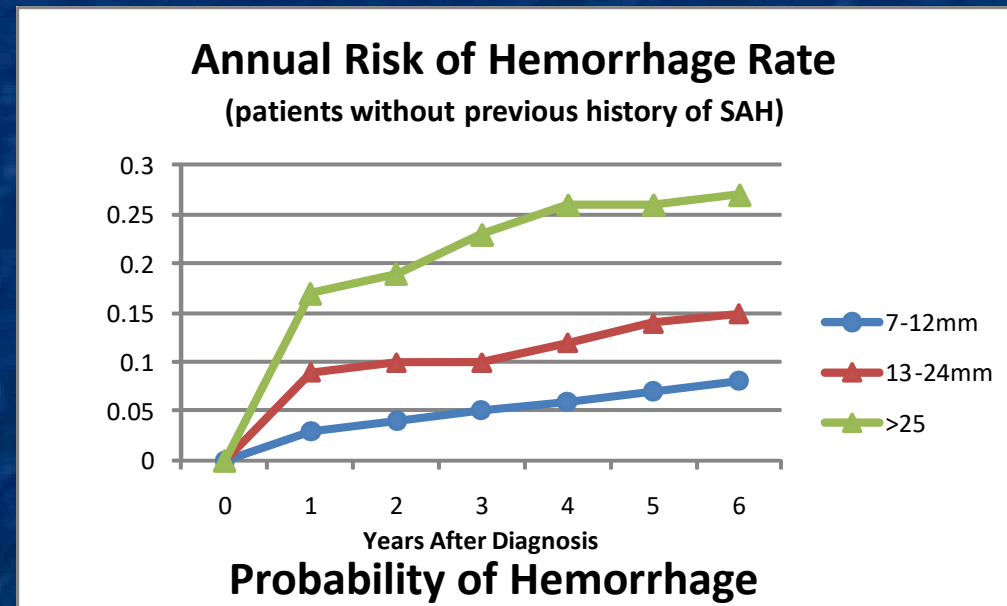
ENDOSACCULAR



Natural History

Large/Giant Size and Aspect Ratio have been identified as statistically significant predictors of subarachnoid hemorrhage (SAH) in multicenter trials.

- ISUIA data suggest that aneurysms >10mm are at critical risk for rupture
- Aneurysms ≥ 25 mm had a 0.17 probability of rupture rate in first year in patients with no prior history of SAH



Source:

3. The International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured Intracranial Aneurysms – Risk of Rupture and Risks of Surgical Intervention. *Neuroradiology*. N Engl J Med 1998; 339:1725-1733

ISAT Lancet 2002

- Patients with ruptured aneurysms deemed **equally suitable for coiling or clipping** enrolled between 1994-2002
- Prospective RCT
 - **22.4% randomized** (2143/9559)
 - 88% WFNS grade I-III
 - small anterior circulation aneurysms (<11mm)
 - 50.5% ACoA
 - 32.5% distal ICA
- 191/801 (23.7%) patients treat with coiling were dead or dependent at 1 year compared to 243/793 (30.6%) of patients treated with clipping (p=0.0019)
- ARR 6.9% and RR reduction of 22.6%

Retreatment

17.4% (191/1096) of coiled aneurysms

46% re-coiled, 54% operated

3.8% (39/1012) of clipped aneurysms

10% re-operated, 90% coiled

Retreatment 4x more likely with coil

Late retreatment 7x more likely with coil

considered a surrogate for recurrence

Retreatment did not cause significant additional morbidity

EVT rebleed latency = 12-68 months

NST rebleed latency = 3 months

Molyneux 2009 Long-term follow-up in ISAT

Mean follow-up = 9 years (6-14 years)

24 rebleeds more than 1 year following treatment

13 from treated aneurysm

10 coil

3 clip

6 de novo

4 pre-existing

1 uncertain

17/24 in coiled group, 7/24 in clipped group

17 endovascular rebleeds (2-5 years)

10 from treated aneurysm

3 dead, 2 disabled, 5 re-treated and independent

3 from de novo

3 from pre-existing

1 uncertain

7 surgical rebleeds (4-7 years)

3 from treated aneurysm

all died

1 rebleed actually a cross-over to GDC;

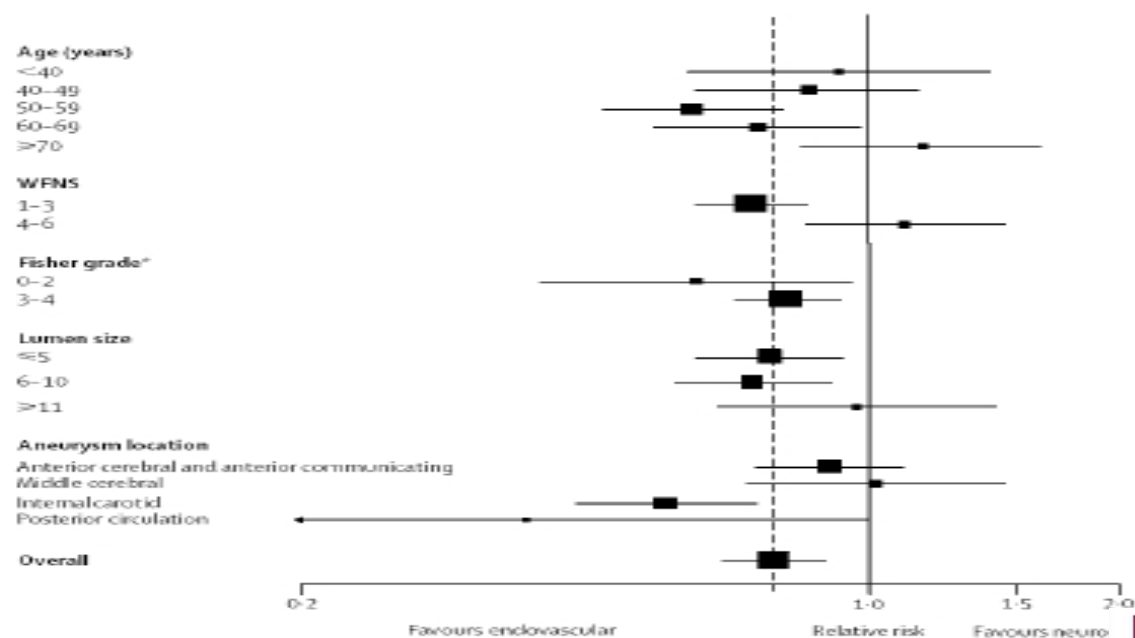
visual confirmation at surgery only for other 2

3 from de novo

1 from pre-existing

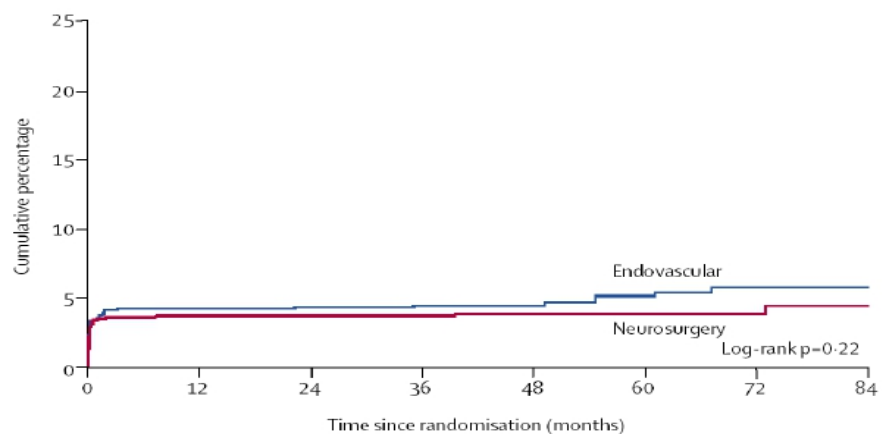
Proportion of patients with mRS < 2, conditional on 5 year survival is 83% (coil) vs. 82% (clip)

Non-significant increased risk for late rebleed from treated aneurysm in coil cohort by intention-to-treat, but significant difference when analyzed by actual treatment-received. No difference in mortality rate for rebleeds



* Fisher grade is a measure of the amount of blood on the CT scan.

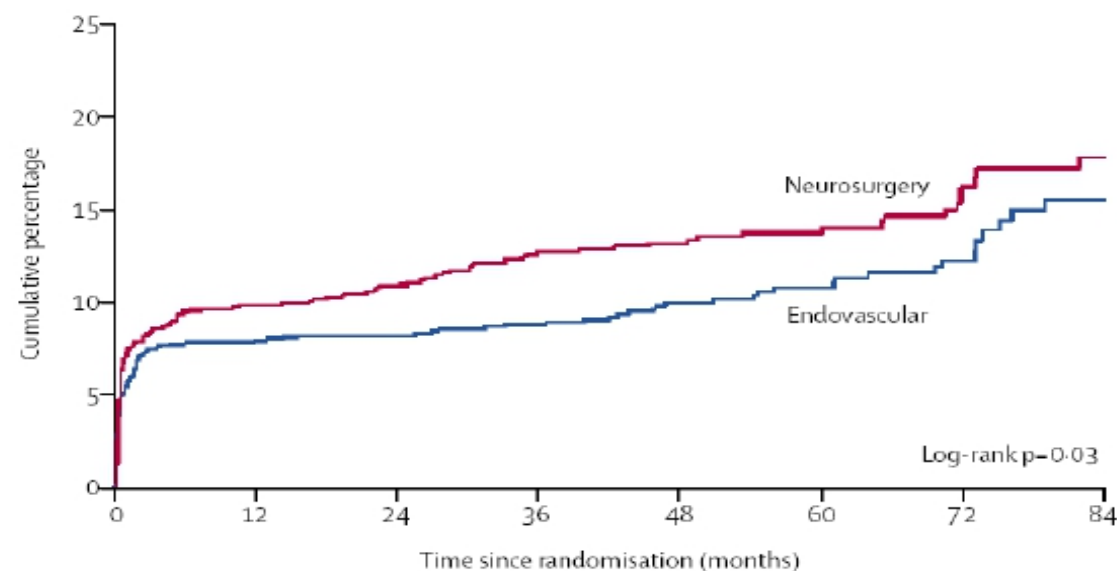
Risk ratio (95% CI)	Number of events		Test of interaction
	Endovascular	Neurosurgery	
0.91 (0.59, 1.39)	34/186	35/174	p=0.04
0.83 (0.61, 1.14)	57/266	67/261	
0.60 (0.47, 0.78)	71/352	121/362	
0.73 (0.55, 0.98)	54/198	72/194	
1.15 (0.82, 1.61)	34/61	31/64	
0.71 (0.61, 0.83)	208/999	291/996	p=0.01
1.11 (0.84, 1.46)	42/64	35/59	
0.61 (0.39, 0.94)	28/245	44/234	p=0.3
0.79 (0.68, 0.92)	222/818	282/821	
0.76 (0.61, 0.93)	137/549	158/560	p=0.4
0.71 (0.57, 0.89)	101/431	139/423	
0.96 (0.65, 1.42)	32/83	29/72	
0.89 (0.73, 1.09)	131/533	147/534	p=0.01
1.01 (0.71, 1.45)	46/162	39/139	
0.56 (0.43, 0.72)	69/344	125/348	
0.38 (0.14, 1.00)	4/24	15/34	
0.76 (0.66, 0.87)	250/1063	326/1055	



Annual number at risk (rebleeding):

	1073 (45)	953 (1)	865 (1)	698 (0)	524 (3)	360 (2)	201 (0)	98
Endovascular	1073 (45)	953 (1)	865 (1)	698 (0)	524 (3)	360 (2)	201 (0)	98
Neurosurgery	1070 (39)	926 (0)	821 (0)	652 (1)	495 (0)	332 (0)	188 (1)	95

Figure 3: Cumulative rebleeding risk from target aneurysm



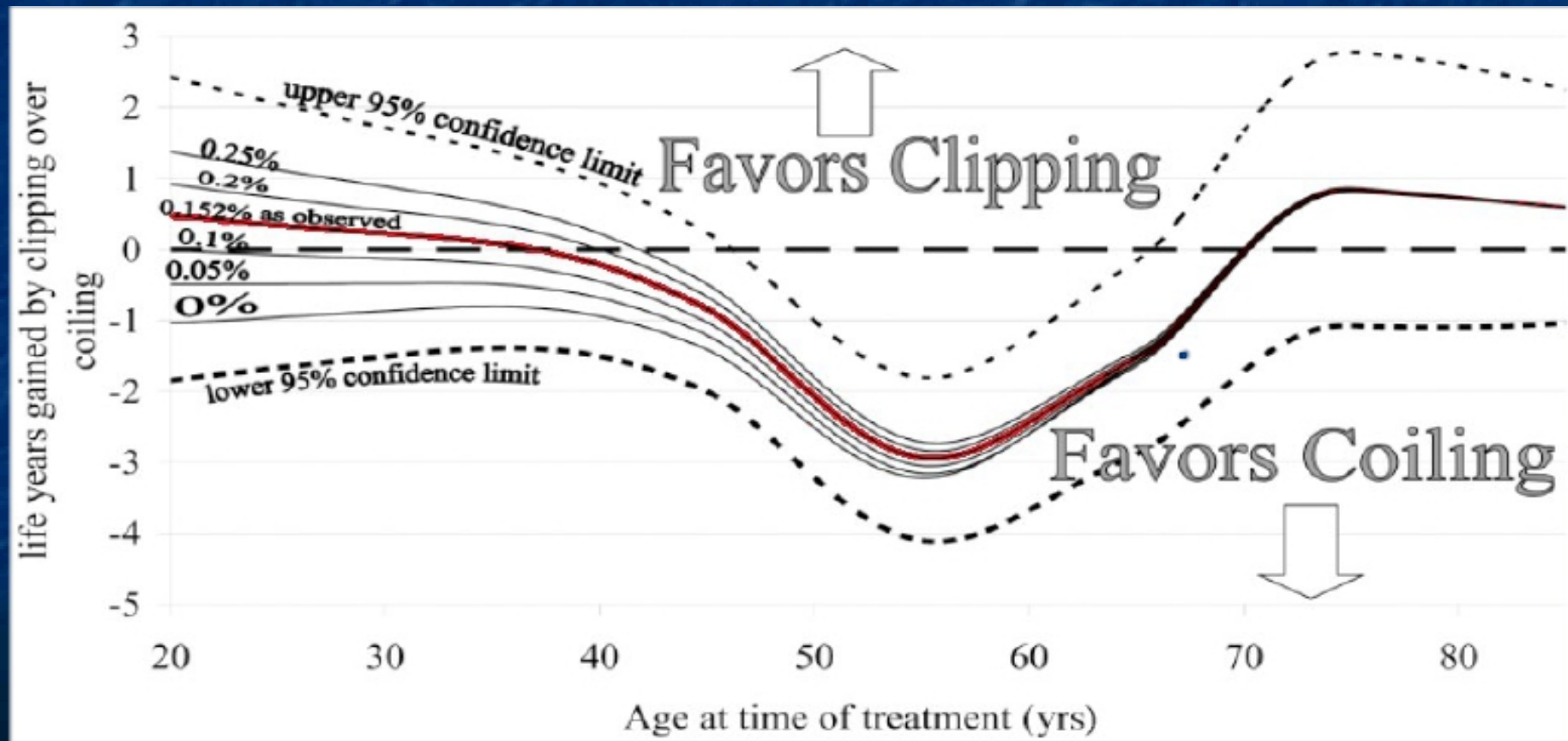
Annual number at risk (deaths):

	1073 (85)	974 (3)	887 (5)	717 (8)	541 (4)	373 (5)	215 (6)	103
Endovascular	1073 (85)	974 (3)	887 (5)	717 (8)	541 (4)	373 (5)	215 (6)	103
Neurosurgery	1070 (105)	944 (10)	842 (16)	663 (3)	503 (3)	340 (7)	192 (3)	98

Figure 2: Kaplan Meier cumulative mortality to 7 years

Could late rebleeding overturn the superiority of cranial aneurysm coil embolization over clip ligation seen in the International Subarachnoid Aneurysm Trial

Mitchell, et al. *J Neurosurgery* 108:437-42, 2008.



International Study of Unruptured Intracranial Aneurysms

Is treating an unruptured aneurysm clinically beneficial?

Retrospective arm analyzed 1449 patients to assess
natural history of UIA

ISUIA I

NEJM 339: 1725-33, 1998

Group I (727 pts with no prior SAH)

ISUIA II

Lancet 362: 103-110, 2003

<10mm	0.05% risk annually
10-24mm	1% risk annually
>25mm	6% risk in first year

Group II (722 pts with prior SAH)

<10mm	0.5% risk annually
>10mm	1% risk annually

Prospective arm analyzed 1172 patients to assess the risk of treatment of UIA

961 Group I (83% surgery)

211 Group II (94% surgery)

Higher morbidity and mortality (endo/surgical) from treatment than previously recognized*

30 day M&M 13.6 -17.5%

1 year M&M 13.1-15.7%

Age was the only predictor of poor outcome. M&M exceeded the 7.5 yr risk of rupture in group I patients with aneurysms smaller than 10mm

<45 yr 6.5%

45-65 yr 14.4%

>65 yr 32%

*mRS 3-5; Mini Mental State Examination <24; Telephone Interview for Cognitive Status <27.
Impaired mental status added substantially to morbidity

ISUIA II

- *Prospective observational* cohort study
- December 1991- 1998
- 4060 patients enrolled
 - 1692 natural history*
 - 1917 surgical clip
 - 451 endovascular

*mean follow-up of 4.1 years (SD=2.0) for 6544 patient years. 727 patients removed from follow-up (534 who were treated and 193 who died).

Investigator decided whether to enroll patient into conservative or treatment arm.

ISUIA 5-year cumulative rate of rupture

<u>Size</u>	<u>ICA, MCA, ACoA</u>	<u>PCoA, basilar apex</u>
<7 mm	0	2.5%
7-12 mm	2.6%	14.5%
13-24 mm	14.5%	18.4%
>24 mm	40%	50%

The Barrow Ruptured Aneurysm Trial

Clinical article

**CAMERON G. McDOUGALL, M.D.,¹ ROBERT F. SPETZLER, M.D.,¹ JOSEPH M. ZABRAMSKI, M.D.,¹
SHAHRAM PARTOVI, M.D.,² NANCY K. HILLS, PH.D.,³ PETER NAKAJI, M.D.,¹
AND FELIPE C. ALBUQUERQUE, M.D.¹**

Results. One year after treatment, 403 patients were available for evaluation. Of these, 358 patients had actually undergone treatment. The remainder either died before treatment or had no identifiable source of SAH. A poor outcome (mRS score > 2) was observed in 33.7% of the patients assigned to aneurysm clipping and in 23.2% of the patients assigned to coil embolization (OR 1.68, 95% CI 1.08–2.61; $p = 0.02$). Of treated patients assigned to the coil group, 124 (62.3%) of the 199 who were eligible for any treatment actually received endovascular coil embolization. Patients who crossed over from coil to clip treatment fared worse than patients assigned to coil embolization, but no worse than patients assigned to clip occlusion. No patient treated by coil embolization suffered a recurrent hemorrhage.

Conclusions. One year after treatment, a policy of intent to treat favoring coil embolization resulted in fewer poor outcomes than clip occlusion. Although most aneurysms assigned to the coil treatment group were treated by coil embolization, a substantial number crossed over to surgical clipping. Although a policy of intent to treat favoring coil embolization resulted in fewer poor outcomes at 1 year, it remains important that high-quality surgical clipping be available as an alternative treatment modality. (DOI: 10.3171/2011.8.JNS101767)

The Barrow Ruptured Aneurysm Trial: 3-year results

Clinical article

**ROBERT F. SPETZLER, M.D.,¹ CAMERON G. McDOUGALL, M.D.,¹
FELIPE C. ALBUQUERQUE, M.D.,¹ JOSEPH M. ZABRAMSKI, M.D.,¹ NANCY K. HILLS, PH.D.,^{2,3}
SHAHRAM PARTOVI, M.D.,⁴ PETER NAKAJI, M.D.,¹ AND ROBERT C. WALLACE, M.D.⁴**

Conclusions. Based on mRS scores at 3 years, the outcomes of all patients assigned to coil embolization showed a favorable 5.8% absolute difference compared with outcomes of those assigned to clip occlusion, although this difference did not reach statistical significance ($p = 0.25$). Patients in the clip group had a significantly higher degree of aneurysm obliteration and a significantly lower rate of recurrence and retreatment. In post hoc analysis examining only anterior circulation aneurysms, no outcome difference between the 2 treatment cohorts was observed at any recorded time point. Clinical trial registration no.: NCT01593267 (ClinicalTrials.gov).

Barrow Ruptured Aneurysm Trial

- 500 eligible patients with SAH
 - 2000-2007, 725 pts screened
- Alternately assigned (last 100 random) 238 clip, 233 coil
- Cross-over was allowed
 - 75 crossed-over to surgery, 4 to coiling
- Primary outcome based on intent-to-treat (right of first refusal). Therefore, one treatment modality could not benefit by crossing over poor-grade patients
- 403 available at 1 year. 358 had undergone treatment

- Poor outcome (mRS 3-6) in ‘intent to treat’ group
 - 33.7% assigned to clip
 - 23.2% assigned to coil (37.7% were switched to surgery)
- Actual treatment
 - 33.9% poor outcome with surgery
 - 20.4% poor outcome with coil
 - Absolute difference = 13.5% *favoring GDC*
- No recurrent hemorrhage in GDC group

- 1996-1998, 1001 patients (9 centers), mean 4 yr f/u
- Risk for rerupture **correlated to degree of occlusion**
 - 1.1% with complete occlusion
 - 2.9% with 91-99% occlusion
 - 5.9% with 70-90% occlusion
 - 17.7% with <70% occlusion
- Higher risk for rerupture with **coiling**
 - 3.4% with coiling
 - 1.3% with surgery
- Risk of rerupture **diminished over time**
 - 1.8% during first year (95%, one-half within first 3 days)
 - After one year, 0.11% with coil and none with surgery
 - Long term follow up necessary due to compaction, etc.



Size of ruptured intracranial aneurysms: a systematic review and meta-analysis

Muhammad Waqas^{1,2} • Felix Chin^{1,2} • Hamidreza Rajabzadeh-Oghaz^{3,4} • Andrew D. Gong^{1,2} • Hamid H. Rai^{1,2} • Maxim Mokin⁵ • Kunal Vakharia^{1,2} • Rimal H. Dossani^{1,2} • Hui Meng^{2,3,4} • Kenneth V. Snyder^{1,2,3,6,7} • Jason M. Davies^{1,2,3,7,8} • Elad I Levy^{1,2,3,7,9} • Adnan H Siddiqui^{1,2,3,7,9}

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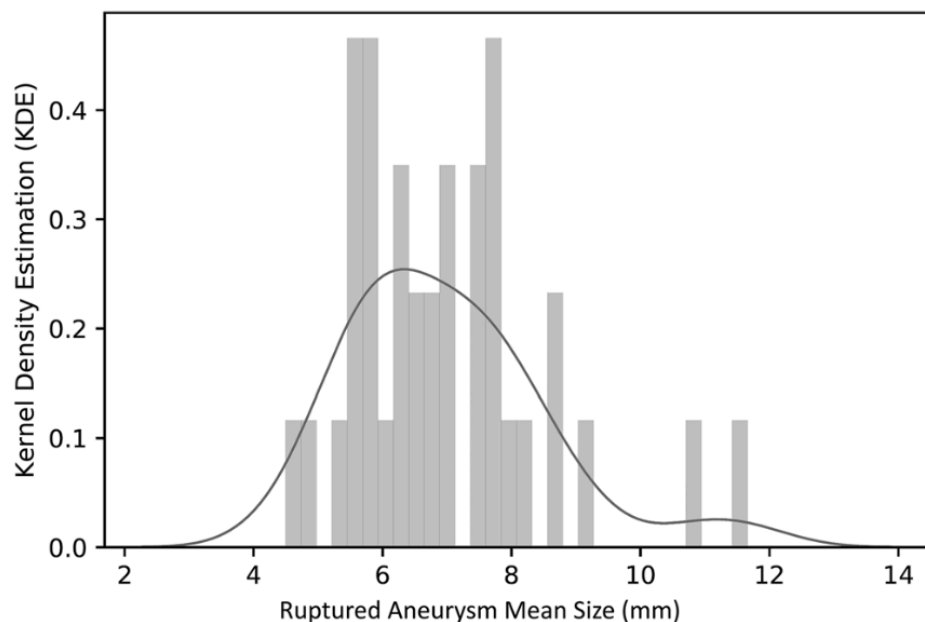
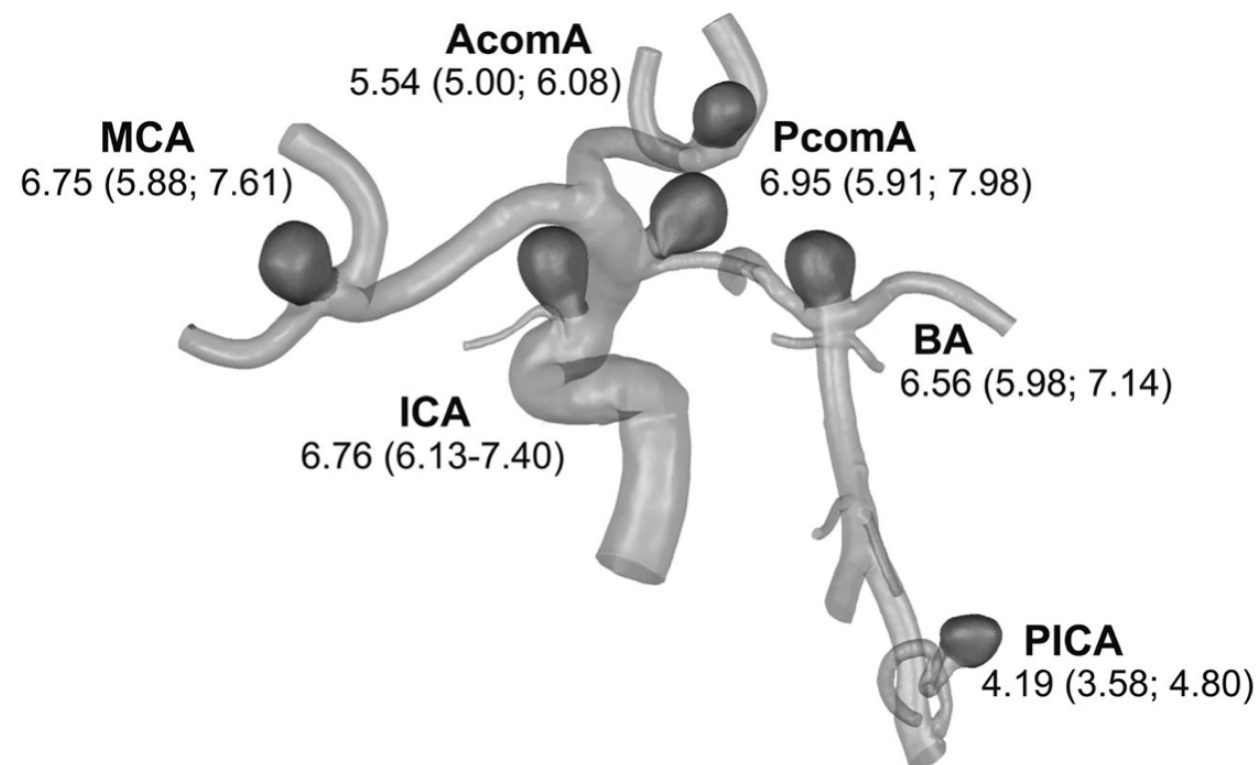


Fig. 2 Histogram displaying mean size of ruptured aneurysms in studies included in the meta-analysis. Kernel density estimates indicate that most studies reported a mean size of < 7 mm as the curve is shifted towards the left



Unruptured Aneurysms

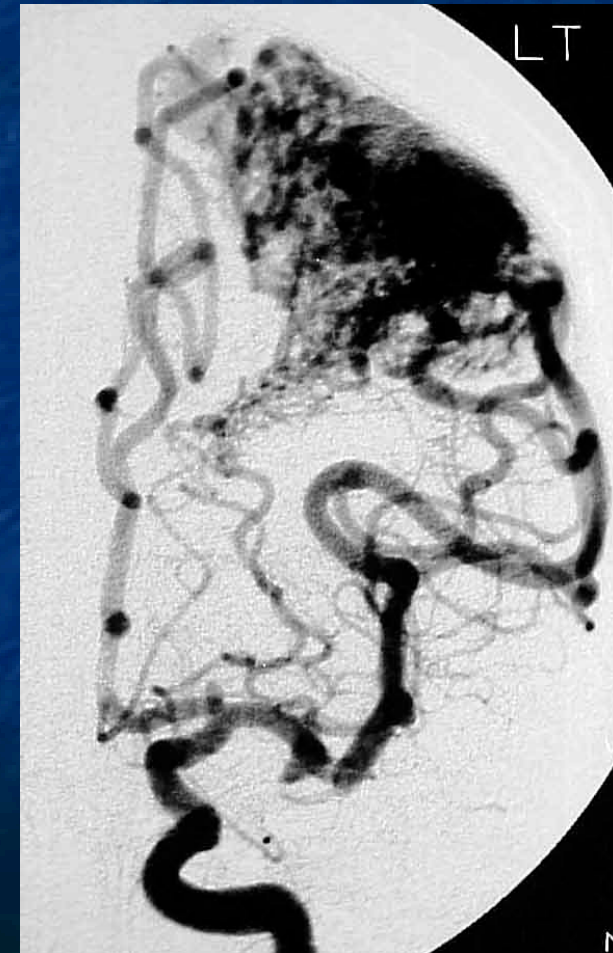
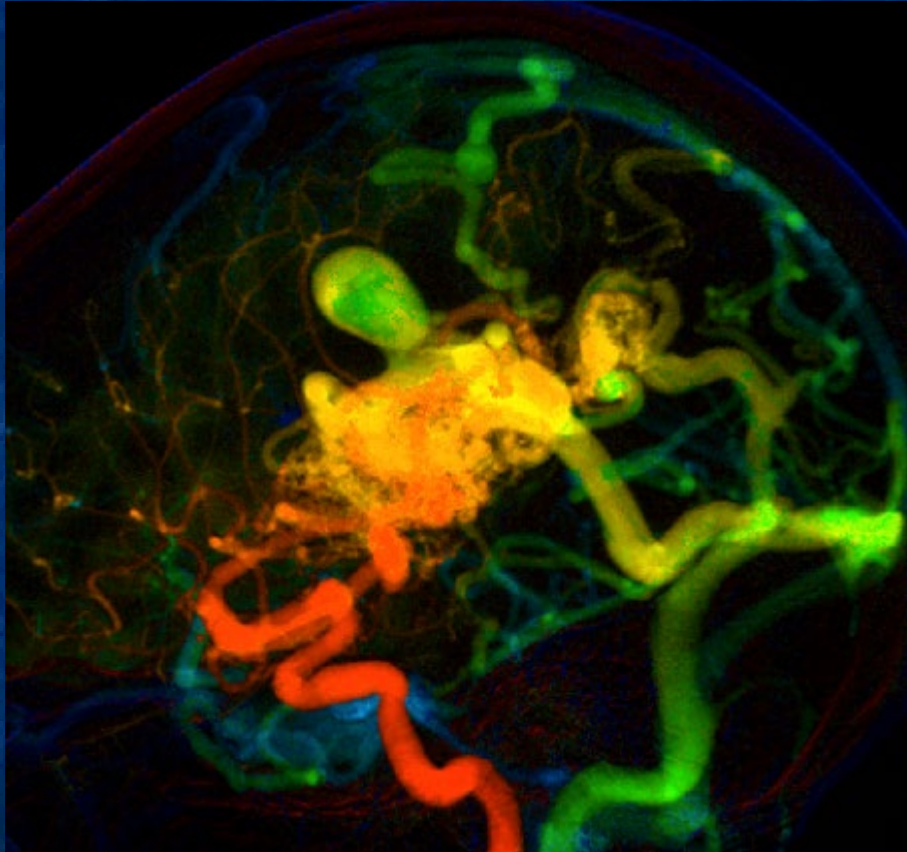
- Rupture Risk Assessment UIATS score, PHASES score
- Complication Rate –HDE, PMA approvals
- Angiographic Cure rate – Raymond Roy Score
- Hemorrhage Rate – Exceeding Low
- Retreatment Rate – Highest w coils alone lowest with Flow Diversion

Ruptured Aneurysms

- Complication Rate HDE, PMA approvals
- Angiographic Cure Rate – Raymond Roy
- Rehemorrhage Rate – Exceedingly low
- Retreatment Rate – Moderate esp with coils

AVMs

- 1 / 10 as common as An.
- Thin and thick walled channels of connected arteries to veins w/o capillary beds
- 15% in posterior fossa
- No intervening normal brain
- 2 to 4 % bleeding risk / year
 - Increased risk if: small, periventricular, deep drainage, intranidal an, venous outflow obstruction



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Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial

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[Claudia S Moy, PhD](#) • [Jessica R Overbey, MS](#) • et al. [Show all authors](#) • [Show footnotes](#)

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Check for updates

Medical Therapy

- Irrespective of randomisation assignment, i.e., all participants receive pharmacological therapy for existing medical disorders (eg, seizures, headaches) or any coexisting vascular risk factors (diabetes, arterial hypertension) as needed.
- Patients in the medical management group who reach the primary endpoint (ie, who develop a symptomatic stroke) related to their brain arteriovenous malformation become candidates for the same interventional options as those randomised to the interventional therapy group but **do not count as crossovers**.
- Cross over considered if the reason for intervention was other than stroke related to their brain arteriovenous malformation.

Interventional therapy

- For patients allocated to the interventional therapy group, interventional therapy includes **ANY neurosurgical, endovascular, or radiotherapy procedure (single or multiple)** deemed appropriate by local ARUBA investigators to achieve complete eradication of the brain arteriovenous malformation
- All patients who switch from interventional therapy to medical management after randomization are defined as crossovers.

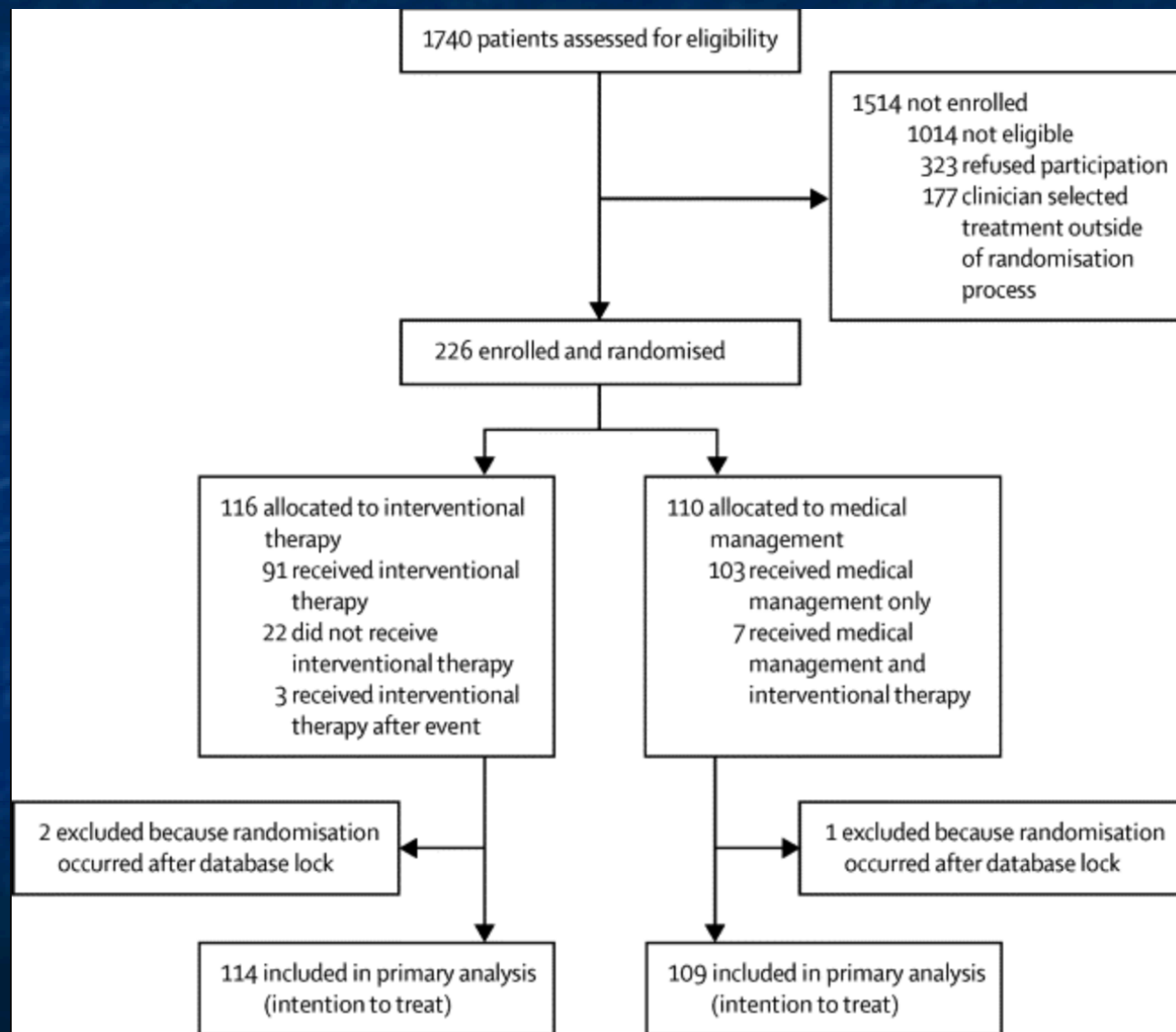
Outcomes

- The primary outcome is time to the composite event of death from any cause or symptomatic stroke.
- The secondary outcome is clinical impairment **at 5 years** with a modified Rankin scale score of 2 or higher

Analysis

- Target sample size of 400 was approved by NIH/NINDS
- Assumed event rate for medical arm was 12% vs 22% in interventional arm, power 80%

Patient Selection in ARUBA



Results

- A total of 223 patients had been enrolled in the trial, with a mean follow-up of approximately **33.3 months**.
- The primary outcome was seen in **11 (10.1%)** of the 109 patients assigned to the medical group and in **35 patients (30.7%)** of the 114 patients assigned to the intervention group

Natural History- ARUBA

- For patients followed up without interventional therapy, ARUBA confirms a low spontaneous rupture rate of 2·2% per year (95% CI 0·9–4·5). These natural history data corroborate earlier reports, even those from cohorts including cases having bled, and our secondary analyses argue against a predictive spontaneous haemorrhage effect from the Spetzler-Martin Grade.

The NASSAU (New ASSEssment of cerebral Arteriovenous Malformations yet Unruptured) Analysis: Are the Results From The ARUBA Trial Also Applicable to Unruptured Arteriovenous Malformations Deemed Suitable for Gamma Knife Surgery?

OBJECTIVE: To confirm or repudiate the ARUBA conclusion that “medical management only is superior to medical management with interventional therapy for unruptured brain arteriovenous malformations.”

METHODS: Data were collected from 1351 patients treated with Gamma Knife Surgery (GKS; Elekta AB, Stockholm, Sweden) for unruptured and untreated AVMs. The follow-up was 8817 yr (median 5.0 and mean 6.5). The results of the analyses were compared to that found in patients randomized to medical management only in the ARUBA trial and extrapolated to a 10-yr time period. Our data were also compared to the natural course in a virtual AVM population for a 25-yr time period.

RESULTS: The incidence of stroke was similar among ARUBA and our patients for the first 5 yr. Thereafter, the longer the follow-up, the relatively better outcome following treatment. Both the mortality rate and the incidence of permanent deficits in patients with small AVMs were the same as in untreated patients for the first 2 to 3 yr after GKS, after which GKS patients did better. Patients with large AVMs had a higher incidence of neurological deficits in the first 3 yr following GKS. The difference decreased thereafter, but the time until break even depended on the analysis method used and the assumed risk for hemorrhage in patent AVMs.

How does Gamma Knife compare with no treatment over extended follow up

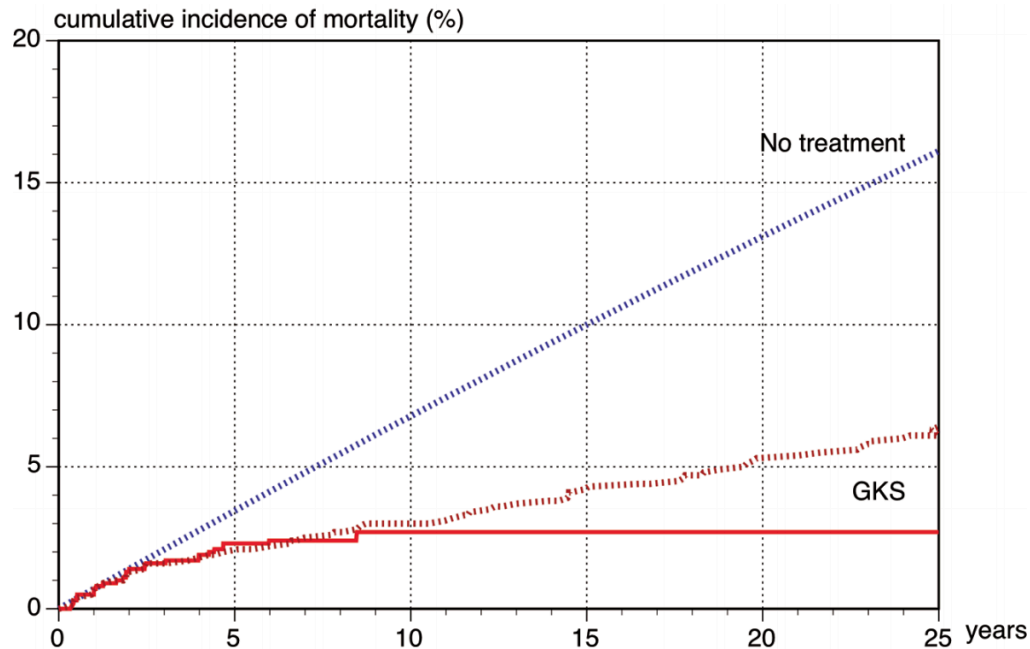


FIGURE 2. Cumulative hemorrhagic mortality rates. The filled red line shows actual data in our patient population while the dotted lines represent the assumption of an annual mortality risk of 0.7% in AVMs not proven to be obliterated. The blue line (no treatment) shows the expected cumulative mortality rate in an untreated (virtual) patient population.

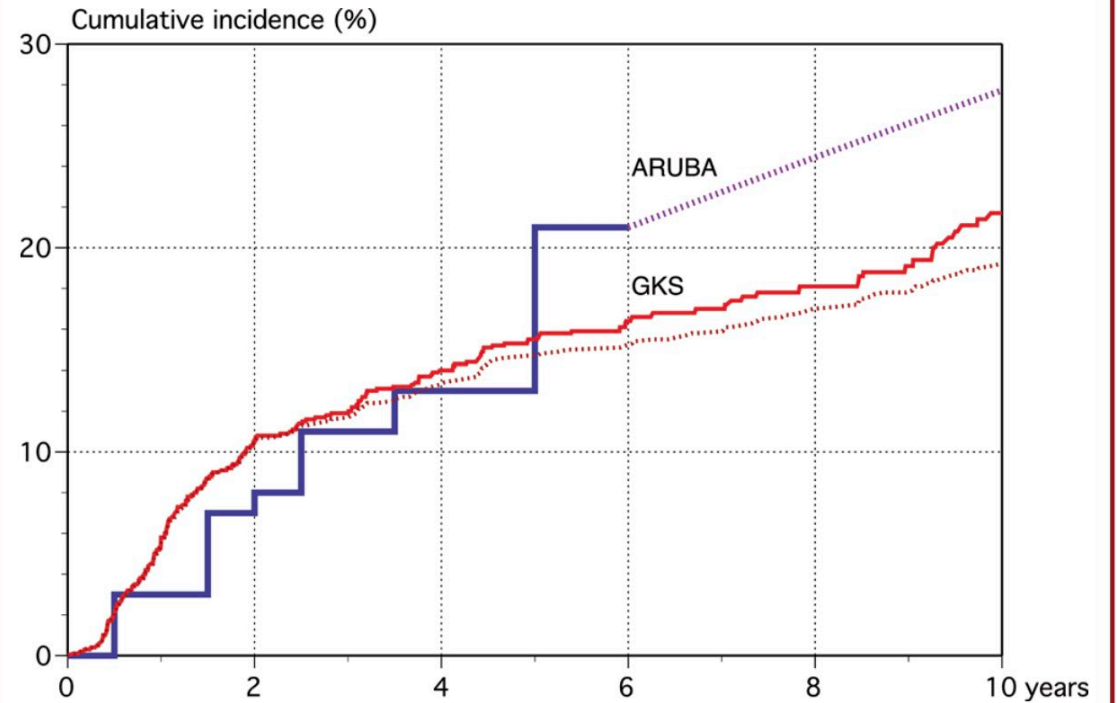


FIGURE 1. Cumulative incidence of strokes in the ARUBA patients randomized to no treatment (blue line) and UE in our patient population (GKS red line). The filled lines represent actual data and the dotted lines the results when using the assumptions of a 0% risk for hemorrhages in obliterated AVMs and a 2.2% risk in the other.

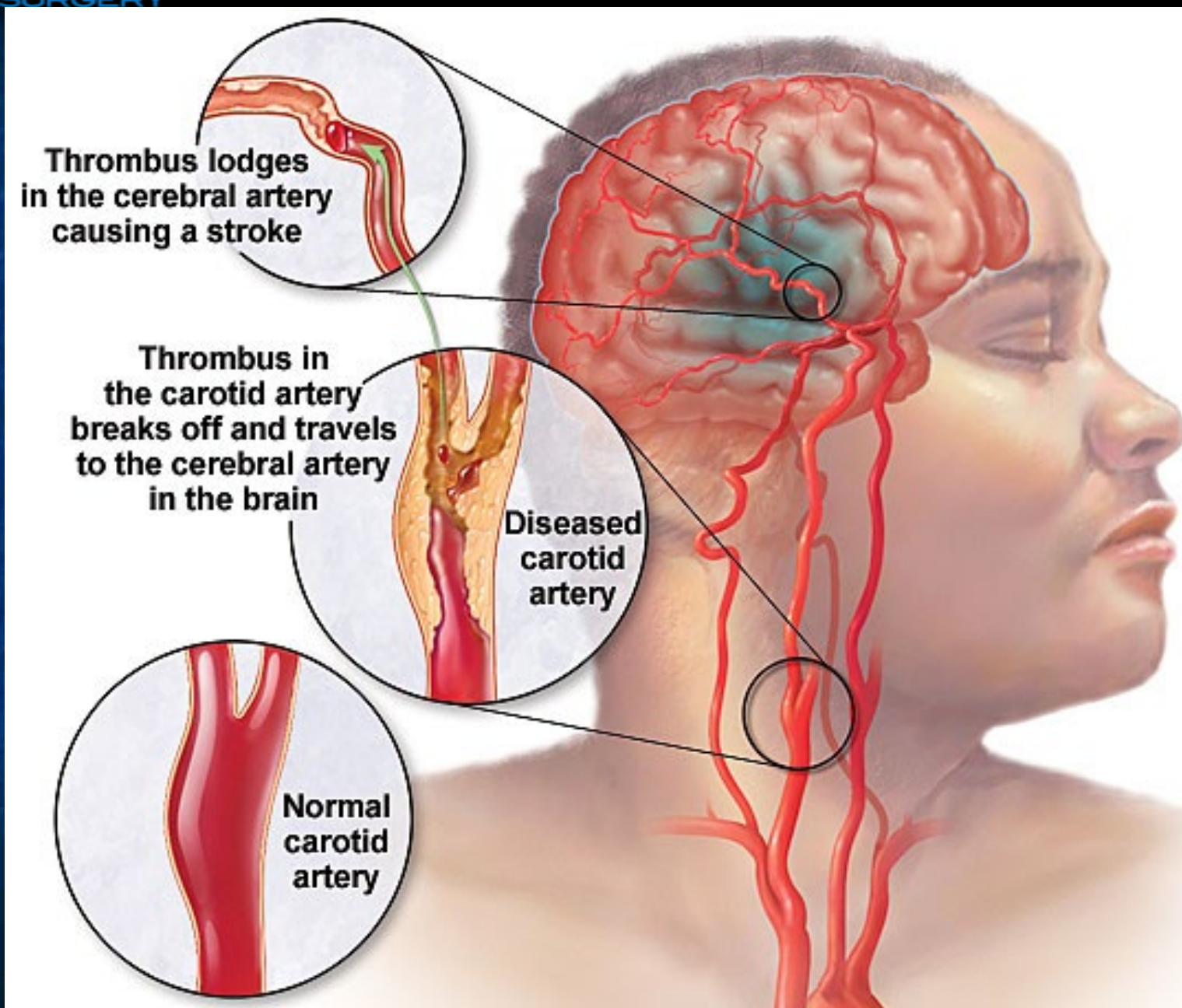
Ruptured AVMs and Fistulae

- Complication Rate
- Angiographic Cure rate
- Rehemorrhage rate
- Retreatment Rate

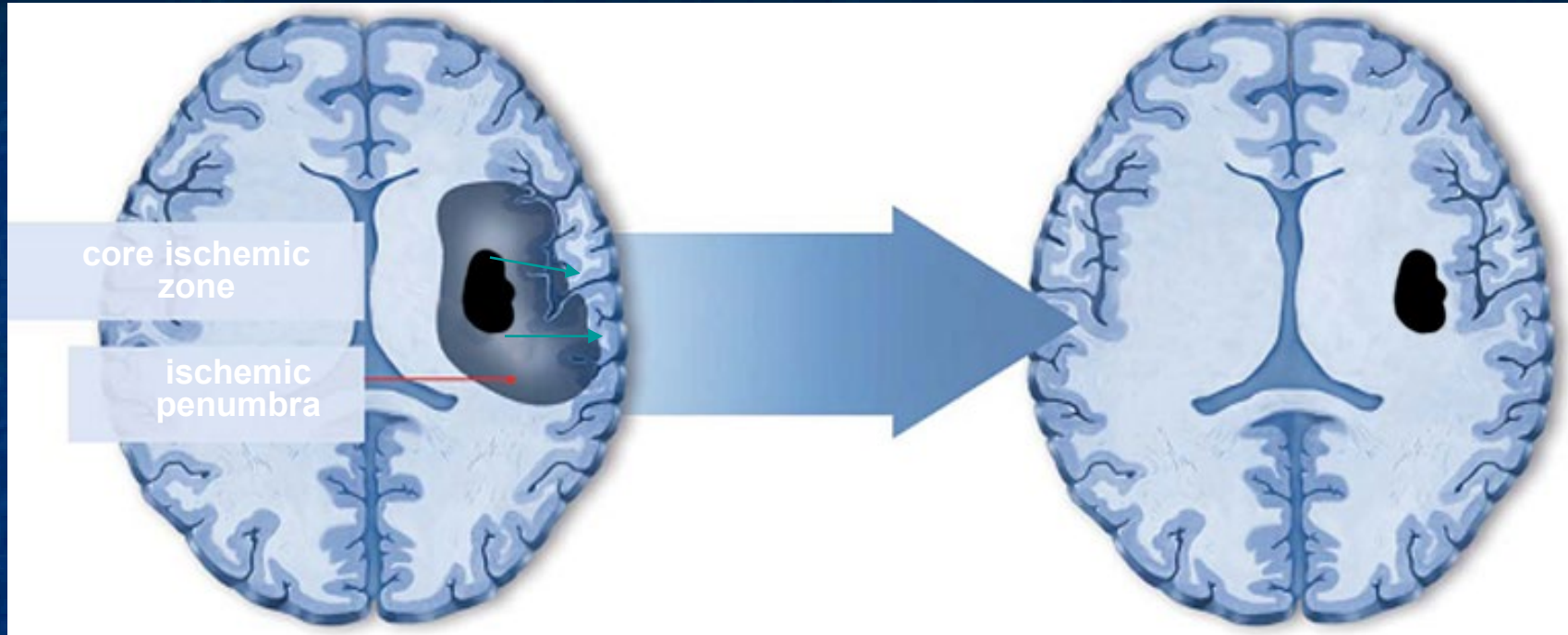
Unruptured AVM & Fistulae

- Complication Rate
- Angiographic Cure rate
- Hemorrhage rate
- Retreatment Rate

Acute Ischemic Stroke

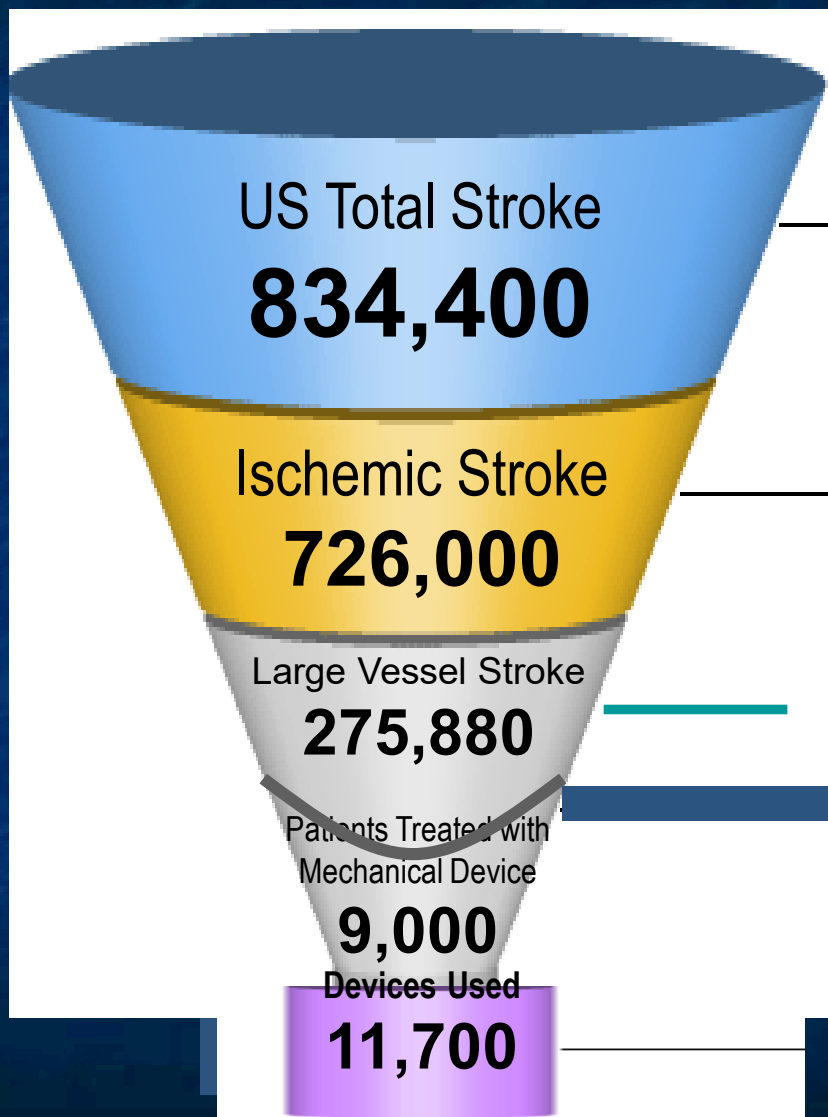


Rapid Reperfusion May Reduce Neurologic Deficit



- Reperfusion of the ischemic penumbra may reduce the extent of damage and improve recovery of function
- Timing is critical
 - The average patient loses 32,000 brain cells/second
 - Fast response is essential

Endovascular Treatment Population



Total Stroke:
Ischemic and
Hemorrhagic

87% of Strokes
are Ischemic

38% of Ischemic
Strokes are Large
Vessel Occlusions
(LVOs) (28-46%)

Only 3% pts. treated

1.3 devices used / patient

Improved stroke networks,
logistics, public awareness,
positive level 1 data & more
effective
endovascular device options
will increase # of patients
treated

Untreated LVO strokes
typically result in
moderate to severe
symptoms

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

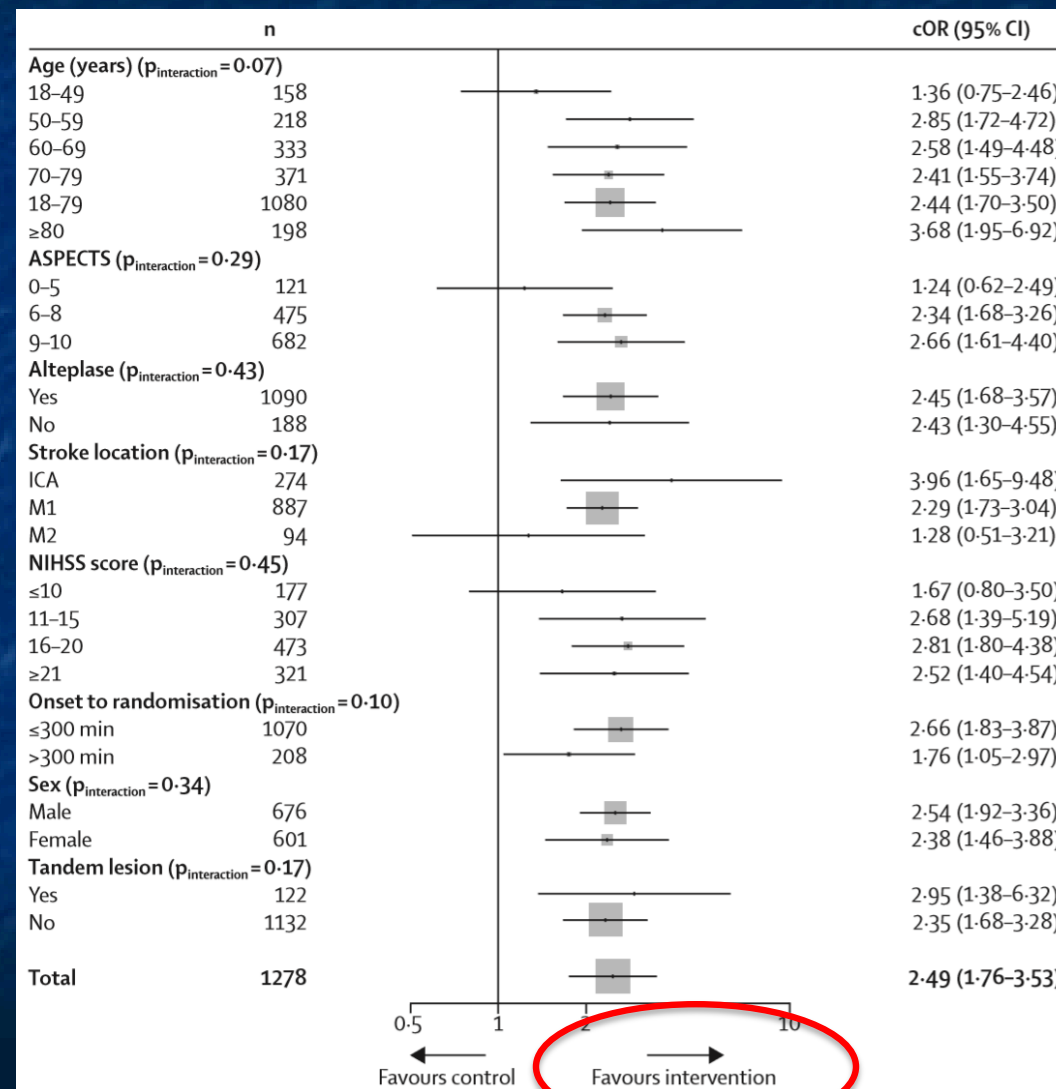
Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Peter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majoie, Aad van der Lugt, Maria A de Miquel, Geoffrey A Donnan, Yvo B W E M Roos, Alain Bonafe, Reza Jahan, Hans-Christoph Diener, Lucie A van den Berg, Elad I Levy, Olvert 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

- Meta-analysis 5 RCTs, thrombectomy vs. medical management for LVO
- N=1287
- Number needed to treat was 2.6 for improvement of 1 point on mRS at 90 days

HERMES

Pre-specified subgroups

- Age
- ASPECTS
- tPA
- Location
- NIHSS
- Onset (>300min)
- Gender
- Tandem lesion



2015 AHA guidelines

KEY NOTES

- **NO** Intervention > 6 hours
- **NO** Utility of CT perfusion / Diffusion weighted imaging
- **NO** Utility of endovascular in posterior circulation, ACA, distal MCA M2/3
- **NO** Utility of aspiration as first line strategy

SINCE AHA GUIDELINES IN 2015

A comparison of direct aspiration versus stent retriever as a first approach ('COMPASS'): protocol.

Turk AS¹, Siddiqui AH², Mocco J³.

- Aspiration thrombectomy vs Stent retriever first line approach
- A non-inferiority trial
- Ratio : 1:1
- Core Lab adjudicated, Open label, blinded outcome
- Primary Outcome: mRS 0-2 at 90 days
- Secondary Outcome: Cost Effectiveness
- Efficacy outcomes: Time metrics to TICI 2b or more, First pass effect, others
- Start Date: June, 2015
- Completion Date: February, 2018
- Publication: March 2019, In Press : the Lancet

Efficacy Endpoints

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	Odds ratio (95% CI)	p value [A1]
Primary efficacy endpoint				
Modified Rankin scale score of 0-2 at 90 days	70 (52%; 43.8-60.3) [A1]	68 (50%; 41.6-57.4) [A1]	NA	0.0014*
Secondary efficacy endpoints				
Median time to TICI 2b or greater (min)	22 (19-28) [A2]	33 (28-37) [A2]	NA	0.0194
90-days global disability Modified Rankin shift [A3]	0.98 (0.64-1.51)	0.9354
0	27 (20.6)	24 (18.5)
1	26 (19.8)	32 (24.6)
2	15 (11.5)	9 (6.9)
3	7 (5.3)	14 (10.8)
4	20 (15.3)	17 (13.1)
5	6 (4.6)	4 (3.1)
6	30 (22.9)	30 (23.1)
TICI 2c or greater within 45 min	50% (66/133)†	44% (59/134)‡	1.3 (0.8-2.1)	0.2998
TICI 3 within 45 min	34% (45/133)†	23% (31/134)‡	1.7 (1.0-3.0)	0.0486
Secondary efficacy outcomes				
TICI 2b or greater on first pass	57% (75/131)§	51% (65/129)¶	1.32 (0.81-2.15)	0.32
TICI 2b or greater within 45 min of access	76% (101/133)†	68% (91/134)‡	1.49 (0.87-2.55)	0.17
Occurrence of emboli in a new territory	3% (4/133)†	2% (2/136)	2.08 (0.37-11.54)	0.44
Presence of vasospasm involving the accessed vascular tree	8% (10/133)†	7% (10/136)	1.02 (0.41-2.55)	1.00
90-days global disability utility weighted modified Rankin shift	0.56 (0.4; n=131)	0.57 (0.4; n=130)**	NA	0.76
Improved (lower [A4]) NIHSS at 24 h	7.5 (9.0; n=133)††	7.3 (8.9; n=132)‡‡	NA	0.86
Improved (lower) NIHSS at 7 days post-treatment or post-discharge	11.0 (8.5; n=117)§§	10.1 (8.7; n=121)¶¶	NA	0.42
Stroke Impact Score 				
Strength	15.8 (4.7)	16.1 (4.2)	NA	0.70
Memory	30.6 (5.8)	30 (6.1)	NA	0.56
Mood	33.7 (5.9)	32.8 (5.5)	NA	0.37
Communication	31.9 (5.2)	31.6 (5.5)	NA	0.77
ADL or IADL	42.8 (10.4)	43.2 (10.8)	NA	0.82
Mobility	36.1 (10.6)	37.1 (9.7)	NA	0.57
Hand function	20.3 (6.4)	21 (5.9)	NA	0.54
Social participation	31.5 (9.0)	31 (9.6)	NA	0.74

Angiographic Outcomes

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	Odds ratio (95% CI)	p value
TICI 2b with primary modality	83% (109/131)*	81% (109/134)†	1.14 (0.60–2.14)	0.75
TICI 2b at final assessment	92% (122/133)‡	89% (121/136)	1.37 (0.61–3.11)	0.54
TICI 2c at final assessment	56% (75/133)‡	56% (76/136)	1.02 (0.63–1.65)	1.00
TICI 3 at final assessment	38% (50/133)‡	29% (39/136)	1.50 (0.9–2.5)	0.15

TICI=thrombolysis in cerebral infarction. *Denominator reflects three patients for whom the core lab was unable to assess TICI after primary modality. †Denominator reflects two patients for whom the core lab was unable to assess TICI after primary modality. ‡Denominator reflects one patient with no available procedural imaging to assess.

Aggregate Supply Chain Cost Analysis

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	p value
Data primary, list price secondary (\$)			
Mean	9540 (7962)	14 081 (4797)	<0.0001
Median	6633 (3885) [A]	12 790.40 (3458.30) [A]	<0.0001
Data secondary, list price primary (\$)			
Mean	10 084 (8873)	15 158 (5223)	<0.0001
Median	6848 (3651) [A]	13 686 (3832) [A]	<0.0001

Safety Endpoints

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	Odds ratio (95%)
All-cause mortality at 3 months	22% (30/134)	22% (30/136)	1.02 (0.57–1.81)
Any identified intracranial haemorrhage	36% (48/134)*	34% (46/135)†‡	1.08 (0.65–1.78)
Symptomatic intracranial haemorrhage ≥ 4 NIHSS	6% (8/134)	6% (8/135)‡	1.01 (0.37–2.77)
Symptomatic intracranial haemorrhage SITS-MOST definition	3% (4/134)	3% (4/135)‡	1.01 (0.25–4.12)
Symptomatic intracranial haemorrhage at 24 h timepoint	6% (8/134)	6% (8/135)‡	1.01 (0.37–2.77)
Asymptomatic intracranial haemorrhage at 24 h timepoint	28% (38/134)	27% (37/135)‡	1.05 (0.62–1.79)
All parenchymatous haemorrhage category 2 within 36 h of randomisation	3% (4/134)	3% (4/135)‡	1.01 (0.25–4.12)
All-cause mortality at 30 days post-randomisation	17% (23/134)	16% (21/133)§	1.11 (0.58–2.11)
Intracranial haemorrhage within 90 days post-randomisation (self-reported)	22% (30/134)	18% (24/136)	1.35 (0.74–2.45)
Procedure-related serious adverse events	13% (17/134)	14% (19/136)	0.89 (0.44–1.814)
Device related serious adverse events up to 48 h post-randomisation	0	0	NA

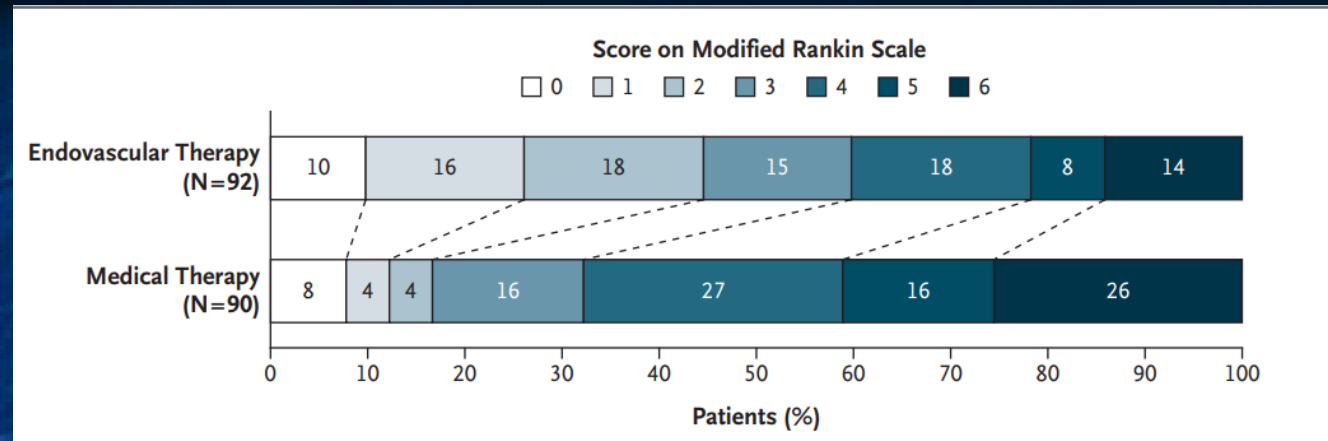
ORIGINAL ARTICLE

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*

- RCT: Thrombectomy vs. Medical
- LVO – M1, supraclinoid ICA, cervical ICA
- LSN 6-16h
- Penumbra on CTP/MRP

DEFUSE-3



- Functional independence at 90 days
 - Thrombectomy: 45%
 - Control: 17%
- Decreased mortality: 14% vs. 26%
- Similar symptomatic ICH: 7% vs. 4%

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

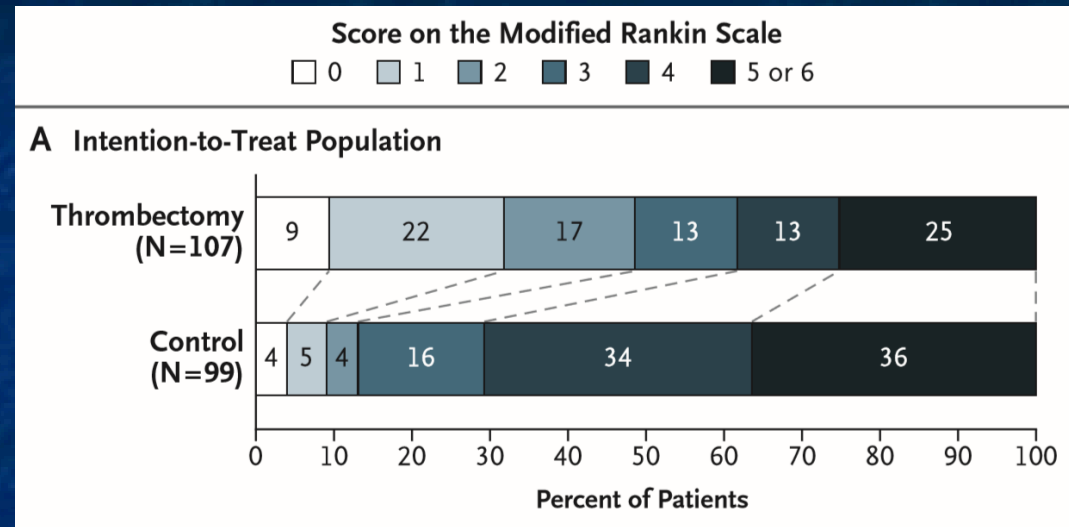
JANUARY 4, 2018

VOL. 378 NO. 1

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*

- RCT: Thrombectomy vs. Medical
- LVO – M1 or supraclinoid ICA
- LSN 6-24h, baseline mRS 0-1
- High NIHSS (≥ 10) with small infarct on MRI or small core perfusion deficit on CTP

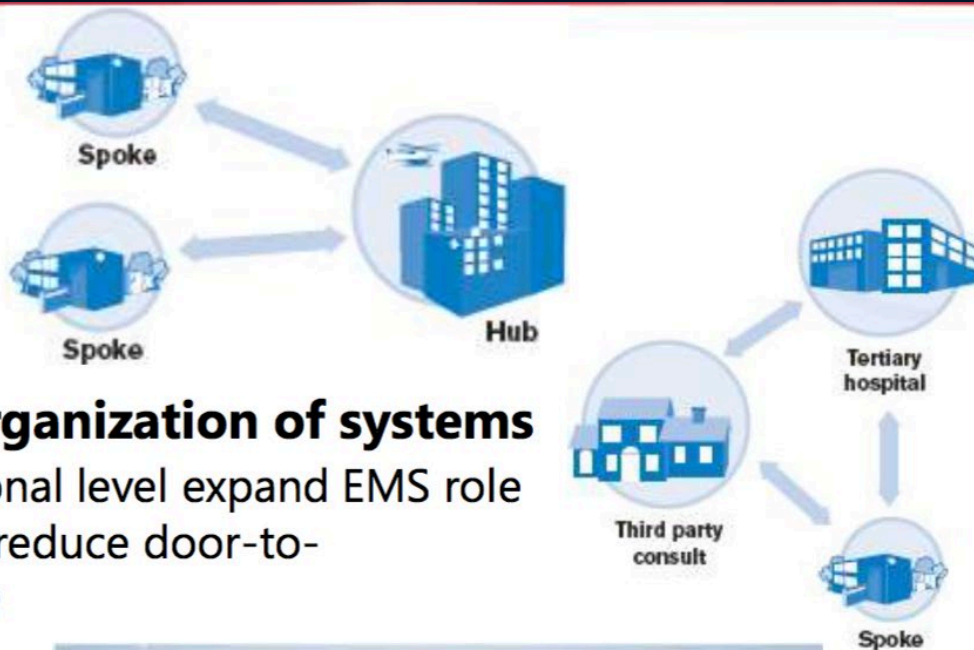


- Functional independence at 90 days
 - Thrombectomy: 49%
 - Control: 13%
- No difference in symptomatic ICH or mortality

Faster workflow and triage

Economical

Telestroke, Organization of systems of care at regional level expand EMS role in stroke triage, reduce door-to-reperfusion time



Viz LVO

A.I. Powered LVO Detection

Viz LVO uses artificial intelligence to automatically identify suspected large vessel occlusion strokes on CT angiogram imaging in your network and to alert your on-call stroke team within minutes.

Environmental

Shift of **focus to Pre-hospital triage** supports mobile triage units, stroke ambulance
Cost and sustainability of mobile stroke units are challenges.

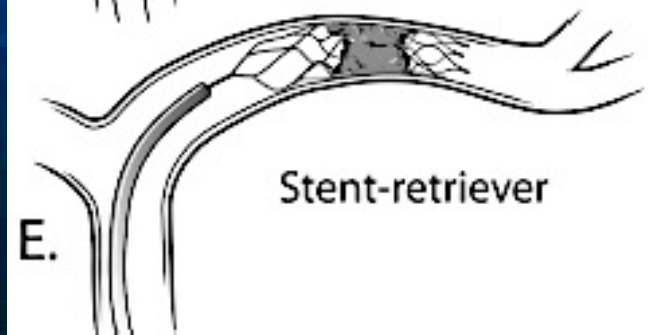
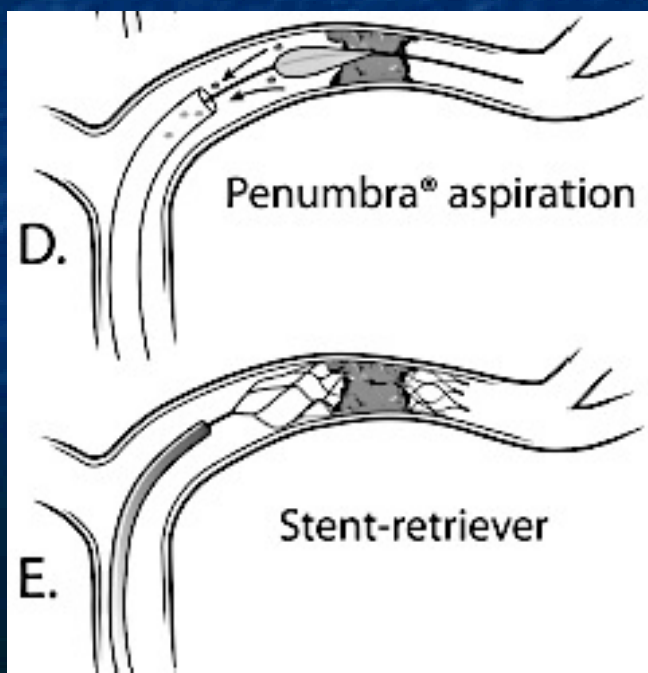
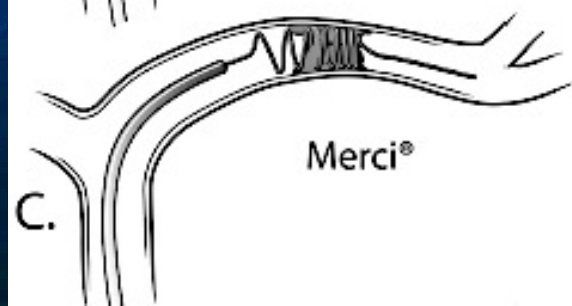
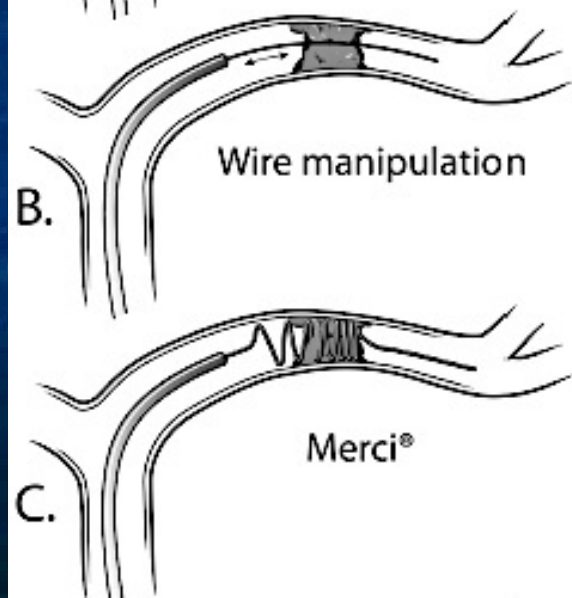
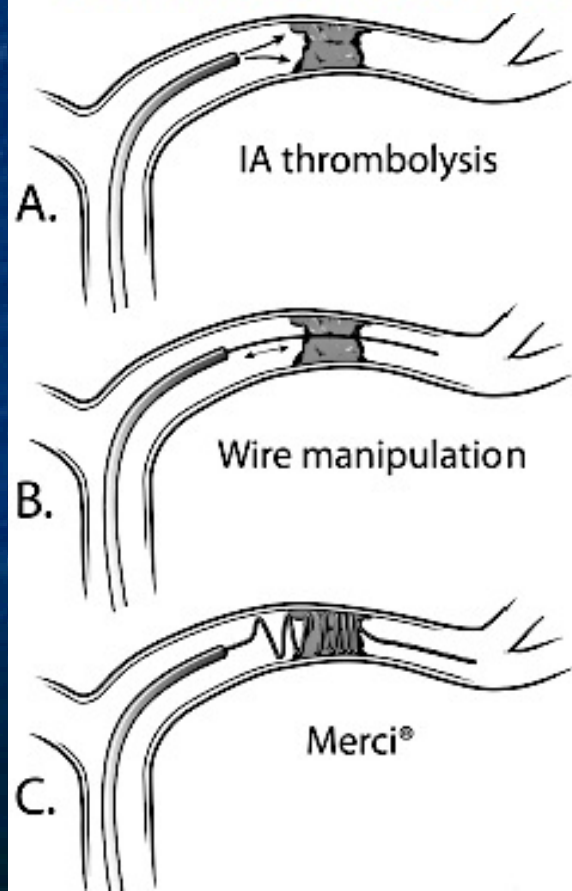


Spoke




Endovascular treatment of acute ischemic stroke: the end or just the beginning?

MAXIM MOKIN, M.D., PH.D.,¹ ALEXANDER A. KHALESSI, M.D., M.S.,³ J MOCCO, M.D., M.S.,⁴ GIUSEPPE LANZINO, M.D.,⁵ TRAVIS M. DUMONT, M.D.,¹ RICARDO A. HANEL, M.D., PH.D.,⁶ DEMETRIUS K. LOPES, M.D.,⁷ RICHARD D. FESSLER II, M.D.,⁸ ANDREW J. RINGER, M.D.,⁹ BERNARD R. BENDOK, M.D.,¹⁰ EROL VEZNEDAROGLU, M.D.,¹¹ ADNAN H. SIDDIQUI, M.D., PH.D.,^{1,2} L. NELSON HOPKINS, M.D.,^{1,2} AND ELAD I. LEVY, M.D., M.B.A.^{1,2}

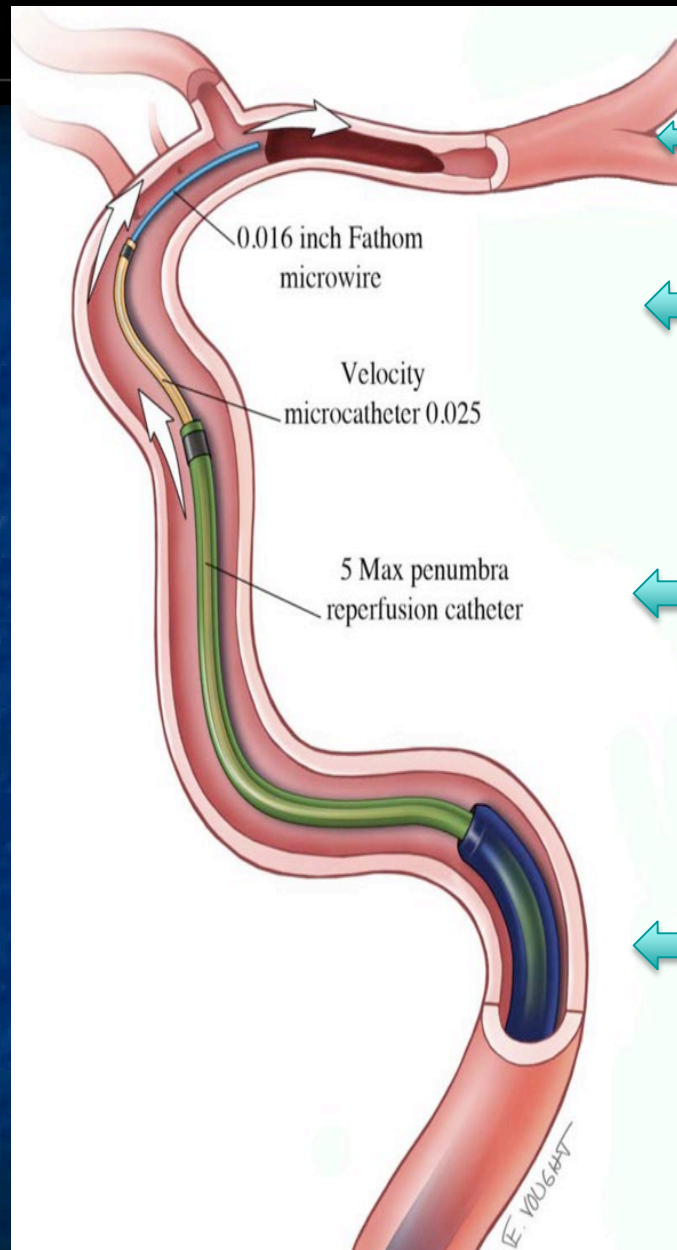
JNS JOURNAL OF
NEUROSURGERY
OFFICIAL JOURNALS OF THE AANS SINCE 1944



Comparison of the most technically-similar, 'stent-retriever'-like neurothrombectomy devices

Device Name (Manufacturer)	Image	Design Overview
EmboTrap® Device (Neuravi Ltd.)		Self-expanding Nitinol stent-like device, attached to guide-wire like shaft. The Nitinol self-expanding portion contains an outer cage and inner flow channel with connected ends and a distal radiopaque tip.
Solitaire FR (Covidien)		Self-expanding Nitinol stent-like device, attached to guide-wire like shaft. The Nitinol self-expanding portion has a seam running along its length, and open ends.
Trevo Pro / ProVue (Stryker)		Self-expanding Nitinol stent-like device, attached to guide-wire like shaft. The Nitinol self-expanding portion has open ends and a guidewire-like radiopaque tip at its distal end.





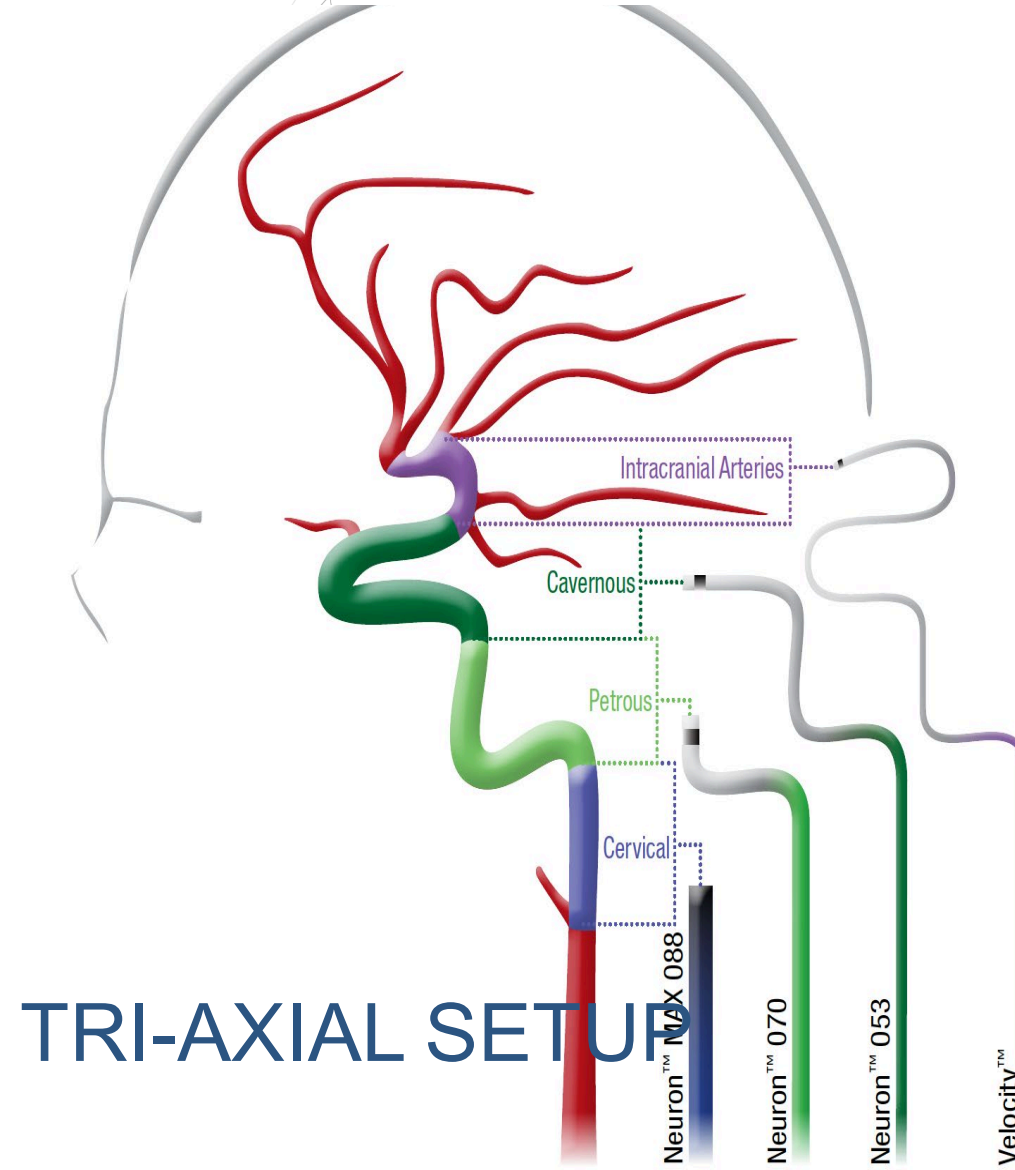
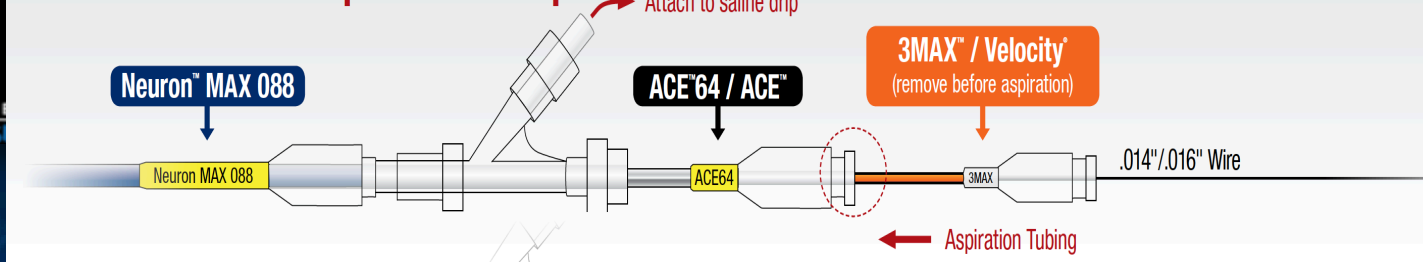
0.014 microwire to
cross clot

0.021+ microcatheter
To deliver stent retriever

5F intermediate
catheter
ID 0.060+
To assist
aspiration &
retrieval

6F long sheath
ID 0.088
Some use
Balloon Guide
instead

Tower of Power



TRI-AXIAL SETUP

What is not in the Guidelines

- Age < 18 years
- NIHSS 0-5
- ASPECTS 0-6
- Time > 24 hours
- Posterior Circulation
- ACA
- Uncertain evidence on M2/3 and Tandem Occlusion
- Prior disability mrS= \neq >3

- Revascularization Rate
-
- 3 month mRS
- Approval Codes
 - NRY – Revascularization
 - POL – Improved Neurological Outcomes

Asymptomatic Carotid Stenosis and Risk of Stroke Study (ACSRs)

**Asymptomatic Patients with Medical
Co-Morbidities And Severe Stenosis...**



**Stroke rate up to 6% per year on
best medical therapy!!**

Carotid Endarterectomy trials

- NASCET (Symptomatic)
 - 70-99% stenosis: 17% (26 to 9%)ARR (65% RRR)/2 yrs
- ECST
 - 70-99% stenosis: 21.2% ARR/5 yrs
- ACAS and ACST (Asymptomatic >60%)
 - 50% RRR in 5 yrs ... less impressive but consistent
 - Standard of care in US

Those for whom CEA is Not a Good Option

Medical Factors

- Pre-op CABG
- Angina pectoris
- CHF
- Recent or evolving MI
- Renal failure

Surgical Factors

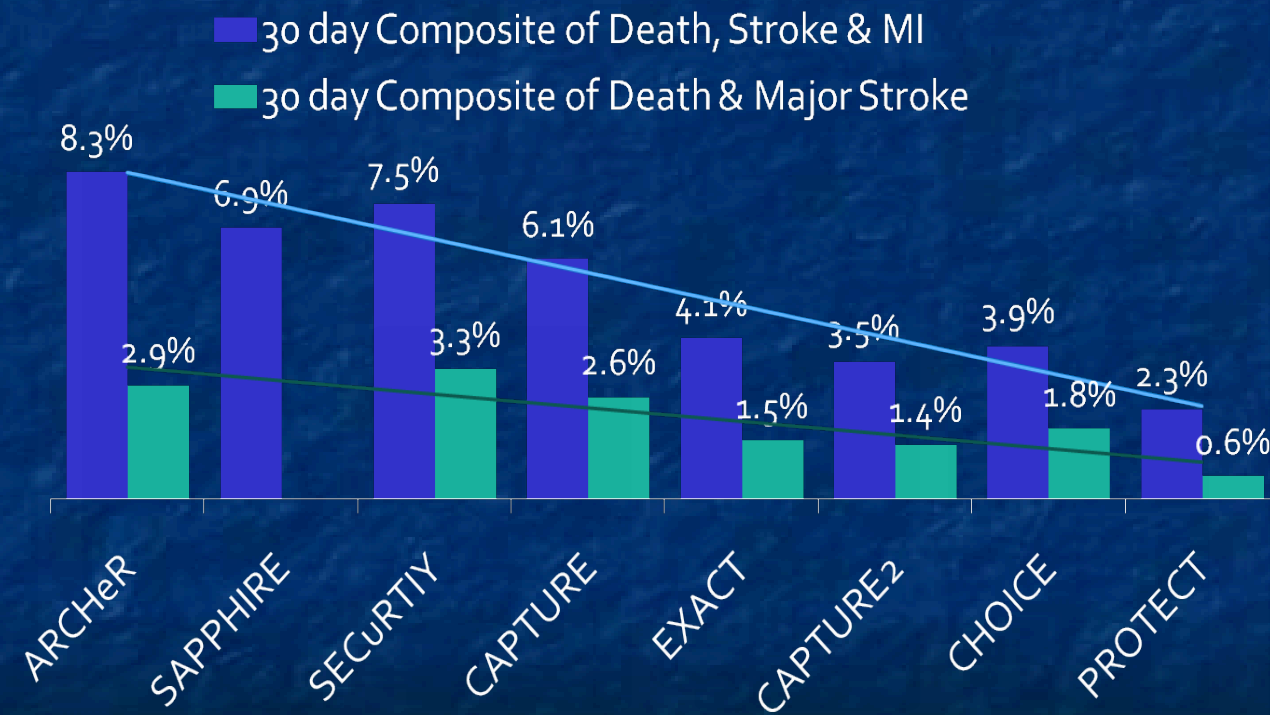
- Recurrent carotid stenosis
- Previous cervical surgery
- Contralateral laryngeal palsy
- Tracheostomy
- Post cervical XRT
- Lesion above C2
- Lesion below clavicle

Outcomes of CAS trials over time

CAS results have vastly improved over time due to:

- (1) more experienced operators
- (2) better patient selection and
- (3) a wider spectrum of technology

CAS outcomes have evolved over time similarly to CEA



CREST

The Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST): Stenting Versus Carotid Endarterectomy for Carotid Disease

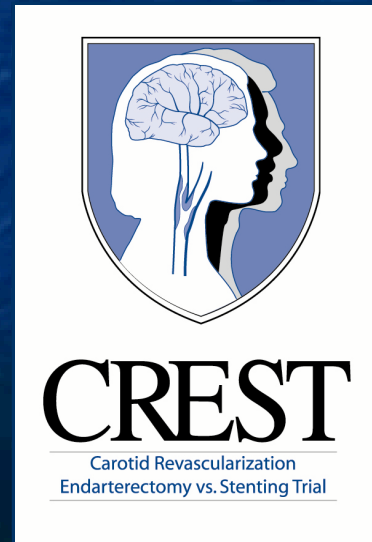
Vito A. Mantese, Carlos H. Timaran, David Chiu, Richard J. Begg and Thomas G. Brott

Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Stroke. 2010;41:S31-S34

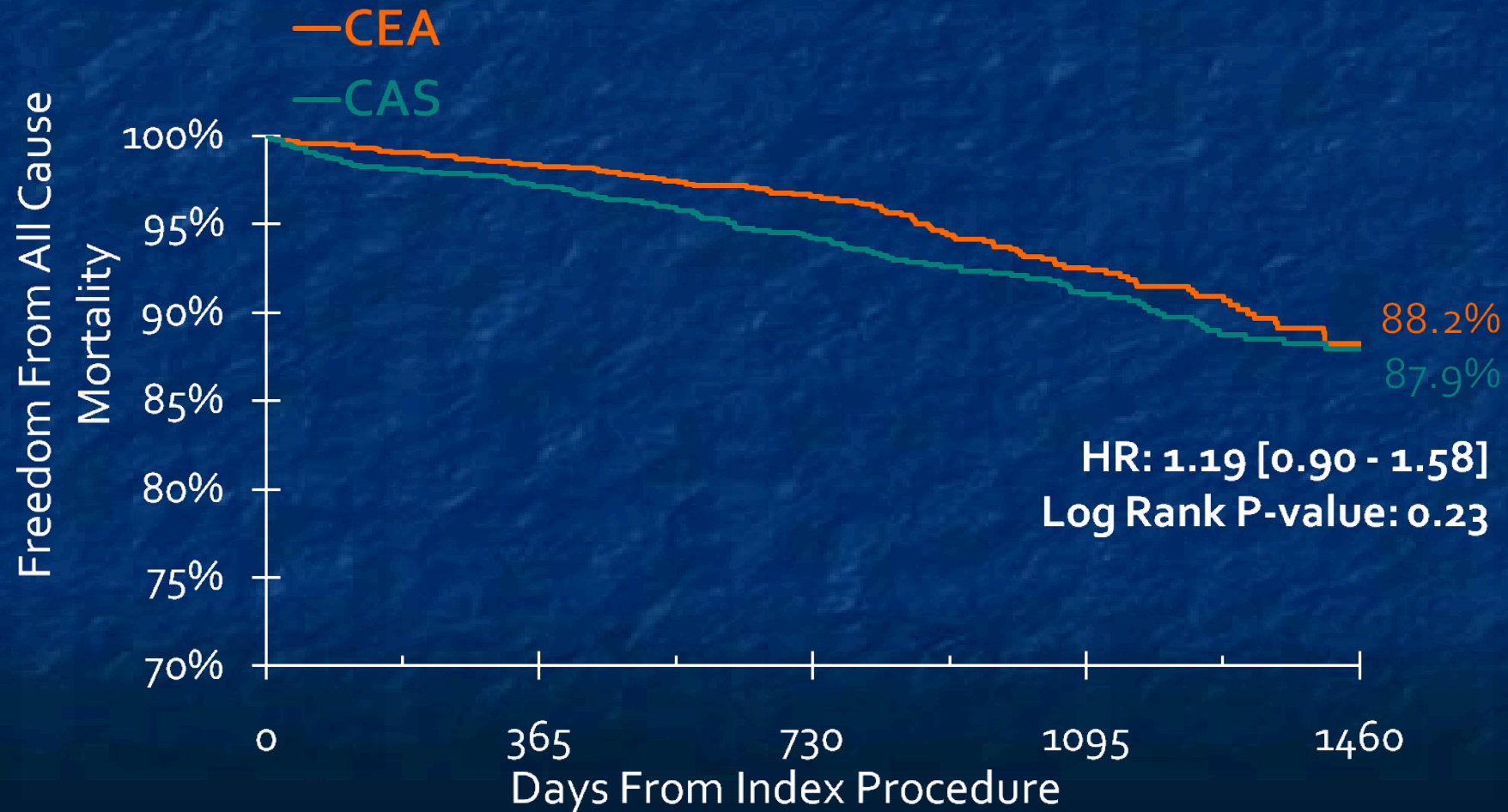
- Landmark trial
- compared outcomes : CEA Vs CAS
- Symptomatic patients > 50% stenosis
- Asymptomatic patients > 60% stenosis
- Rigorous certification process



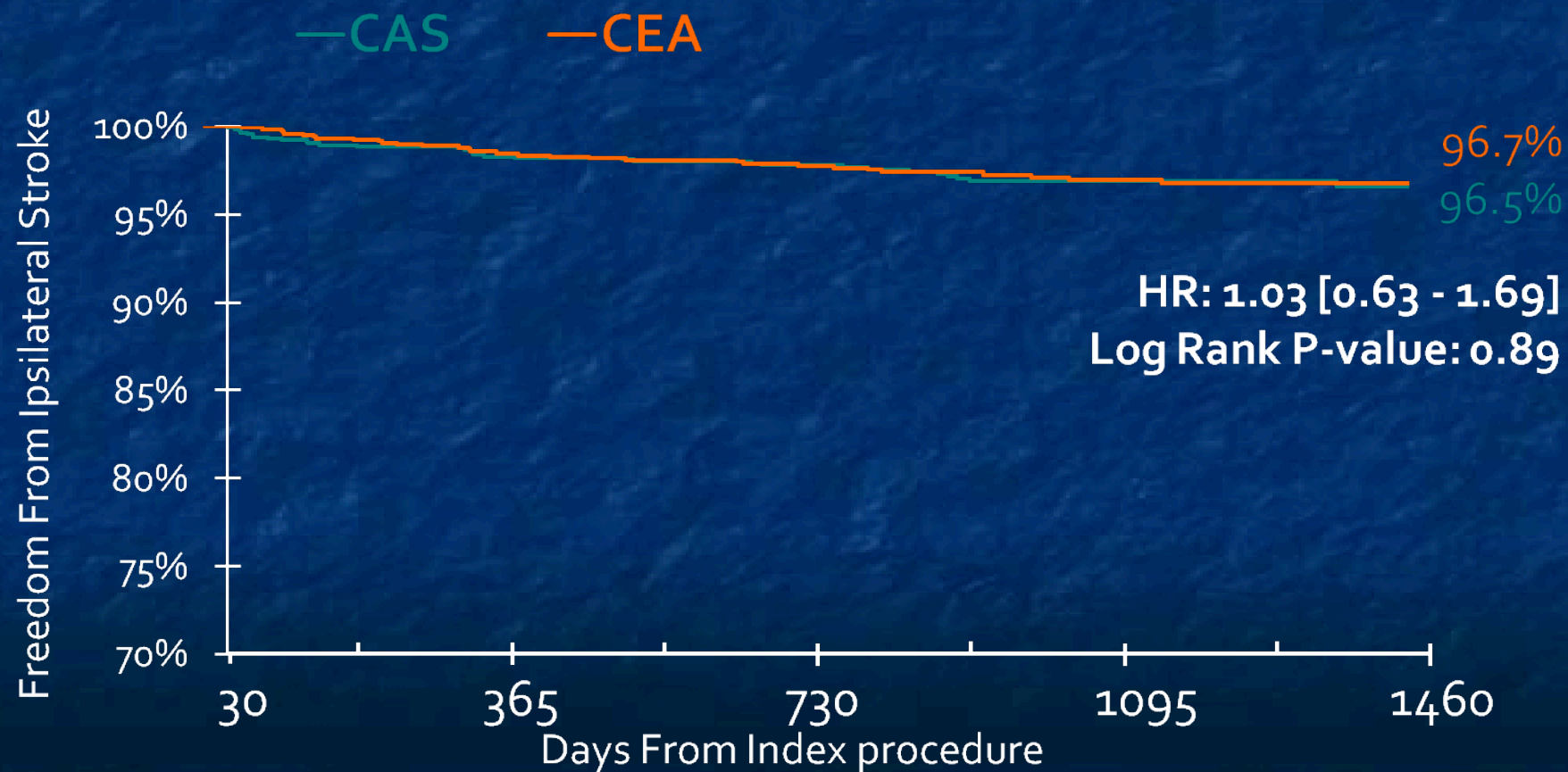
Per protocol	CAS N = 1,131	CEA N = 1,176	Difference	Unadjusted p-value*
All Death, Stroke, or MI	5.8% (65)	5.1% (60)	0.7%	0.5200
Death	0.53% (6)	0.26% (3)	0.27%	0.3335
Any Stroke	4.1% (46)	1.9% (22)	2.2%	0.0019
Major Stroke	0.9% (10)	0.4% (5)	0.5%	0.2005
Minor Stroke	3.2% (36)	1.5% (18)	1.7%	0.0088
MI	2.0% (22)	3.4% (40)	-1.5%	0.0387

* Fisher's exact p-values were not adjusted for multiple comparisons; p-values for descriptive purposes only

Similar Mortality up to 4 Years



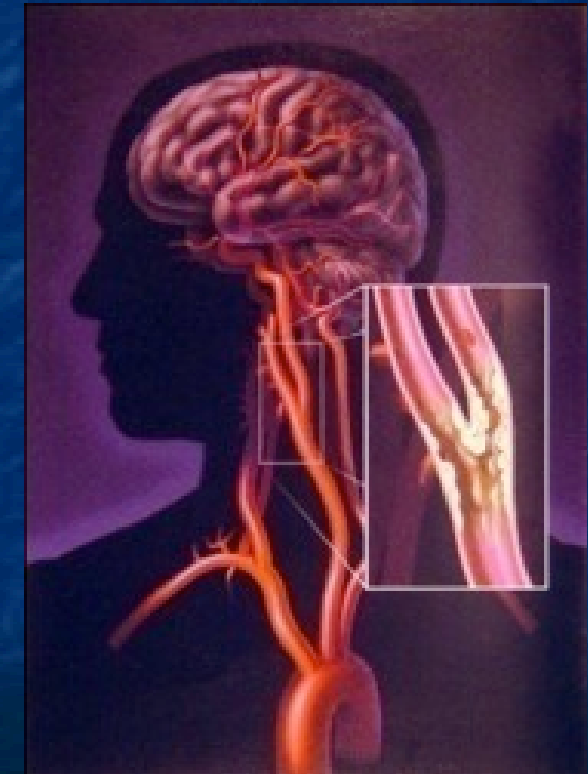
Similar Freedom from Ipsilateral Stroke Day 31 to 4 Years



CAS Risk Factors Identified in Trials

(*BEFORE Proximal EP*)

1. *Sx (hot) lesion...*
2. *Elderly pts (tortuosity+Arch Access)...*
3. *Low Gray Scale Median...*
4. *Duration Filter...*
5. *Pre dil without EP...*
6. *Tortuosity- severe...*
7. *Multiple stents...*
8. *Concentric calcium...*
9. *Aortic Arch disease...*
10. *Renal Failure...*



High-Risk Factors in Symptomatic Patients Undergoing Carotid Artery Stenting With Distal Protection: Buffalo Risk Assessment Scale (BRASS)

Andrew A. Fanous, MD*†

Sabareesh K. Natarajan, MD,
MS*†

Patrick K. Jowdy, BS*†

Travis M. Dumont, MD*†§

Maxim Mokin, MD, PhD*†¶

Jihnhee Yu, PhD||

Adam Goldstein*†

Michael M. Wach, BS*†

James L. Budny, MD*†

L. Nelson Hopkins, MD*†##**††

Kenneth V. Snyder, MD,
PhD*†###§§

Adnan H. Siddiqui, MD,
PhD*†####

Elad I. Levy, MD, MBA*†##

TABLE 6. Buffalo Risk Assessment Scale for Carotid Artery Stenting^a

Variable	Points
Carotid tortuosity (any)	2
Difficult distal landing zone	2
Concentric calcification	1
Carotid pseudo-occlusion	1
Difficult femoral access	1
NIHSS score ≥ 10	1
Renal disease	1
Maximum scale points	9
Total score	
BRASS I (low risk)	0-2
BRASS II (moderate risk)	3-4
BRASS III (high risk)	5-9



Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal

Christopher J. Kwolek, MD,^a Michael R. Jaff, DO,^b J. Ignacio Leal, MD,^c L. Nelson Hopkins, MD,^d
Rasesh M. Shah, MD,^e Todd M. Hanover, MD,^f Sumaira Macdonald, MD,^g and Richard P. Cambria, MD,^a
Boston, Mass; Toledo, Spain; Buffalo, NY; Norfolk, Va; Greenville, SC; and Sunnyvale, Calif

Conclusions: The results of the ROADSTER trial demonstrate that the use of the ENROUTE Transcarotid NPS is safe and effective at preventing stroke during CAS. The overall stroke rate of 1.4% is the lowest reported to date for any prospective, multicenter clinical trial of CAS. (J Vasc Surg 2015;62:1227-35.)

Proximal or distal protection? More evidence...

The PROFI Study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting)

A Prospective Randomized Trial

Klaudija Bijuklic, MD, Andreas Wandler, MD, Fadia Hazizi, MD, Joachim Schofer, MD, PhD

Hamburg, Germany

Results: When evaluated with DWI MRI, cases with MO.MA protection, when compared with distal filters, showed significantly reduced embolic load (both number and size of DW lesions)

Study	Procedure	Embolic Protection	#subjects	%w/New DWI lesions
ICSS ¹	Transfemoral	Distal Filter	51	73
ICSS ¹	CEA	Clamp, backbleed	107	17
PROFI ²	Transfemoral CAS	Distal field(Emboshield)	31	87
Leal ⁵	Transfemoral	Distal Filter	33	33
PROFI ²	Transfemoral CAS	Proximal occlusion(MoMA)	31	45
DESERVE ⁴	Transfemoral CAS	Proximal occlusion(MoMA)	127	30
PROOF ³	Transcervical CAS	High flow rate reversal	48	16.7
Leal ⁵	Transcervical CAS	Flow Reversal	31	12.9

1. Lancet Neurol. 2010 Apr;9(4):353-62
2. J Am Coll Cardiol. 2012;59:1383-1389
3. JVS 2011;54:1317-1323

4. Rubino P, EuroPCR 2011
5. JVS 2012;56:1585-1590

Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy

Alison Halliday, Richard Bulbulia*, Leo H Bonati, Johanna Chester, Andrea Craddock-Bamford, Richard Petot†, Hongchao Pan†, for the ACST-2 Collaborative Group‡*

Findings Between Jan 15, 2008, and Dec 31, 2020, 3625 patients in 130 centres were randomly allocated, 1811 to CAS and 1814 to CEA, with good compliance, good medical therapy and a mean 5 years of follow-up. Overall, 1% had disabling stroke or death procedurally (15 allocated to CAS and 18 to CEA) and 2% had non-disabling procedural stroke (48 allocated to CAS and 29 to CEA). Kaplan-Meier estimates of 5-year non-procedural stroke were 2·5% in each group for fatal or disabling stroke, and 5·3% with CAS versus 4·5% with CEA for any stroke (rate ratio [RR] 1·16, 95% CI 0·86–1·57; $p=0·33$). Combining RRs for any non-procedural stroke in all CAS versus CEA trials, the RR was similar in symptomatic and asymptomatic patients (overall RR 1·11, 95% CI 0·91–1·32; $p=0·21$).

Interpretation Serious complications are similarly uncommon after competent CAS and CEA, and the long-term effects of these two carotid artery procedures on fatal or disabling stroke are comparable.

EDITORIAL COMMENT

Asymptomatic Carotid Stenosis: The Not-So-Silent Disease

Changing Perspectives From
Thromboembolism to Cognition*

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- Evidence of chronic carotid stenosis having progressive effect on cognitive decline
- Cognitive evaluation should be an important part of initial asymptomatic carotid disease evaluation



The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study

Health and Hope for Patients at Risk for Stroke

CREST-2 offers three

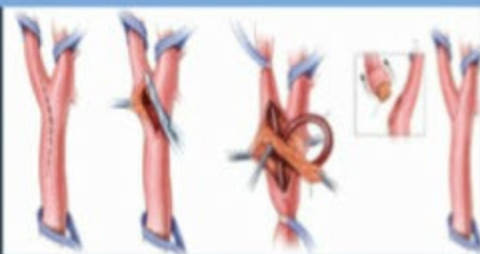
STROKE PREVENTION OPTIONS

1



Medical Management

2



Carotid Endarterectomy
+ Medical Management

3



Carotid Artery Stenting
+ Medical Management



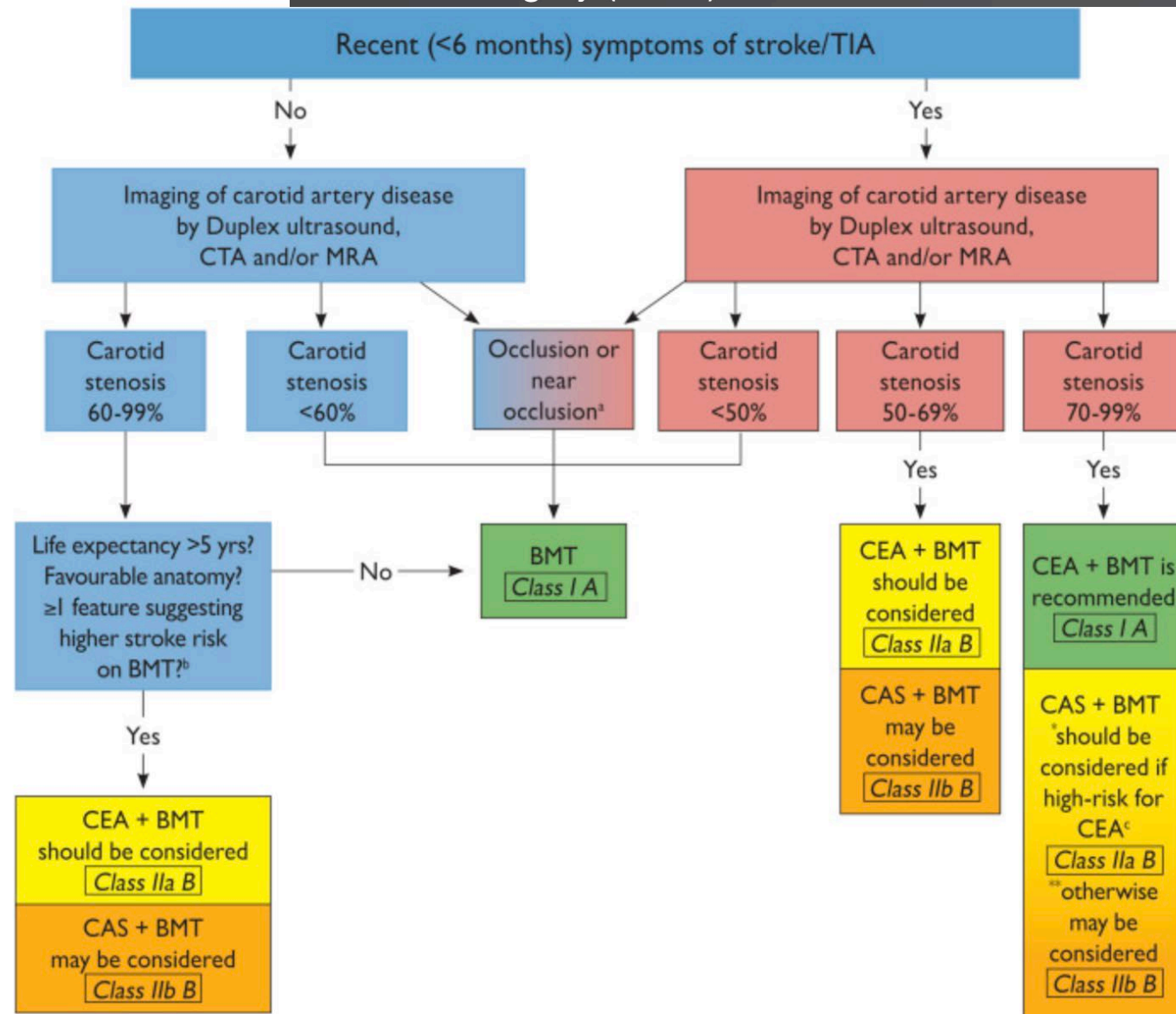
The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study

Health and Hope for Patients at Risk for Stroke

Goal:

In patients with $\geq 70\%$ asymptomatic stenosis, to assess:

- The treatment differences between medical management and CEA.
- The treatment differences between medical management and CAS.



Asymptomatic Carotid Disease

- Complications: Stroke, MI, Death, Cranial Nerve Injury
- Recurrent Stenosis needing retreatment
- Stroke

Symptomatic carotid Disease

- Complications: Stroke, MI, Death, Cranial Nerve Injury
- Recurrent Stenosis needing retreatment
- Stroke

Intracranial Atherosclerosis Treatment Past, Present, and Future

Brent Flusty, DO; Adam de Havenon, MD; Shyam Prabhakaran, MD;
David S. Liebeskind, MD; Shadi Yaghi^{ID}, MD

Timeline of ICAD events

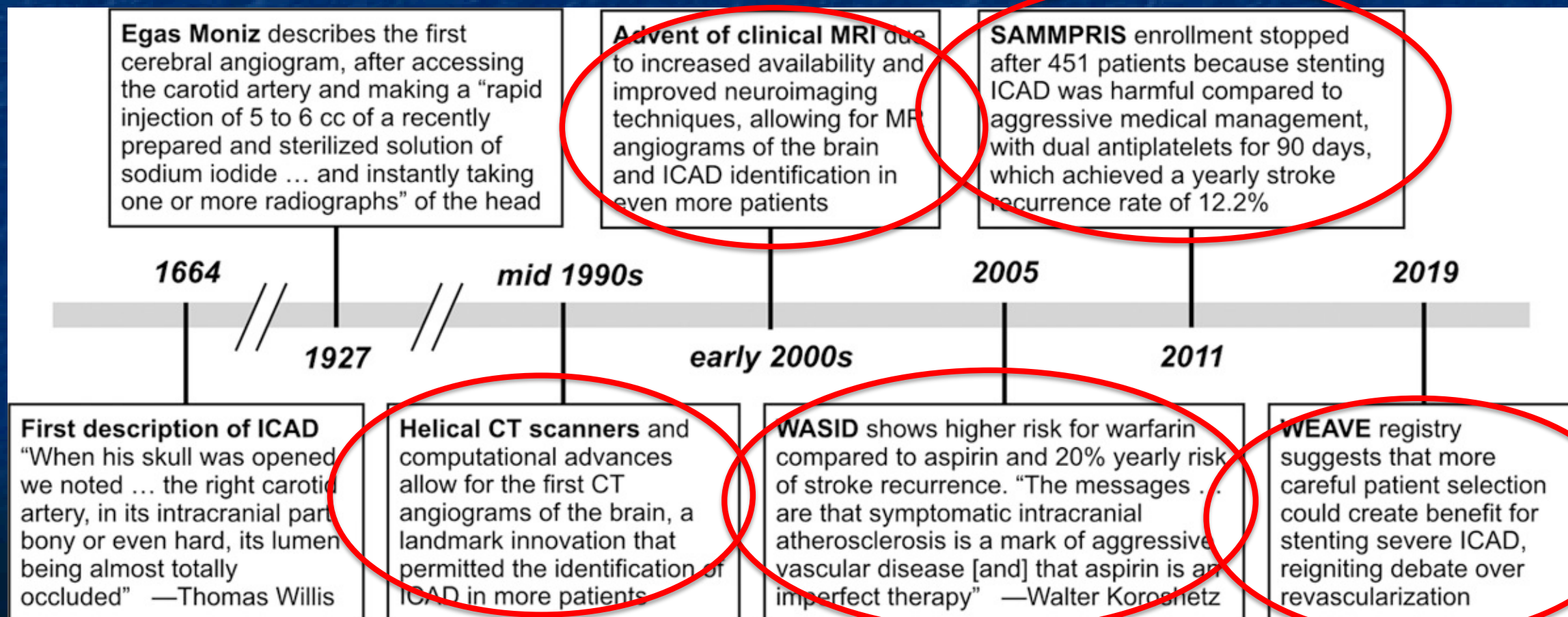


Table. Completed and Ongoing Clinical Trials Testing Medical and Interventional Treatments for Intracranial Atherosclerotic Disease

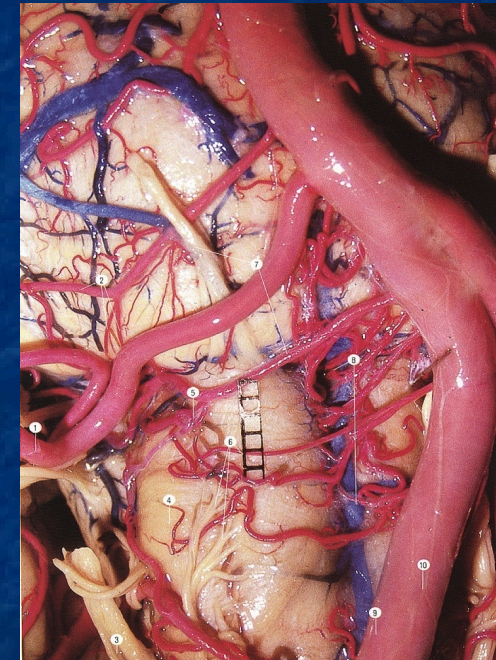
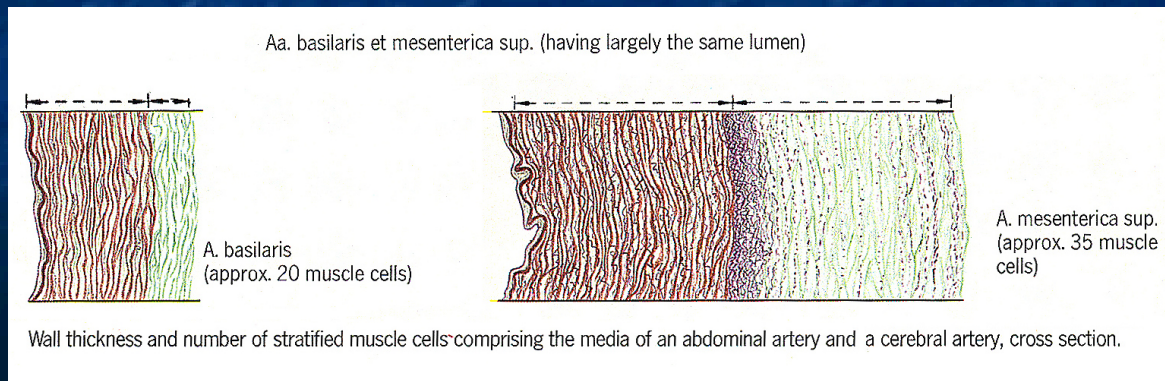
Trial	Location	Intervention	Outcome	Sample Size	Completion
International cooperative study of extracranial/intracranial arterial anastomosis (EC/IC Bypass)	North America, Europe, Asia	STA-MCA bypass surgery vs medical management	Surgery resulted in more strokes and adverse events	1377	1985
Comparison of warfarin and aspirin for symptomatic intracranial atherosclerosis (WASID)	North America	Warfarin vs aspirin	Warfarin nonsuperior for stroke prevention and harmful	569	2005
Stenting vs aggressive medical management for intracranial atherosclerosis (SAMMPRIS)	United States	Stenting vs medical management	Stenting resulted in more strokes and death	451	2011
Stenting vs medical treatment in patients with symptomatic vertebral artery stenosis (VAST)	Holland	Stenting vs medical management	Stenting did not lower the risk of stroke and more adverse events	115	2015
Effect of a balloon-expandable intracranial stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis (VISSIT)	United States, China, Europe	Stenting vs medical management	Stenting resulted in more strokes and death	112	2015

Aggressive Medical Management (Stroke and death at 1 year)

- WASID (ASA 1300 mg, 2005): ~10%
 - 70-99% symptomatic stenosis (~20%)
 - < 30 days higher recurrence rate than those enrolled 30-90 days.
- SAMMPRIS (ASA and Plavix, 2011) = 12%
- VISIT (ASA and Plavix, 2015) = 15%

Many Lessons in ICAD from Cardiology...

- However, the cerebrovascular anatomy is unique:
 - Surrounded by CSF
 - Less Intima, media, and Adventitia
 - Greater % smooth muscle
 - Large deficit from occlusion of small perforators
 - Bony walls within petrous cervical and vertebral arteries



SAMMPRIS (2011,2014) and VISSIT (2015)

- SAMMPRIS: 451 patients randomized to aggressive medical therapy and lifestyle modification vs the above + aggressive angioplasty and stenting with Wingspan stent
 - Halted Early
 - 15% and 20% 30-day and 1 year stroke rate in stenting arm
 - 5% and 12% 30-day and 1 year stroke rate in medical arm
 - ICH within 30 days 30% in stent group vs 0% in medical
- VISSIT: Multicenter, prospective randomized trial to evaluate the PHAROS Vitesse Neurovascular BMS. 110 of 250 pts enrolled.
 - 24.1% and 36.2% 30 day and 1-year stroke/TIA rate for Stent
 - 9.4% and 15.1% 30 day and 1 year stroke/TIA rate in medical group
 - ICH within 30 days occurred in 8.6% in the stent group vs 0 in the medical arm.

SAMMPRIS (2011,2014) and VISSIT (2015)

- In SAMMPRIS trial, all of 30-day stroke or death (14.7%,33/224) in the PTAS group occurred within 1 day after the procedure (75.8%,25/33) or 2 to 6 days later(24.2%,8/33).
- In 3 year follow up, still only difference was that from initial 7 days
- After SAMMPRIS and VISSIT...significant decline in Stenting for ICAD in US.

SAMMPRIS Conclusions

Based on SAMMPRIS results, general conclusions were:

1. Medical therapy was more effective than anticipated (*earlier WASID data which showed recurrent stroke risk of 18% per year when taking aspirin alone*)
2. Intracranial stenting was less effective and more risky than anticipated (*based on earlier registries which demonstrated lower complication risk*)

Conclusions: patients with intracranial stenosis should be treated with medical therapy alone and should not be stented

Failure of SAMMPRIS trial to demonstrate benefit of intracranial stenting **DOES NOT** equal failure of endovascular treatment of intracranial atherosclerotic disease

Questions remain

Was procedure protocol appropriately chosen? Could high complication rate be explained by design of this first-generation device (Gateway/Wingspan system)?

SAMMPRIS protocol - treatment included the following steps:

1. Pre-angioplasty of the lesion
2. Stenting
3. Post-stenting plasty, if needed

Each step has risk of embolic complications, thus having three steps should triple the risk

Endovascular options after SAMMPRIS for ICAD

1. Improve medical therapies (new better agents)
2. Balloon angioplasty alone (Submaximal angioplasty)
3. Staged stenting (later, once plaque is stable)
4. Different stent design (closed vs open cell, balloon mounted stent,..) Note similar result from the VISSIT trial
5. Improve patients selection – decision making based on CT perfusion, MRI plaque study
6. Stenting of selected patients only (avoid perforator-rich territories such as mid BA or proximal M1)



WINGSPAN ONLY

For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than the Wingspan stent is unknown and is considered investigational (*Class IIb; Level of Evidence C*).

1. Change from 50% to 99% stenosis to 70% to 99% stenosis
2. Rewording to mention Wingspan device used in SAMMPRIS

For patients with severe stenosis (70%–99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel therapy, achievement of systolic BP <140 mm Hg, and high-intensity statin therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational (*Class IIb; Level of Evidence C*).

New recommendation

ANGIOPLASTY AND OTHER STENTS ARE INVESTIGATIONAL

NOT EVEN FOR SEVERE STENOSIS PROGRESSING SYMPTOMS AFTER ASPIRIN AND CLOPIDOGREL

For patients with severe stenosis (70%–99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational (*Class IIb; Level of Evidence C*).

New recommendation

FDA RECOMMENDATION

- The FDA conducted a panel review of the Wingspan stent system in March 2012, including assessment of the data from all of the Wingspan trials and registries and renewed the FDA clearance of the device but with revised on-label criteria.
- **INCREASED** the minimum degree of stenosis from 50% to 70%
- **REVISED** the recommended clinical criteria to patients who had 2 strokes in the vascular territory of the stenotic intracranial artery, although no trial has utilized 2 strokes as a criterion for stenting. The original HDE approval trial only required 1 stroke and recurrent symptoms.

WEAVE Trial

Final Results in 152 On-Label Patients

Michael J. Alexander ✉, Alois Zauner, John C. Chaloupka, Blaise Baxter, Richard C. Callison, Rishi Gupta, Shlee S. Song, Wengui Yu,
on behalf of the **WEAVE Trial Investigators**
and WEAVE Trial Sites and Interventionalists

The WEAVE trial (Wingspan Stent System Post Market Surveillance) is a postmarket surveillance trial mandated by the Food and Drug Administration to assess the periprocedural safety of the Wingspan Stent system in the treatment of symptomatic intracranial atherosclerotic disease.

- This was a prospective, single-arm, consecutive enrollment, post-market surveillance study.
- The WEAVE trial was an FDA mandated study to evaluate the rate of stroke and death within 72 hours post-stenting in patients treated with the Wingspan Stent System according to the Instructions for Use.

METHODS

- Patients enrolled in the trial in the primary analysis were 22 to 80 years old, with a symptomatic ICAD lesion of 70% to 99% in an artery 2 mm or larger, who had a baseline mRS ≤ 3 , who had experienced 2 strokes, and were stented with Wingspan ≥ 8 days after their last stroke.
- Poststenting balloon dilation within the stent was discouraged unless the residual stenosis remained $\geq 50\%$ after stenting.

Table 4. Primary End Point Results

	Primary Analysis Trial / On Label
Enrolled	N=152
Subjects without stroke or death within 72 h	97.4% (148/152)
Subjects with death within 72 h	1.3% (2/152)
Subjects with stroke (without death) within 72 h	1.3% (2/152)
Total percentage of patients with stroke or death within 72 h	2.6% (4/152)

COMPARISON OF WEAVE WITH OTHER TRIALS

Table 5. Comparison of Multicenter Wingspan Trials (Table view)

Trial	Percent Stenosis	Qualifying Event Stroke	Refractory to Medical Therapy	Median Time to Stent, d	Periprocedural Event Rate
HDE trial ¹	50%–99%	95%	100%	22	4.5%
NIH registry ²	50%–99%	59%	Not reported	10	6.2%
US registry ³	50%–99%	61%	75%	Not reported	6.2%
SAMMPRIS ⁶	70%–99%	63%	64%	7	14.7%
WEAVE trial	70%–99%	100%	100%	22	2.6%

HDE indicates Humanitarian Device Exemption; NIH, National Institutes of Health; SAMMPRIS, Stenting and Aggressive Medical Management for the Prevention of Recurrent Stroke in Intracranial Stenosis; and WEAVE, Wingspan Stent System Post Market Surveillance.

Now that the periprocedural event rate has been reduced, intracranial stents may be evaluated

CONCLUSION

STENTING WORKS IN SELECTED CASES

- The WEAVE trial demonstrated periprocedural safety of the Wingspan stent with a 2.6% periprocedural stroke and death rate, which was better than the target of 4% event rate set by the FDA.
- This was the largest on-label Wingspan stent trial for ICAD with the most homogenous patient population of all the US stenting trials because there was 100% on-label usage for the trial.

Symptomatic Intracranial Atherosclerotic Disease

- Complication Rate (Only HDE devices approved)
- Restenosis Rate
- Recurrent stroke rate

What the physician Societies want to do

- Get a Coverage for Evidence Development (CED) to fund an interventional registry to collect real world data to support these interventions
- SNIS, CV Section and SVIN have signed on to NVQI-QOD to collect ALL cases performed for
 - Intracranial Aneurysms
 - Arteriovenous Malformations
 - Acute Ischemic Stroke
 - Extracranial and Intracranial atherosclerotic Disease

NVQI-QOD proposed data fields

Current Living Status
Date of Death
Cause
Current Smoking
30 Day Modified Rankin Score
30 Day NIHSS
30 Day NIHSS NA
Re-admission within 30 days
90 Day Modified Rankin Score
90 Day NIHSS
90 Day NIHSS NA
Re-admission within 90 days
1 Year Modified Rankin Score
1 Year NIHSS
1 Year NIHSS NA

Re-admission within 1 year
Antiplatelet or DAPT type and duration of therapy
“Verify now” instrument data or similar
Cerebral target (treated) vessel re-occlusion
Death within 30 days
Death within 90 days
Death within 1 year
New cerebral infarct within 30 days
New cerebral infarct within 90 days
New cerebral infarct within 1 year
Discharge Disposition
Rehab
Nursing Facility
Hospice
Home

NVQI-QOD proposed data fields

mRS 2 years

mRS 3 years

mRS 5 years

Health Economics Data

- Total hospital charges - This may include what is documented on UB04 billing forms
- DRG Code - Diagnosis related group (DRG) code use for billing the hospital admission
- Total Payments - Total payments received by the hospital for each patient admission
- Insurance payer - Insurance payer for each payment and hospital admission
- Net financial gain or loss - Net financial gain or loss for the hospital, calculated as the difference between total cost and total reimbursement or payment
- Length of stay - Length of hospital stay
- Cost of all devices used during procedure - Includes femoral sheaths, contrast, procedural medications, guidewires, catheters
- Hospital direct costs - Including cost of devices, but also including surgeries, nursing care, medications, imaging, and equipment costs
- Hospital indirect costs -Projected costs of utilities, human resources, maintenance, legal, insurance
- Total hospital cost = direct + indirect

CMS FDA NIH / US Government Agencies Work Closely Together

- The Devices used for Acute Ischemic Stroke Intervention (DAISI) Initiative was developed with a focus on acute ischemic stroke that allows the capture of data from actual patient encounters with medical devices and was launched by the FDA on November 9, 2017.
- Medical Device Development-Clinical Trial Phase and Marketing Applications
- Good collaboration exists across the US Federal Government to date

There may be an opportunity to work across US Government Agencies

- To make sure physicians and patients understand the levels of evidence for any given device
- Recommend reconciling CMS decisions with the understanding of sponsor requirements based on the level of evidence
- Also recommend FDA, CMS, NIH take a joint approach to the development of stroke devices, including where possible class based decisions (combining decisions for NRY and POL devices where additional evidence exists).
- A Coverage for Evidence Development will allow us to collect high quality data to support marketing devices and reimbursement of procedures

Thank you!

