Diagnosis and Management of TIA

June 12th, 2018

Thomas Jeerakathil BSc, MD, MSc, FRCP(C),
Professor
Division of Neurology, U of A
Northern Stroke Lead CV/S Strategic Clinical Network, AHS
Associate Director, Edmonton Stroke Program

Faculty/Presenter Disclosure

- **Faculty:** Thomas Jeerakathil

- **Relationships with financial sponsors:**
  - **Grants/Research Support:** AIHS, CIHR, HSFC, CSN, University Hospital Foundation
  - **Speakers Bureau/Honoraria:** Bayer (2 consultation boards).
  - **Consulting Fees:** None
  - **Patents**: None
  - **Other:** None

Mitigating Potential Bias

- The topic of this talk is unrelated to my disclosures
- I have no ongoing relationships with any companies

Objectives

- To review preventive lifestyle, medical and interventional strategies in stroke and TIA
- To review TIA diagnosis and risk triaging
- Apply the information on TIA recognition and management to one's own practice

Patient #1 Don

- A 62 year old man sees you in clinic
- He experienced blurring of vision present upon awakening that lasted a few minutes
- There was no specific visual field defect
- He also had tingling of both hands
- PMH - smoker, prior CAD, DM
- Exam - truncal obesity; BP 135/ 80; otherwise normal
- Currently on clopidogrel
- Was this a TIA?

Patient #2 Jane

- A 65 year old lady sees you in clinic
- She is referred for transient inability to speak with severe word finding difficulties lasting 15 minutes
- PMH includes hypertension
- Was this a TIA?

Approach to Stroke in 6 Lines

1. **Diagnosis and localization***
2. **Neuronal Salvage:** thrombolysis, surgical evacuation, neuroprotection, glucose, temperature, BP
3. **Etiology:** MRI/A, doppler, TTE/TEE, angio, TCD, thrombophilia, HT, DM, homocysteine, lipids; (standard workup, young stroke workup, vasculitic workup, proximal embolic workup, coagulopathic workup)*

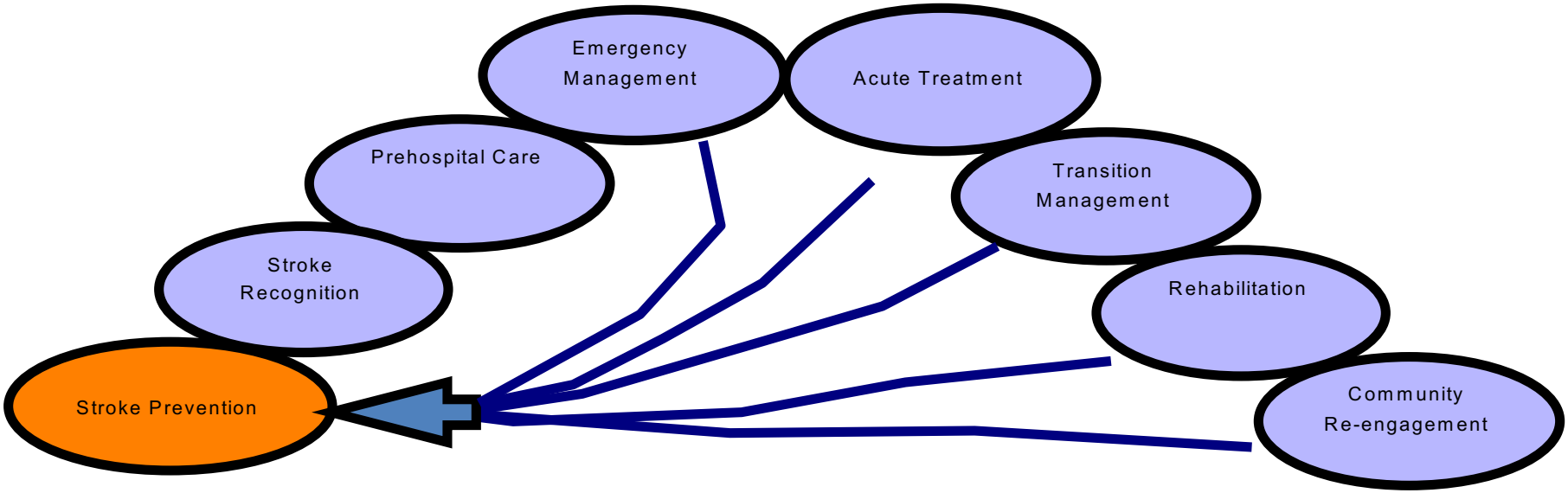
* Relevant to TIA as well

Approach to Stroke in 6 Lines

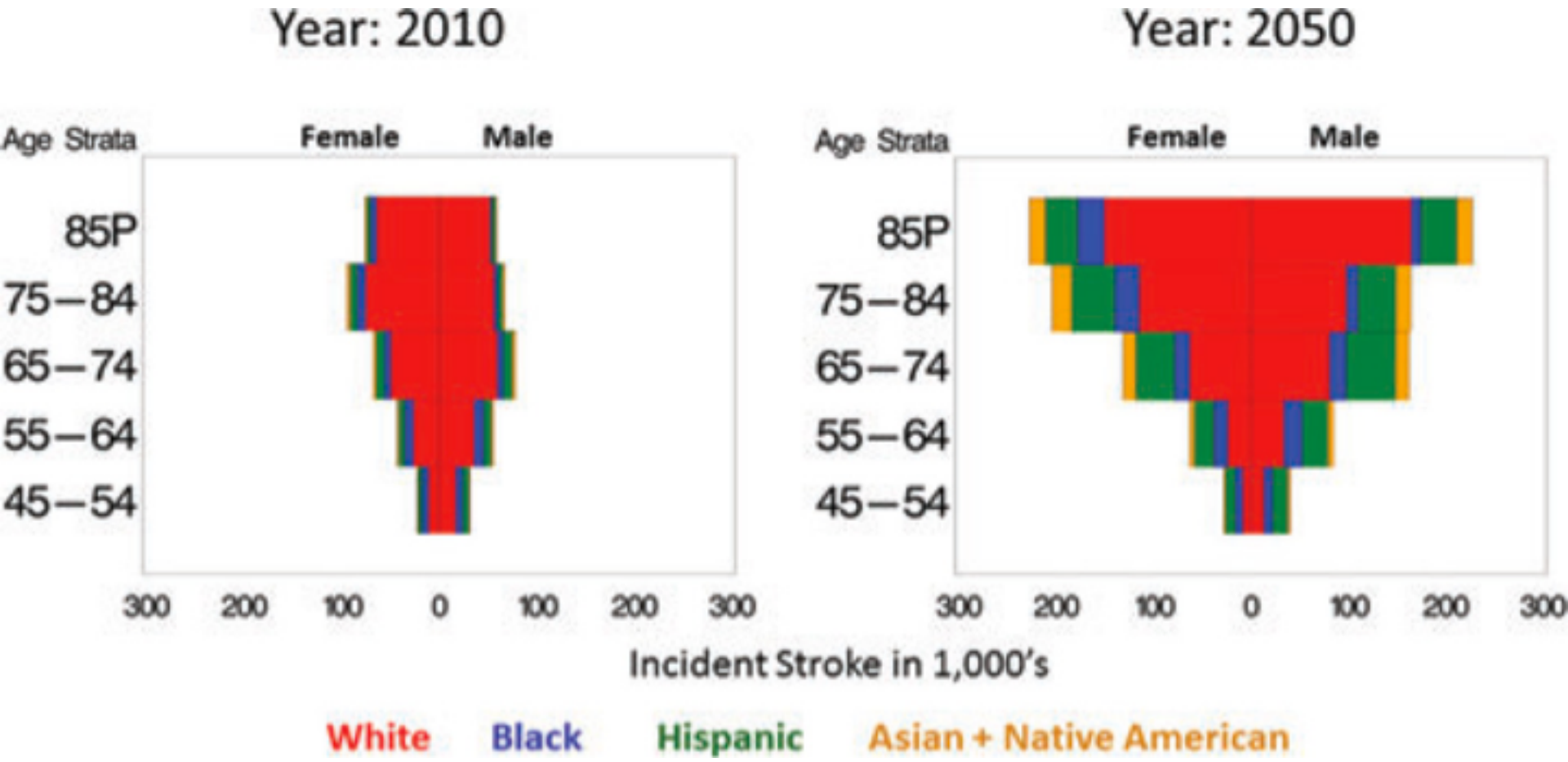
4. **Prevention of Recurrence:** antiplatelets, heparin, warfarin, endarterectomy, statins, ACE inhibitors*
5. **Prevention of Medical Complications:** DVT/PE prophylaxis, swallowing, infection
6. **Rehabilitation and Reintegration:** PT/OT, speech, inpatient rehab, driving, occupation, cognition, emotional health

* Relevant to TIA as well

Stroke Continuum

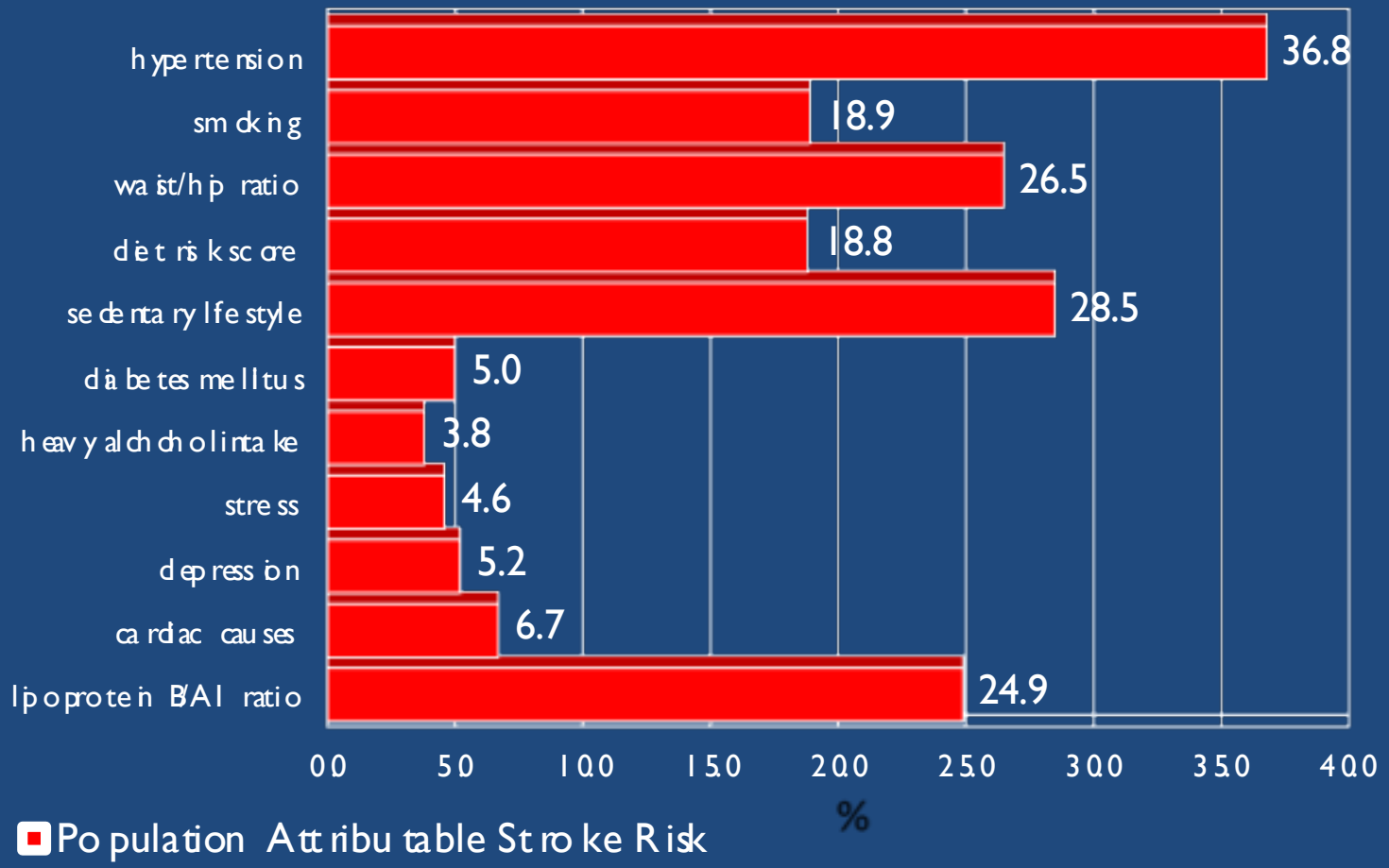


Stroke Occurrence - USA



Heart Disease and Stroke Statistics , AHA

10 Risk Factors Explain 90% of Stroke Risk



Interstroke O'Donnell et al; Lancet 2010: 376; 112–23

Optimal BMI - WHO

BMI Categories General Population:

- Underweight = <18.5
- Normal weight = 18.5-24.9
- Overweight = 25-29.9
- Obesity = BMI of 30 or greater

BMI Categories Asians:

- Underweight = <18.5
- low/mod risk= 18.5- 23
- Mod/high = 23.1- 27.5
- High/ very high risk = BMI of 27.1 or greater

Optimal BMI and Waist Circumference

	MALE	FEMALE
European/Caucasian, Sub-Saharan Africans, Eastern Mediterranean, Middle Eastern	102 cm/40 in	88 cm/ 35 in
South Asian, Malaysian, Asian, Chinese, Japanese, Ethnic South and Central Americans	90 cm/ 35in	80cm/ 32 in

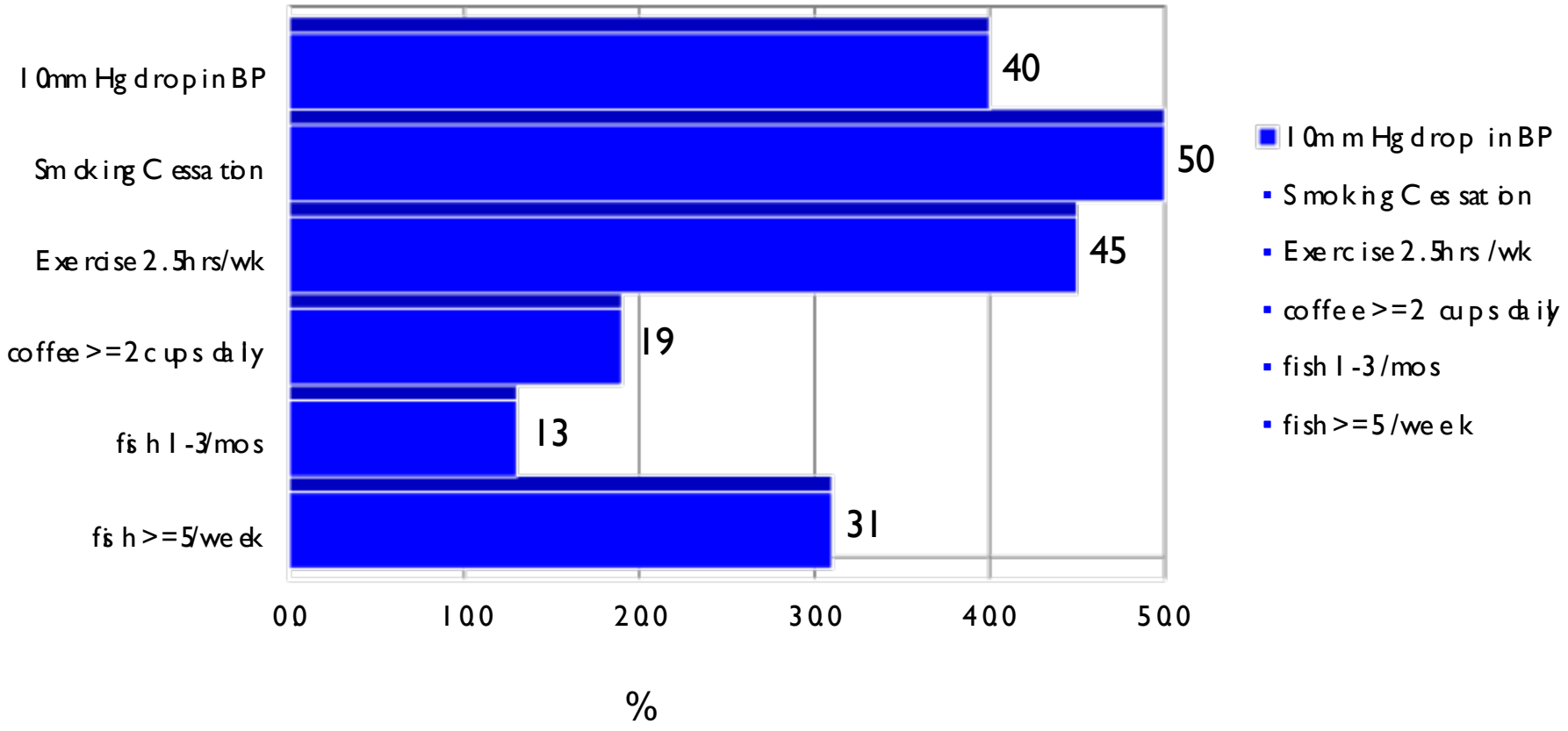
Multiple choice - Recommended minimum adult weekly physical activity

1. 2.5 hours moderate OR 1.25 hours vigorous aerobic activity and 2 muscle strengthening (in bouts of >=10 min)
2. 5 hours moderate OR 3 hours vigorous aerobic activity and 2 muscle strengthening (in bouts of >= 1 hour)
3. 2 hours vigorous aerobic activity
4. ‘pumping iron’ 2 hours a day

Multiple choice - Recommended minimum adult weekly physical activity

1. 2.5 hours moderate OR 1.25 hours vigorous aerobic activity and 2 muscle strengthening (in bouts of >=10 min)
2. 5 hours moderate OR 3 hours vigorous aerobic activity and 2 muscle strengthening (in bouts of >= 1 hour)
3. 2 hours vigorous aerobic activity
4. ‘pumping iron’ 2 hours a day

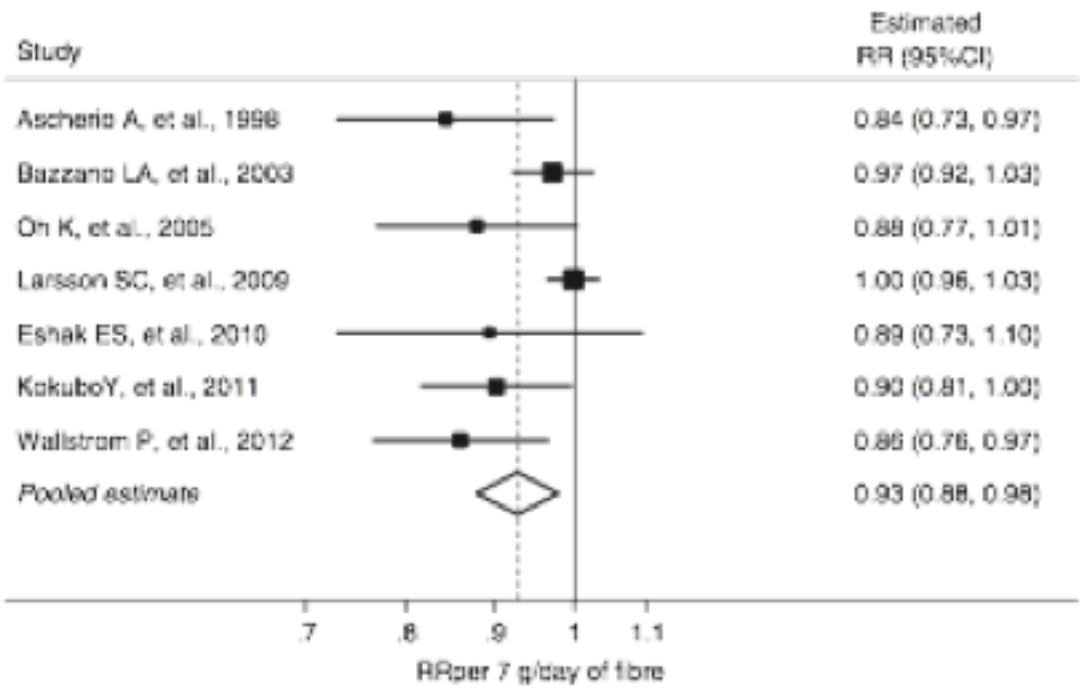
Relative Risk Reductions for stroke from lifestyle modification



Dietary Fiber Intake and Risk of First Stroke

A Systematic Review and Meta-Analysis

Diane E. Threapleton, MSc; Darren C. Greenwood, PhD; Charlotte E.L. Evans, PhD; Cristine L. Cleghorn, MSc; Camilla Nykjaer, MSc; Charlotte Woodhead, MSc; Janet E. Cade, PhD; Chris P. Gale, MBBS; Victoria J. Burley, PhD



Meta-analysis of 8 cohort studies; found that for every 7g increase in fibre intake a 7% decrease in the RR of stroke

Stroke 2013:44:00-00;

What is a TIA?

- Definition:
- Ischemic focal neurological deficit lasting < 24 hr

- Proposed tissue based definition:
- Rapidly resolving neurologic symptoms, typically lasting <1 hour, with no evidence of infarction on MRI (DWI) (Albers et al. New Engl J Med; 2002; 347: 1713-1716)

- 40% – 60% of clinically diagnosed TIA patients have ischemic injury on DWI

(Ay et al. Cerebrovasc Dis; 2002; 14: 177-186)

Diagnosing ‘spells’

- Phenomenology: before, during, after the event
- Was the event witnessed? What did witnesses observe?
- What is the setting? (vascular risk factors, elderly, young without risk factors)

Top 6 symptoms likely to be a TIA-1

6. Vertigo only if present with brainstem symptoms
5. Hemibody numbness
4. Double vision, crossed numbness or weakness, slurred speech, ataxia of gait

Top 6 symptoms likely to be a TIA - 2

3. Monocular or hemifield visual loss (not blurring of entire visual field)

2. Speech disturbance for a defined period of time (definite dysarthria, muteness or marked word finding difficulty, paraphasic speech)

1. Hemibody weakness

Symptoms unlikely to be a TIA - 2

- Positional and recurrent numbness of one limb or tingling of all 4 extremities
- Scintillating or flashing visual disturbances
- Symptoms of duration < 30 seconds
- Seizure or convulsions at onset
- Isolated syncope
- Postural dizziness alone

Features supportive of TIA or Stroke

- A well-defined onset time
- Definite focal neurological symptoms
- Presence of neurological signs on examination
- Being able to lateralize signs to the left or right side of the brain
- Being able to determine a clinical stroke subclassification

The Brain Attack Study; Stroke 2006; 37; 769-775

Patient #1 Don

- A 62 year old man sees you in clinic
- He experienced blurring of vision present upon awakening that lasted a few minutes
- There was no specific visual field defect
- He also had tingling of both hands
- PMH - smoker, prior CAD, DM
- Exam - truncal obesity; BP 135/ 80; otherwise normal
- Currently on clopidogrel
- Was this a TIA?

Patient #2 Jane

- A 65 year old lady sees you in clinic
- She is referred for transient inability to speak with severe word finding difficulties lasting 15 minutes
- PMH includes hypertension
- Was this a TIA?

Stroke Risk

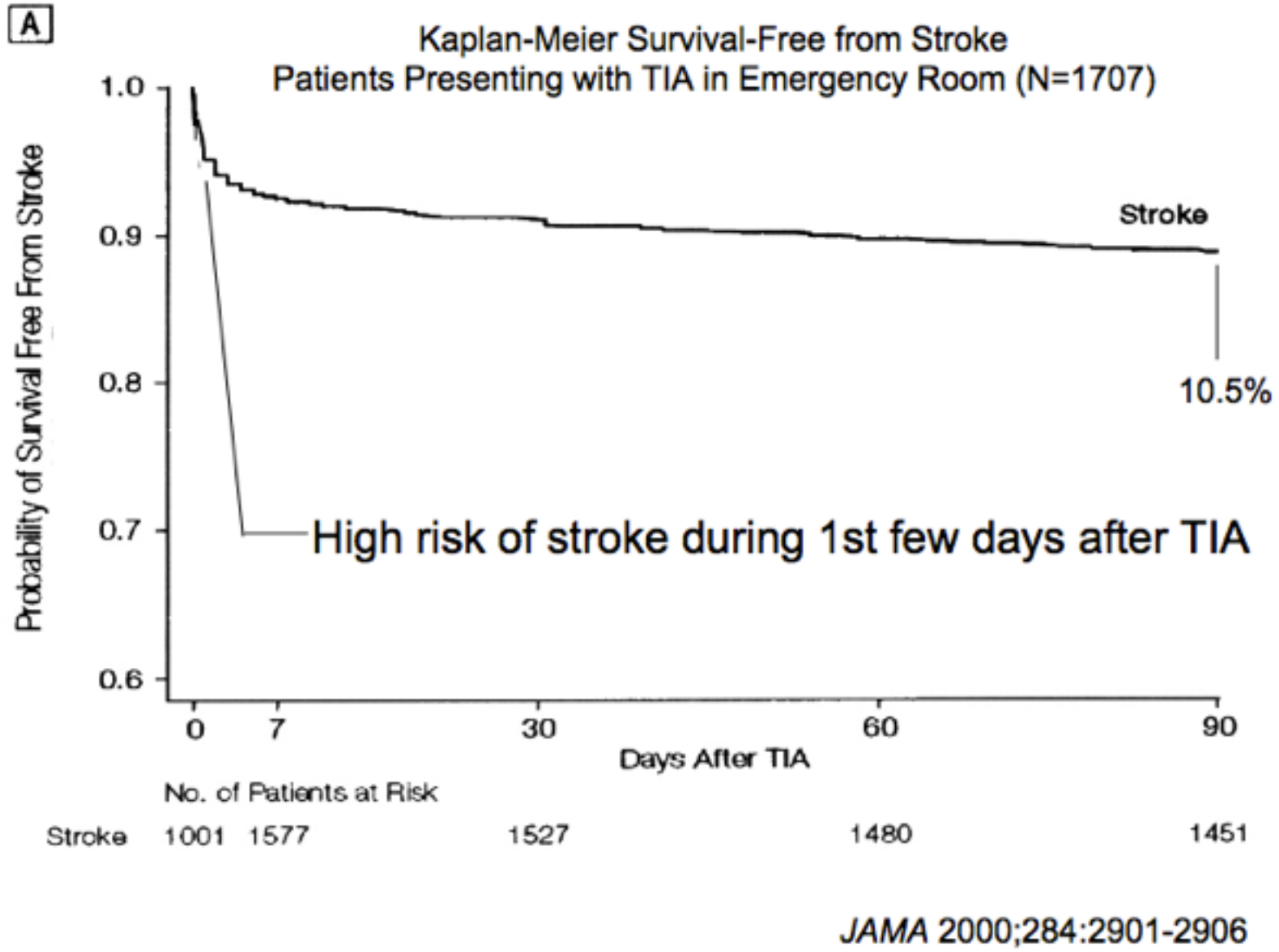
- Risk of stroke following a TIA is high:
- As high as10-20% within 90 days
- 50% of these within the first 48 hours

(Johnston et al. JAMA 2000; 284: 2901-06)

- **~ 20%-40% of strokes are preceded by a TIA or non disabling stroke**

(Rothwell et al. Lancet Neurol 2006; 5: 323-331)

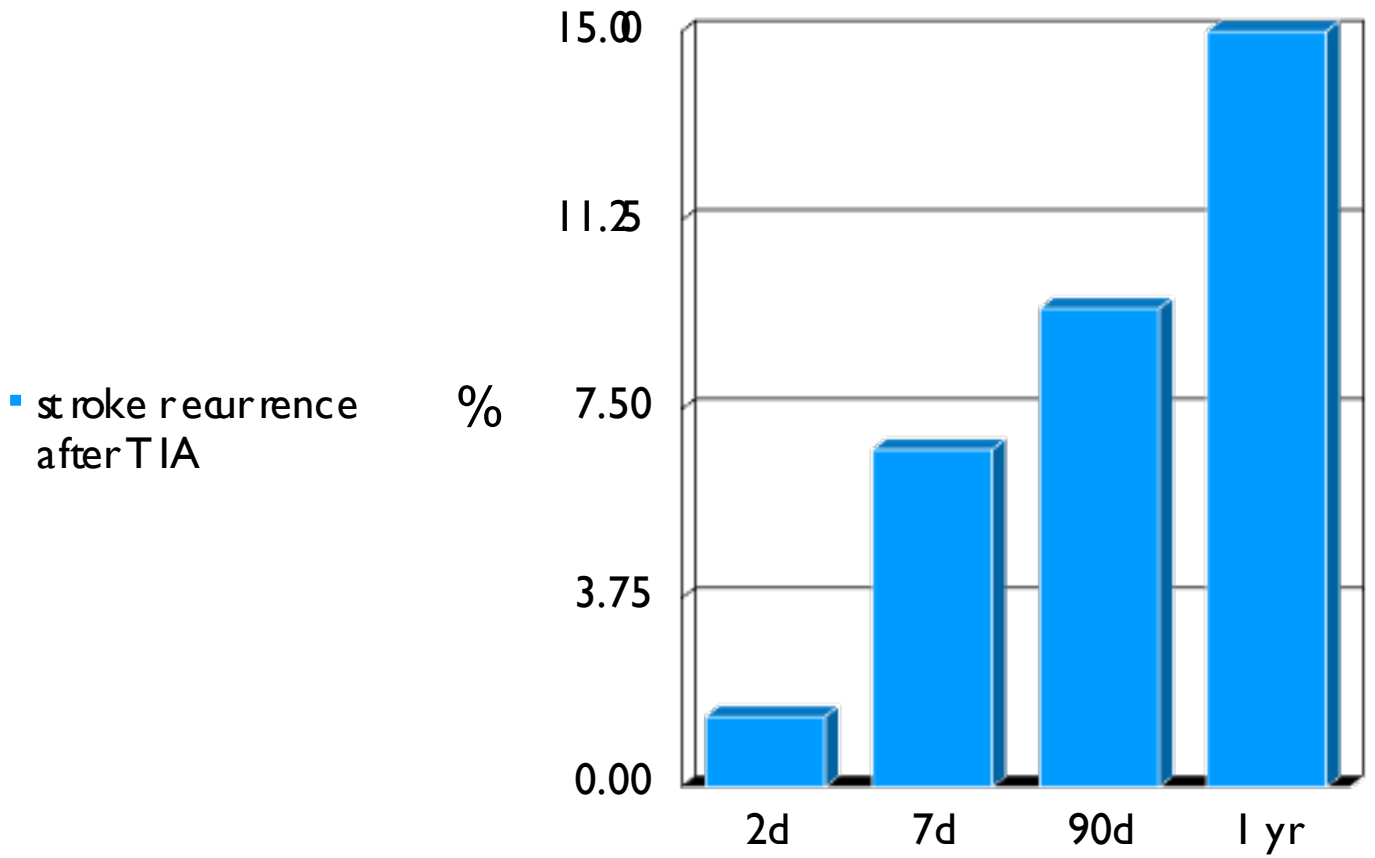
- Golden Opportunity for Stroke Prevention!



In 2000 the stroke rate after TIA was 10.5% at 3 months! 1/2 this risk is in the 1st 48 hours and ¾ of this risk occurs by 7 days.

Alberta TIA Study 2004

Hill et al Neurology 2004;62;2015-20



2285 ED visits for TIA across Alberta in one fiscal year; 10% stroke recurrence at 3 months; 15% at one year;

ABCD² Score

Rothwell et al. Lancet; 2007; 369: 283-292

	Yes	No
Age >= 60 yrs	**1**	**0**
Bp >= 140/90	**1**	**0**
Clinical Features		
• **Unilateral weakness (with or without speech disturbance)**	**2**	**0**
• **Speech deficit without weaknes**	**1**	**0**
Duration		
> 10 min < 59 min	**1**	**0**
>= 60 min	**2**	**0**
Diabetes	**1**	**0**

Score >= 4 = High Risk

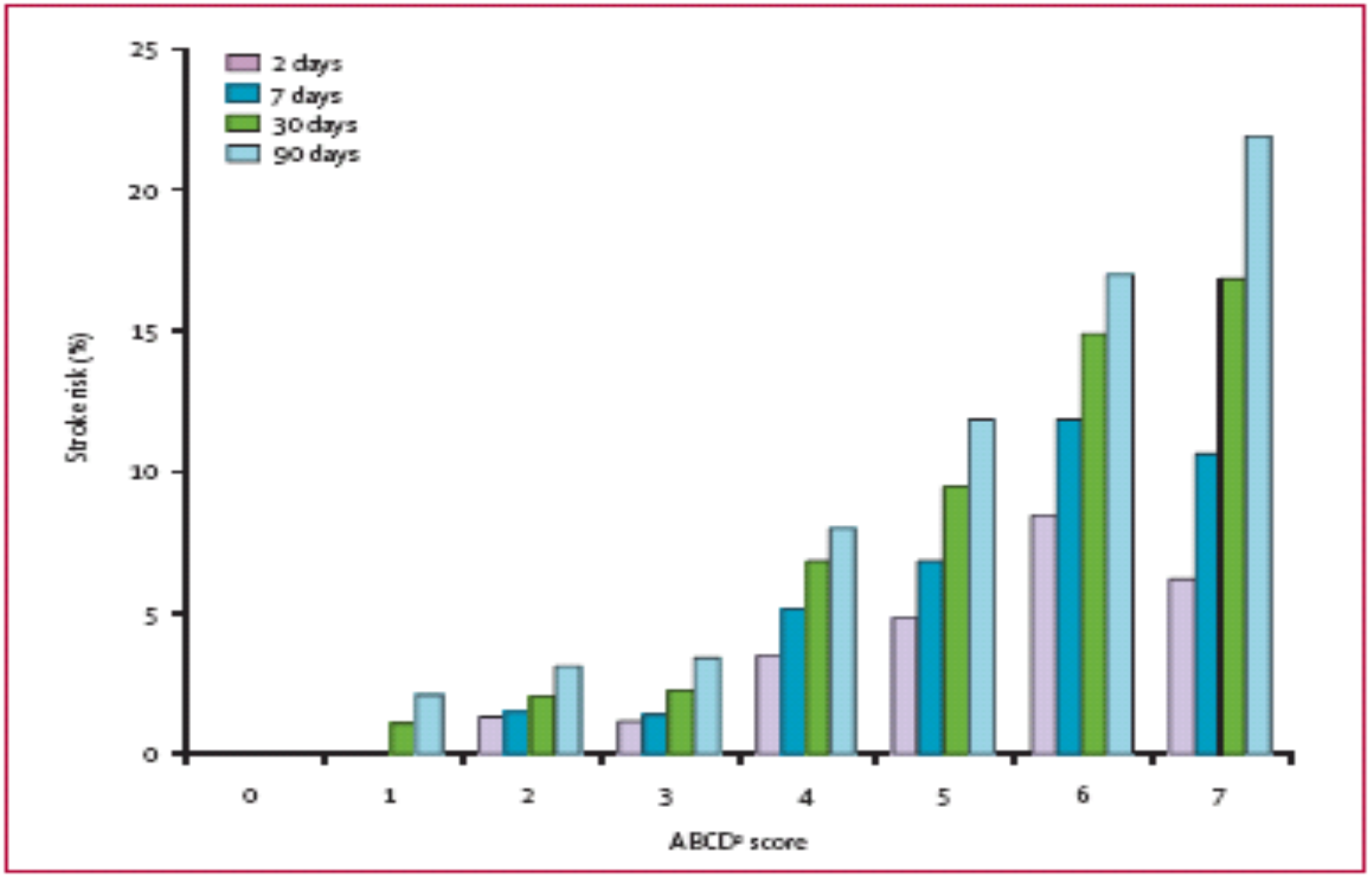


Figure: Short-term risk of stroke by ABCD² score in six groups combined (n=4799)

Stroke risk after TIA increases with increasing ABCD2 score Risk. Risk is 22% at 90d for ABCD2 score of 7

Very High Risk TIA

TIA symptoms in the last 48 hours with high risk symptoms **(speech disturbance or weakness of the face, arm or leg)** or lower risk symptoms (hemianopsia, monocular visual loss, brainstem syndrome, hemisensory loss)

Immediate actions:

Proceed immediately to the nearest ED with capacity for advanced stroke care:

Brain imaging and imaging of the neck vessels (CTA neck vessels or carotid doppler) within 24 hours of health system contact.

Immediate EKG;

If no blood on CT initiate immediate therapy with antiplatelet agents.*
Canadian Best Practice Recommendations for Stroke Care (Secondary Prevention of Stroke Update 2017)

*(if fully resolved antiplatelet agents could be started prior to CT – expert consensus)

Canadian Best Practice Recommendations for Stroke Care (Secondary Prevention of Stroke Update 2017)

High Risk TIA

TIA symptoms occuring 48 hours to 2 weeks ago with high risk symptoms (speech disturbance or weakness of the face, arm or leg)

Immediate actions:

Clinical evaluation and investigations by a professional with stroke expertise ASAP **ideally initiated** within 24 hours of first contact with the health system:

Brain imaging and imaging of the neck vessels (CTA neck vessels or carotid doppler); (ie completed within 48 hours – not specified)

EKG;

If no blood on CT initiate immediate therapy with antiplatelet agents.*

*(if fully resolved antiplatelet agents could be started prior to CT – expert consensus)

Canadian Best Practice Recommendations for Stroke Care (Secondary Prevention of Stroke Update 2017)

Moderate Risk TIA

TIA symptoms in the last 48 hours – 2 weeks with lower risk symptoms (eg. monocular visual loss, hemianopsia, brainstem syndrome, numbness)

Immediate actions:

Clinical evaluation and investigations by a professional with stroke expertise ASAP **ideally initiated** within two weeks of first contact with the health system:

Brain imaging and imaging of the neck vessels (CTA neck vessels or carotid doppler). (not specified – suggest completed within two weeks)

EKG;

If no blood on CT initiate immediate therapy with antiplatelet agents.*

Canadian Best Practice Recommendations for Stroke Care (Secondary Prevention of Stroke Update 2017)

*(if fully resolved antiplatelet agents could be started prior to CT – expert consensus)

Lower Risk TIA

TIA symptoms more than 2 weeks ago regardless of symptoms.

Immediate actions:

Referral to clinic with capacity for advanced stroke care or neurological expertise to be seen within one month from first contact with the healthcare system.

Canadian Best Practice Recommendations for Stroke Care (Secondary Prevention of Stroke Update 2017)

Atypical and other symptoms unlikely to be TIA

Imaging and referral to general neurologist, urgent neurology clinic or a stroke prevention clinic based on presentation and clinical judgement.

Edmonton Zone TIA Triaging Algorithm 2018

If you need help with TIA Triaging

Alberta-wide
For any Increased Risk TIA or higher (or any TIA syndrome you are not sure of) call:

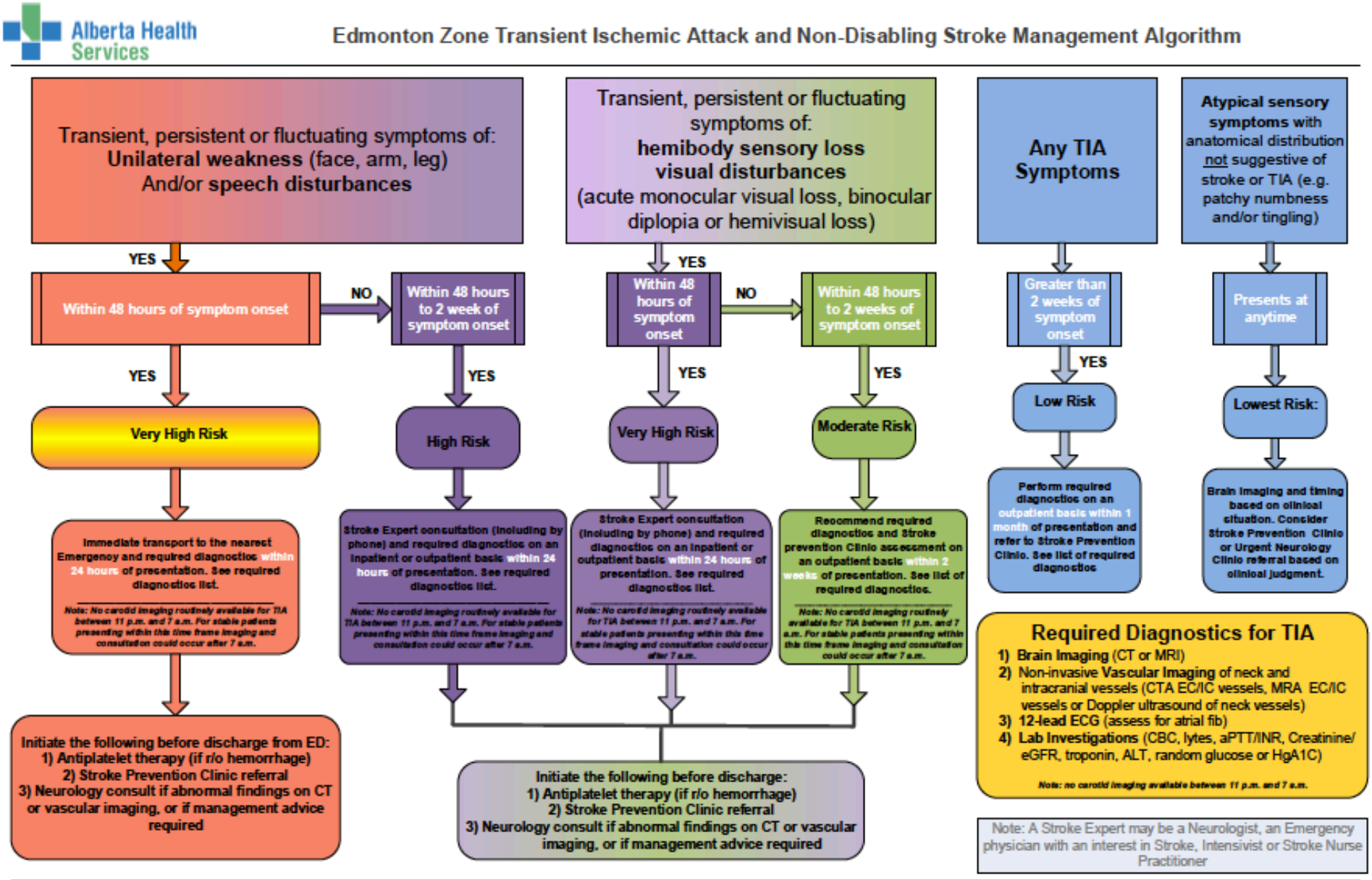
RAAPID North
1-800-735-0812

or RAAPID South
1-800-661-1700

To speak to a stroke neurologist about urgent TIA care (if required). However the Edmonton Zone TIA Algorithm can guide you quite well. (on CCPG)

https://www.albertahealthservices.ca/info/Page9356.aspx

Newest version – not yet on website!



Patient Phil

- A 52 year old man shows up in your general neurology office booked in urgently
- Transient symptoms of weakness of the right arm and leg and aphasia (duration 15 minutes) (yesterday)
- BP 150/90 at home right after the event
- PMH - smoker, no meds prior but asa for 24 hrs
- What is his Triage Level?

Patient Phil

- A 52 year old man shows up in your general neurology office booked in urgently
- Transient symptoms of weakness of the right arm and leg and aphasia (duration 15 minutes) (yesterday)
- BP 150/90 at home right after the event
- PMH - smoker, no meds prior but asa for 24 hrs
- What is his Triage Level? Very high (immediate referral)

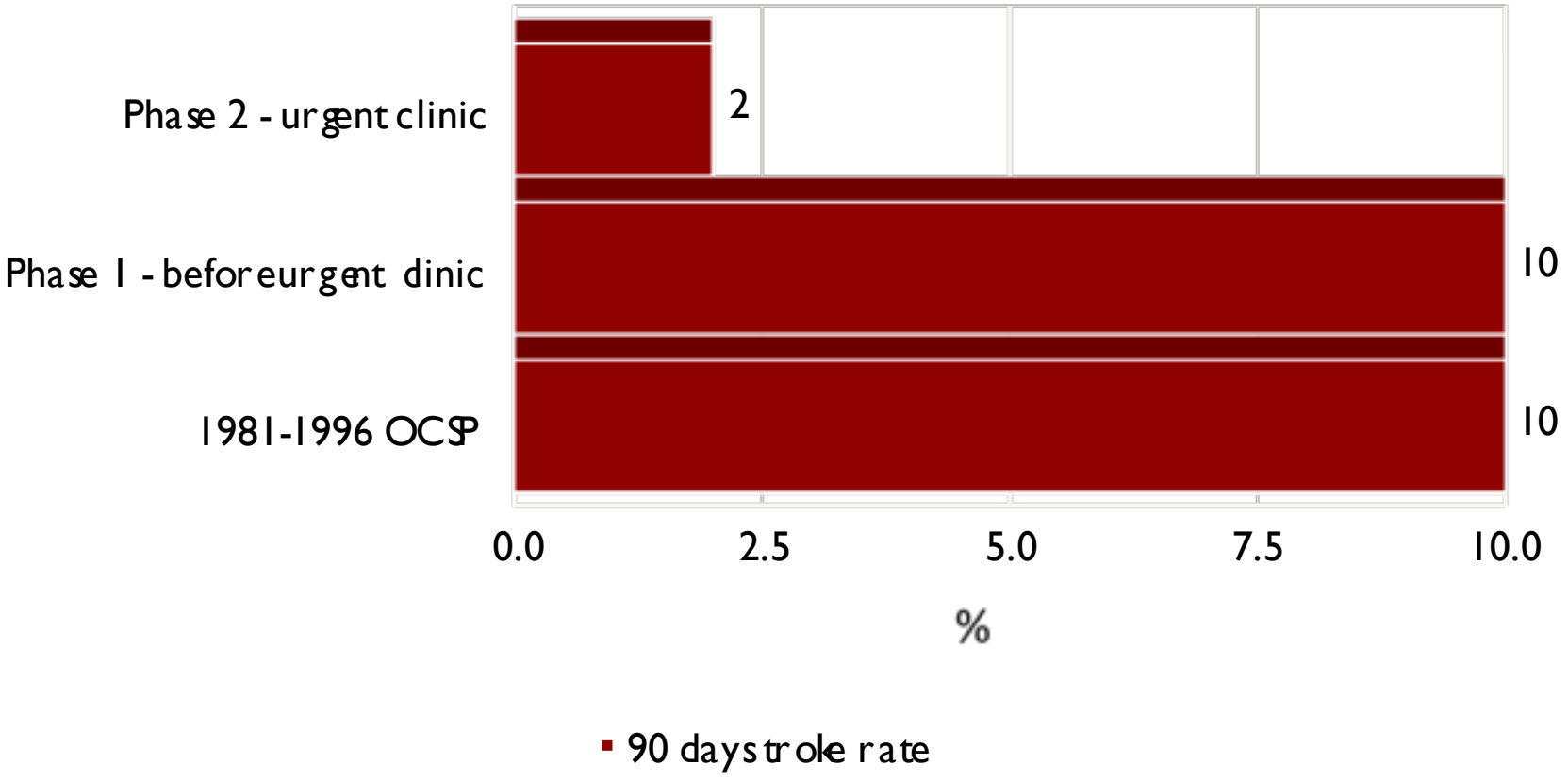
Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison

Peter M Rothwell, Matthew F Giles, Arvind Chandratheva, Lars Marquardt, Olivia Geraghty, Jessica N E Redgrave, Caroline E Lovelock, Lucy E Binney, Linda M Bull, Fiona C Cuthbertson, Sarah J V Welch, Shelley Bosch, Faye Carasco-Alexander, Louise E Silver, Sergei A Gutnikov, Ziyah Mehta, on behalf of the Early use of Existing Preventive Strategies for Stroke (EXPRESS) study

- Health services research study
- Population based – prospective case capture in a 'captive' population in Oxfordshire
- Evaluated the effect of implementation of an urgent access TIA clinic on stroke recurrence rates following TIA
- 1278 patients with TIA

Lancet 2007; 370; 1432-42

The EXPRESS Study: Effect of rapid treatment of TIA



Are we making progress with TIA?

- In several areas across the world, stroke recurrence rates after TIA are dropping in the last decade– from 10% to 3-4% at 90 days.
- Surveillance tends to be in those systems with organized stroke and TIA care
- Better secondary prevention following TIA may be a factor
- There is scarce data for undeveloped stroke systems or the developing world

Patient Phil

If you are in private practice and seeing Phil today in your clinic what options are available to you to expedite his care?

Patient Phil

If you are in private practice and seeing Phil today in your clinic what options are available to you to expedite his care?

1) arrange assessment on an inpatient basis via an emergency department

2) Follow the CBPSC recommendations or the SPEZ or similar algorithm

3) If unsure call RAAPID and speak to the stroke neurology (South) or telestroke (North) teams

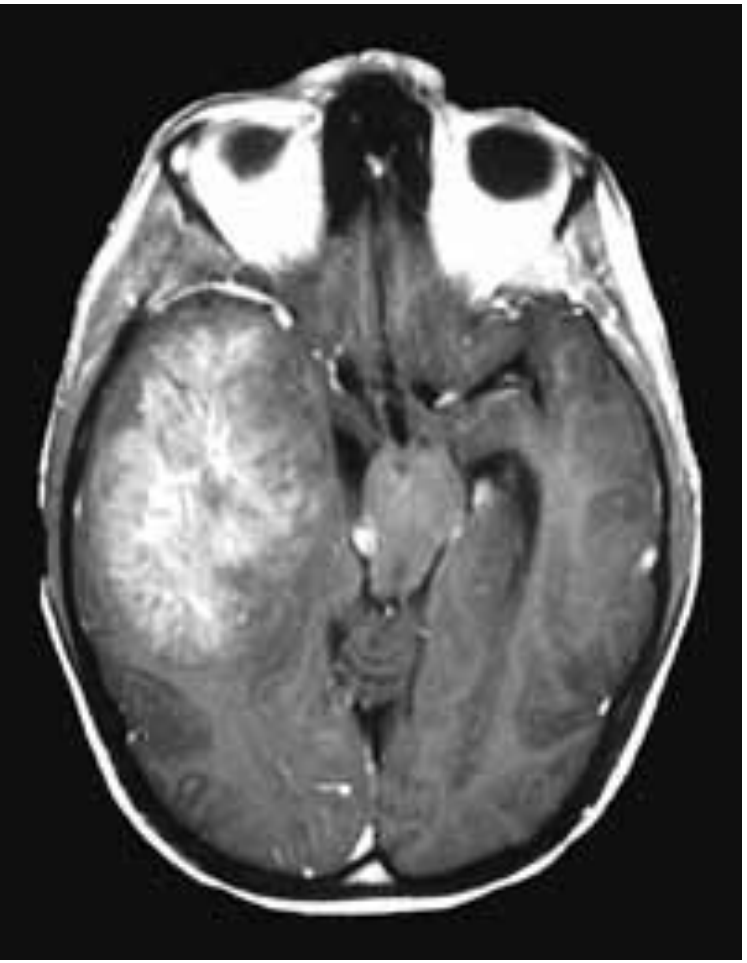
Patient Phil

- A 52 year old man shows up in your general neurology office booked in urgently
- Transient symptoms of weakness of the right arm and leg and aphasia (duration 15 minutes)
- PMH - smoker, no meds prior but asa for 24 hrs
- Exam - truncal obesity and general obesity
- What questions or tests could we use to fully determine his future stroke risk?

“Standard workup” for TIA or stroke

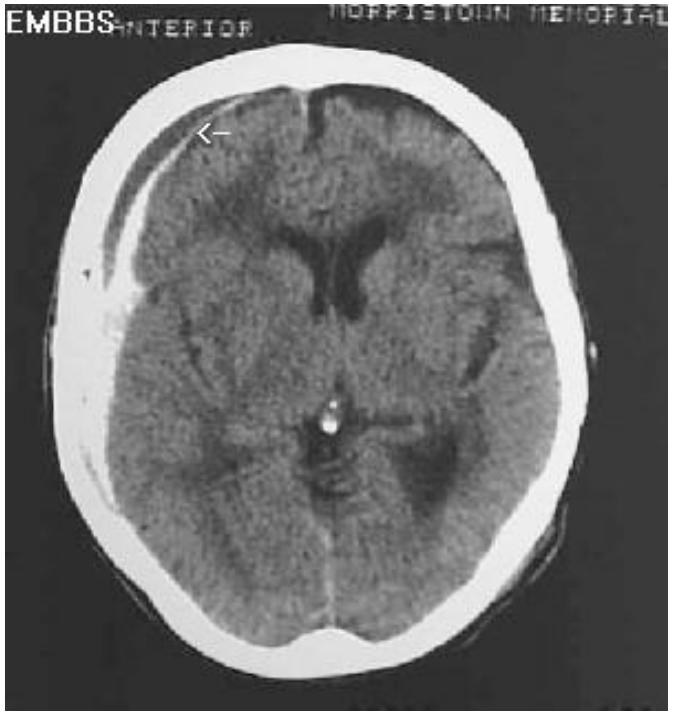
- Brain imaging (CT plain or MRI with DWI)
- Vascular imaging – CTA neck and brain preferred over carotid ultrasound although it still has a role
- Holter monitor (long term cardiac monitor?)
- Consider TTE (criteria are not clear cut)

Brain Imaging - for TIA Mimics

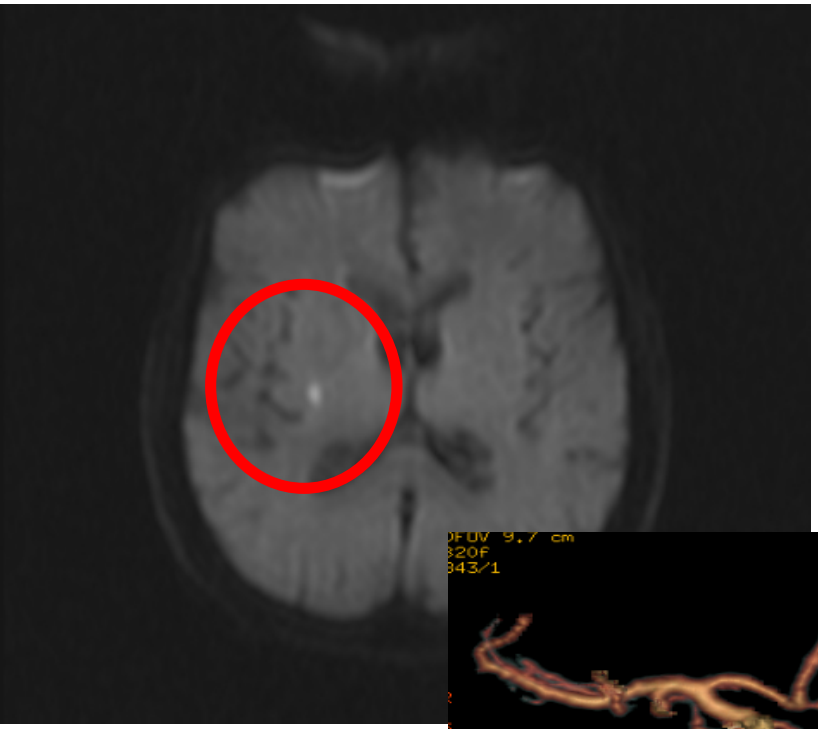


Brain CT is sufficient

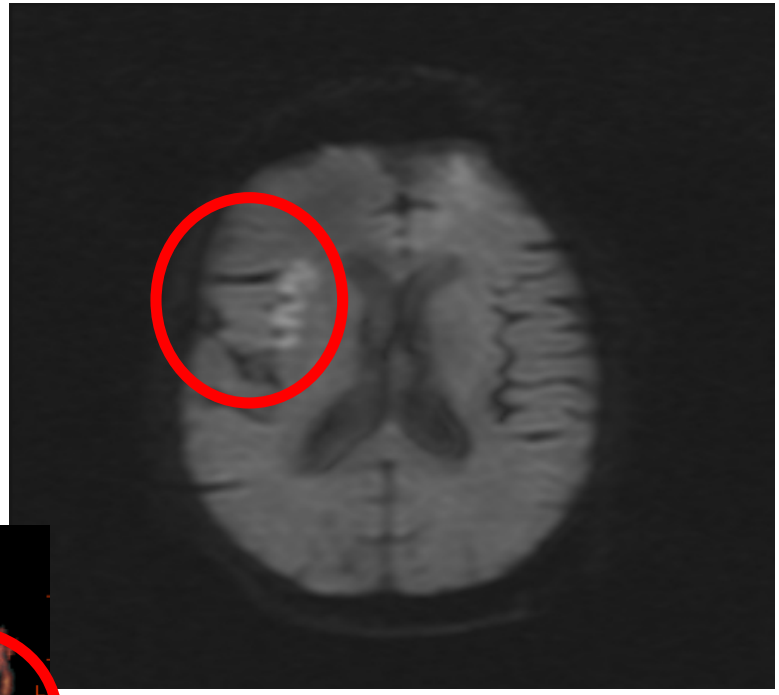
Brain MRI is best but less available

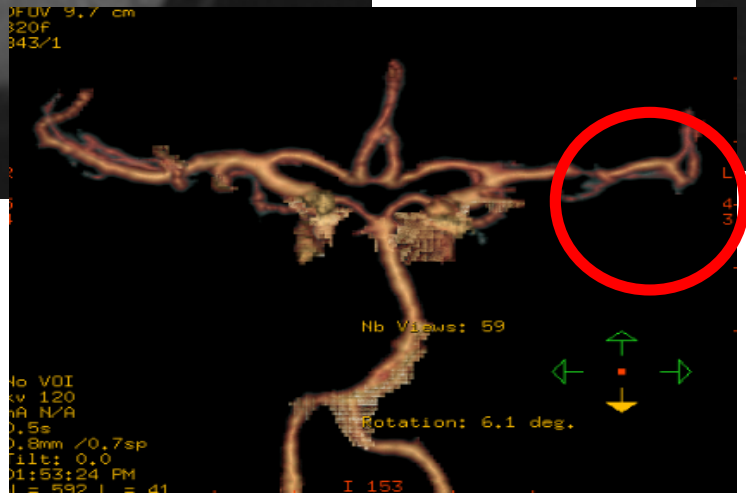


Brain Imaging - for TIA Diagnosis/Prognosis



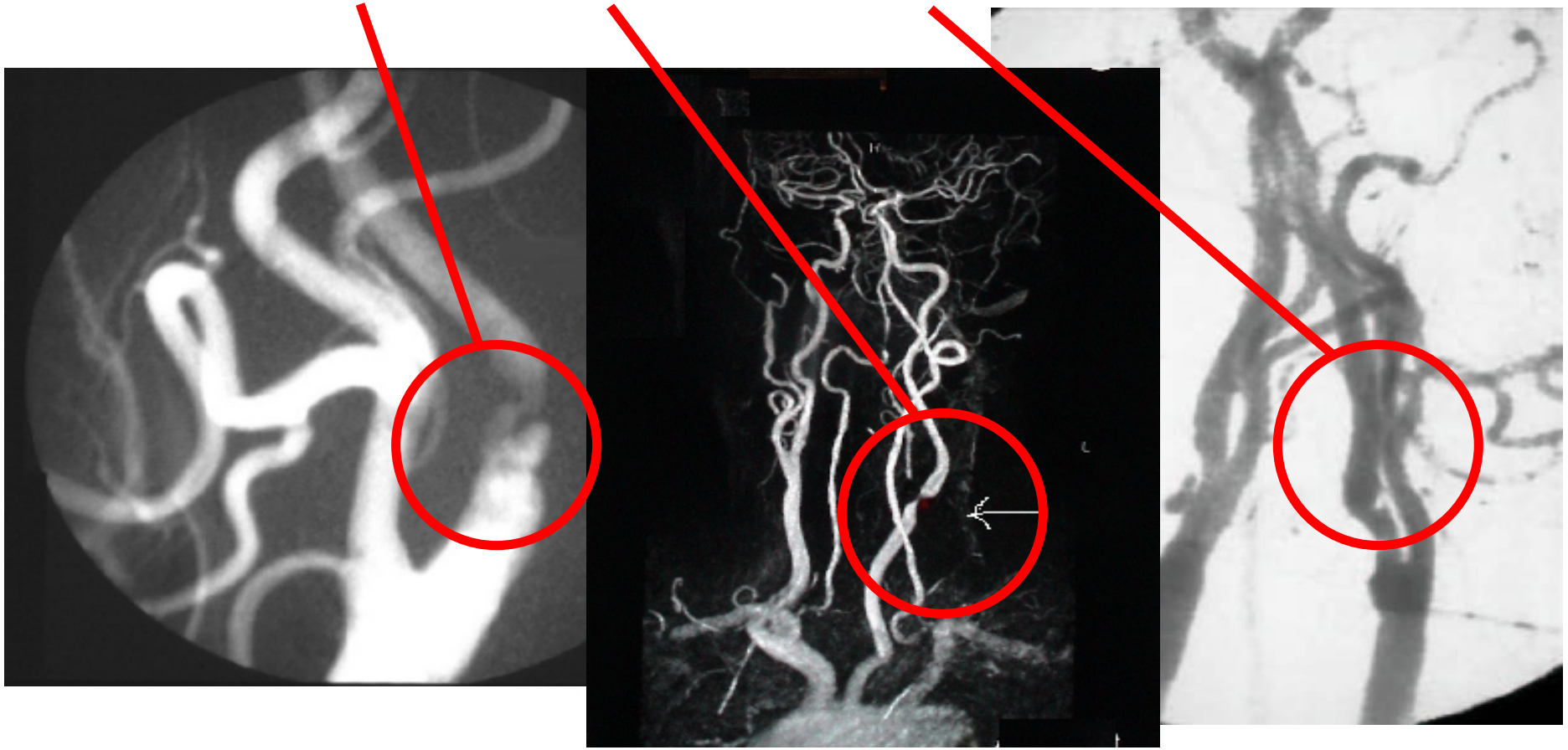
MRI/DWI is best for brain tissue



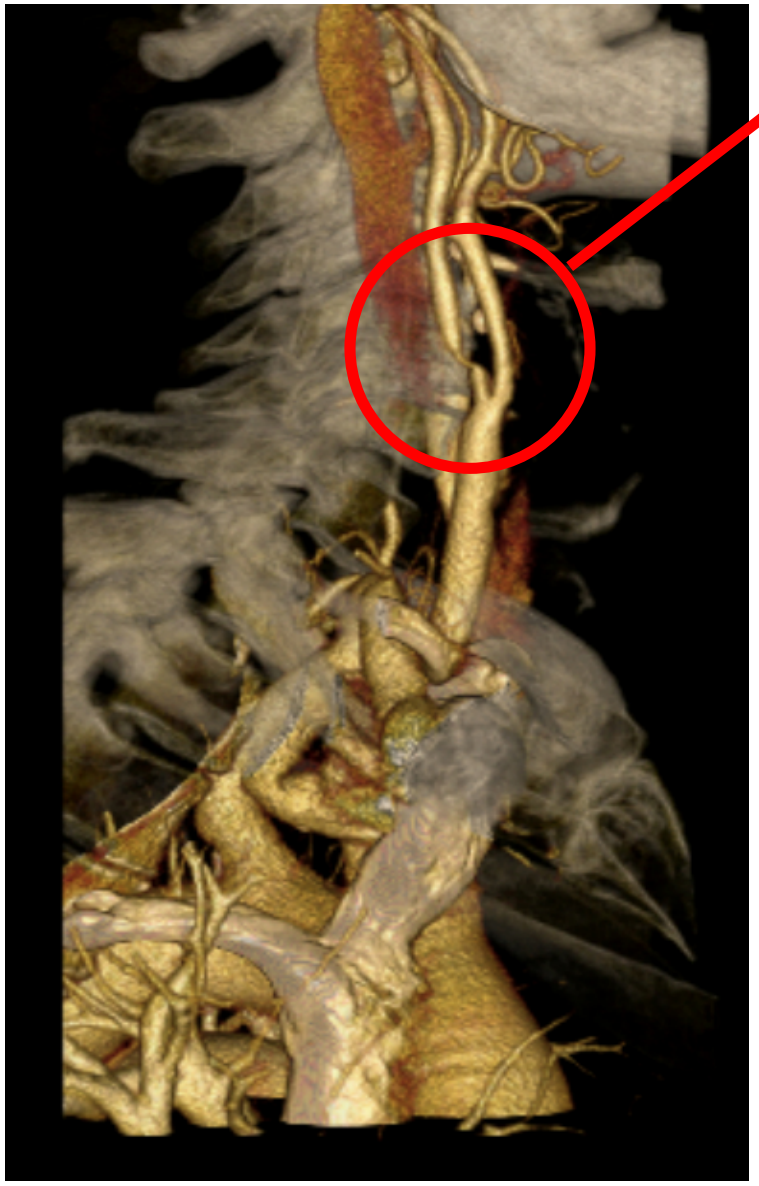


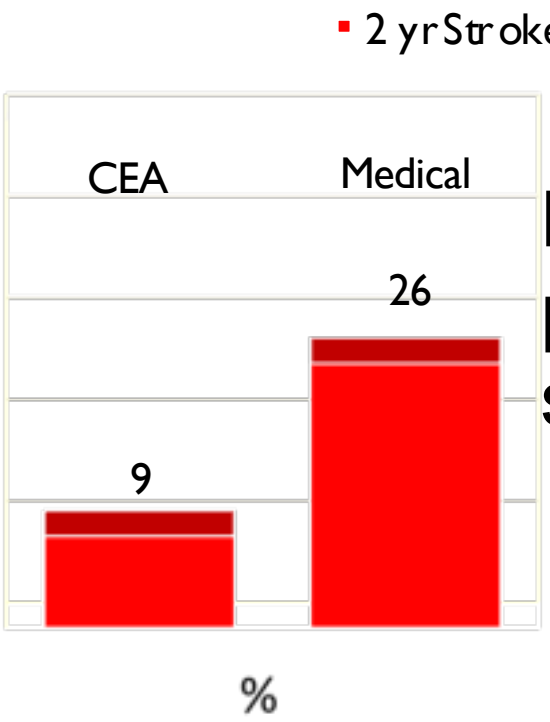
CTA neck and intracranial arteries is best for blood vessels

Symptomatic Carotid stenosis
-stroke risk as high as 42% at 2 years;



Symptomatic Carotid Stenosis



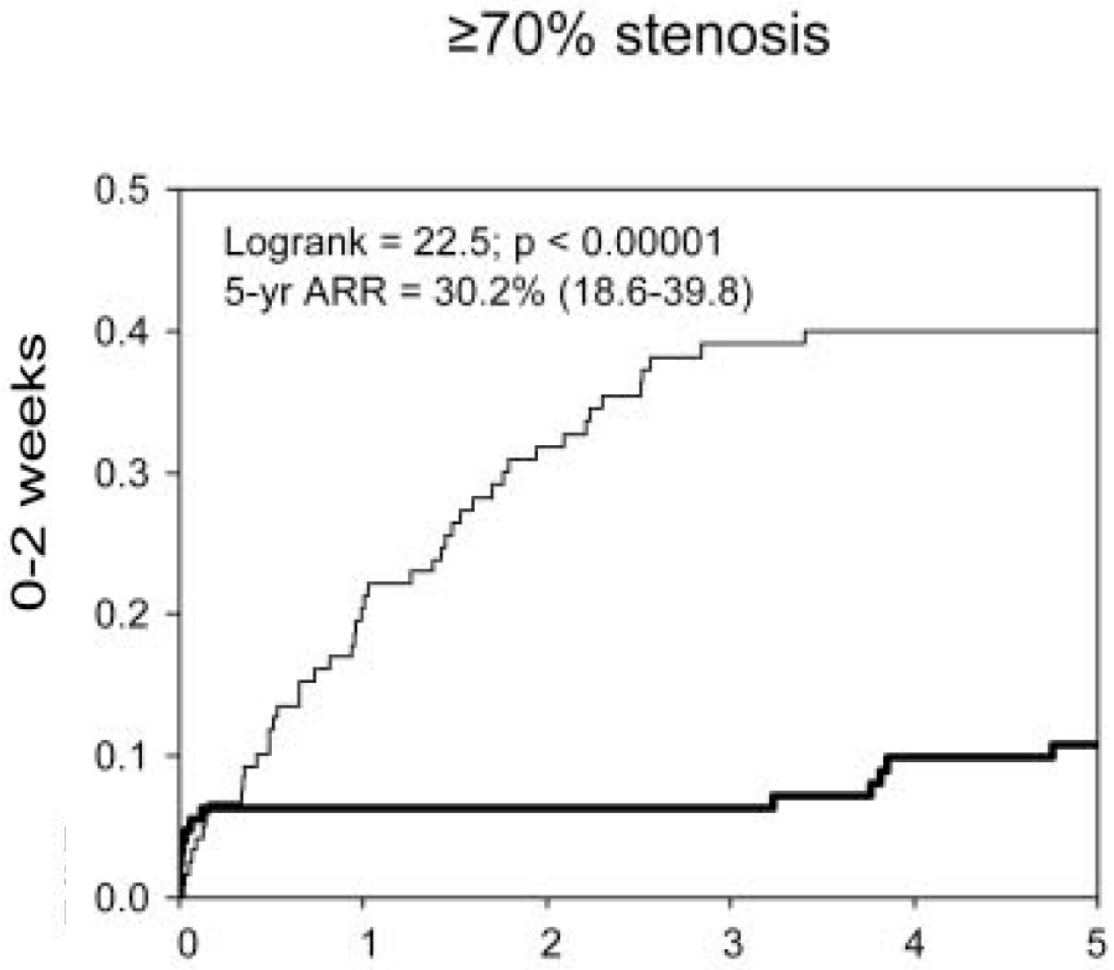


NNT = 5.6 to prevent 1 stroke

This benefit occurs if carotid endarterectomy (CEA) performed within 6 months of symptoms.

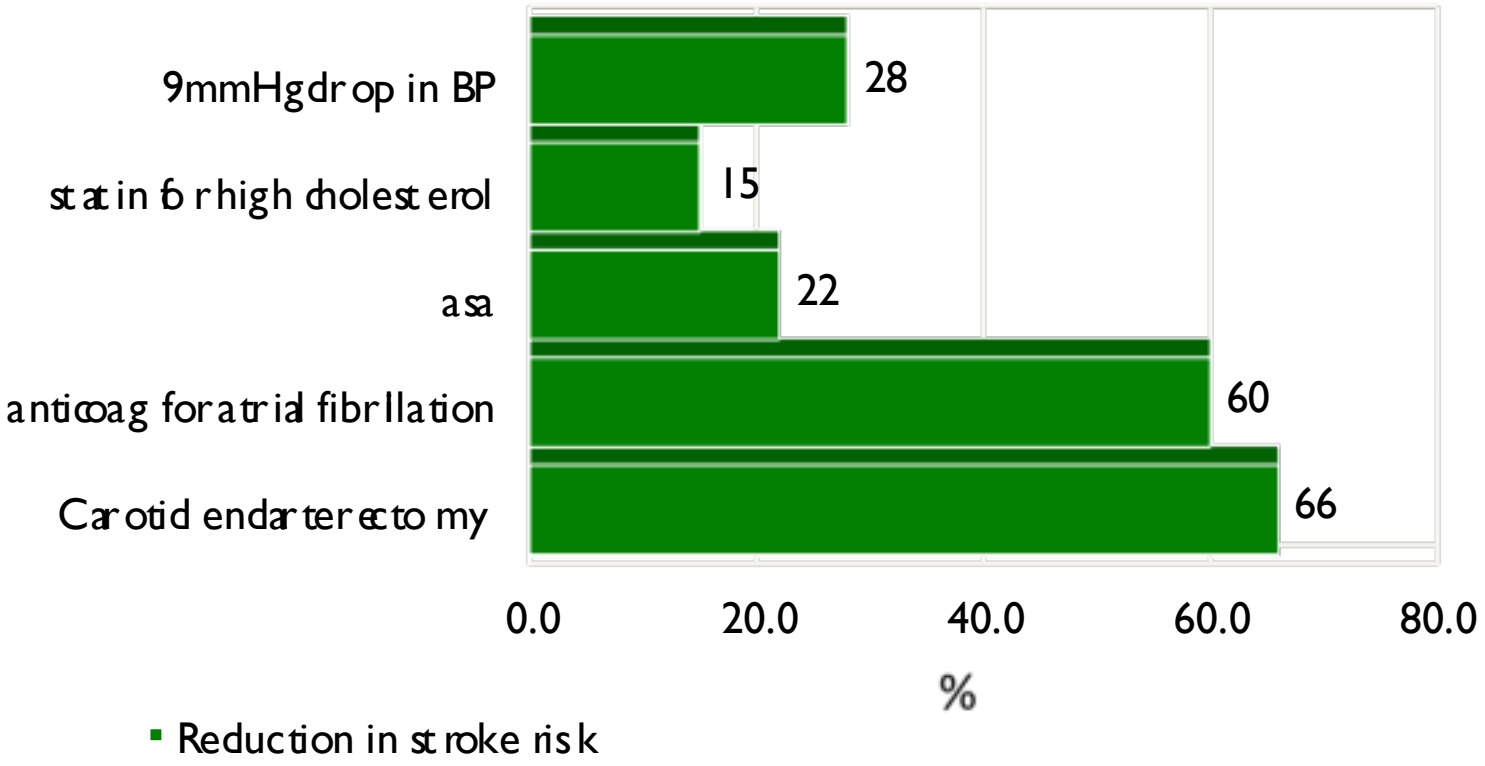
Early Carotid Surgery Much Better

Rothwell PM et al. Stroke 2004;35:2855-2861.

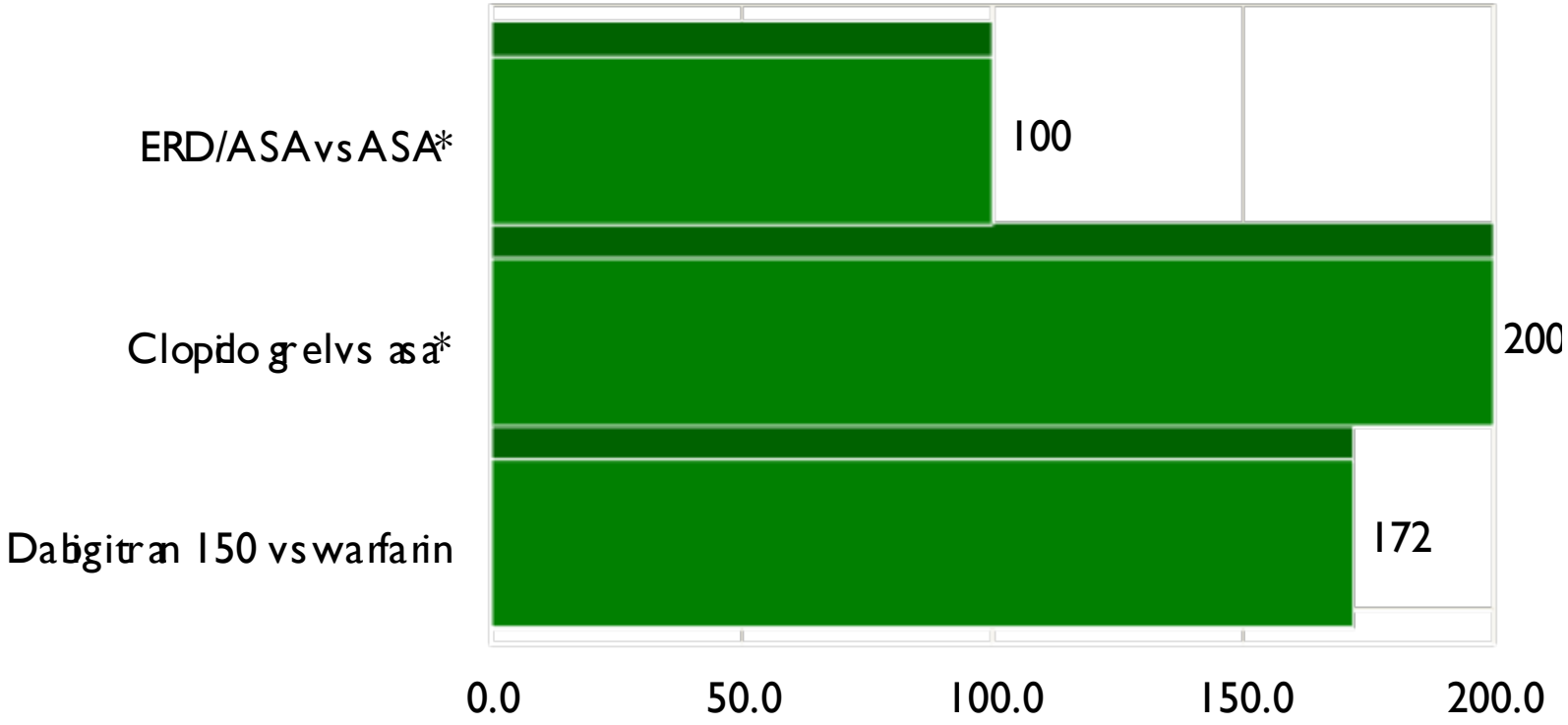


NNT is 3 to prevent 1 stroke if CEA done <2wks from TIA or minor stroke! Benefit MAY be neutral after 2 weeks in women and 12 weeks in men

Relative Risk Reductions for secondary stroke prevention



NNT over baseline therapy to prevent 1 stroke at 1 year



* these therapies are similar in head to head comparison

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

- 'CHANCE' - RDBPC Trial
- 114 Centres in China - 5170 patients within 24 hours of high risk TIA or minor stroke
- Clopidogrel load 300mg then 75mg per day for 90 days and Asa 75-300 mg per day on day 1; then 75mg daily for 21 days
- vs aspirin 75mg/d and clopidogrel placebo for 3 months

NEJM 2013; 369: 11-19

Table 2. Efficacy and Safety Outcomes.

Outcome	Aspirin (N=2586)		Clopidogrel and Aspirin (N=2584)		Hazard Ratio (95% CI)	P Value
	Patients with Event no.	Event Rate %	Patients with Event no.	Event Rate %		
Primary outcome						
Stroke	303	11.7	212	8.2	0.68 (0.57–0.81)	<0.001
Secondary outcomes						
Stroke, myocardial infarction, or death from cardiovascular causes	307	11.9	216	8.4	0.69 (0.58–0.82)	<0.001
Ischemic stroke	295	11.4	204	7.9	0.67 (0.56–0.81)	<0.001
Hemorrhagic stroke	8	0.3	8	0.3	1.01 (0.38–2.70)	0.98
Myocardial infarction	2	0.1	3	0.1	1.44 (0.24–8.63)	0.69
Death from cardiovascular causes	5	0.2	6	0.2	1.16 (0.35–3.79)	0.81
Death from any cause	10	0.4	10	0.4	0.97 (0.40–2.33)	0.94
Transient ischemic attack	47	1.8	39	1.5	0.82 (0.53–1.26)	0.36
Safety outcomes						
Bleeding[A]						
Severe	[illegible]	0.2	4	0.2	0.94 (0.24–3.79)	[illegible]
Moderate	4	0.2	3	0.1	0.73 (0.16–3.26)	0.68
Mild	19	0.7	30	1.2	1.57 (0.88–2.79)	0.12
Any bleeding	41	1.6	60	2.3	1.41 (0.95–2.10)	0.09

- 'CHANCE' - results
- 32% lower stroke risk at 90 days
- Lower stroke/MI/vascular death (but all driven by stroke!)
- No significant bleeding excess

NEJM 2013; 369: 11-19

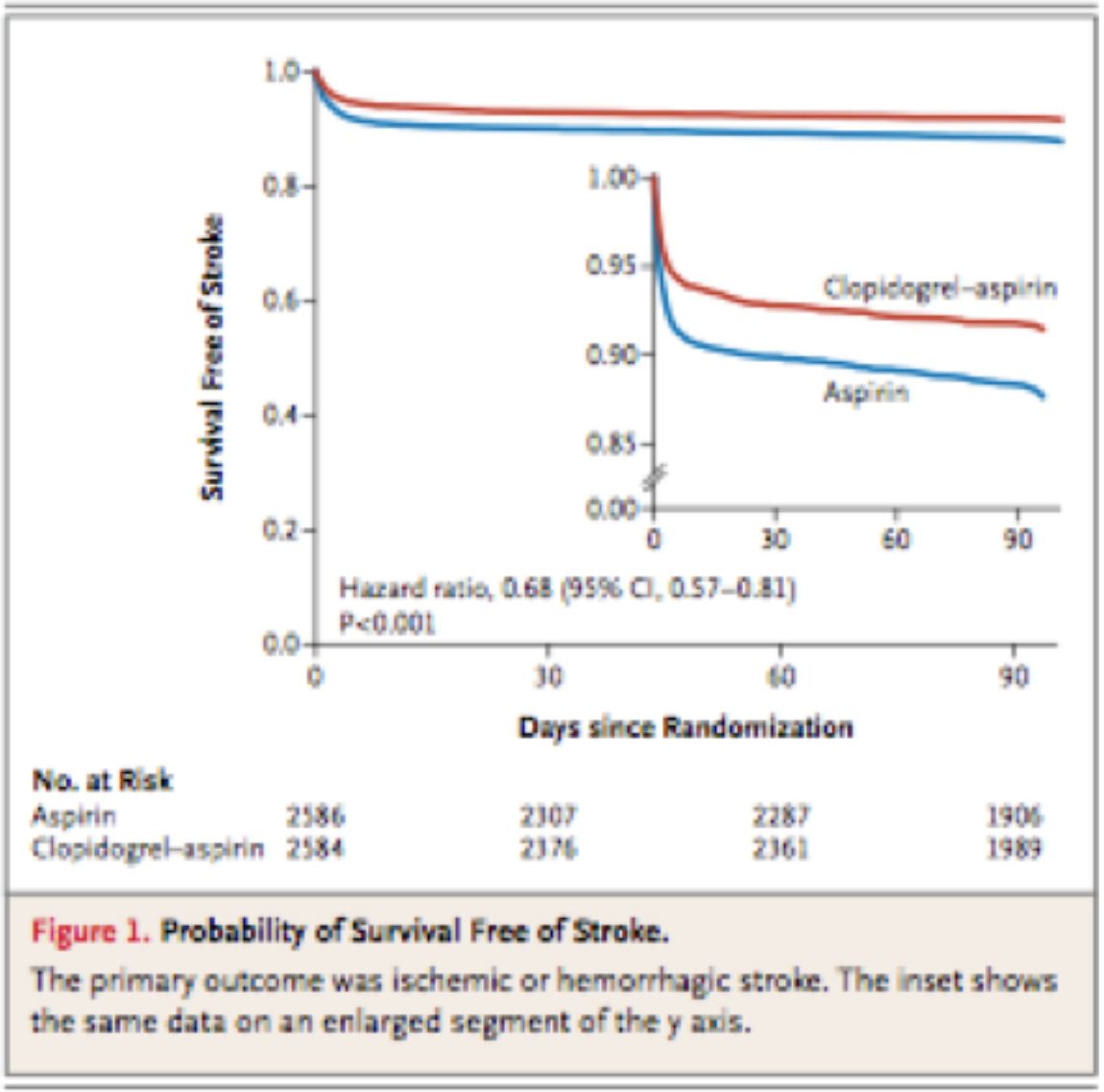


Figure 1. Probability of Survival Free of Stroke.

The primary outcome was ischemic or hemorrhagic stroke. The inset shows the same data on an enlarged segment of the y axis.

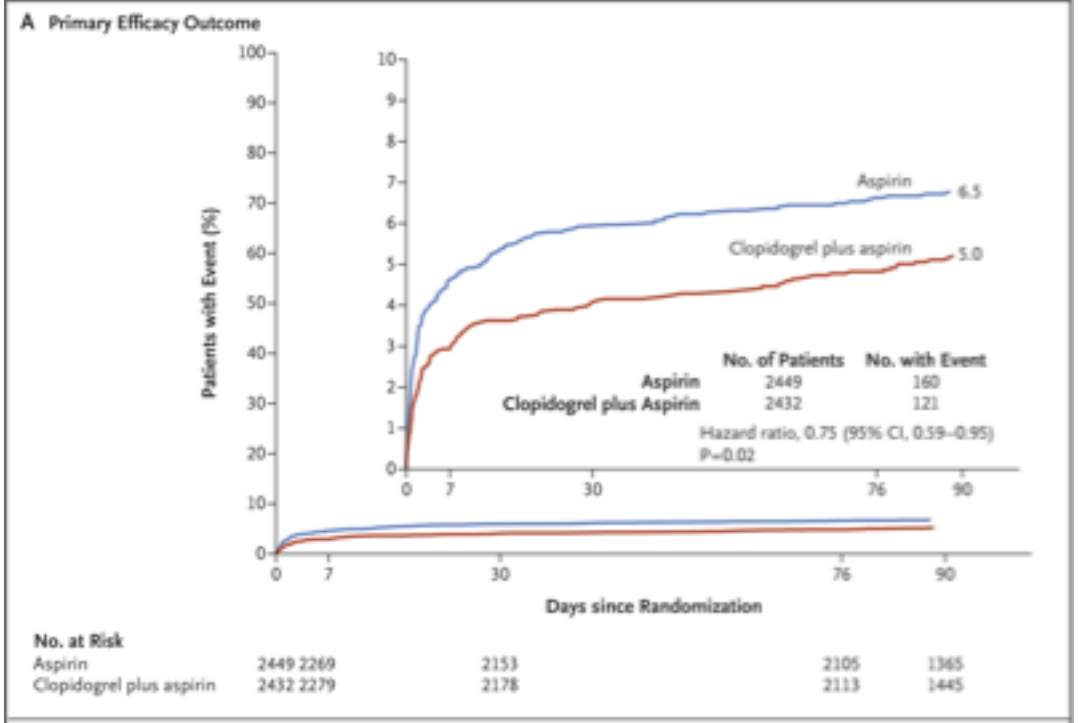
- 'CHANCE' - results
- The curves separated in the first week then remained parallel

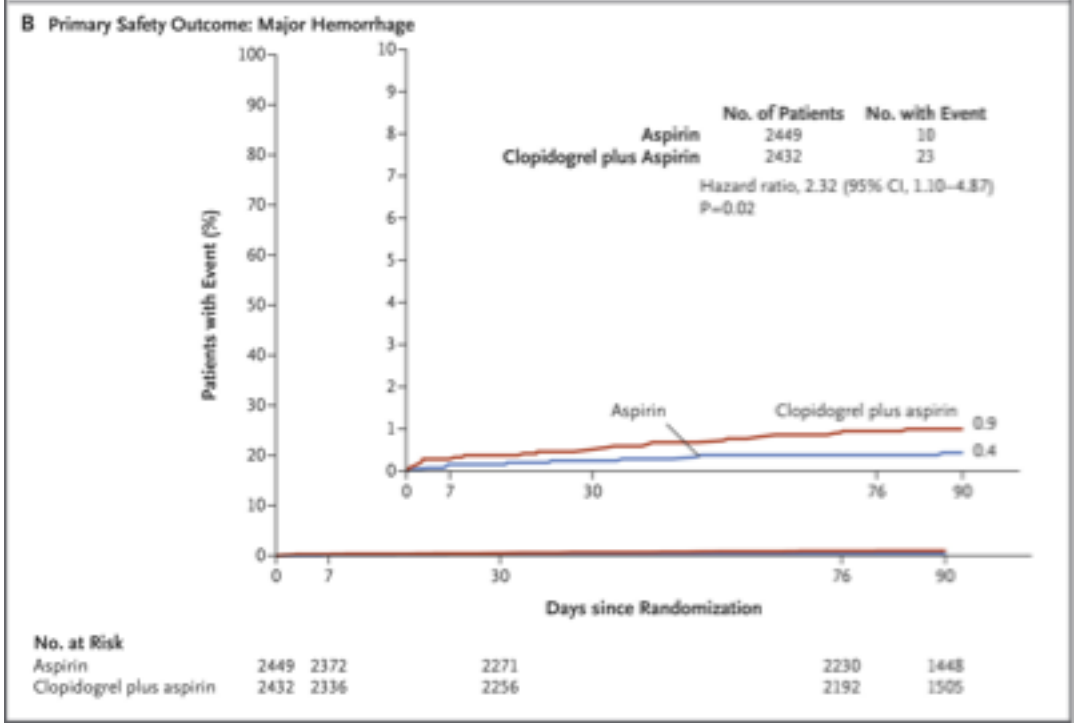
Bottom line: Dual treatment with asa and clopidogrel for three weeks following TIA is an option but confirmatory trials are underway

POINT Trial

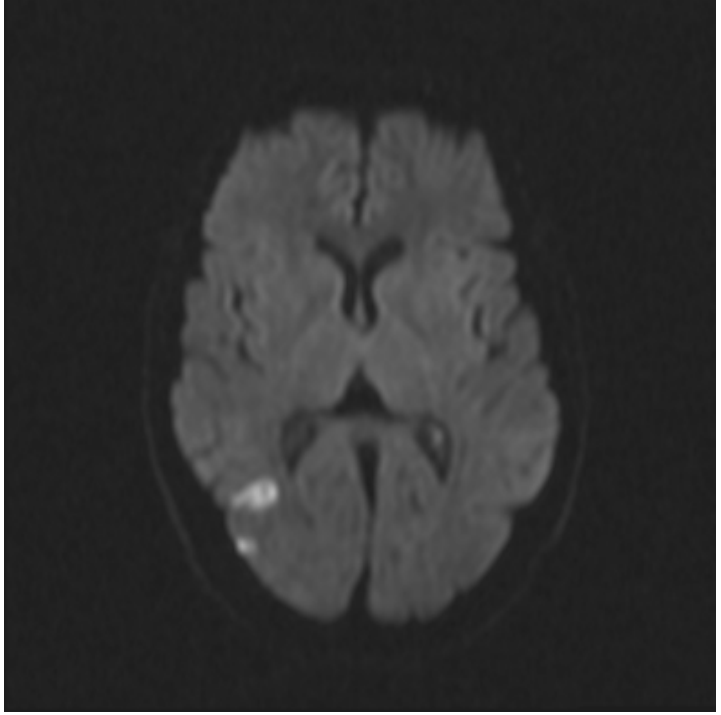
NEJM 2018:10.1056/NEJMoa1800410

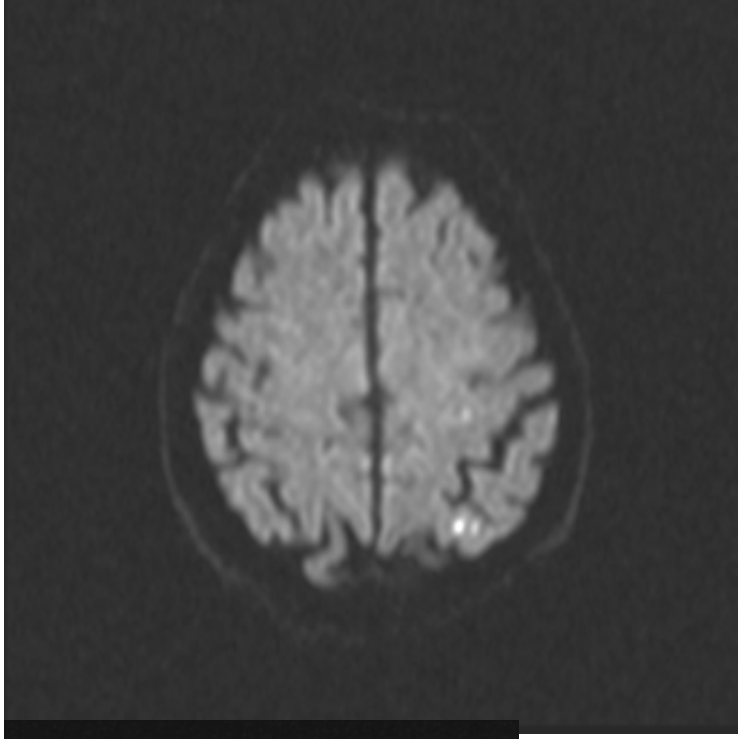
- RDBPC Trial; 4881 patients; >280 international sites
- Clopidogrel 600 mg then 75 mg daily plus asa 50-325 mg daily for three months
- vs asa alone
- Composite of IS, MI, vascular death at 90 days
- Stopped early after interim analysis showed a significant reduction in composite event and an increase in major hemorrhage in the intervention arm

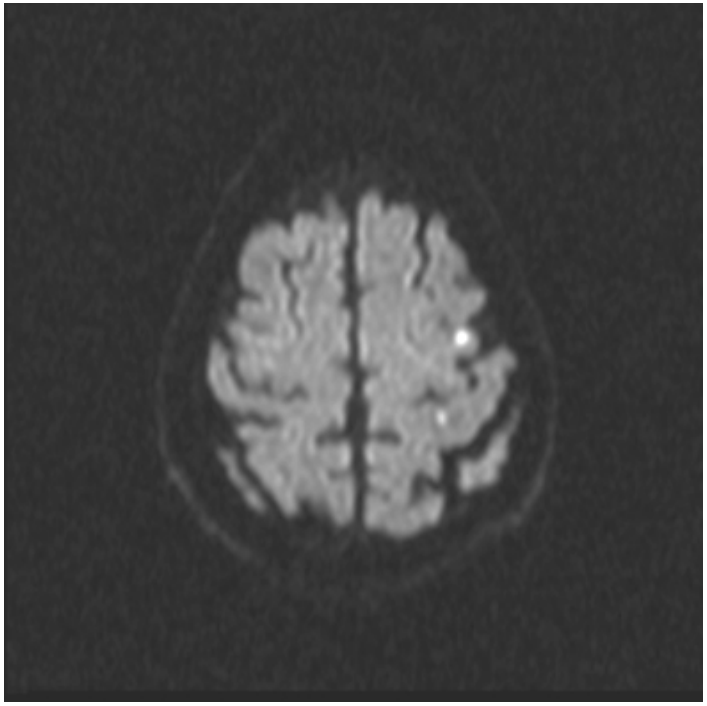


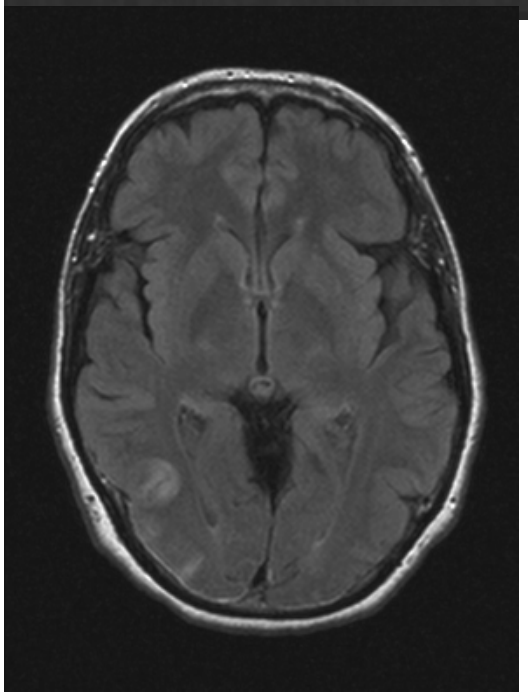


The benefit of dual therapy manifested by 21 days with no major difference in hemorrhage rate at that time
The sweet spot for dual treatment likely 21-30 days;

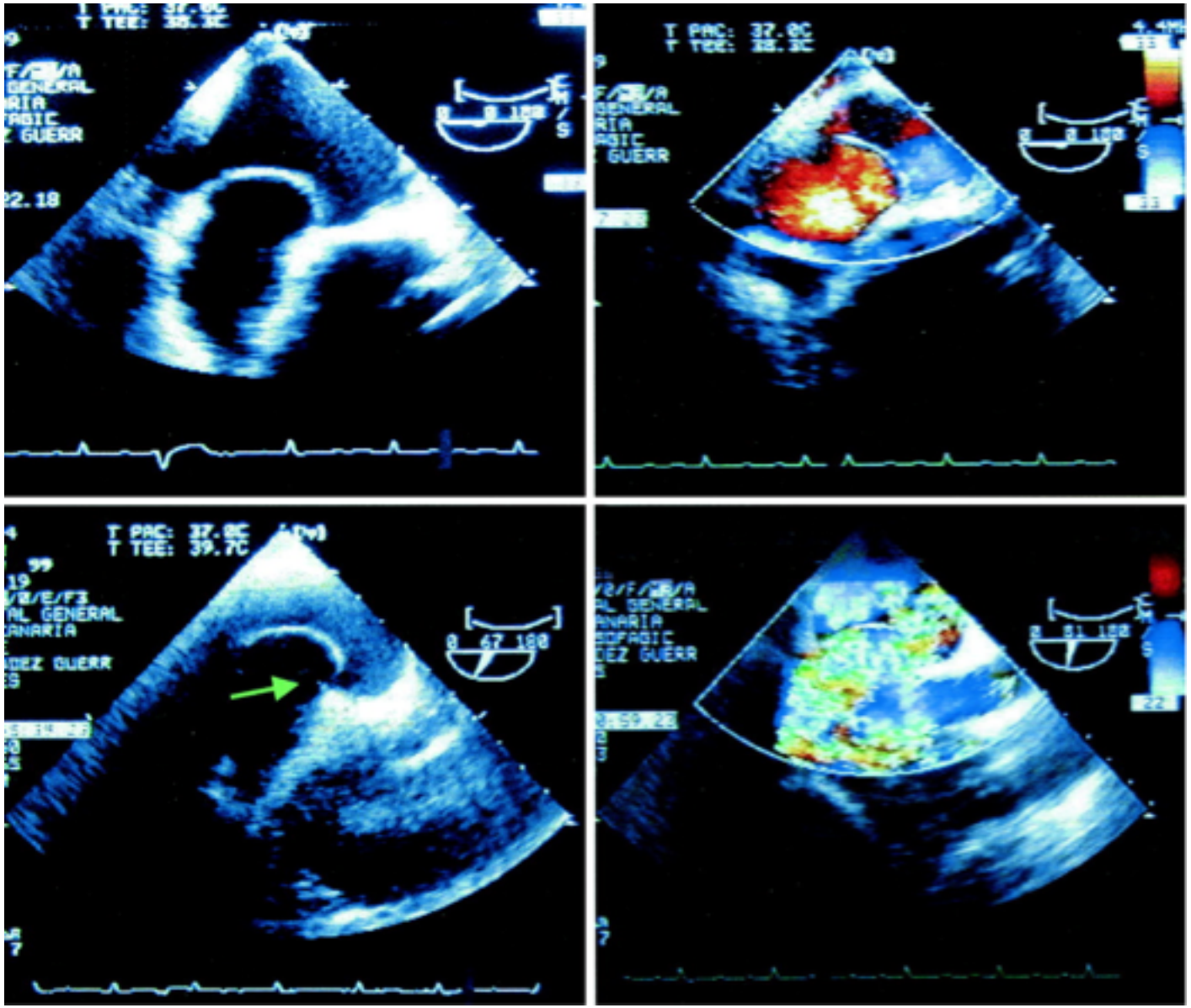








Multiple Acute Strokes in a 45 year old healthy male with no risk factors



PFO with R to L shunt on TEE

Summary of PFO closure in 2018

- Prior trials of PFO closure in stroke showed no clear benefit
- 3 randomized trials published results on PFO closure in 2017
- Some evidence that PFO closure with new devices can reduce stroke risk in those 16 to 60 years of age with a recent cryptogenic stroke with PFO and atrial septal aneurysm or at least moderately large shunt
  - 0.5% to 1% annual stroke risk reduction per 100PY;
  - Approximately 50% RRR but NNT is 100-200 to prevent one stroke yearly
- Devices generally safe but post procedure atrial fibrillation risk long term needs to be better quantified (is as high as 6.6% initially)

Objectives

- To review preventive lifestyle, medical and interventional strategies in stroke and TIA
- To review TIA diagnosis and risk triaging
- Apply the information on TIA recognition and management to one's own practice

Thank-you