

Stroke: Current Approaches to Prevention and Treatment

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I have no conflicts of interest

Outline

- **Epidemiology**
- **Definitions of TIA**
- **Imaging (which type is best)**
- **New time standard in catheter based treatment**
- **Cardiac Holter monitoring**

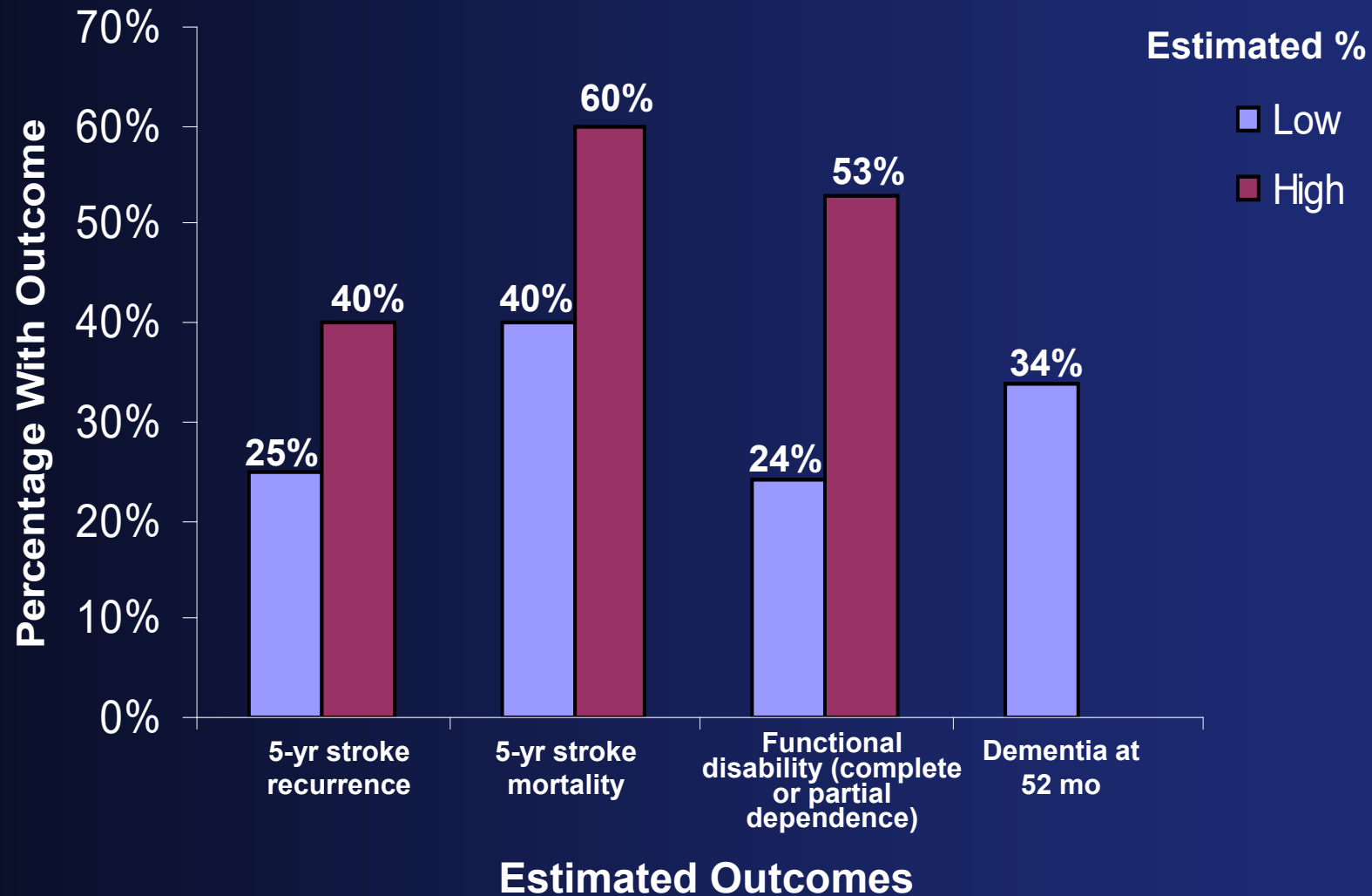
Key Points:

- Time has very limited function in determining a stroke and cerebral imaging allows for a more accurate diagnosis, determine mechanism of the event and helps with early treatment and prognosis.
- Next best steps: Utilize dual antiplatelet therapies for 21 days after stroke when ABCD2 score is ≥ 4 and NIH ≤ 3 then monotherapy with a single antiplatelets and consider longer Holter monitoring as outpatients to improve the diagnosis of A Fib that would require anticoagulation.

Stroke in the US

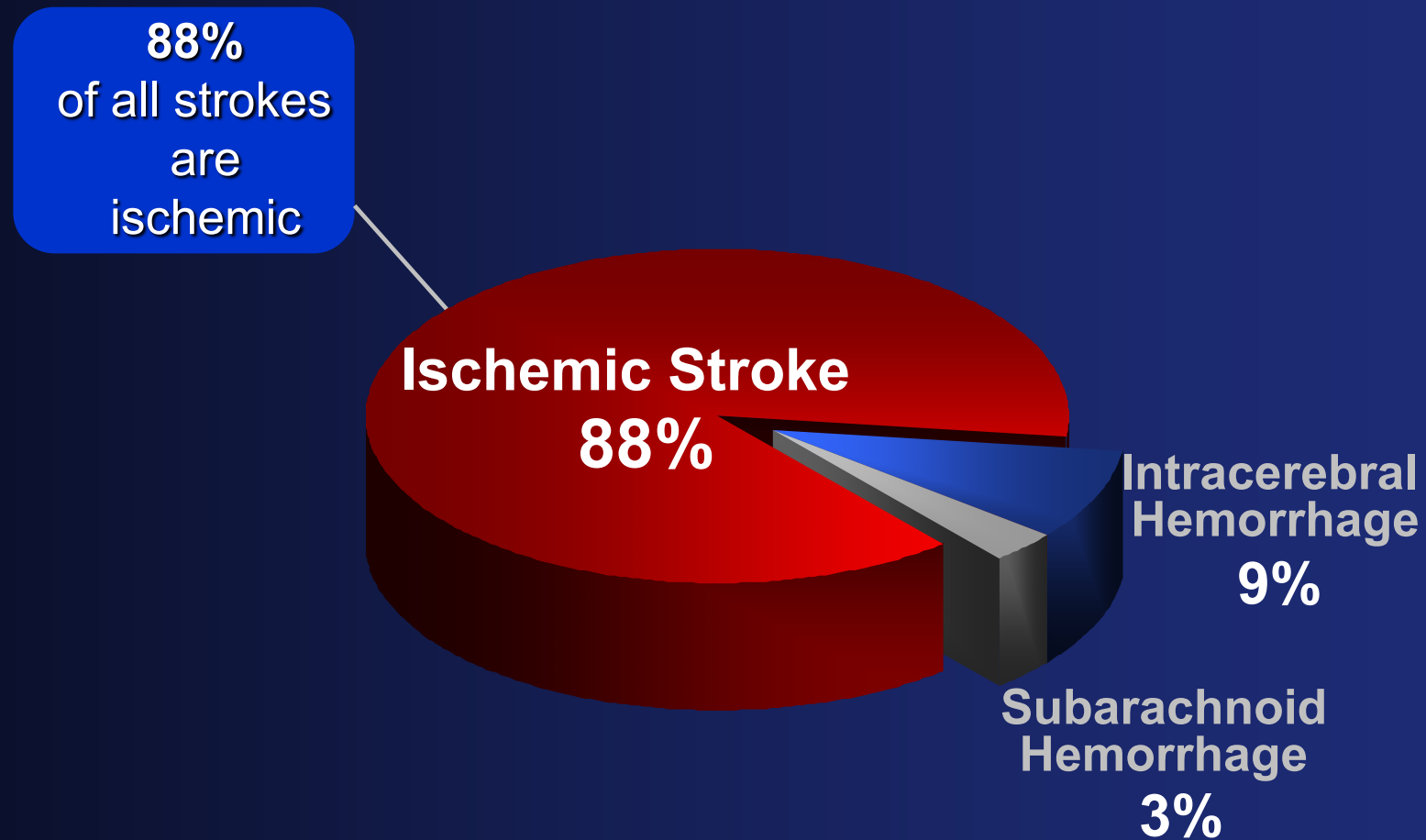
- 795 000 people experience a new or recurrent stroke.
 - Approximately 610 000 of these are first attacks, and 185 000 are recurrent attacks.
- 137 000 stroke deaths annually in the United States.
- Leading cause of serious, long-term disability
- Third leading cause of death in the U.S.; second leading cause worldwide
- Second-leading cause of hospital admission among older adults

Estimated Outcomes After Ischemic Stroke



Adapted with permission from Sacco RL. *Neurology*. 1997;49(5 suppl 4):S39.

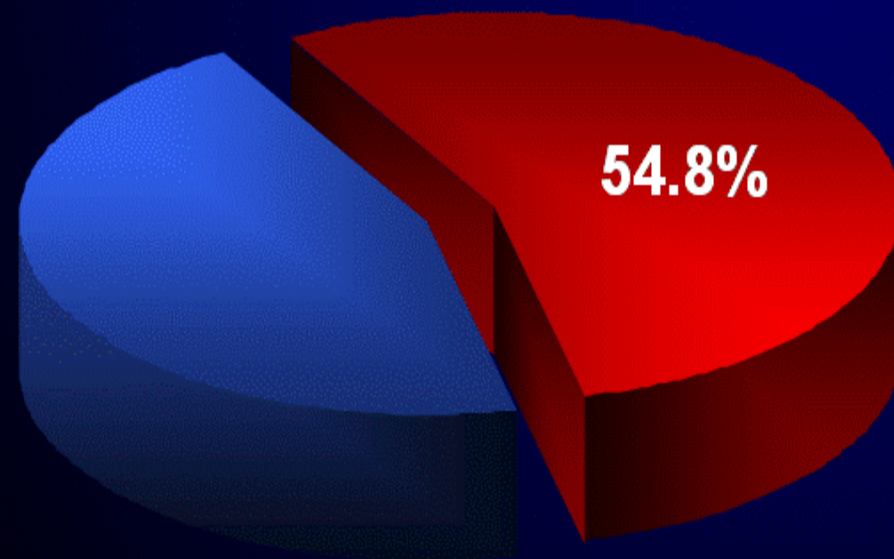
Prevalence of Ischemic Stroke



Common Causes – Not a single disease

- Atherothrombosis
 - Large-vessel
 - Extracranial
 - Aortic
 - Cervical ICA
 - Cervical CCA
 - Intracranial
 - ICA
 - MCA
 - Vertebral artery
 - Basilar artery
 - Small vessel
 - Lacunar
- Cardiac source
 - Atrial fibrillation
 - Dilated cardiomyopathy
- Nonatherosclerotic arteriopathies, eg:
 - Vasculitis
 - Migraine
- Prothrombotic disorders

The Prevalence of PAD in Ischemic Stroke Patients



A study of 852 patients with TIA or ischemic stroke found **54.8%** patients had a form of PAD. This included:

- **50.8%** of the total population had an ABI ≤ 0.9
- **10.0%** of the total population had intermittent claudication

ABI=ankle-brachial index.

This study was funded by sanofi-aventis.

Weimar C et al. *J Neurol*. 2007 Aug 3; [Epub ahead of print].

Risk Factors for Stroke

Modifiable

- Hypertension
- Diabetes
- Cardiac disease
- Atrial fibrillation
- TIA/prior stroke
- Metabolic syndrome
- Dyslipidemia
- Cigarette smoking
- Alcohol abuse
- Obesity
- Physical inactivity
- Carotid stenosis

Nonmodifiable

- Age
- Gender
- Race/ethnicity
- Heredity

INTERSTROKE: Population-attributable risk for common risk factors

Risk factor	Population-attributable risk, % (99% CI)
Hypertension	34.6 (30.4–39.1)
Smoking	18.9 (15.3–23.1)
Waist-to-hip ratio (tertile 2 vs tertile 1)	26.5 (18.8–36.0)
Dietary risk score (tertile 2 vs tertile 1)	18.8 (11.2–29.7)
Regular physical activity	28.5 (14.5–48.5)
Diabetes	5.0 (2.6–9.5)
Alcohol intake	3.8 (0.9–14.4)
Cardiac causes	6.7 (4.8–9.1)
Ratio of apolipoprotein B to A1 (tertile 2 vs tertile 1)	24.9 (15.7–37.1)
Psychological factors	
• Stress	4.6 (2.1–9.6)
• Depression	5.2 (2.7–9.8)

*For the protective factor of physical activity, the population-attributable risks are provided for individuals who do not participate in regular physical activity.

O'Donnell MJ et al. *Lancet* 2010; available at: <http://www.thelancet.com>.

Sleep Apnea

- **OSA increased stroke rate 2-5x**
- **Prevalence of OSA in patient with stroke/TIA up to 70%**
- **Screening**
 - **Sleep questionnaire**
 - **Nocturnal polysomnographic diagnostic testing**

Sleep Apnea

Epworth Sleepiness Scale

0=would never doze or sleep

1=Slight chance

2=Moderate chance

3=High chance

Chance of Dozing or Sleeping

Sitting and reading

Watching TV

Sitting inactive in a public area

Being a passenger in a motor vehicle for an hour
or more

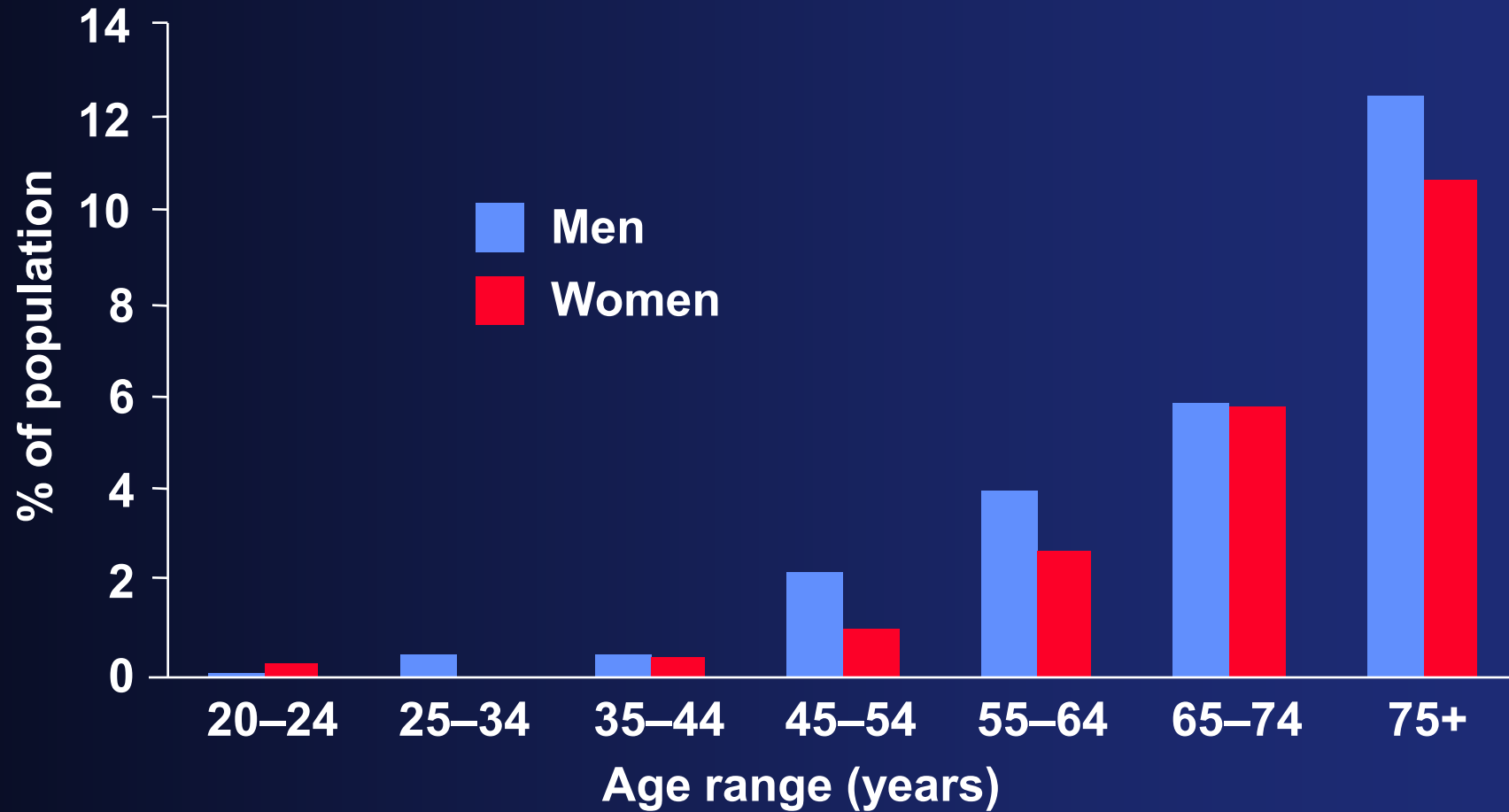
Sitting and talking to someone

Sitting quietly after lunch (no alcohol)

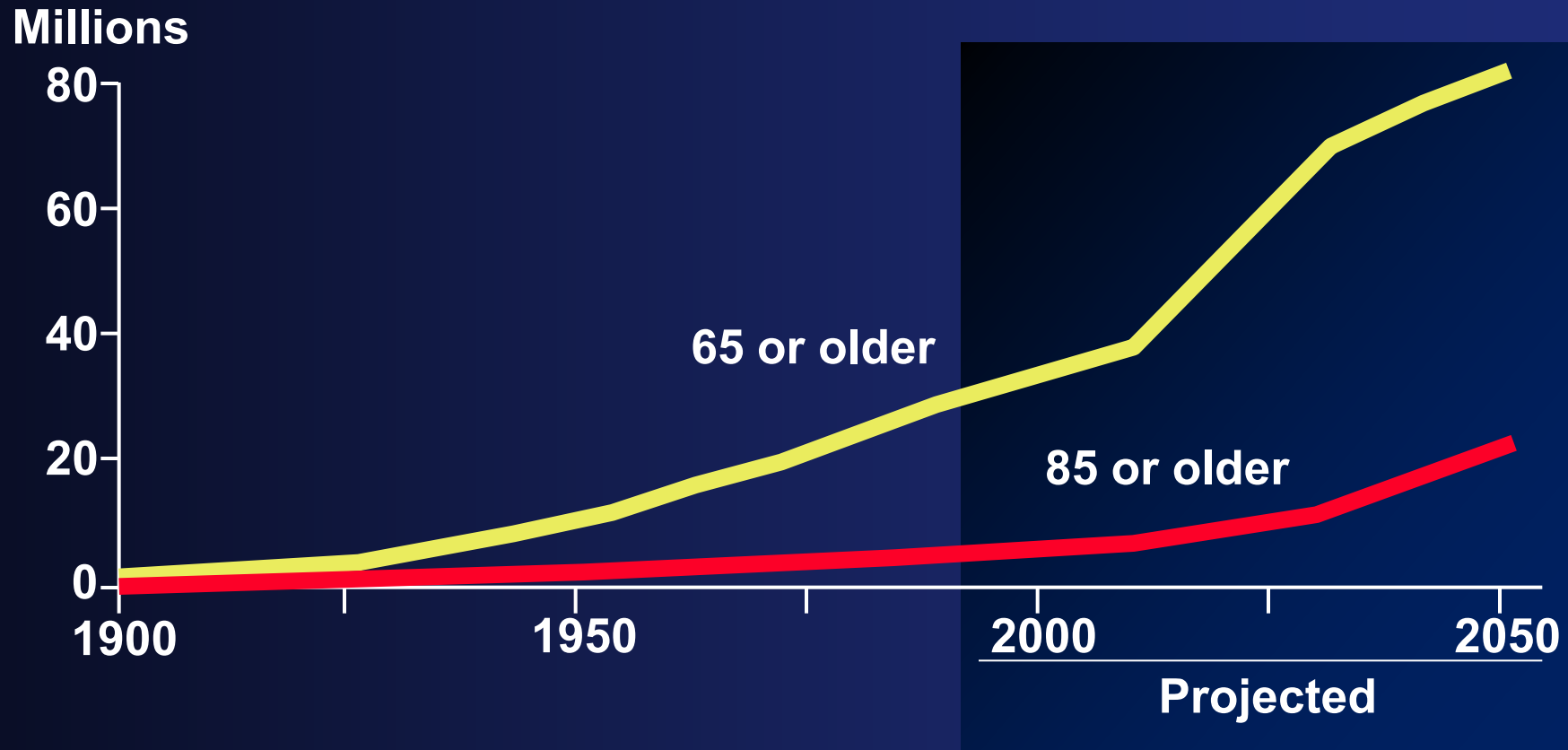
Stopped for a few minutes in traffic while driving

Total score: up to “9” WNL

Prevalence of Stroke by Age



Total Number of Elderly by Age Group: 1900 to 2050



Note: data for the years 2000 to 2050 are middle-series projections of the population.
Reference population: these data refer to the resident population.
US Census Bureau. *Decennial Census Data and Population Projections*, 2003.

Transient Ischemic Attacks (TIAs)

Historic Definition

Temporary focal brain or retinal deficits caused by vascular disease that *resolve within 24 hours*

New Definition of TIA

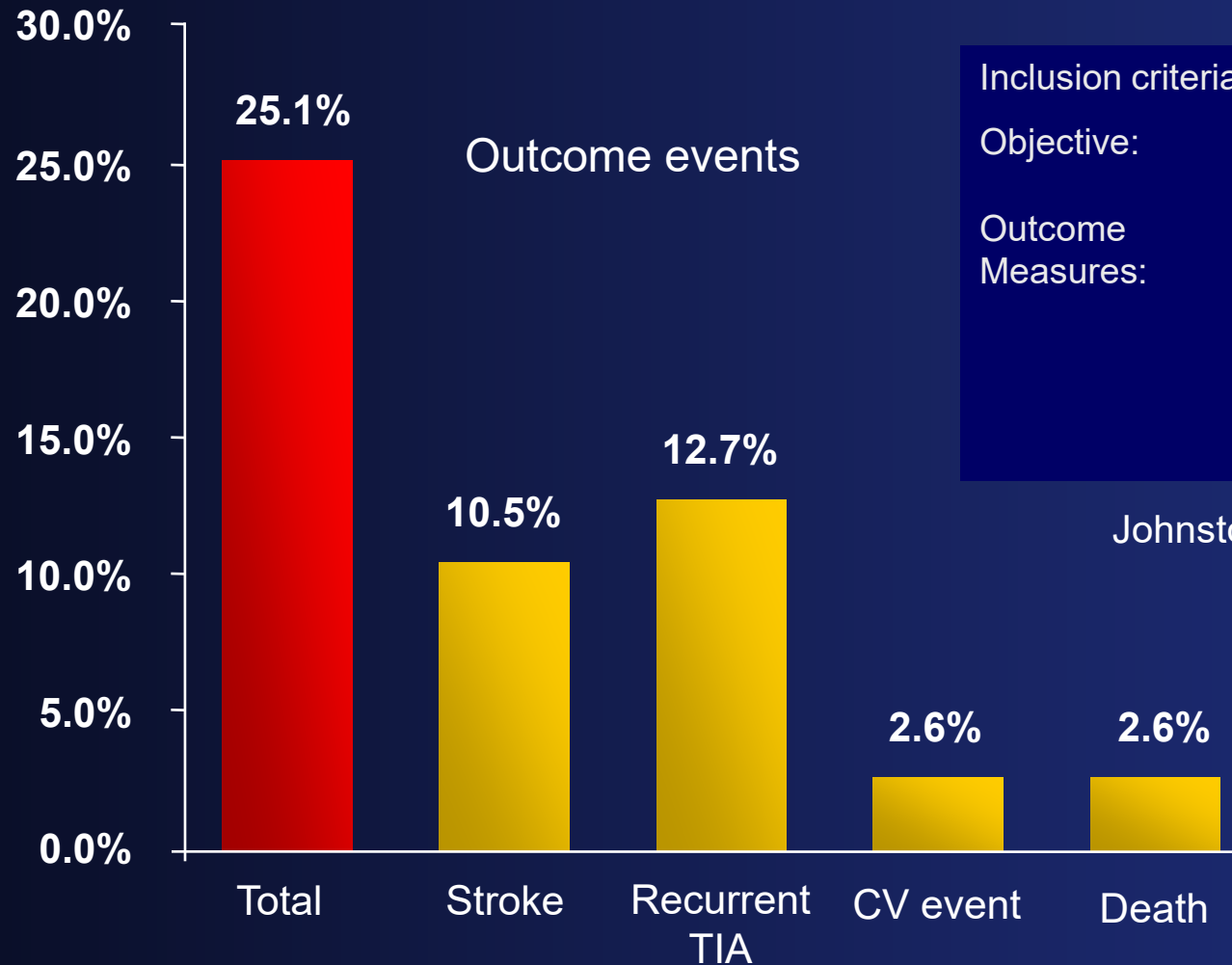
TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting *less than one hour*, and *without evidence of acute infarction*

N Engl J Med, Vol. 337, Nov 21, 2002, 1713-1717.

Stroke, Vol 37, 2006, 577-617.

Stroke. 2009;40:2276.

Short-term Prognosis after Emergency Department Diagnosis of TIA



Inclusion criteria: TIA by ED physicians

Objective: Short-term risk of stroke after ED diagnosis

Outcome Measures: Risk of stroke and other events during the 90 days after index TIA

Johnston SC. et al. JAMA 2000; 284: 2901-2906

ABCD² of TIA

- **Patients with TIA score points for each of the following factors:**
 - Age 60 years (1 point)
 - Blood pressure 140/90 mm Hg on first evaluation (1 point)
 - Clinical symptoms of focal weakness with the spell (2 points) or speech impairment without weakness (1 point)
 - Duration 60 minutes (2 points) or 10 to 59 minutes (1 point)
 - Diabetes (1 point).
 - 2-day risk of stroke:
 - 0% for scores of 0 -1
 - 1.3% for 2 -3
 - 3, 4.1% for 4-5
 - 8.1% for 6-7

Admit to the Hospital?

- Reasonable to hospitalize patients with TIA if they present within 72 hours of the event and any of the following criteria are present:
 - ABCD² score of 3 or greater
 - ABCD² score of 0-2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient

Working up TIA

- Neuroimaging evaluation within 24 hours of symptom onset.
 - MRI, including DWI, is the preferred brain diagnostic imaging modality.
- Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation
- Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis
- Patients with suspected TIA should be evaluated as soon as possible after an event
- ECG/ECHO/Holter

CT vs MRI in acute stroke

- **CT is widely available and fast**
 - **Noncontrast CT, CT angiography and CT perfusion can be performed in under 15 minutes**
 - **Superior to MRA in evaluating the vessels**
 - **Less artefacts and better quantification of lesions**
- **MRI stroke protocol takes longer**
 - **Conventional MRI, DWI, MRA and PWI**
 - **No radiation**
 - **Can be performed without contrast**
 - **Arterial spin labelling, time-of-flight**
- **The two modalities are equally useful for evaluating acute stroke**
 - **Equivalent depiction of the penumbra**

Imaging approach to acute stroke

- **Four P's**
 - **Parenchyma**
 - Assess early signs of acute stroke
 - Rule out haemorrhage
 - **Pipes**
 - Assess extracranial circulation (carotid & vertebral) and intracranial circulation for evidence of intravascular thrombus
 - **Perfusion**
 - Assess Cerebral blood volume (CBV), Cerebral blood flow (CBF) and Mean transit time (MTT)
 - **Penumbra**
 - Assess tissue at risk of dying if ischemia continues without recanalization of intravascular thrombus

Evaluation of Tissue Status: Noncontrast Head CT

Advantages

- Almost universally available
- Rapid
- High sensitivity for detection of hemorrhage (100% ICH, 90% SAH)

Disadvantages

- Often normal in hyperacute phase
- Insensitive to lacunar and posterior fossa strokes

Evaluation of Tissue Status: Multimodal MRI (including DWI)

Advantages

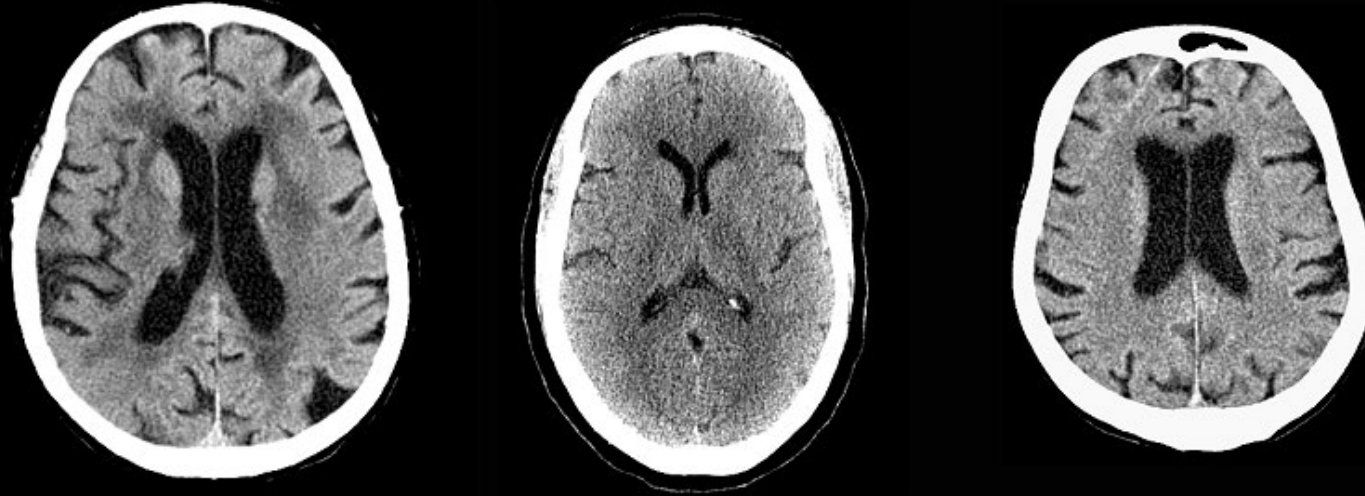
- More sensitive to acute ischemia
- More sensitive to posterior fossa lesions
- More sensitive to small vessel, lacunar lesions

Disadvantages

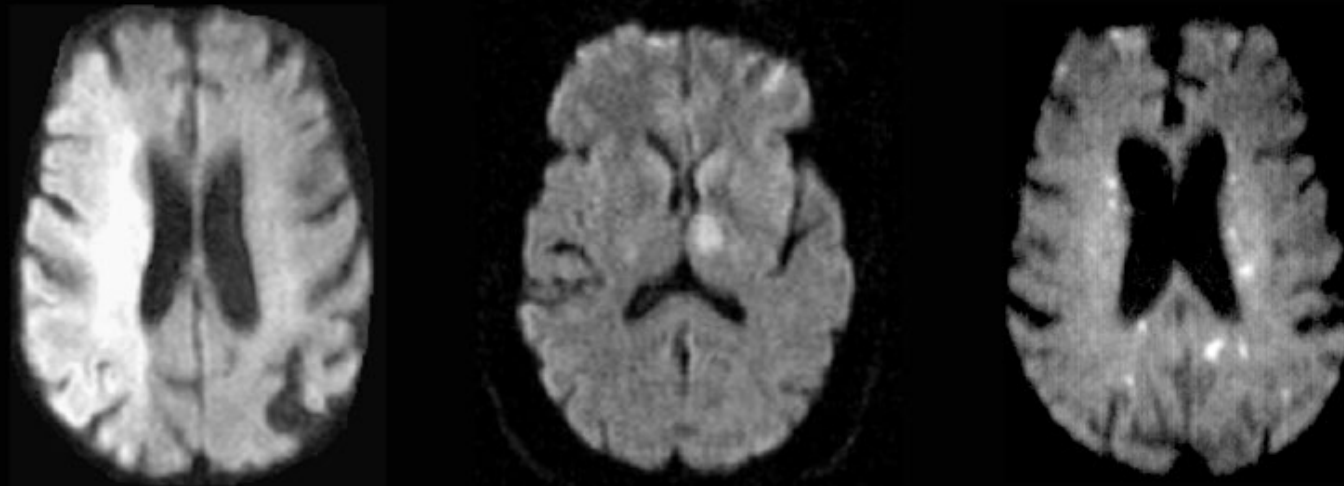
- Not universally available
- Longer scanning time
- Patient contraindications (e.g. pacemaker)

MRI - Tissue Status: Ischemia

CT



DWI



Evaluation of Vessel Status

1. CT Angiography
2. MR Angiography
3. Ultrasound Techniques
4. Catheter Angiography

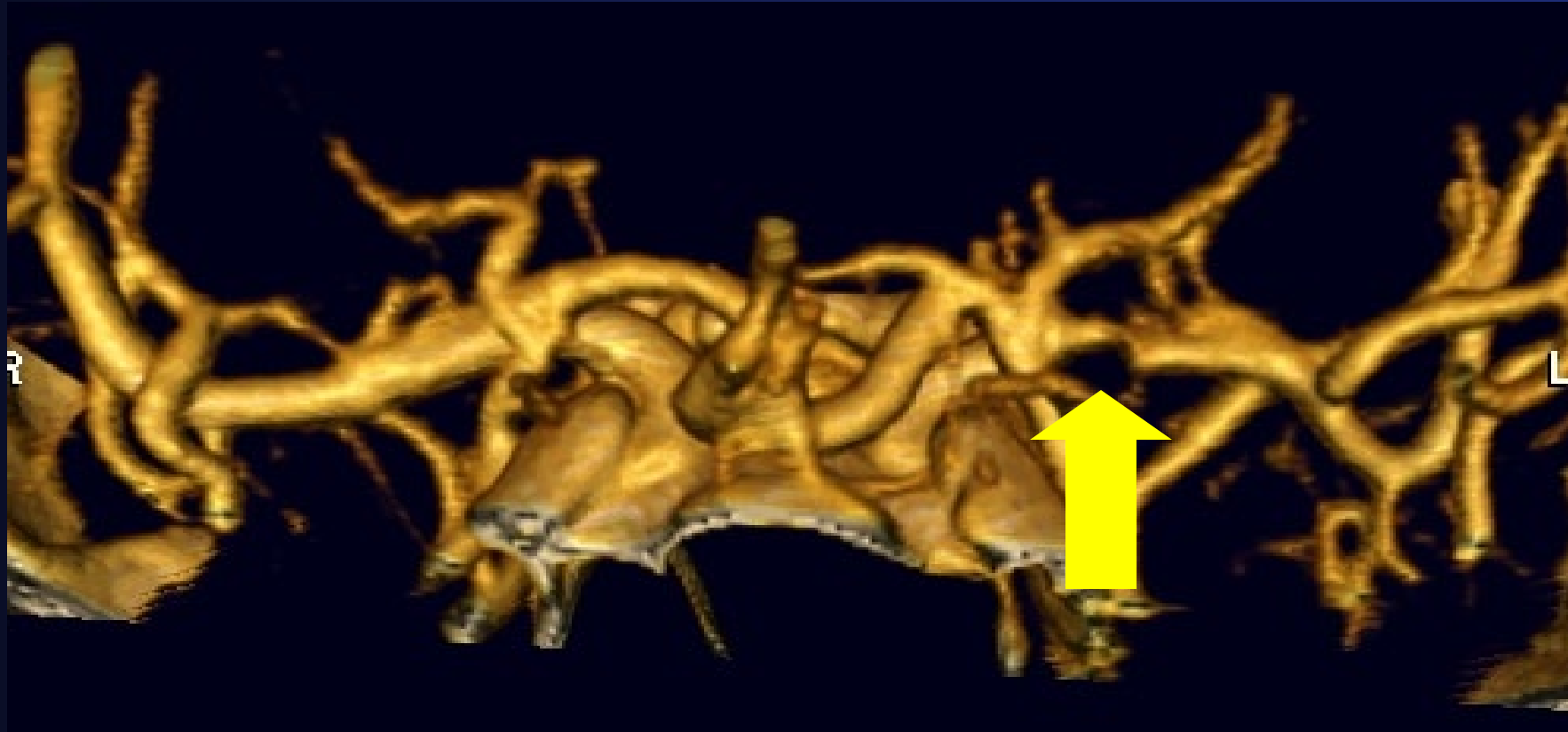
CT Angiography

- **Requires injection of intravenous contrast agent**
- **New generation helical scanners allow rapid evaluation of aortic arch, neck, and intracranial vessels with 1 injection**
- **80-100% accuracy compared with catheter angiography**
- **Disadvantages: iodinated contrast agent, radiation exposure**

CTA: Carotid Stenosis



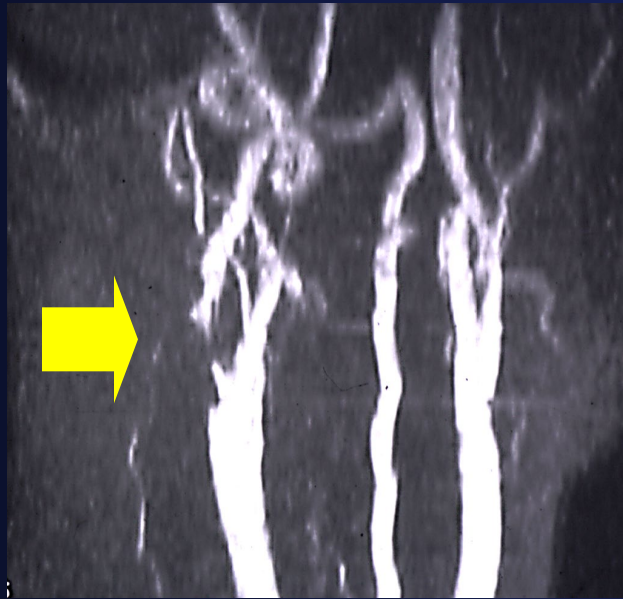
CTA: MCA Stenosis



MR Angiography

- **Noninvasive means to evaluate neck and intracranial vessels**
- **Time of flight technique may overestimate stenoses**
- **Not reliable in identifying distal or branch intracranial occlusions**
- **Sensitivity and specificity 70-100% compared to catheter angiography**
- **Power-injector, contrast-enhanced techniques – increased sensitivity**
- **Subject to limitations of standard MRI**

MR Angiography



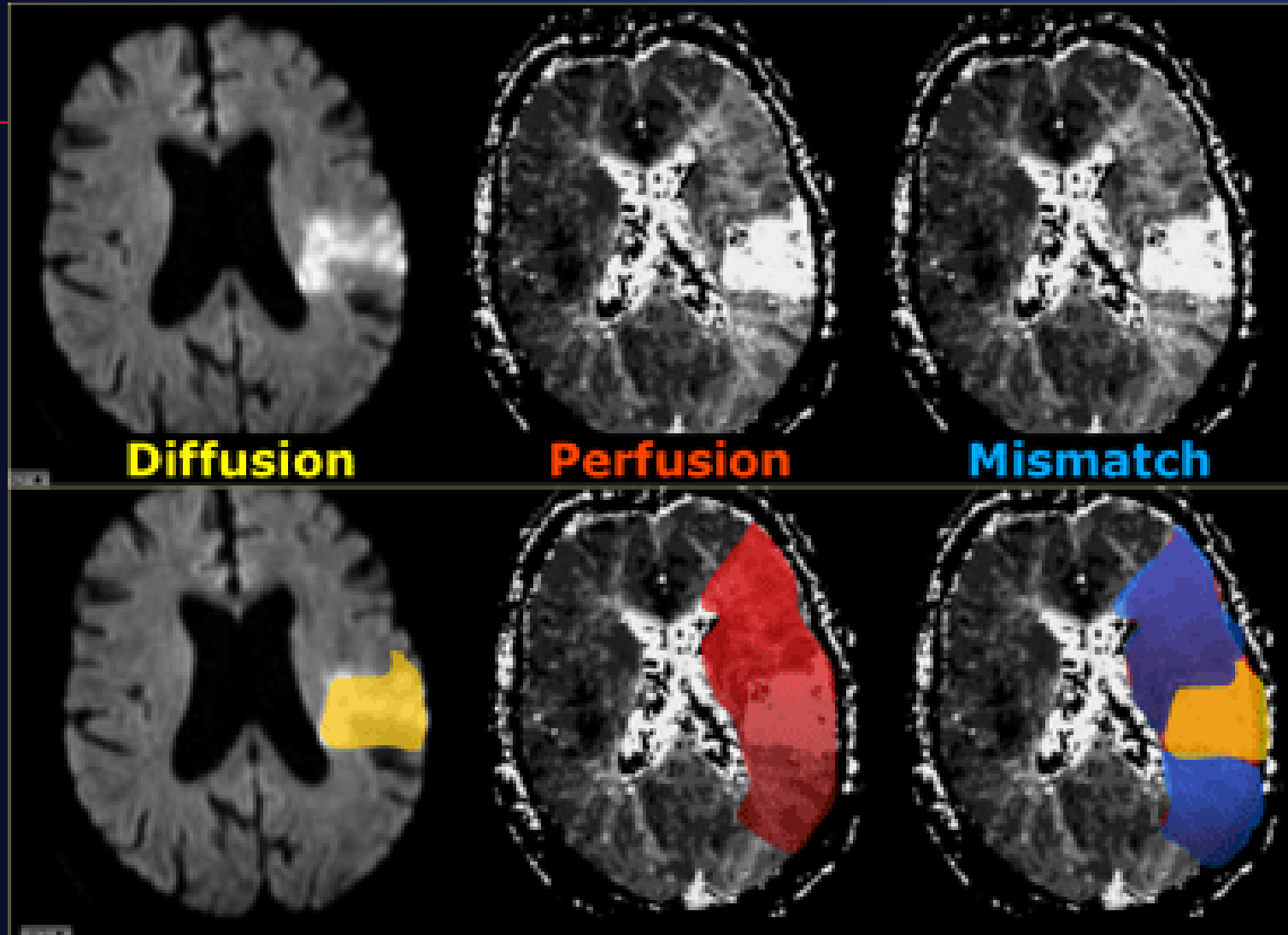
Neck MRA: Right
Carotid Stenosis



Intracranial MRA:
Left ICA Occlusion

Evidence-based guideline: The role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke

- **DWI should be considered superior to noncontrast CT scan for the diagnosis of acute ischemic stroke in patients presenting within 12 hours of symptom onset (Level A).**
- There is insufficient evidence to support or refute the value of PWI in diagnosing acute ischemic stroke (Level U).
- Baseline DWI volume should be considered useful in predicting baseline clinical stroke severity and final lesion volume in anterior-circulation stroke syndromes (Level B).



Whics scan to order?

- Office practice MRI/MRA
- In ED and symptomatic CT/CTA
- In ED and asymptomatic MRI/MRA
- When there is a consideration of thrombolysis IV/IA Either
- IV TPA < 4.5 hours CT is min.

Acute Ischemic Stroke: ASA/AAN/ACCP Guidelines

- Pharmacotherapies
 - tPA (tissue plasminogen activator) within 3 hours of stroke onset
 - Aspirin for acute stroke (within 48 hours of symptom onset) (Grade 1A) to reduce stroke mortality and decrease morbidity; ONLY if no contraindications or if patient will not be given rtPA¹
 - Heparin and low molecular weight heparin (LMWH): not indicated and may increase bleeding complications;
 - LMWH and heparinoids may be considered for DVT prophylaxis in at-risk patients¹
- Early consultation by neurologist or stroke team critical²

1. Coull BM et al. *Stroke*. 2002;33:1934-1942.

2. Adams HP et al. *Stroke*. 2003;34:1056-1083.

IV tPA, the “Gold Standard”

- Systemic “Clot Buster”
- FDA Approved for the treatment of AIS in 1996
- Only 8% of ischemic stroke patients are eligible for IV tPA
 - Narrow time window
 - Risk of cerebral and systemic hemorrhage
 - Achieves early reperfusion in only 13-50% of large vessel occlusions

National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581-1587. Kleindorfer DO, Broderick JP, et al. Emergency department arrival times after acute ischemic stroke during the 1990s. Neurocrit Care. 2007;7(1):31-5. del Zoppo GJ, Poeck K, Pessin MS, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol 1992;32:78-86. 6. Bhatia R, Hill MD, Shobha N, et al. Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: realworld experience and a call for action. Stroke 2010;41:2254-8.

35-40% of Ischemic Strokes are Considered “Large Vessel”

- This subset of ischemic stroke comprises blockages in the:
 - Internal Carotid Artery (ICA)
 - Middle Cerebral Artery (MCA)
 - Vertebral / Basilar Artery
- Patient prognosis with these types of stroke is poor

Vessel	Mortality Rate
ICA	53% ¹
MCA	27% ²
Basilar Artery	89-90% ³

1. Jansen O, et al.

2. Furlan A et al. PROACT II Trial

3. Brückmann H et al.

Turning Point

The Era of Stent-Retrievers

Technological advances

- Stent-retriever technology for safe, reliable performance
- Significant improvement in revascularization and patient outcomes vs older technology, proven in randomized clinical trials*

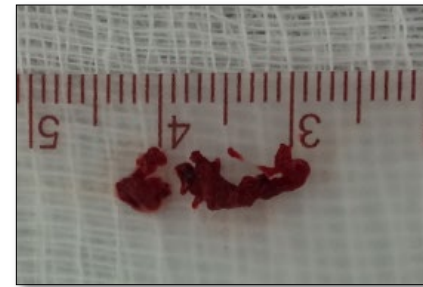
Goal of Ischemic Stroke Treatment



Before Intervention



After Successful Intervention



Original Article

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

Raul G. Nogueira, M.D., Ashutosh P. Jadhav, M.D., Ph.D., Diogo C. Haussen, M.D.,
Alain Bonafe, M.D., Ronald F. Budzik, M.D., Parita Bhuva, M.D., Dileep R.
Yavagal, M.D., Marc Ribo, M.D., Christophe Cognard, M.D., Ricardo A. Hanel, M.D.,
Cathy A. Sila, M.D., Ameer E. Hassan, D.O., Monica Millan, M.D., Elad I. Levy, M.D.,
Peter Mitchell, M.D., Michael Chen, M.D., Joey D. English, M.D., Qaisar A.
Shah, M.D., Frank L. Silver, M.D., Vitor M. Pereira, M.D., Brijesh P. Mehta, M.D.,
Blaise W. Baxter, M.D., Michael G. Abraham, M.D., Pedro Cardona, M.D., Erol
Veznedaroglu, M.D., Frank R. Hellinger, M.D., Lei Feng, M.D., Jawad F. Kirmani, M.D.,
Demetrius K. Lopes, M.D., Brian T. Jankowitz, M.D., Michael R. Frankel, M.D., Vincent
Costalat, M.D., Nirav A. Vora, M.D., Albert J. Yoo, M.D., Ph.D., Amer M. Malik, M.D.,
Anthony J. Furlan, M.D., Marta Rubiera, M.D., Amin Aghaebrahim, M.D., Jean-Marc
Olivot, M.D., Wondwossen G. Tekle, M.D., Ryan Shields, M.Sc., Todd Graves, Ph.D.,
Roger J. Lewis, M.D., Ph.D., Wade S. Smith, M.D., Ph.D., David S. Liebeskind, M.D.,
Jeffrey L. Saver, M.D., Tudor G. Jovin, M.D., for the DAWN Trial Investigators

N Engl J Med
Volume 378(1):11-21
January 4, 2018



The NEW ENGLAND
JOURNAL of MEDICINE

PHANTOM-S: The Pre-Hospital Acute Neurological Therapy and Optimization of Medical Care in Stroke Patients - Study "PHANTOM-S"



S1474-

4422(12)70057-1. Epub 2012 Apr 11.

Telestroke

- AAN and ASA are supporters of bipartisan legislation which was recently introduced in Congress, the *Furthering Access to Stroke Telemedicine (FAST) Act* (H.R. 2799).
- This bipartisan bill expands access to stroke telemedicine (also called “telestroke”) treatment in Medicare. Similar legislation (S.1465) has been introduced in the Senate.

Lowering Blood Pressure

ASA Treatment Guidelines: Ischemic Stroke Not Eligible for Thrombolytic Therapy

BP Level (mm Hg)	Treatment
SBP <220 OR DBP <120	No treatment unless end-organ involvement
SBP >220 OR DBP <121-140	Nicardipine or labetalol to 10% -15% ↓ in BP
DBP >140	Nitroprusside to 10% -15% ↓ in BP

ASA = American Stroke Association; IS = ischemic stroke; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Adams HP, et al. *Stroke*. 2007;38:1655-1711.

ASA Treatment Guidelines: Ischemic Stroke Eligible for Thrombolytic Therapy

BP Level (mm Hg)	Treatment
Pretreatment SBP >185 or DBP >110	Labetalol (may repeat once), nitropaste , or nicardipine If BP not reduced and maintained, do not administer rt-PA
During and after rt-PA	
SBP 180-230 OR DBP 105-120	
SBP >230 OR DBP 121-140	

rt-PA = recombinant tissue plasminogen activator.

Adams HP, et al. *Stroke*. 2007;38:1655-1711.

Blood Pressure and Stroke

What to Conclude

- All studies support detection and aggressive treatment of blood pressure for both primary and secondary prevention
- Reduction of stroke by 35%-40% possible¹
- Thiazide-type diuretic recommended as first therapeutic agent¹
- ACEI and ARBs are more effective in reducing progression of renal disease and are recommended as first-choice medications for patients with diabetes

1. Chobanian AV et al, and the National High Blood Pressure Education Program Coordinating Committee. *JAMA*. 2003;289:2560-2572.

2. *Stroke*, Vol 37, 2006, 577-617.

3. Schrader J. *Stroke*. 2003;34:1199-1703.

Questions for the future

- Which out-of-hospital stroke scale to use for identifying large artery occlusions?
- Would telemedicine directed by a remote stroke physician be a better triage technique?
- Should primary stroke centers be bypassed to transport patients to comprehensive centers, even if it means delaying the start of intravenous tissue plasminogen activator (tPA)?
- How much delay in bypass is acceptable?
- Would a mobile stroke unit with computed tomographic capability

Antiplatelets

In patients with a history of noncardioembolic ischemic stroke or TIA, we recommend long-term treatment with:

- Aspirin (75-100 mg once daily)
- Clopidogrel (75 mg once daily)
- Aspirin/extended-release dipyridamole (25 mg/200 mg bid)
- Cilostazol (100 mg bid)

Over

- No antiplatelet therapy (Grade 1A)
- Oral anticoagulants (Grade 1B)
- Combination of clopidogrel plus aspirin (Grade 1B)
- Triflusal (Grade 2B)

Original Article

Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

Yongjun Wang, M.D., Yilong Wang, M.D., Ph.D., Xingquan Zhao, M.D., Ph.D., Liping Liu, M.D., Ph.D., David Wang, D.O., F.A.H.A., F.A.A.N., Chunxue Wang, M.D., Ph.D., Chen Wang, M.D., Hao Li, Ph.D., Xia Meng, M.D., Ph.D., Liying Cui, M.D., Ph.D., Jianping Jia, M.D., Ph.D., Qiang Dong, M.D., Ph.D., Anding Xu, M.D., Ph.D., Jinsheng Zeng, M.D., Ph.D., Yansheng Li, M.D., Ph.D., Zhimin Wang, M.D., Haiqin Xia, M.D., S. Claiborne Johnston, M.D., Ph.D., for the CHANCE Investigators

N Engl J Med
Volume 369(1):11-19
July 4, 2013



The NEW ENGLAND
JOURNAL of MEDICINE

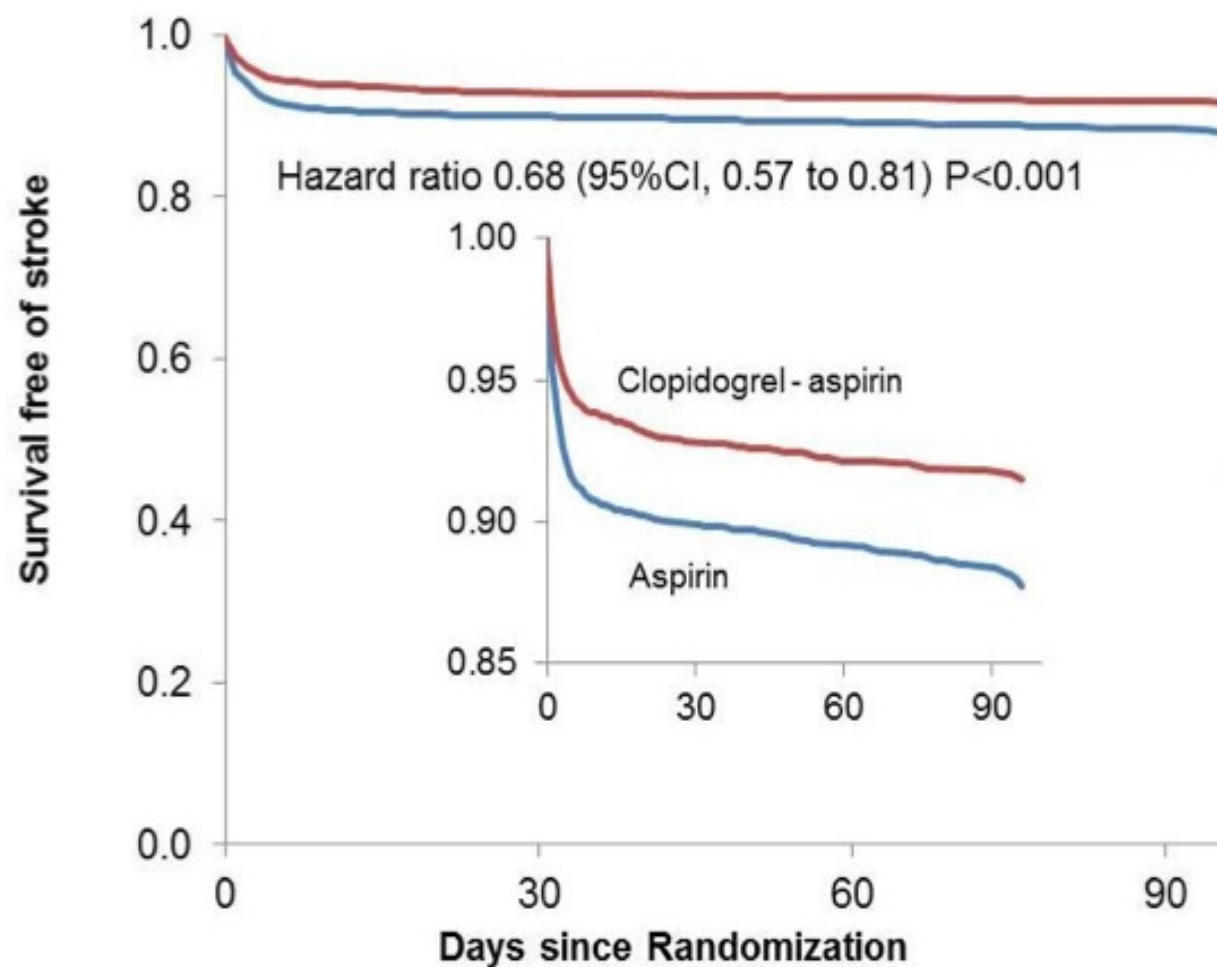
Primary objective of the CHANCE trial

- To assess the efficacy of a 3-month regimen of clopidogrel-aspirin (300 mg load followed by 75 mg/day) vs. aspirin alone on reducing the 3-month risk of new stroke (ischemic or hemorrhagic) when initiated within 24 hours of symptom onset in patients with high-risk TIA or minor stroke.

CHANCE trial

- Age ≥ 40 years;
- Either:
Non-disabling ischemic stroke(NIHSS ≤ 3), or
TIA with moderate-to-high risk of stroke recurrence
(ABCD2 score ≥ 4).
- Study drug can be given within 24 h of symptom onset.

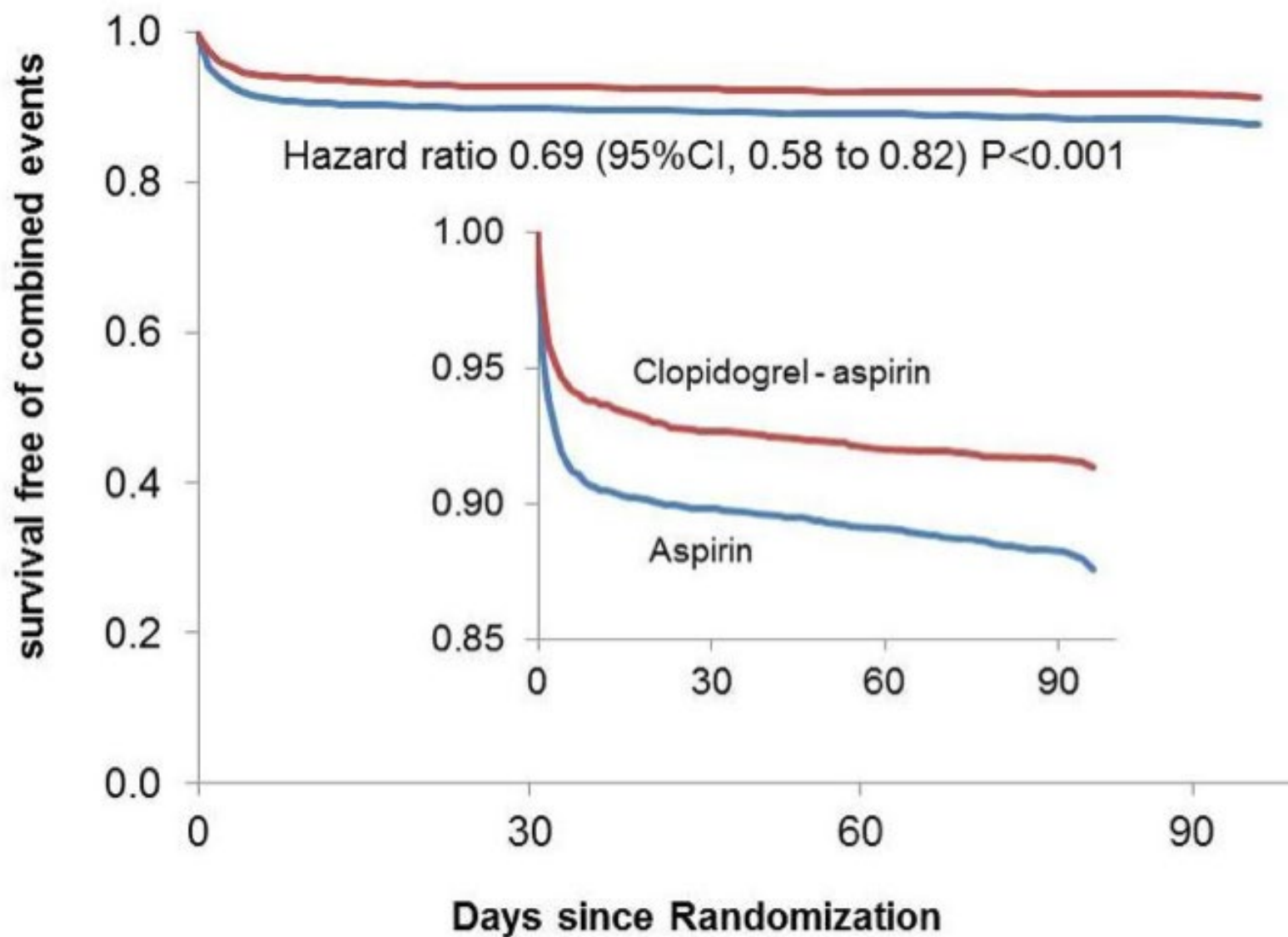
Primary outcome: stroke



No. at Risk

Aspirin	2586	2307	2287	1906
Clopidogrel - aspirin	2584	2376	2361	1989

Secondary combined outcome



CHANCE Trial Summary

- TIA and minor ischemic stroke are a treatable emergency
- Clopidogrel with a 300 mg load plus aspirin reduces subsequent stroke risk compared to aspirin alone.
- Clopidogrel-aspirin is safe in this setting with no increase in bleeding.
- Even more aggressive interventions after acute TIA and minor stroke may be indicated but require clinical trials.

Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA

S. Claiborne Johnston, M.D., Ph.D., J. Donald Easton, M.D., Mary Farrant, M.B.A., William Barsan, M.D., Robin A. Conwit, M.D., Jordan J. Elm, Ph.D.,

Anthony S. Kim, M.D., Anne S. Lindblad, Ph.D., and Yuko Y. Palesch, Ph.D., for the Clinical Research Collaboration, Neurological Emergencies Treatment Trials Network, and the

POINT Investigators

ABSTRACT

BACKGROUND

Combination antiplatelet therapy with clopidogrel and aspirin may reduce the rate of recurrent stroke during the first 3 months after a minor ischemic stroke or transient ischemic attack (TIA). A trial of combination antiplatelet therapy in a Chinese population has shown a reduction in the risk of recurrent stroke. We tested this combination in an international population.

METHODS

In a randomized trial, we assigned patients with minor ischemic stroke or high-risk TIA to receive either clopidogrel at a loading dose of 600 mg on day 1, followed by 75 mg per day, plus aspirin (at a dose of 50 to 325 mg per day) or the same range of doses of aspirin alone. The dose of aspirin in each group was selected by the site investigator. The primary efficacy outcome in a time-to-event analysis was the risk of a composite of major ischemic events, which was defined as ischemic stroke, myocardial infarction, or death from an ischemic vascular event, at 90 days.

RESULTS

A total of 4881 patients were enrolled at 269 international sites. The trial was halted after 84% of the anticipated number of patients had been enrolled because the data and safety monitoring board had determined that the combination of clopidogrel and aspirin was associated with both a lower risk of major ischemic events and a higher risk of major hemorrhage than aspirin alone at 90 days. Major ischemic events occurred in 121 of 2432 patients (5.0%) receiving clopidogrel plus aspirin and in 160 of 2449 patients (6.5%) receiving aspirin plus placebo (hazard ratio, 0.75; 95% confidence interval [CI], 0.59 to 0.95; $P=0.02$), with most events occurring during the first week after the initial event. Major hemorrhage occurred in 23 patients (0.9%) receiving clopidogrel plus aspirin and in 10 patients (0.4%) receiving aspirin plus placebo (hazard ratio, 2.32; 95% CI, 1.10 to 4.87; $P=0.02$).

CONCLUSIONS

In patients with minor ischemic stroke or high-risk TIA, those who received a combination of clopidogrel and aspirin had a lower risk of major ischemic events but a higher risk of major hemorrhage at 90 days than those who received aspirin alone. (Funded by the National Institute of Neurological Disorders and Stroke; POINT ClinicalTrials.gov number, NCT00991029.)

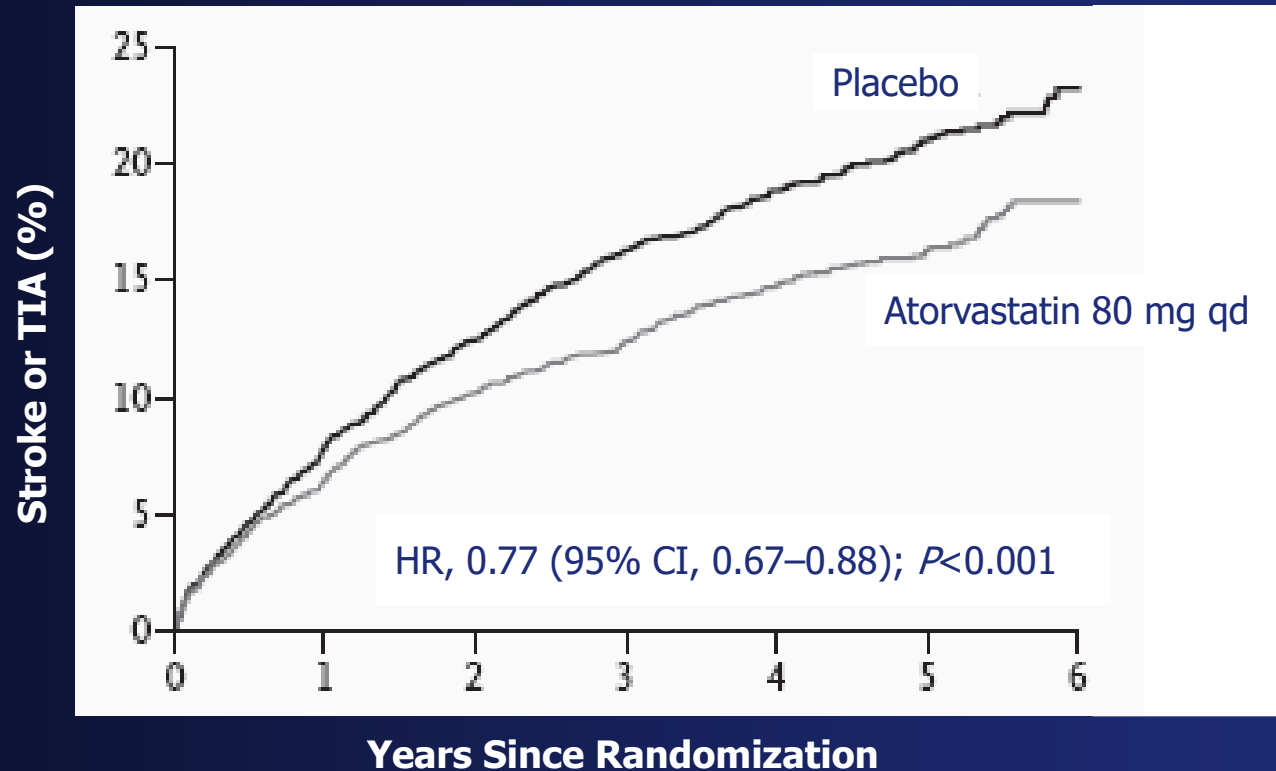
BMJ 2018;364k1508

- Meta analysis and systemic review involving 10K patients, dual antiplatelet therapy with clopidogrel and aspirin given within 24 hours after high risk TIA or minor stroke reduces subsequent stroke (20 in 1000). Benefit after 21 days is unlikely.**

Effect of statins on all strokes, fatal stroke, and hemorrhagic stroke

Studies	Relative risk reduction
All stroke (total)	0.82 (0.77–0.87)
•All stroke (primary-prevention studies)	0.81 (0.75–0.87)
•All stroke (secondary prevention: SPARCL, HPS, LIPID, and CARE)	0.88 (0.78–0.99)
Fatal stroke (total)	0.87 (0.73–1.03)
•Fatal stroke (primary-prevention studies)	0.90 (0.76–1.05)
•Fatal stroke (secondary prevention: SPARCL)	0.59 (0.36–0.97)
Hemorrhagic stroke (total)	1.03 (0.75–1.41)
•Hemorrhagic stroke (primary-prevention studies)	0.81 (0.60–1.08)
•Hemorrhagic stroke (secondary prevention: SPARCL and HPS)	1.73 (1.19–2.50)

Effects of High-dose Atorvastatin After Stroke or TIA

**No. at Risk**

Atorvastatin	2365	2148	2023	1933	1837	871	119
Placebo	2366	2132	1998	1871	1780	803	126

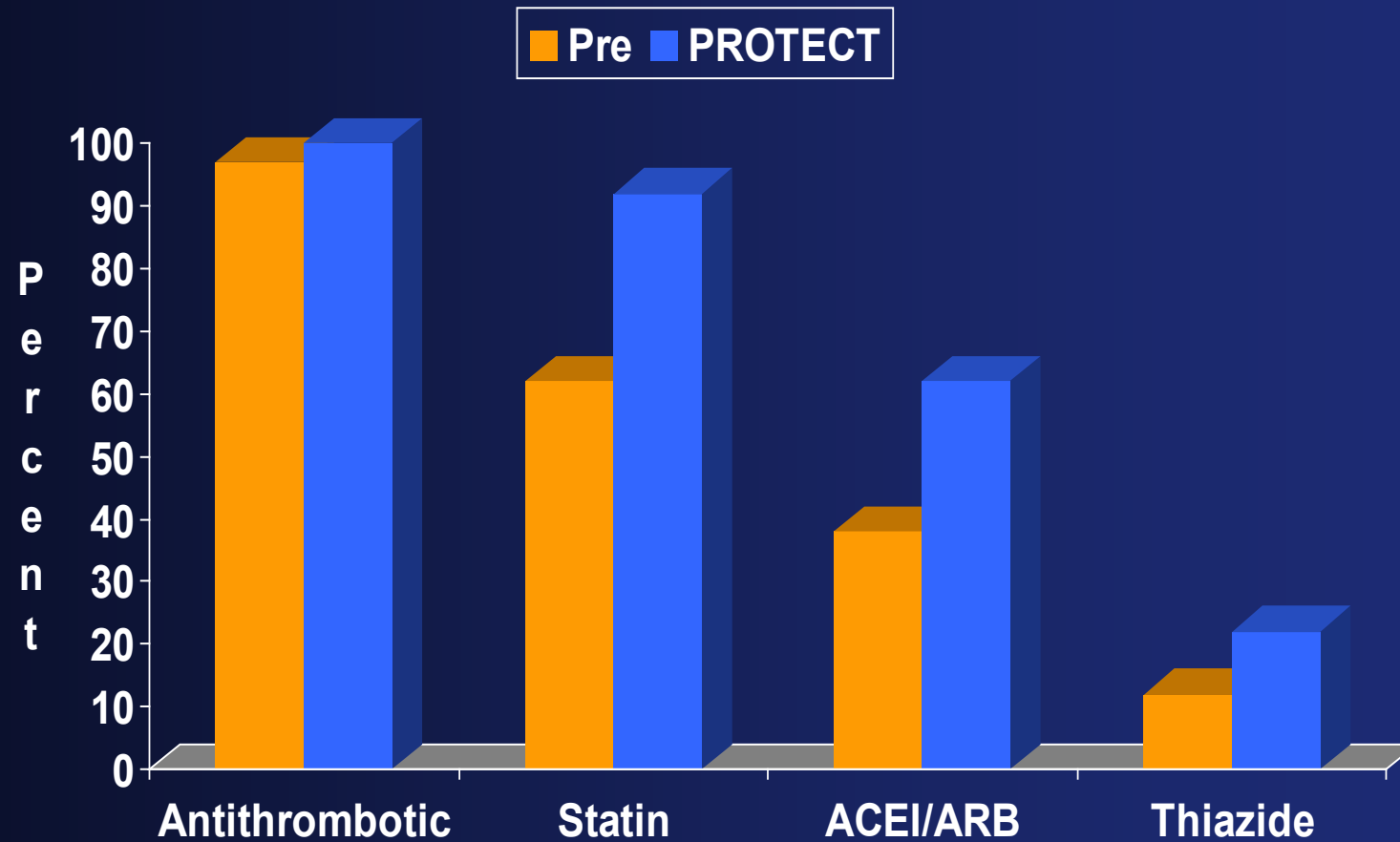
SPARCL=Stroke Prevention by Aggressive Reduction in Cholesterol Levels.

SPARCL Investigators. *N Engl J Med.* 2006;355:549-559.

ACC/AHA Guidelines for the Treatment of Blood Cholesterol in Primary Prevention

- **Recommendations based on the 10 year risk for cardiovascular disease**
- **Shifts away from specific cholesterol goals**
- **Estimated risk dictates intensity of statin Rx: high risk mandates high intensity statin Rx**
- **Atorvastatin 10 mg is moderate intensity statin Rx and 40 to 80 mg is high intensity**
- **10 year Risk calculator**

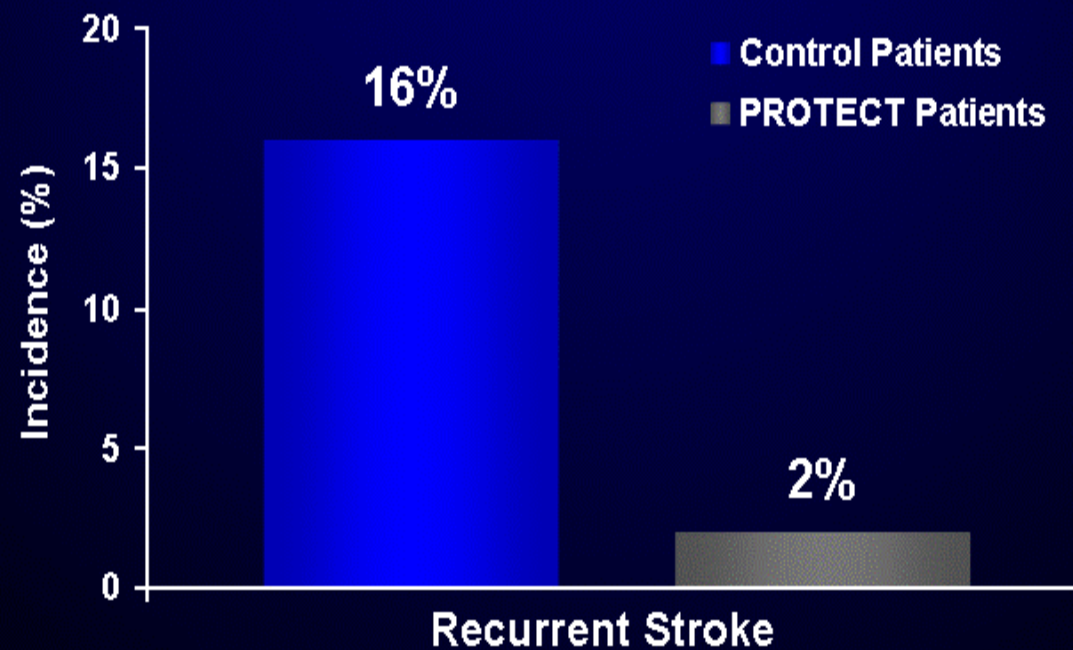
Impact of PROTECT pilot phase on Treatment Rates at Discharge



--Ovbiagele et al, Stroke 2003

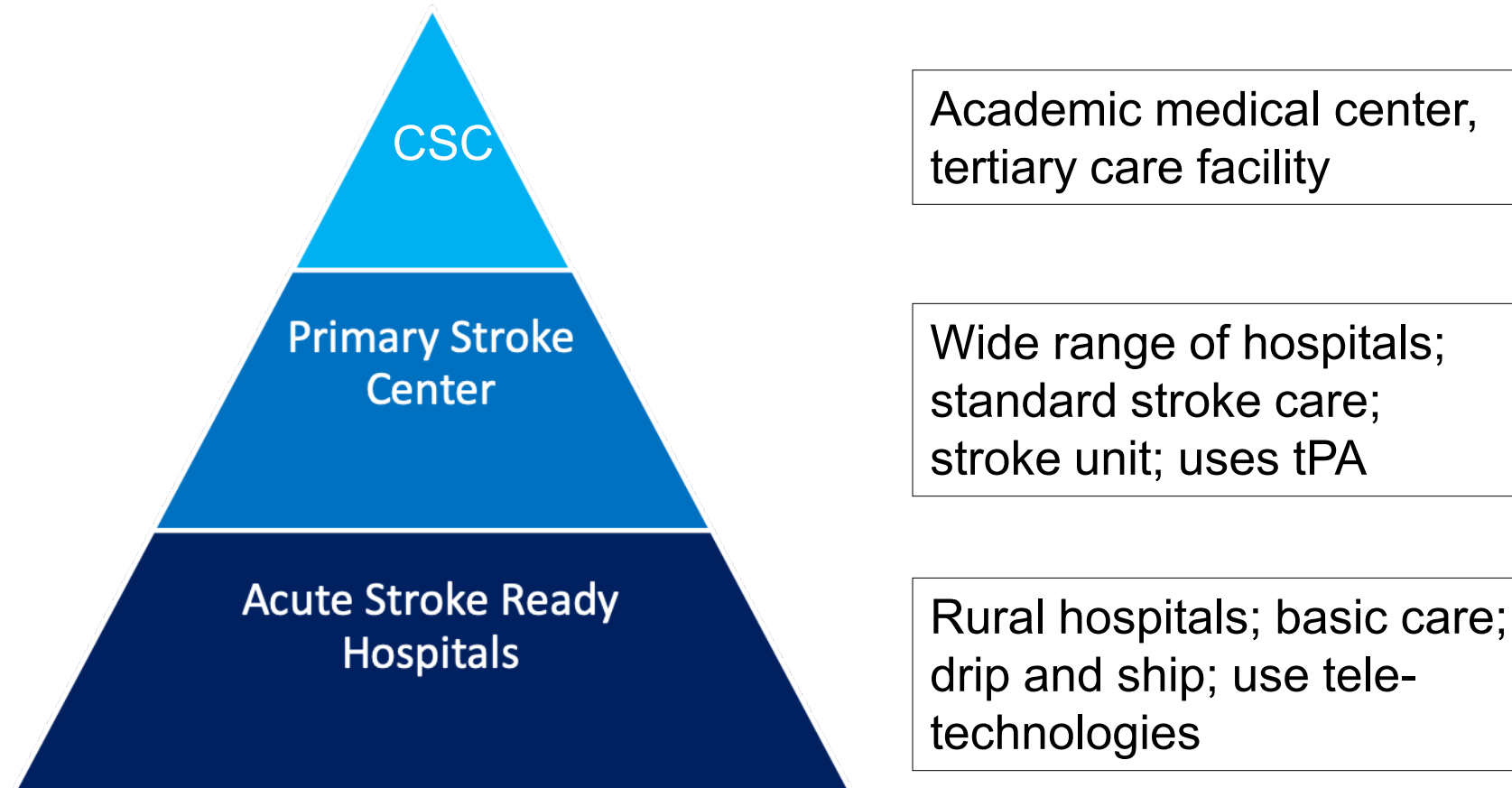
PROTECT: Incidence of Recurrent Stroke

A significant difference was observed at 90 days with regard to the incidence of recurrent strokes



$P=0.045$.
Rahiman A et al. *Stroke*. 2005;36:429. Abstract 58.

Models of Stroke Care



Benefits of Certification

- **Builds the structure required for a systematic approach to clinical care**
- **Reduces variability and improves the quality of patient care**
- **Pushes you to look at yourself more closely**
- **Creates a loyal, cohesive clinical team**
- **Provides an objective assessment of clinical excellence**
- **Differentiates clinical care in the marketplace**
- **Promotes achievement to referral sources**

Work-up of TIA and Ischemic Stroke

All Patients

- Brain Imaging
- Neurovascular imaging
- Blood glucose
- Serum electrolytes
- CBC w/ Platelets
- PT/PTT/INR
- 12 lead EKG/ROMI
- Holter monitoring
- TTE/TEE
- Supplemental O₂
- Fever reduction

• Lipids

Selected Patients

- Hepatic functions
- Toxicology
- Blood alcohol level
- Pregnancy
- Hypercoagulable w/u
- EEG
- LP

Original Article

Atrial Fibrillation in Patients with Cryptogenic Stroke

David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., Martin O'Donnell, M.B., Ph.D., Andreas Laupacis, M.D., Robert Côté, M.D., Mukul Sharma, M.D., John A. Blakely, M.D., Ashfaq Shuaib, M.D., Vladimir Hachinski, M.D., D.Sc., Shelagh B. Coutts, M.B., Ch.B., M.D., Demetrios J. Sahlas, M.D., Phil Teal, M.D., Samuel Yip, M.D., J. David Spence, M.D., Brian Buck, M.D., Steve Verreault, M.D., Leanne K. Casaubon, M.D., Andrew Penn, M.D., Daniel Selchen, M.D., Albert Jin, M.D., David Howse, M.D., Manu Mehdiratta, M.D., Karl Boyle, M.B., B.Ch., Richard Aviv, M.B., Ch.B., Moira K. Kapral, M.D., Muhammad Mamdani, Pharm.D., M.P.H., for the EMBRACE Investigators and Coordinators

N Engl J Med
Volume 370(26):2467-2477
June 26, 2014



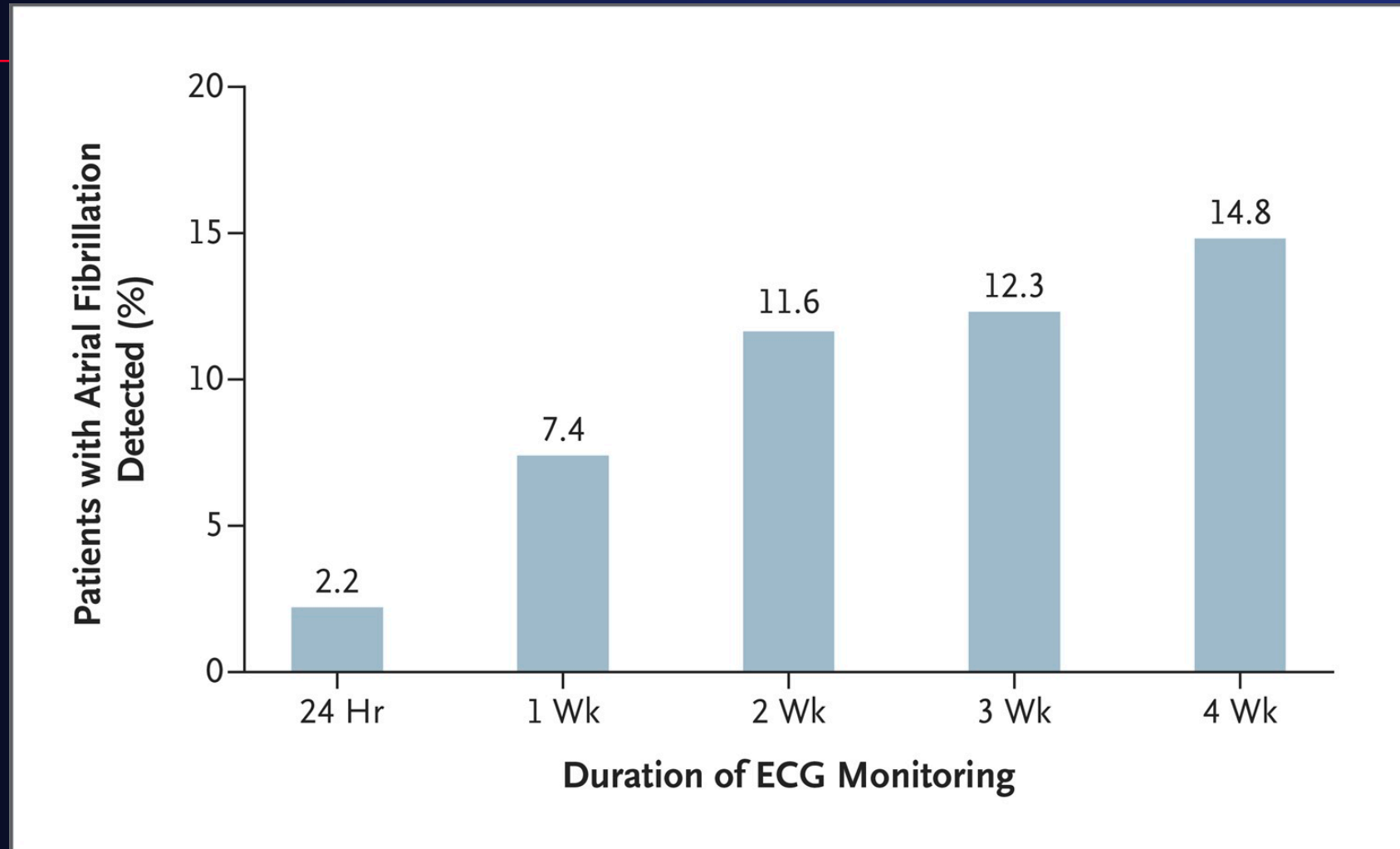
The NEW ENGLAND
JOURNAL of MEDICINE

Study Overview

- In this study, patients with cryptogenic stroke who were randomly assigned to undergo intensive ECG monitoring for 30 days had a higher incidence of detected atrial fibrillation (16%) than those assigned to receive standard 24-hour monitoring (3%).



Incremental Yield of Prolonged ECG Monitoring for the Detection of Atrial Fibrillation in Patients with Cryptogenic Stroke or TIA.



Gladstone DJ et al. N Engl J Med 2014;370:2467-2477



The NEW ENGLAND
JOURNAL of MEDICINE

Conclusions

- Among patients with a recent cryptogenic stroke or TIA who were 55 years of age or older, paroxysmal atrial fibrillation was common.
- Noninvasive ambulatory ECG monitoring for a target of 30 days significantly improved the detection of atrial fibrillation by a factor of more than five and nearly doubled the rate of anticoagulant treatment, as compared with the standard practice of short-duration ECG monitoring.



Warfarin Coagulopathy Reversal

- **Vitamin K 10 mg IV**
- **Options include FFP or PCC**
 - Most recent guidelines recommend weight-based dosing of PCC when available
 - The PCC dose is adjusted based on the INR

INR	4-factor PCC dose	Max dose
2-3.9	25 units/kg	2500 units
4-6	35 units/kg	3500 units
>6	50 units/kg	5000 units

Other Coagulopathy Reversal

MEDS	REVERSAL
UFH	Protamine
Antiplatelets	Consider DDAVP (0.4 mcg/kg) Platelets NOT recommend unless undergoing neurosurgical procedure
Factor Xa inhibitors -Rivaroxaban -Apixaban -LMWH	• FFP and vitamin K are not effective • Consider activated charcoal (50 gm) if last oral dose was within 2 hours • No evidence for FEIBA or 4-factor PCC 30 IU/kg for rivaroxaban or apixaban • Andexxa (coagulation factor Xa [recombinant] for rivaroxaban or apixaban • Protamine for LMWH given < 8 hrs for partial rev.
Direct Thrombin Inhibitors	For Dabigatran (idarucizumab*), emergent dialysis, consider rVIIa 80µg/kg or FEIBA (Factor VIII inhibitor bypassing activity)

*Pollack et al. NEJM 2015; 373:511-20

Discharged with:

- **Blood pressure control**
 - **Diabetics ACEI/ARBs**
- **Antiplatelets**
- **Statins**
- **Lifestyle changes**

Summary

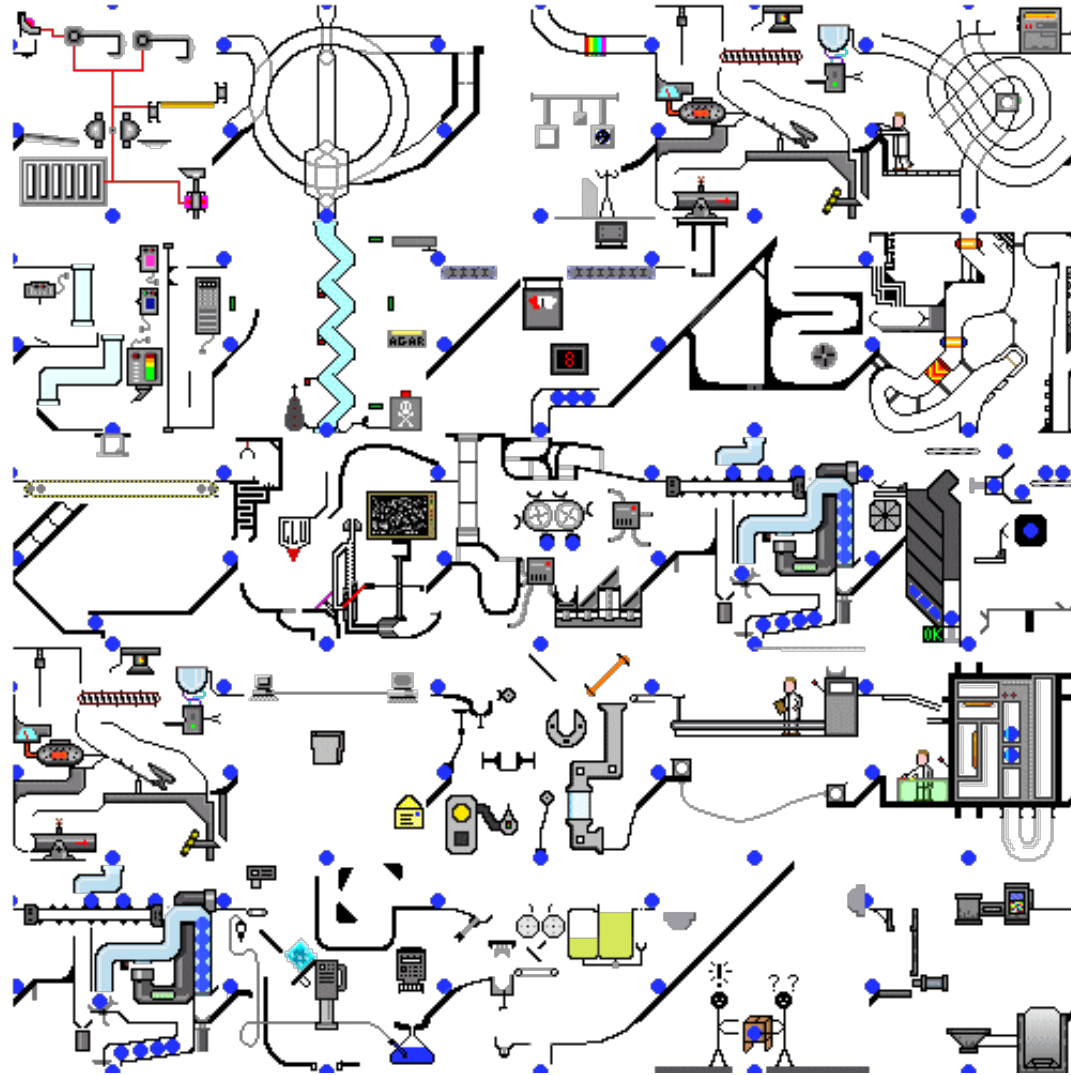
- **Epidemiology**
- **Definitions of TIA**
- **Imaging (which type is best)**
- **New time standard in catheter based treatment**
- **Cardiac Holter**

Key Points:

- Time has very limited function in determining a stroke and cerebral imaging allows for a more accurate diagnosis, determine mechanism of the event and helps with early treatment and prognosis.
- Next best steps: Utilize dual antiplatelet therapies for 21 days after stroke when ABCD2 score is ≥ 4 and NIH ≤ 3 then monotherapy with a single antiplatelet and consider longer Holter monitoring as outpatients to improve the diagnosis of A Fib that would require anticoagulation.

I have no conflicts of interest

Thank you for your Attention



Question 1

Mr. Jones has 4 hours of sudden onset dysarthria and arm/hand weakness and then symptoms completely resolve.

Is this a:

- A. Stroke**
- B. TIA**
- C. RIND**
- D. Complicated migraine**

Answer to Question 1

- Then answer is A.
- The definition of TIA is < 1 hour and negative imaging
- Reversible ischemic neurologic deficit is no longer a valid term
- Migraine symptoms are not sudden

Question 2

What is the most practical cerebral imaging study within 3 hours of stroke signs and symptoms?

- A. CT of brain**
- B. CT of brain/CT angiogram of head and neck**
- C. MRI of brain**
- D. MRI of brain/MRA of head and neck**

Answer to Question 2

- The answer is B.
- CT/CTA scans seem to to be the most practical cerebral imaging study in the EDs, ICUs, and for other inpatients.

Question 3

Mr. Jones 83 years old right handed male has a NIHSS of 12, had a witnessed onset of his stroke and is within 13 hours with a neg. CT and positive left MCA thrombus

- A. Too old to consider to give TPA**
- B. Give ASA only**
- C. If there are no protocol exclusions, performing a thrombectomy**
- D. Give Clopidogrel only**

Answer to Question 3

- The answer is C.
- The patient should be taken to thrombectomy.
- ASA or Clopidogrel should be given ASAP only if the patient is not a TPA candidate

Question 4

Which is the most appropriate antiplatelet therapy for noncardioembolic stroke?

- A. Aspirin**
- B. Clopidogrel**
- C. Asp/dyp combination**
- D. Asp/Clopidogrel**
- E. Any listed above**

Answer to Question 4

- The answer is E.
- Ischemic stroke is a very heterogeneous disease and the treatment regimen depends on the etiology of the patient's ischemic event.

Question 5

How do I workup the patient with the diagnosis of TIA?

- A.** Cardiac Echo
- B.** EKG/Holter
- C.** Brain imaging (CT or MRI)
- D.** Vascular imaging (CTA or MRA)
- E.** All of these above

Answer to Question 5

- The answer is E.
- Echo to r/o PFO, to evaluate ejection fraction, and evaluate wall motion abnormality
- EKG and Holter to r/o Afib.
- We always need brain imaging with neurovascular imaging

Reference:

- **2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association**
 - Stroke. 2018;49:e46–e99. DOI: 10.1161/STR.0000000000000158.)