Advances in Stroke

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I have no conflicts of interest

Outline and Learning Objectives

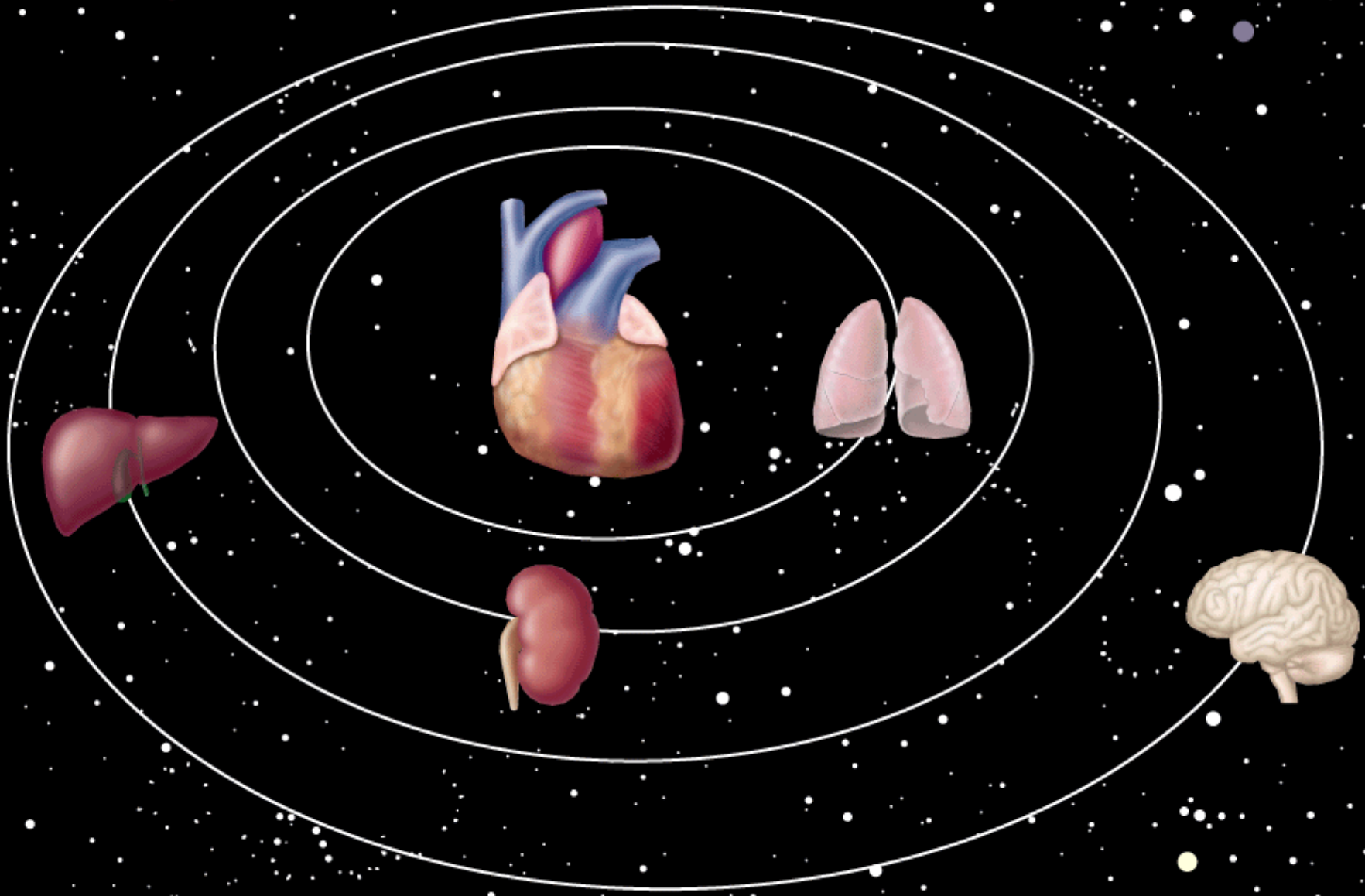
- Review epidemiology
- Review polyvascular disease
- Discuss new definitions of TIA
- Review medical interventions
  - Thrombolysis
  - Antihypertensives
  - Statin therapy
  - Anticoagulants
  - Antiplatelet therapy
- Review barriers to improve outcomes
- Discuss promotion of stroke centers
- Review stroke workup

Stroke in the US

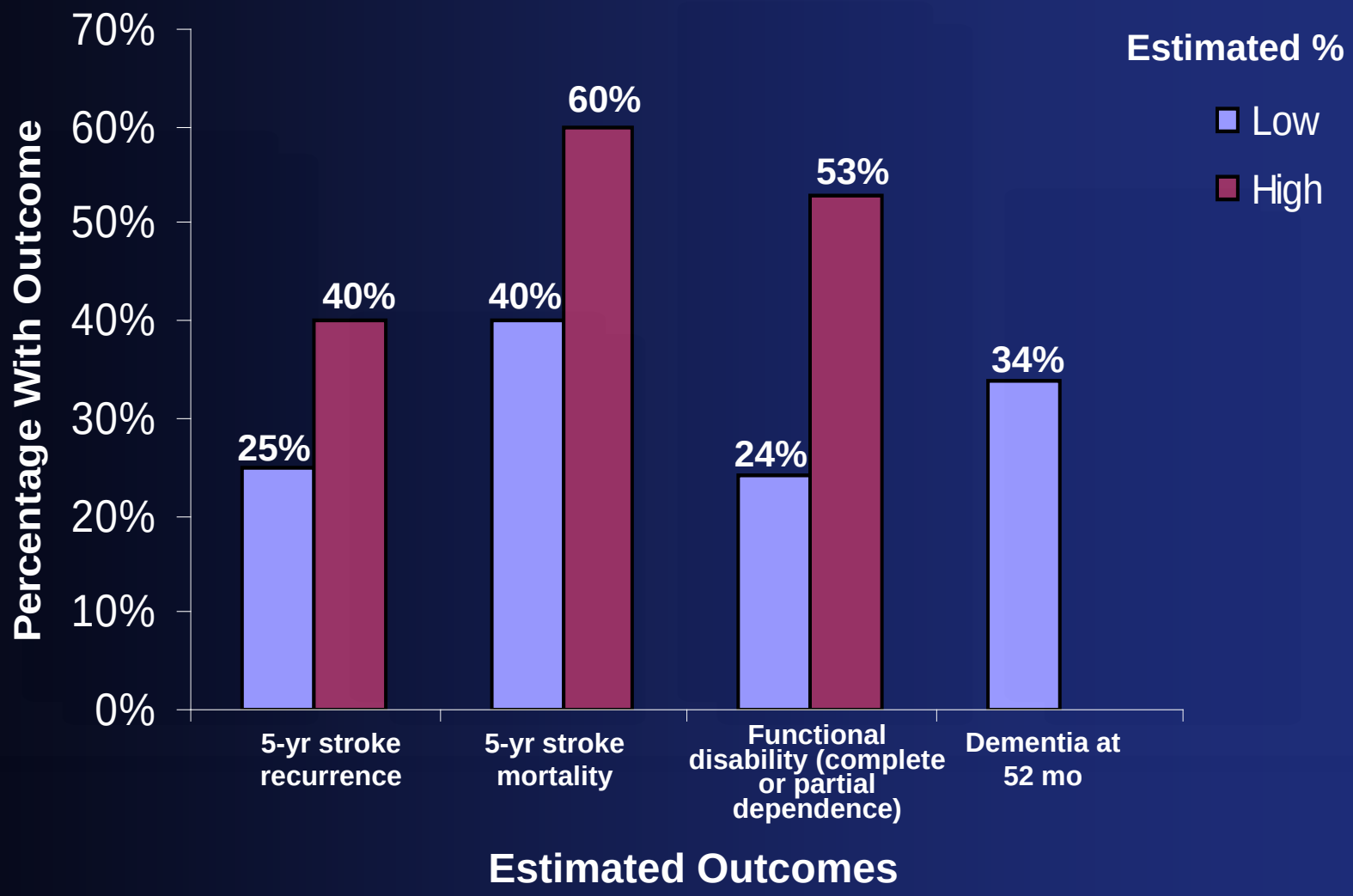
- 795 000 people experience a new or recurrent stroke.
  - Approximately 610 000 of these are first attacks, and 185 000 are recurrent attacks.
- 137 000 stroke deaths annually in the United States.
- Leading cause of serious, long-term disability
- Third leading cause of death in the U.S.; second leading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

AHA, 2014

Cardio-Centric Universe

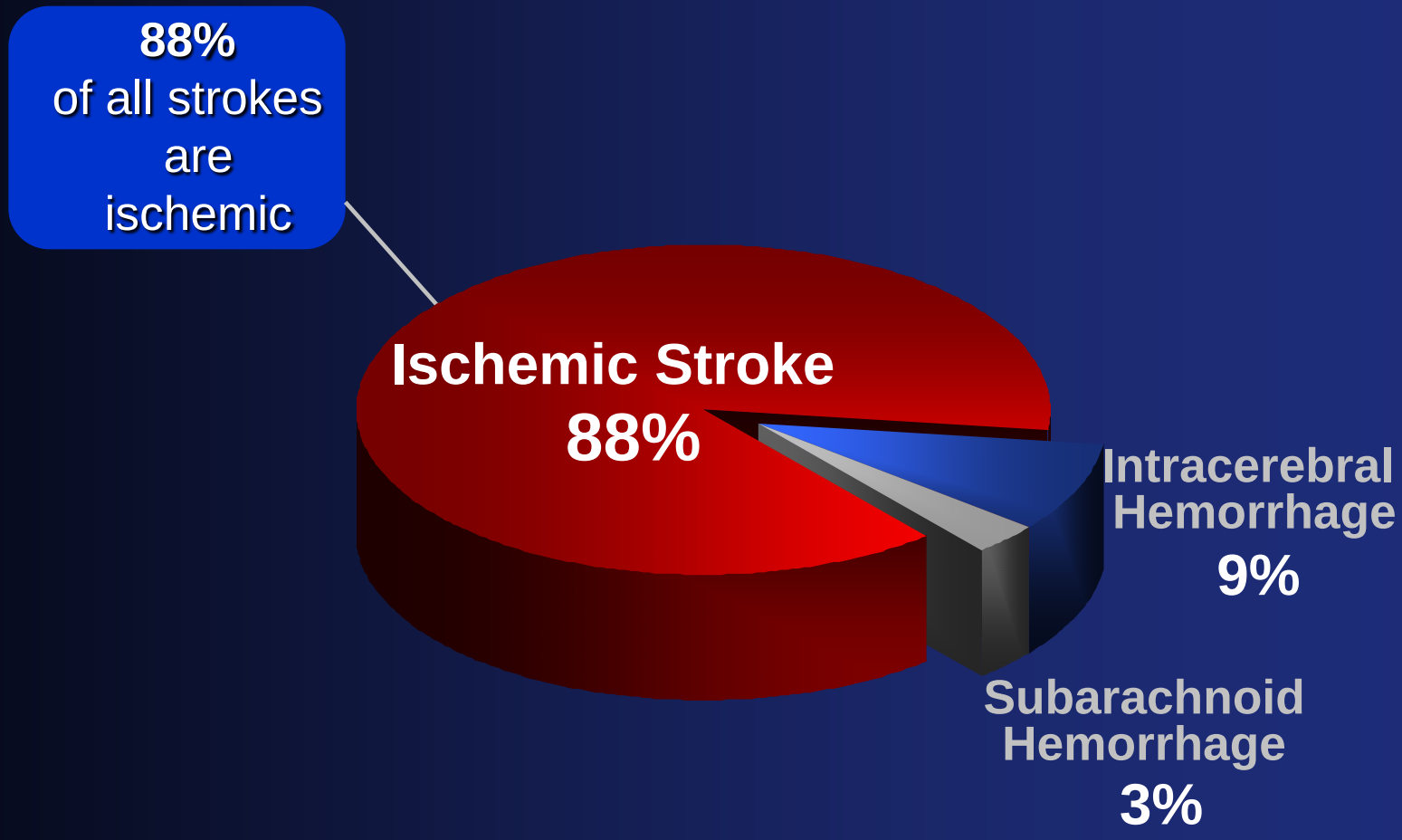


Estimated Outcomes After Ischemic Stroke



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

Prevalence of Ischemic Stroke



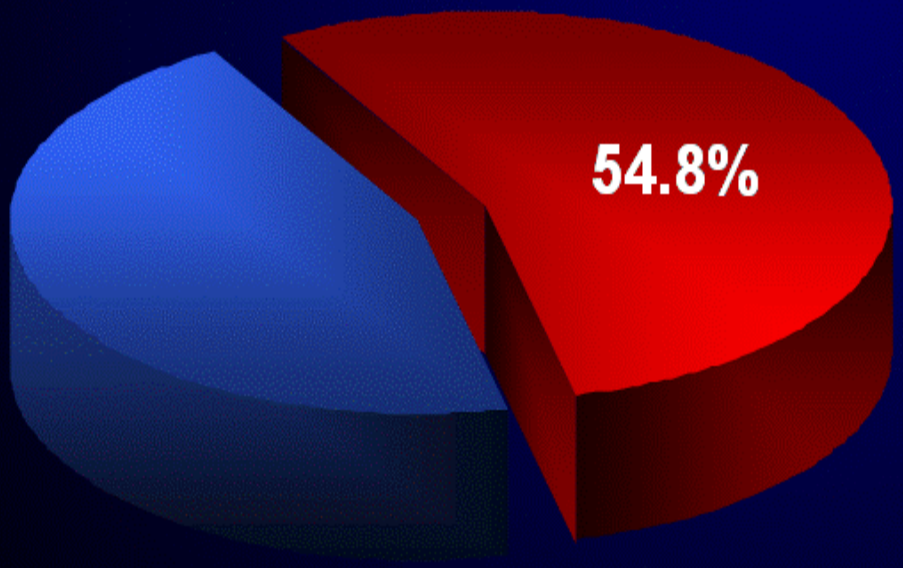
American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. 2005.

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

Helgason CM et al. *Circulation*. 1997;96:701-707.

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

Goldstein L et al. *Circulation*. 2001;103:163-182.
Broderick J et al. *Stroke*. 1998;29:415-421.
Brown WV. *Clin Cornerstone.* 2004;6 Suppl 3:S30-S34.

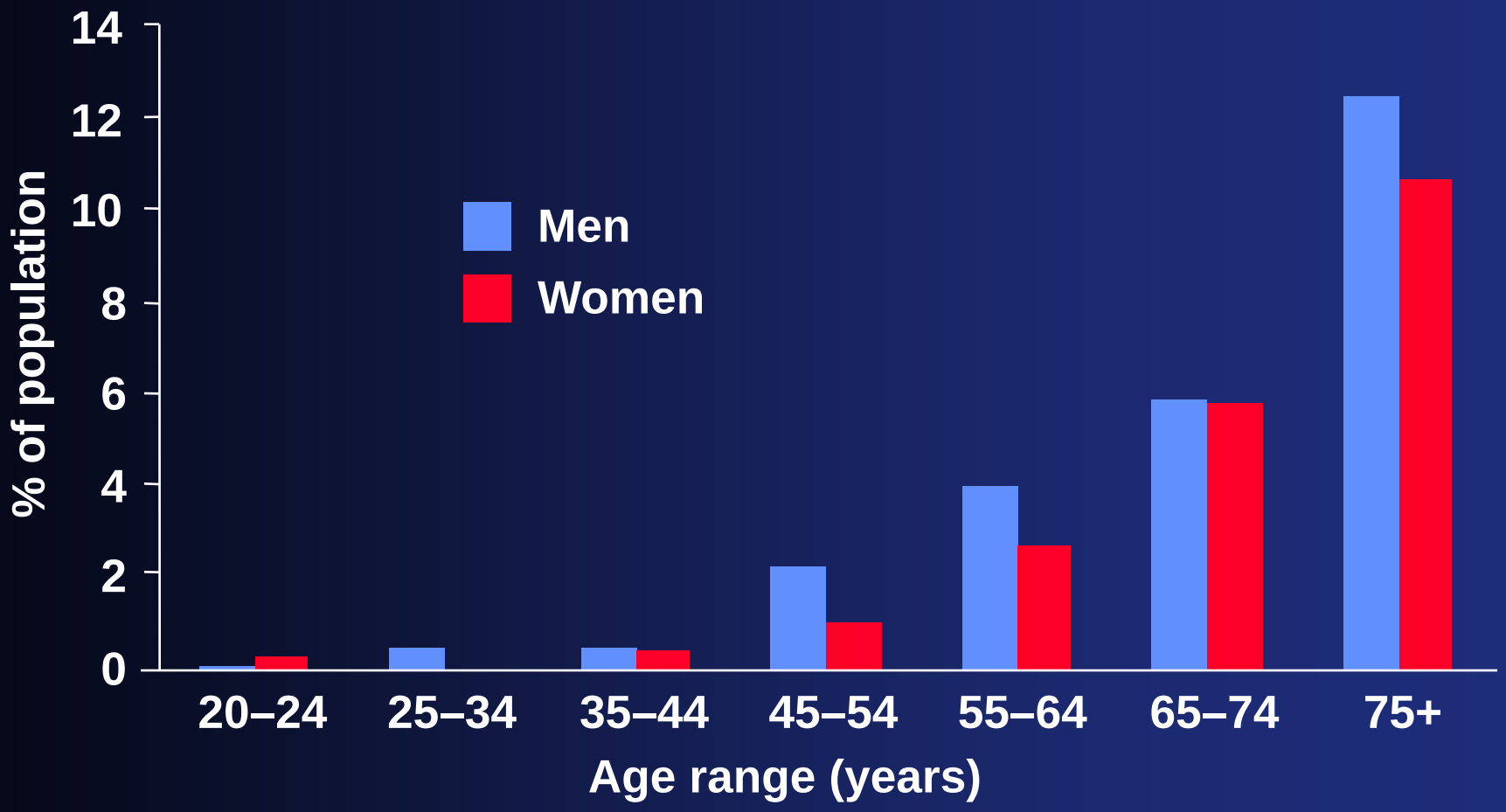
INTERSTROKE: Population-attributable risk for common risk factors

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.

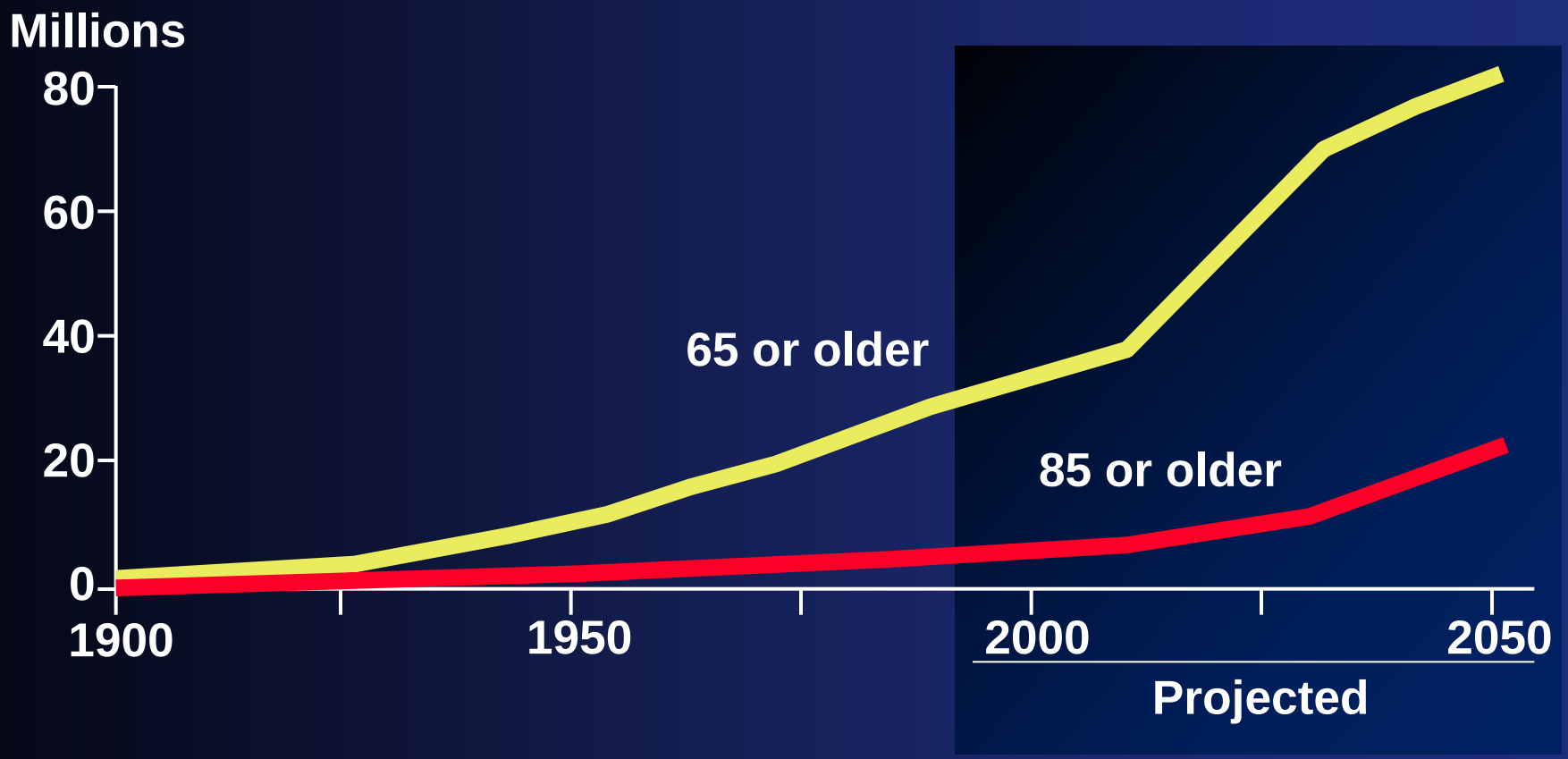
O'Donnell MJ et al. *Lancet* 2010; available at: http://www.thelancet.com.

Prevalence of Stroke by Age



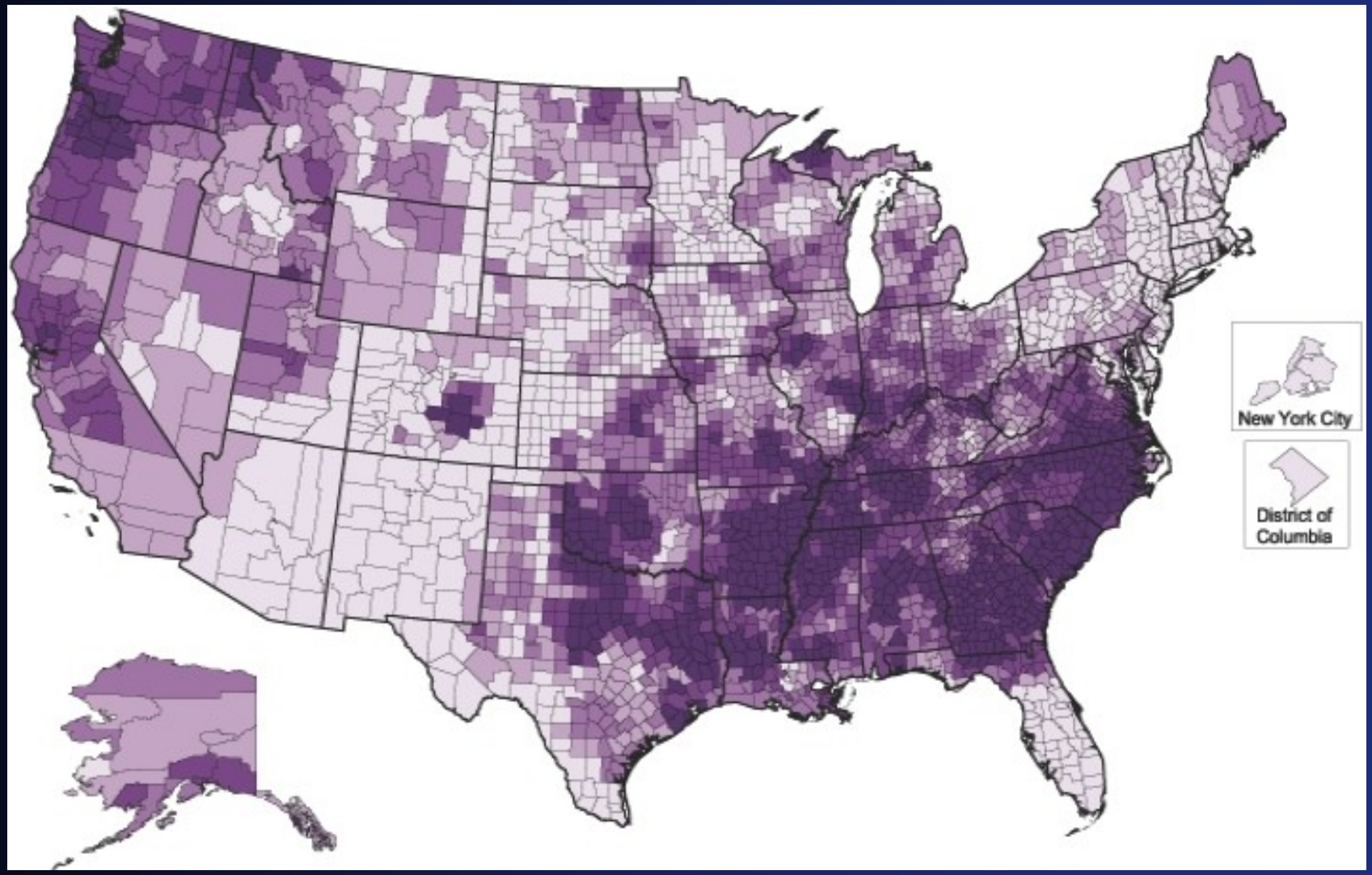
AHA. *Heart Disease and Stroke Statistics—2004 Update*.

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.*

Stroke Mortality Rates



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

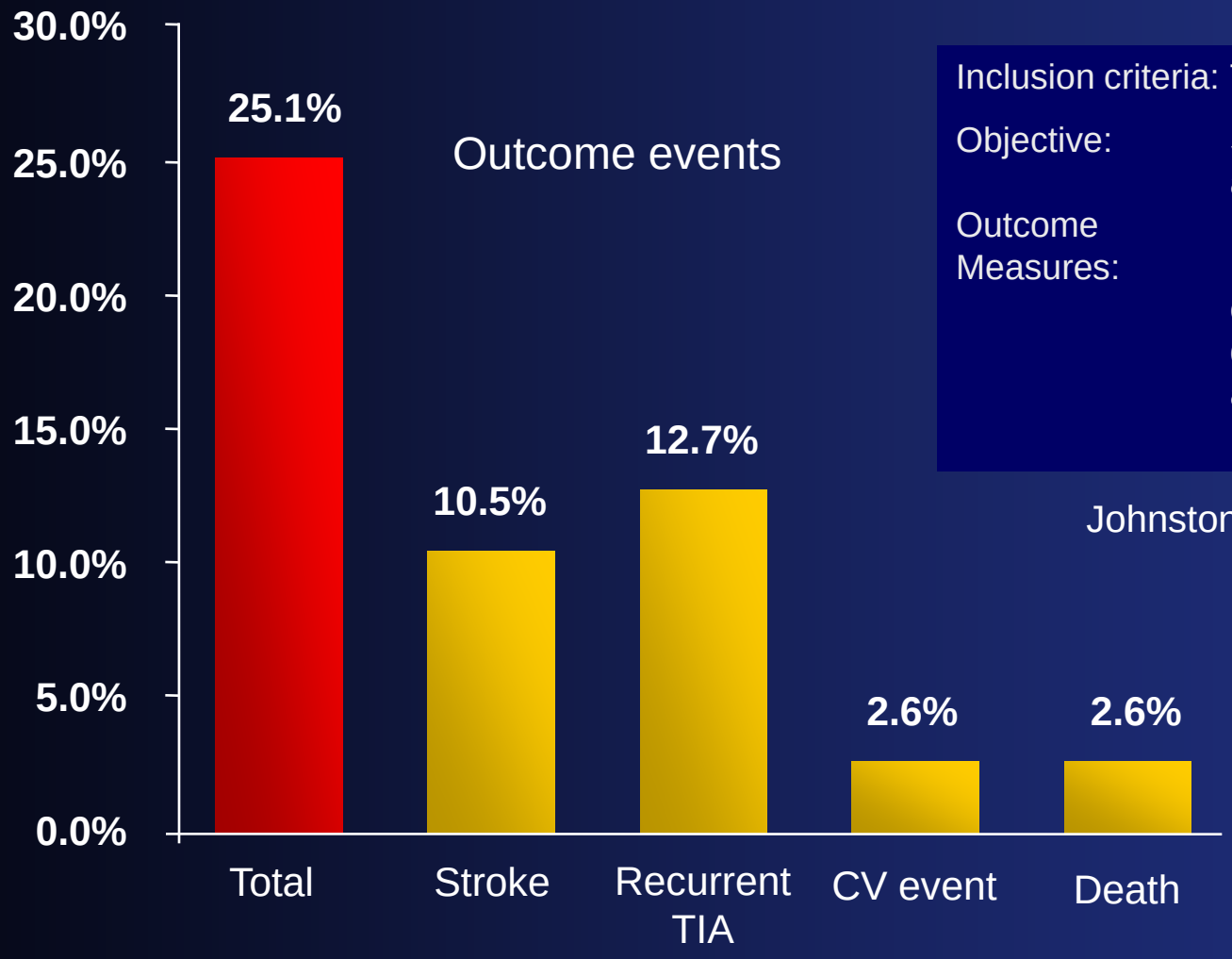
TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting *less than one hour*, and *without evidence of acute infarction*

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

ABCD^2 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 (1point)
  - 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

Stroke. 2009;40:2276.

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:
  - $ABCD^2$ score of 3 or greater
  - $ABCD^2$ score of 0-2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient

Stroke. 2009;40:2276.

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

Stroke. 2009;40:2276

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

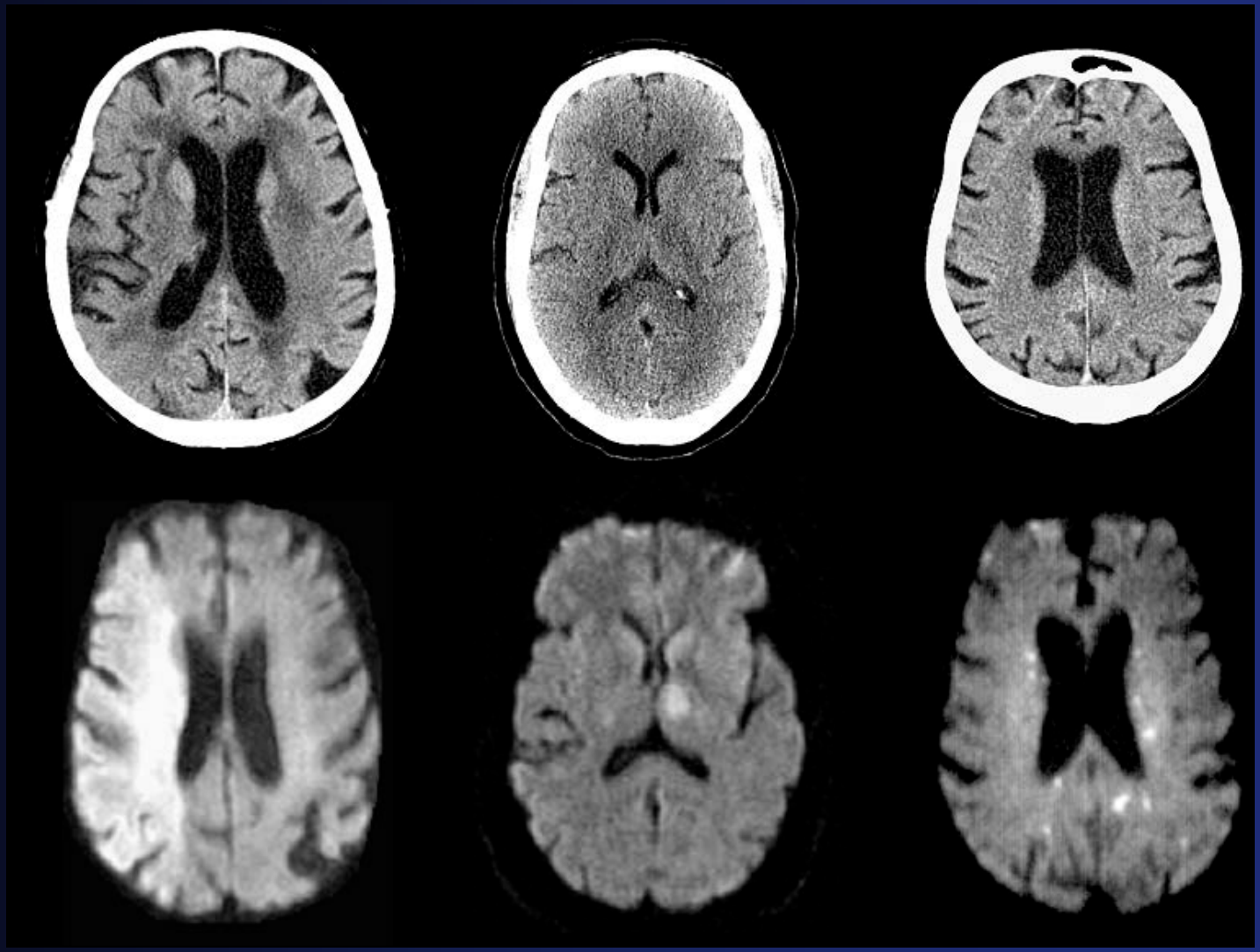
- More sensitive to acute ischemia
- More sensitive to posterior fossa lesions
- More sensitive to small vessel, lacunar lesions

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

MRI - Tissue Status: Ischemia

CT

DWI



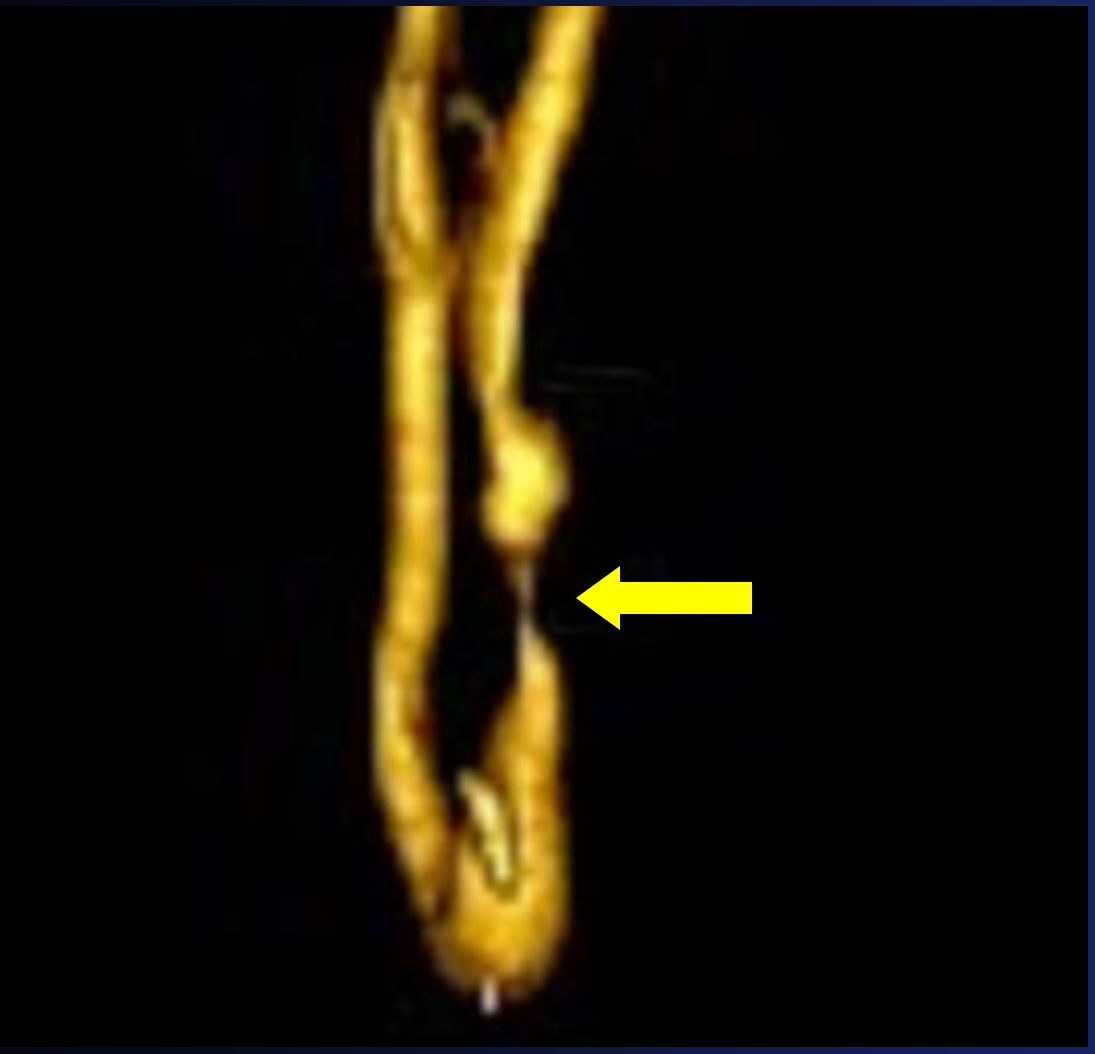
Evaluation of Vessel Status

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

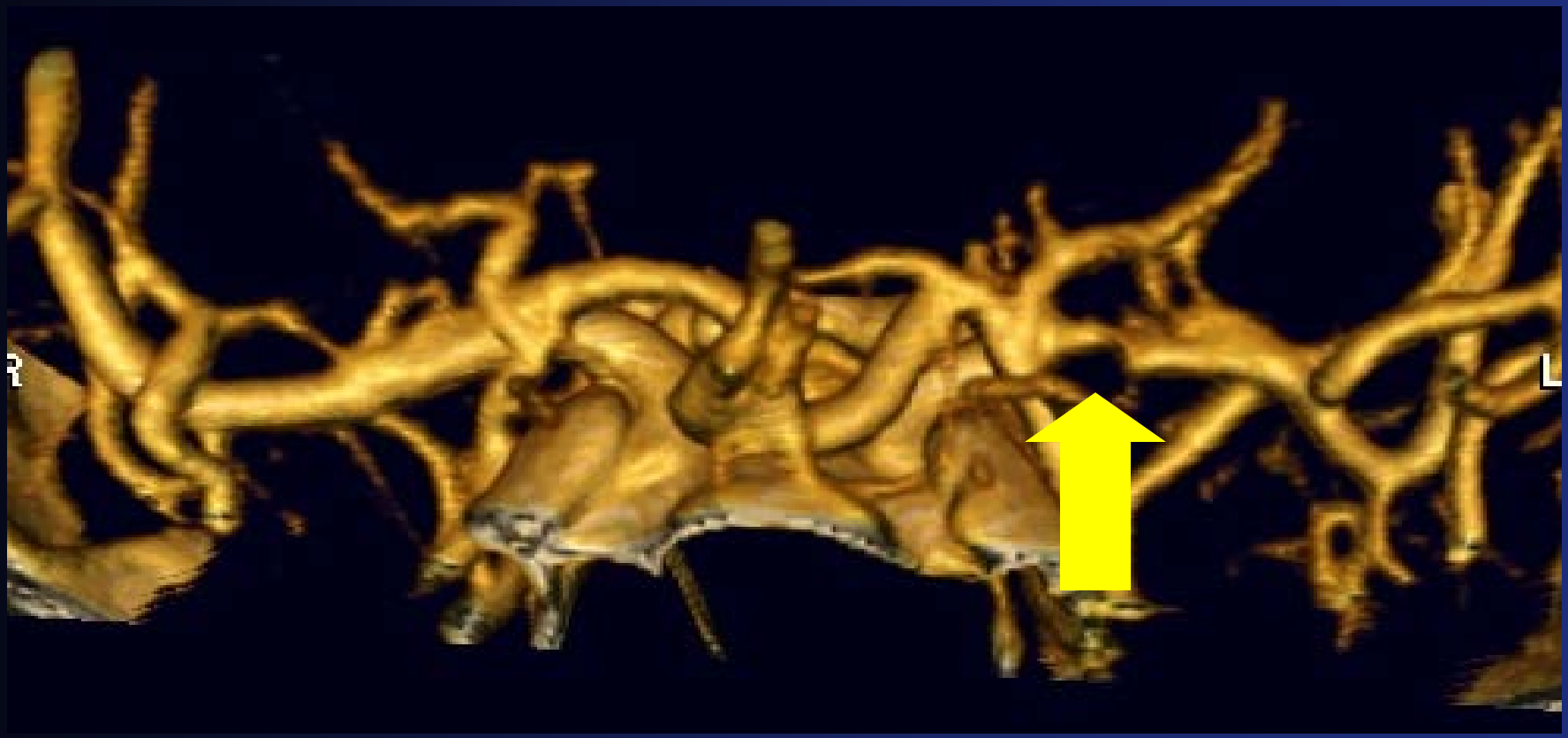
CT Angiography

- 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



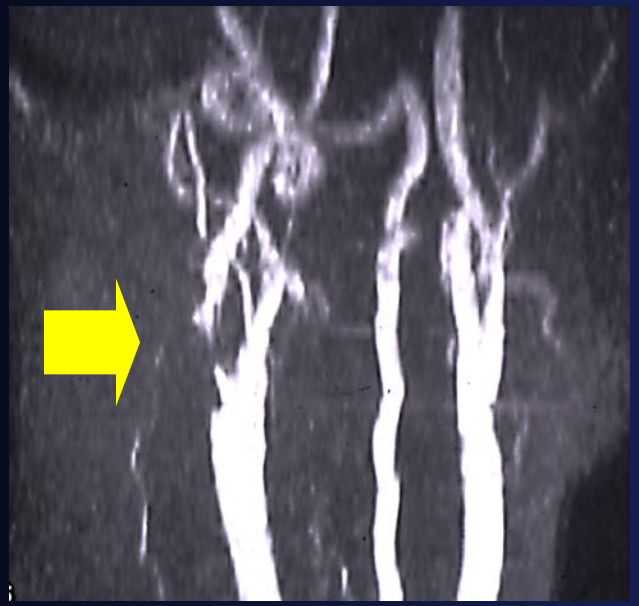
CTA: MCA Stenosis



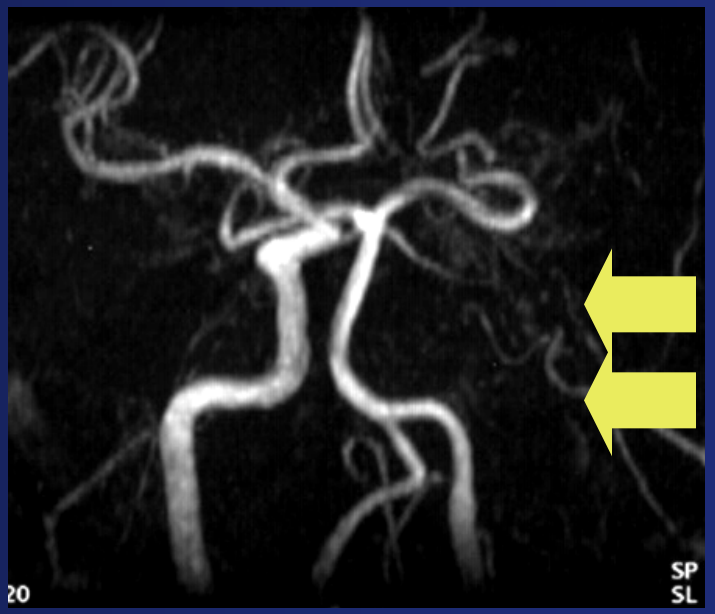
MR Angiography

- 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).

NEUROLOGY 2010;75:177-185

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): 160 to 325 mg/day) (Grade 1A) to reduce stroke mortality and decrease morbidity; ONLY if no contraindications or if patient will not be given rtPA[1]
  - 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 patients[1]
- Early consultation by neurologist or stroke team critical[2]

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

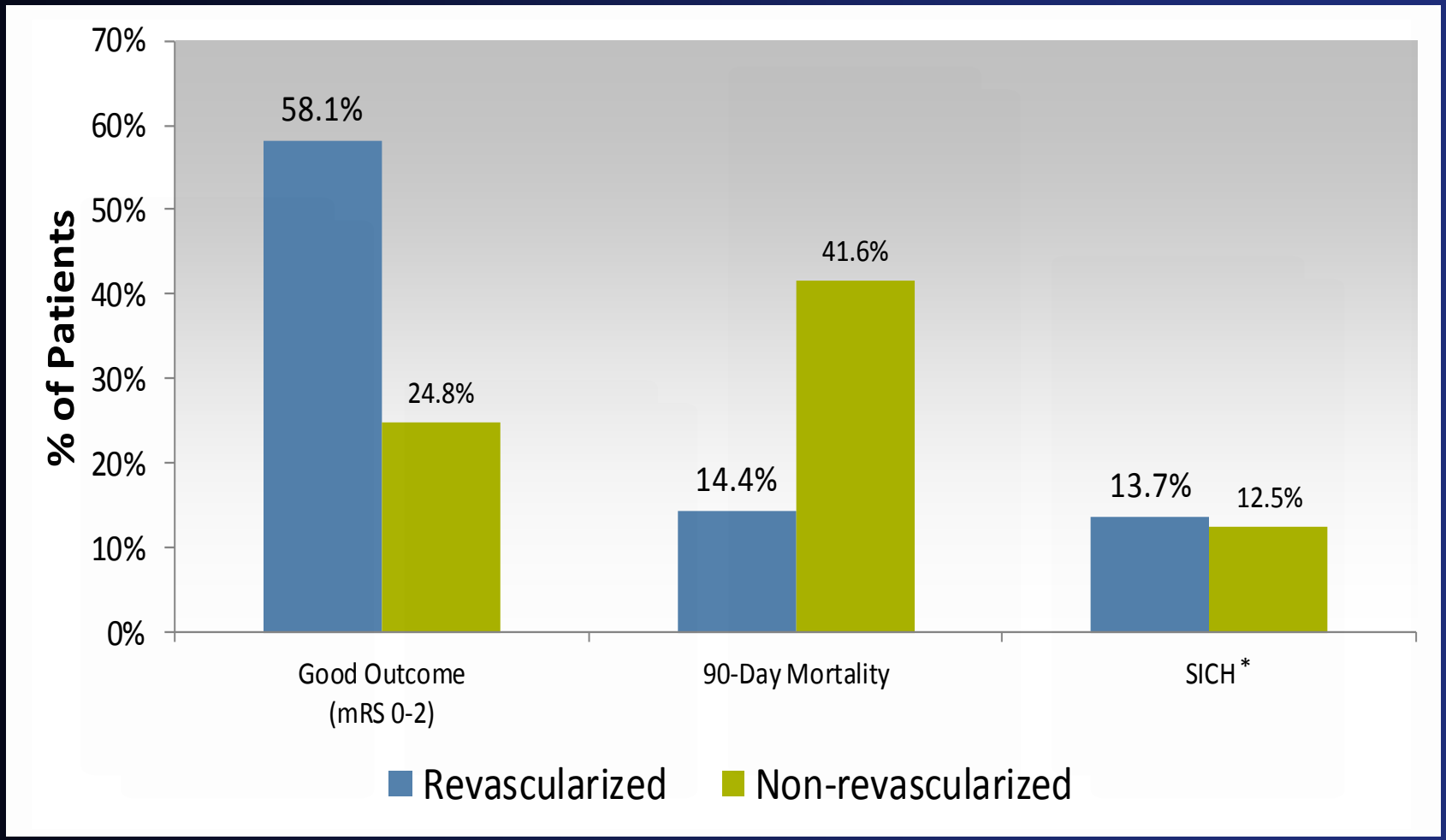
National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581-1587. Kleindorfer DO, Broderick JP, et al. Emergency department arrival times after acute ischemic stroke during the 1990s. Neurocrit Care. 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.

In patients with acute ischemic stroke:

- ≤ 3 hours for IV r-tPA (Grade 1A)
- 3 ≤ 4.5 hours we suggest IV r-tPA over no IV r-tPA (Grade 2C)
- Cannot be initiated ≤ 4.5 h of symptom onset, we recommend against IV r-tPA (Grade 1B)

CHEST. 2012;141(2_suppl):1S-1S. doi: 10.1378/chest.1412S1

Meta-analysis Shows a Strong Correlation Between Revascularization and Good Patient Outcomes



*Differences in sICH were not statistically significant between the revascularized and non-revascularized groups

Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke. 2007 Mar;38(3):967-73.

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

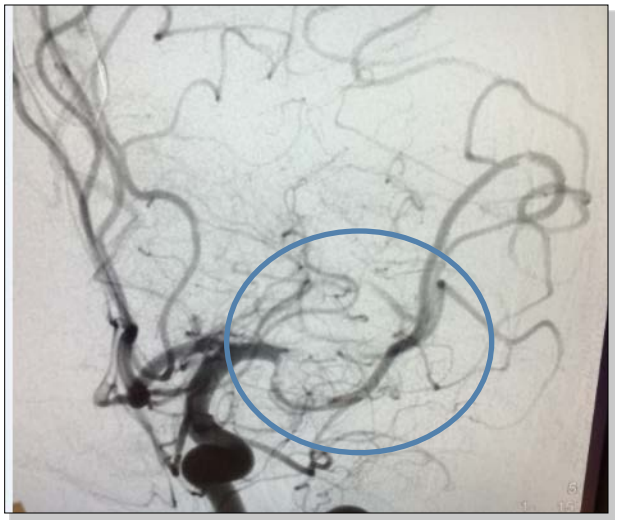
Vessel	Mortality Rate
ICA	53%[1]
MCA	27%[2]
Basilar Artery	89-90%[3]

1. Jansen O, et al.
2. Furlan A et al. PROACT II Trial
3. Brückmann H et al.

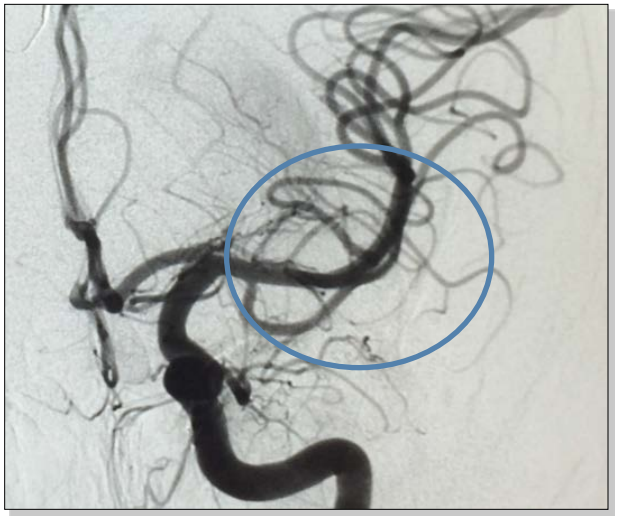
Trial Summary

Trial	Imaging Required to Confirm Occlusion Prior to Randomization?	Device(s) Used in Intervention Arm	TICI 2b/3 Revascularization Rate in the Intervention Arm	mRS 0-2		
				Intervention Arm	Control Arm	Odds Ratio (95% CI)
IMS III	No	IA Lytic (138), Merci Retriever® (95), EKOS (22), Penumbra (54), Solitaire FR (5)	38% ICA 44% M1 44% M2 23% multi M2	40.8% (N=415)	38.7% (N=214)	0.02 (-0.06 to 0.09)
MR RESCUE	No	Merci Retriever®, EKOS, IA Lytic, Penumbra	24% pen (n=34) 27% nonp (n=30)	21% pen (n=34) 17% nonp (n=30)	26% pen (n=34) 10% nonp (n=20)	NS
MR CLEAN	Yes	97% Stent Retrievers, 2% other Mechanical	58.7% (N=196)	33% (N=233)	19% (N=267)	2.16 (1.39-3.38)
ESCAPE	Yes	86% Stent Retriever	72.4% (n=156)	53.0% (n=164)	29.3% (n=147)	1.8 (1.4-2.4)
SWIFT PRIME	Yes	100% Stent Retriever	88.0% (n=83)	60.2% (n=98)	35.5% (n=93)	2.75 (1.53,4.95)
EXTEND-IA	Yes	100% Stent Retriever	86.2% (n=29)	71% (n=35)	40% (n=35)	4.2 (1.3-13)

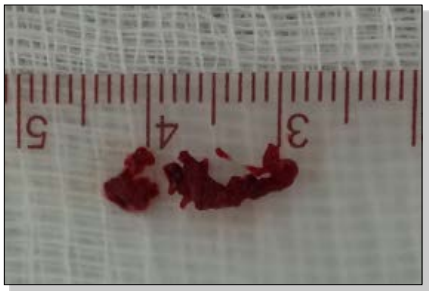
Goal of Ischemic Stroke Treatment



Before Intervention



After Successful Intervention



Images courtesy of Dr. Joey English – Used with Permission. Results from case studies are not predictive of results in other cases. Results in other cases may vary.

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

Lancet Neurol. 2012 May;11(5):397-404. doi: 10.1016/S1474-4422(12)70057-1. Epub 2012 Apr 11.

Lowering Blood Pressure

HYPERTENSION

7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

BP Classification	SBP* (mm Hg)	DBP* (mm Hg)	Lifestyle Modification	Initial Drug Therapy	
				Without Compelling Indications	With Compelling Indications
Normal	**<120**	**and <80**	**Encourage**		
Pre-hypertension	**120-139**	**or 80-89**	**Yes**	**No antihypertensive drug indicated**	**Drug(s) for compelling indications†**
Stage 1 Hypertension	**140-159**	**or 90-99**	**Yes**	**Thiazide-type diuretics‡**	**Drug(s) for compelling indications† Other antihyper-tensives**
Stage 2 Hypertension	**≥160**	**or ≥100**	**Yes**	**2-drug combination therapy**	

*Treatment determined by highest category.

†Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mm Hg.

‡May consider ACEI, ARB, BB, CCB, or combination.

Adapted from Chobanian AV, et al. *JAMA*. 2003;289:2560-2572.

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**	**Labetalol**
SBP >**230** OR DBP **121-140**	**Nicardipine** or **labetalol** If BP not controlled, consider nitroprusside

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% possible[1]
- Thiazide-type diuretic recommended as first therapeutic agent[1]
- 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.

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)

CHEST. 2012;141(2_suppl):1S-1S. doi: 10.1378/chest.1412S1

Which antiplatelet is better?

- **Of the recommended antiplatelet regimens, we suggest clopidogrel or aspirin/extended release dipyridamole over aspirin (Grade 2B) or cilostazol (Grade 2C)**

- ***Remarks:*** **With long-term use (> 5 years), the benefit of clopidogrel over aspirin in preventing major vascular events may be offset by a reduction in cancer-related mortality with regimens that contain aspirin.**

CHEST. 2012;141(2_suppl):1S-1S. doi: 10.1378/chest.1412S1

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.**

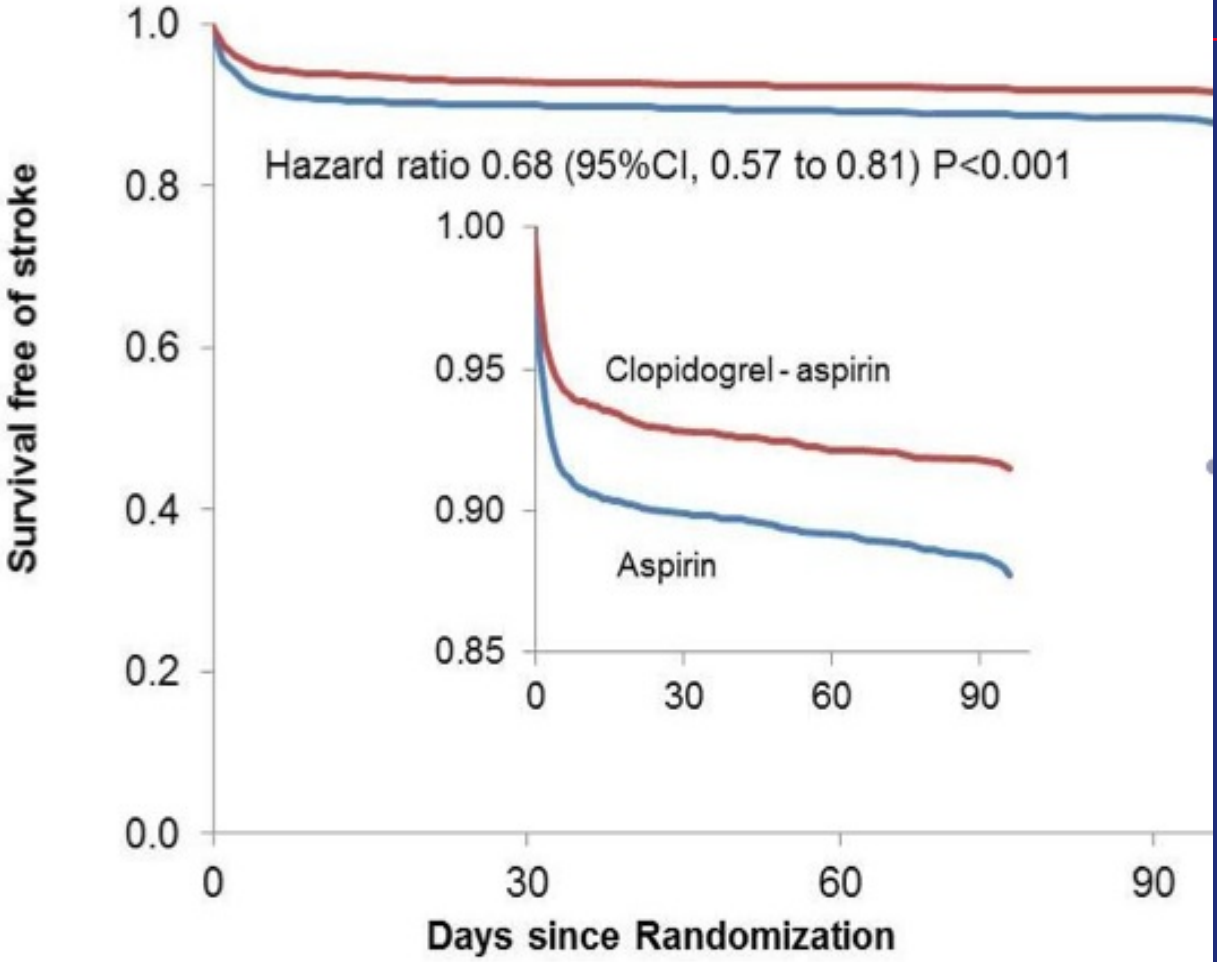
N Engl J Med Volume 369(1):11-19 July 4, 2013

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.

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

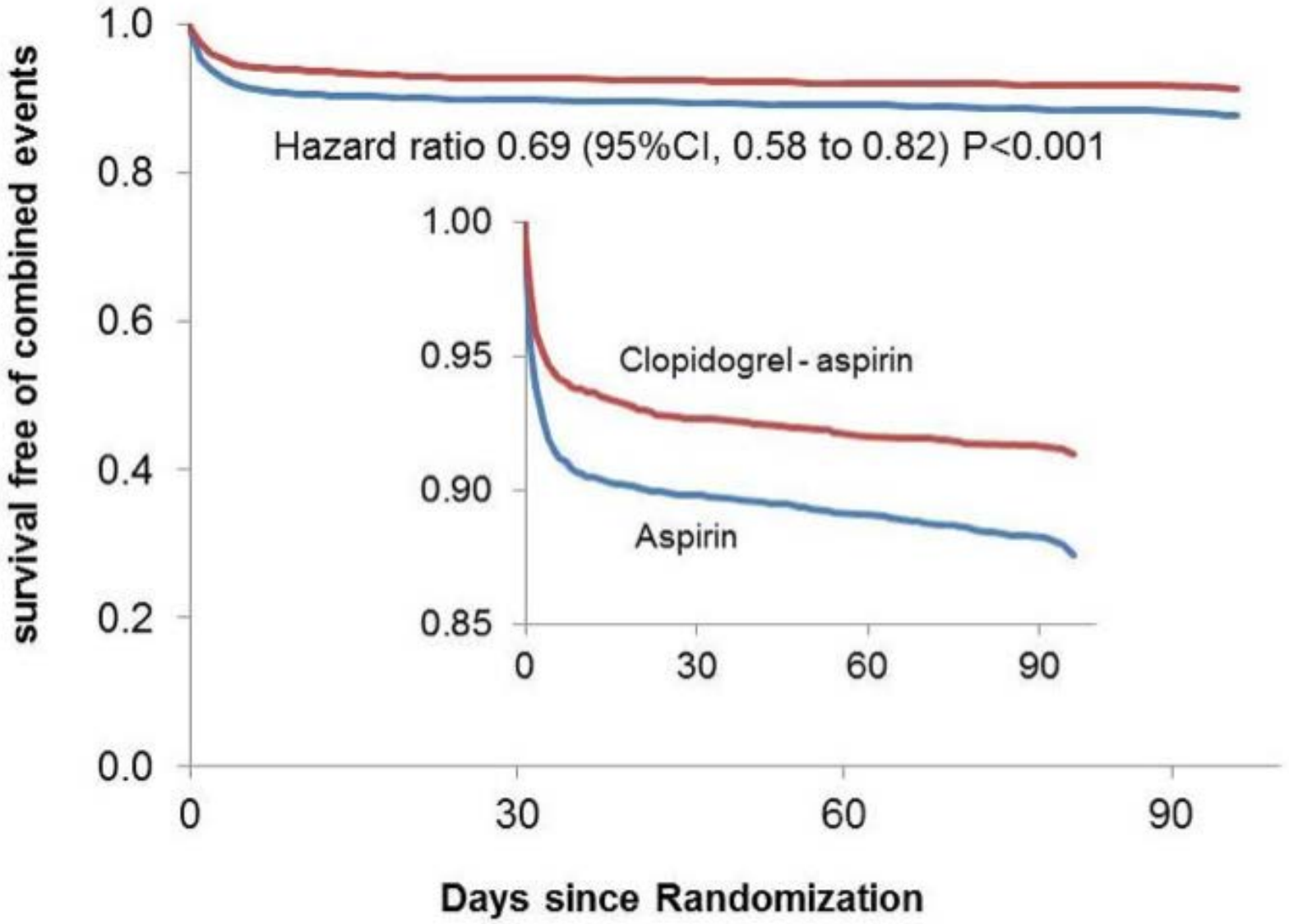
Primary outcome: stroke



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.

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

Patients with a history of ischemic stroke or TIA and atrial fibrillation (AF), including paroxysmal AF

- **Oral anticoagulation over no antithrombotic therapy** (Grade 1A)**, aspirin** (Grade 1B)**, or combination therapy with aspirin and clopidogrel** (Grade 1B)

- **Oral anticoagulation with dabigatran 150 mg bid over adjusted-dose VKA therapy (target range, 2.0-3.0)** (Grade 2B)

CHEST. 2012;141(2_suppl):1S-1S. doi: 10.1378/chest.1412S1

Reversal of Treatments

- ***Warfarin***
  - Vitamin K
  - Fresh frozen plasma
  - Protein complex concentrates

- ***Dabigatran – Direct Thrombin Inhibitor***
  - No antidote
  - Hemodialysis

- ***Rivaroxaban/Apixiban – Direct Factor Xa Inhibitor***
  - Hemostatics PCC, rFVIIa may be considered but not been evaluated
  - NOT dialyzable

BWH Policy

- **Vitamin K antagonists (i.e. warfarin)**
  - **Administer:**
    - *4-Factor Prothombin Complex* Concentrate (4PCC)
      - Dose based on actual body weight and most recent INR
      - Kcentra
      - Vitamin K 10mg IV x1

BWH Policy: Oral Factor Xa Inhibitors (i.e. rivaroxaban, apixaban)

- **Check PT and Anti-Xa (Heparin/LMWH) STAT, if elevated administer below products**

- **Administer:**
  - If last dose within last 3 hours, give activated charcoal 50 gm PO x1
  - 4PCC 50 units/kg IV x1
    - Dose based on actual body weight
  - If patients with worsening symptoms or radiological expansion, a second dose of 4PCC 50 units/kg or recombinant Factor VII activated 90 mcg/kg IV x1

BWH Policy:Oral Direct Thrombin Inhibitors

- **Check Thrombin Time (TT) and PTT STAT, if elevated administer below products**
- **Administer:**
  - If last dose within last 3 hours, give activated charcoal 50 gm PO x1
  - ***FEIBA*** 25 units/kg IV x1
    - Dose based on actual body weight
  - If patients with worsening symptoms or radiological expansion, a second dose of FEIBA 25 units/kg or recombinant Factor VII activated 90 mcg/kg IV x1

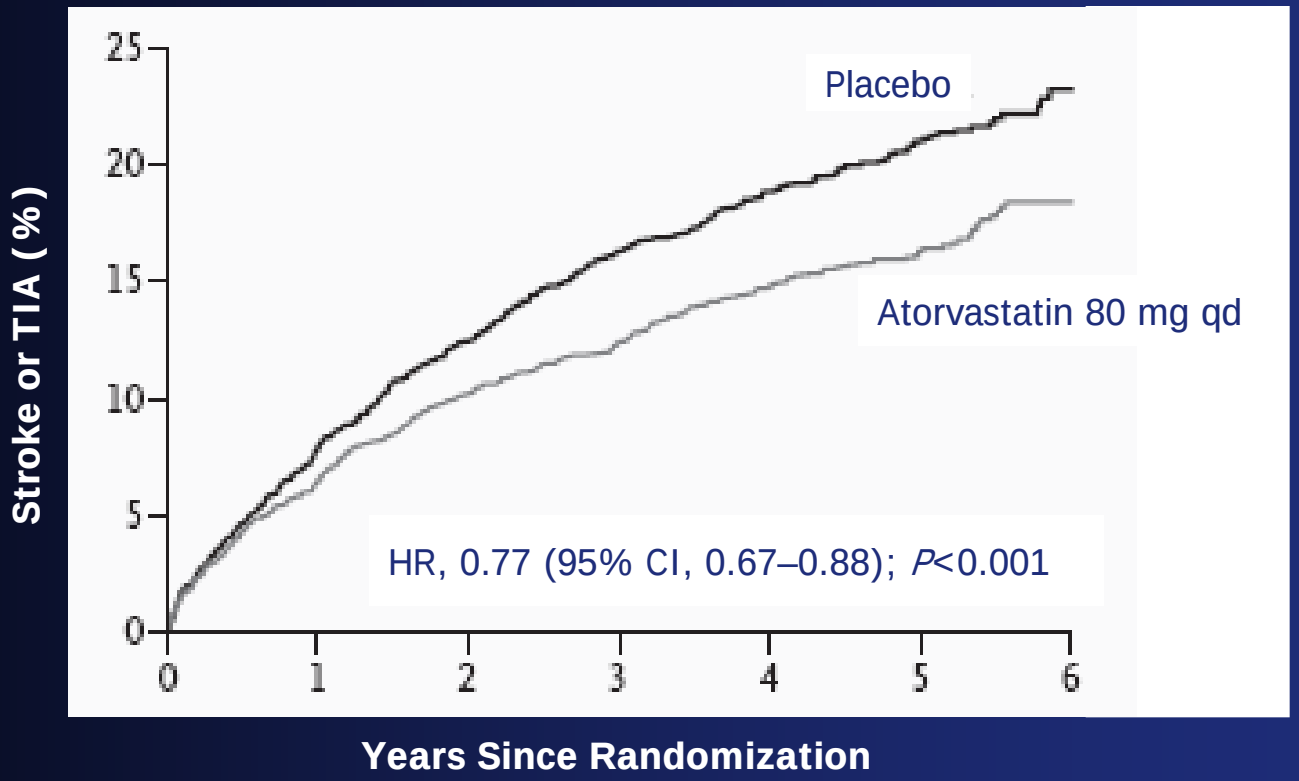
Effect of statins on all strokes, fatal stroke, and hemorrhagic stroke

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)

Amarenco P, Labreuche J. *Lancet Neurol* 2009; 8:453-463.

SPARCL

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.

AHA/ASA Recommendations for Lipid Management

- Ischemic stroke or TIA patients with elevated cholesterol, comorbid coronary artery disease, or evidence of an atherosclerotic origin should be managed according to NCEP III guidelines, which include lifestyle modification, dietary guidelines, and medication recommendations. ***Class I, Level A***

- Statin agents are recommended, and the target goal for cholesterol lowering for those with CHD or symptomatic atherosclerotic disease is an LDL-C level of **100 mg/dL**. An LDL-C **70 mg/dL** is recommended for very high-risk persons with multiple risk factors. ***Class I, Level A***

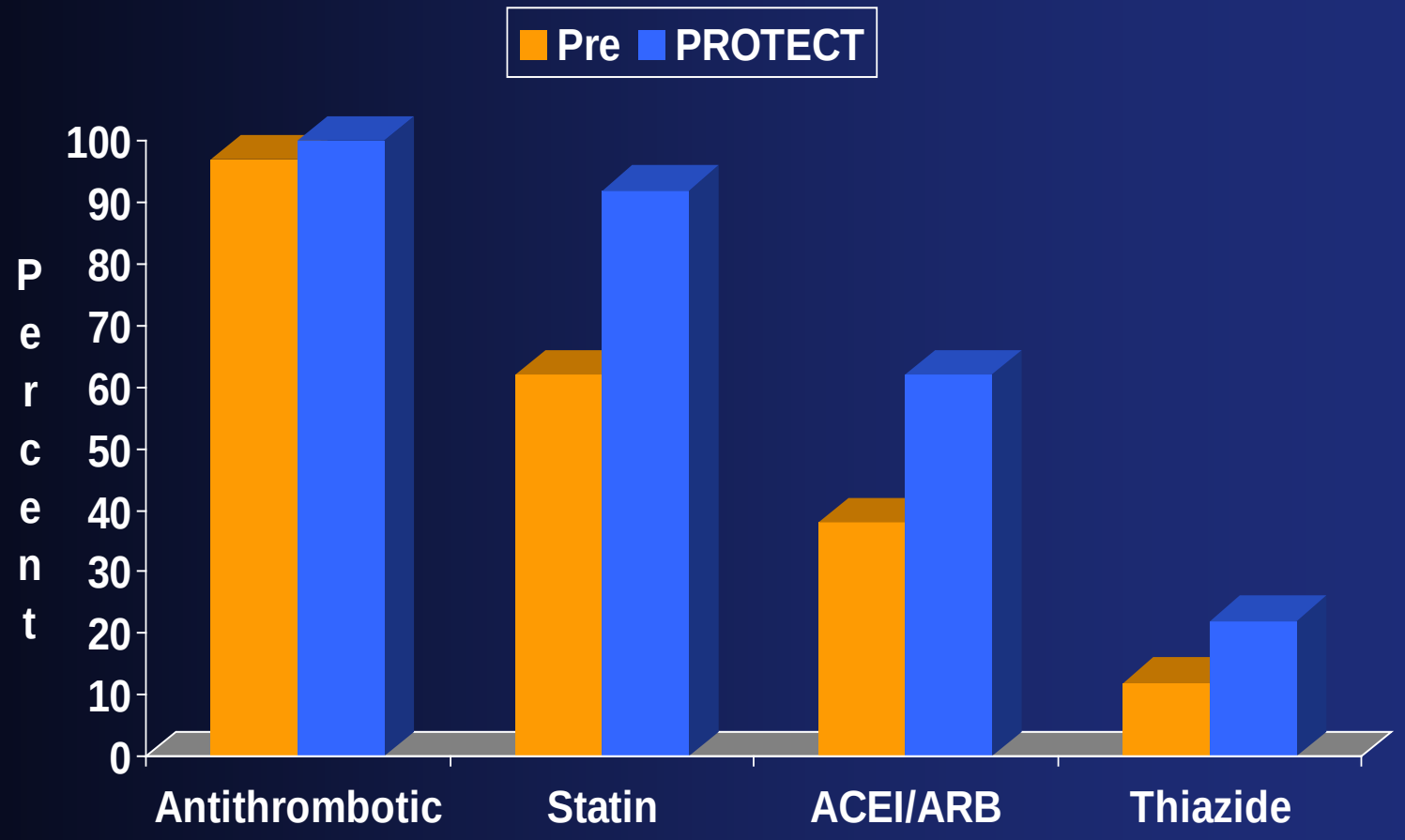
***Stroke*. 2008;39:1-6.**

Brain Attack Coalition

Types of Stroke Care Centers

- ***Primary Stroke Centers***
  - The primary stroke center stabilizes and provides emergency care to acute stroke patients.
  - Primary stroke centers ultimately transfer patients to a comprehensive stroke center or admit patients for further care, based on level of need.
- ***Comprehensive Stroke Center***
  - The comprehensive stroke center provides complete care to patients experiencing the most complex strokes that require specialized testing and other interventions.
  - These centers typically include tertiary care centers or hospitals with appropriate infrastructure.

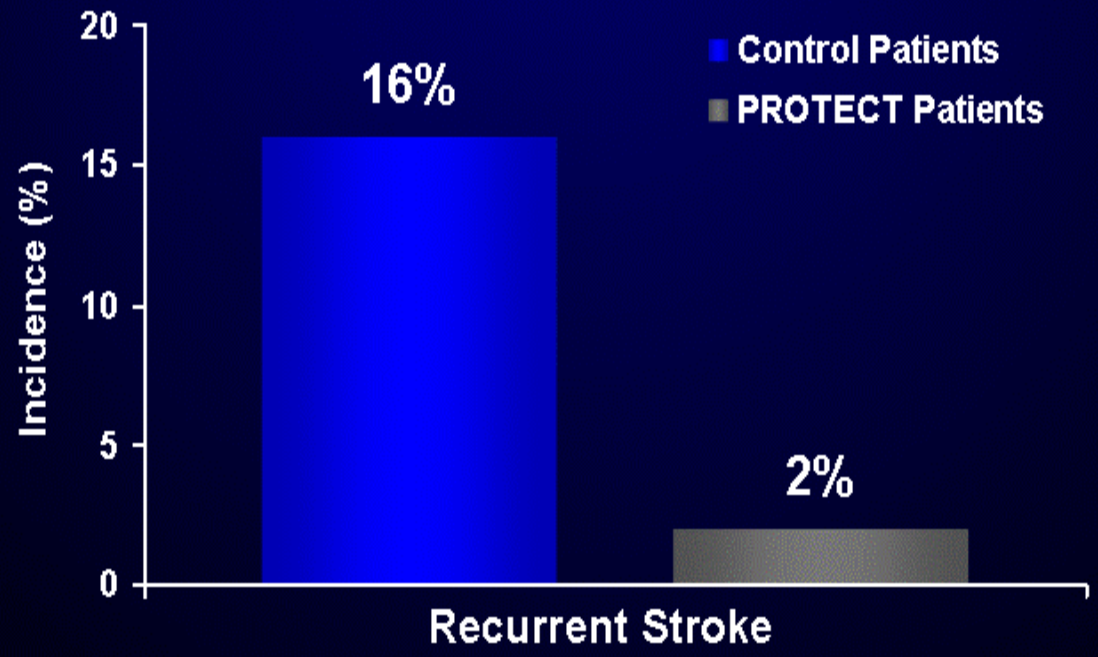
Impact of PROTECT pilot phase on Treatment Rates at Discharge



--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.

Evidence of Better Outcomes in Stroke Centers

- Stroke unit trialists' collaboration meta-analysis
  - OR death: 0.82 (0.69, 0.98)
  - OR death/inst: 0.76 (0.64, 0.90)
  - OR death/dep: 0.71 (0.61, 0.84)
- In-hospital death less frequent in facilities with vascular neurologist; adjusted OR=0.49, $P<0.0001$
- Trend toward fewer deaths in facilities with dedicated stroke team available by pager
- JCAHO credentialing of stroke centers ensures that patients receive proper care
  - www.jointcommission.org/

Indredavik B, et al. *Stroke*. 1999;30:917-923.
Indredavik B, et al. *Stroke*. 1997;28:1861-1866.
Indredavik B, et al. *Stroke*. 2000;31:2989-2994.
Goldstein LB, et al. *Neurology.* 2003;61:792-796.
Alberts MJ, et al. *JAMA.* 2000;283:3102-3109.
Gillum LA, et al. *Stroke*. 2001;32:2137-2142.

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 O_2
- 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
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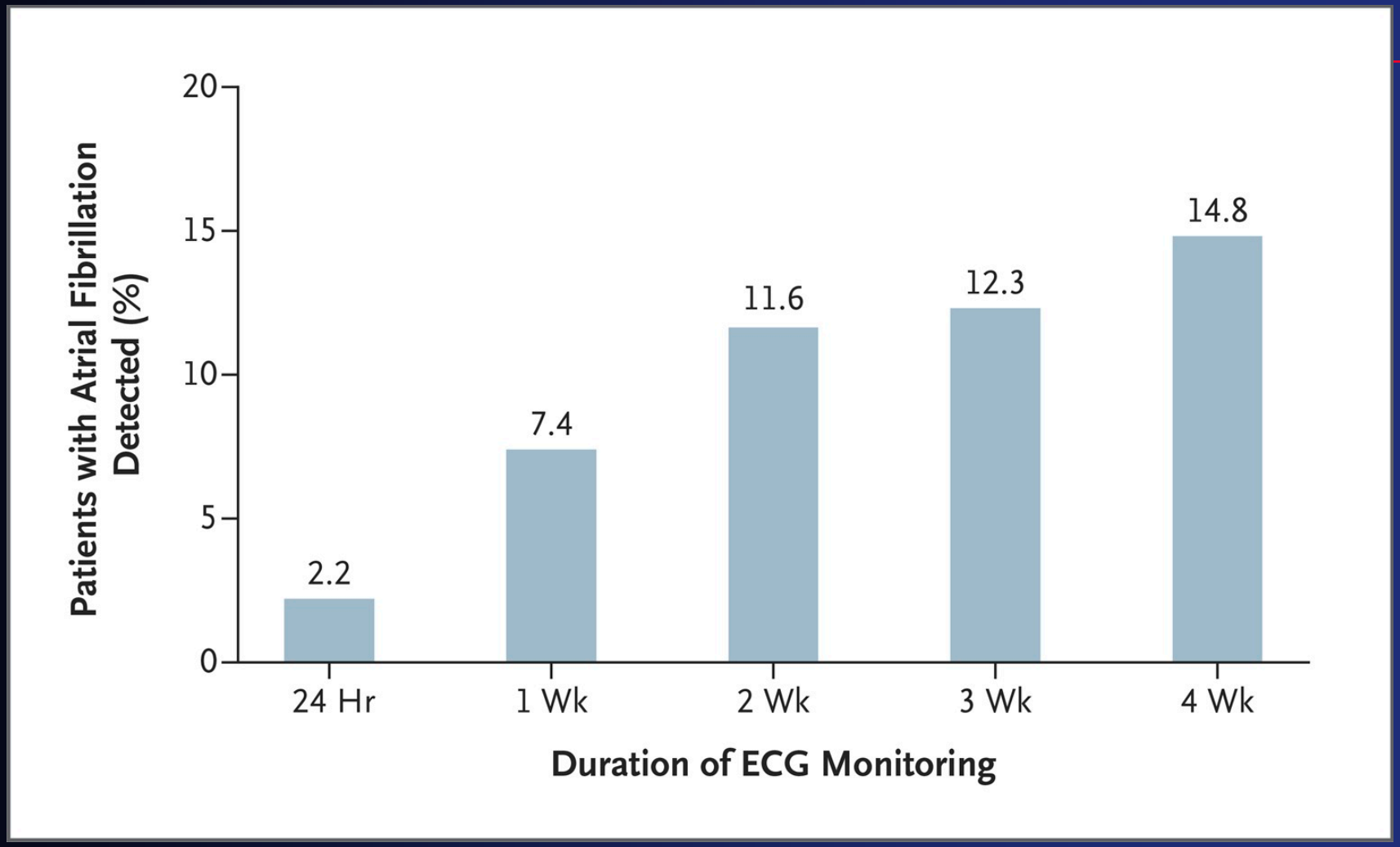
Study Overview

- 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%).

The NEW ENGLAND JOURNAL of MEDICINE

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.

The NEW ENGLAND JOURNAL of MEDICINE

Discharged with:

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

Controversial or Investigational Secondary-Prevention Strategies

Table 2. Controversial or Investigational Secondary-Prevention Strategies.*

Target	Possible Strategy	Comments
Early recurrent stroke	Combined aspirin and clopidogrel for 90 days from stroke onset	Increased risk with combination therapy vs. aspirin or clopidogrel alone, but meta-analysis suggests possible benefit of combination therapy after a TIA or minor stroke[35]; POINT (NCT00991029): combination therapy vs. aspirin, ongoing
Carotid stenosis	Carotid-artery stenting	Higher risks of periprocedural stroke and death with stenting than with endarterectomy,[36-39] although risks similar with the two treatments among patients 70 years of age or younger[40]
Aortic-arch atheroma	Antiplatelet therapy vs. anticoagulation	Common cause of stroke; most effective treatment unknown; ARCH (NCT00235248)[41]: aspirin plus clopidogrel vs. warfarin, ongoing
Intracranial arterial stenosis	Intracranial stenting	Higher rates of stroke and death with intracranial stenting than with aggressive medical therapy in one trial (SAMMPRIS),[42] but other trials ongoing
Carotid dissection	Antiplatelet therapy vs. anticoagulation	Optimal treatment unclear; CADISS (NCT00238667): aspirin vs. warfarin, ongoing
Patent foramen ovale	Percutaneous closure device vs. medical therapy	No benefit observed with percutaneous closure in CLOSURE I[43]; other trials ongoing

* ARCH denotes Aortic Arch Related Cerebral Hazard, CADISS Cervical Artery Dissection in Stroke Study, CLOSURE I Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale, POINT Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke, and SAMMPRIS Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis.

Davis SM, Donnan GA. N Engl J Med 2012;366:1914-1922

Stroke Risk Factors Unique to Women in Review

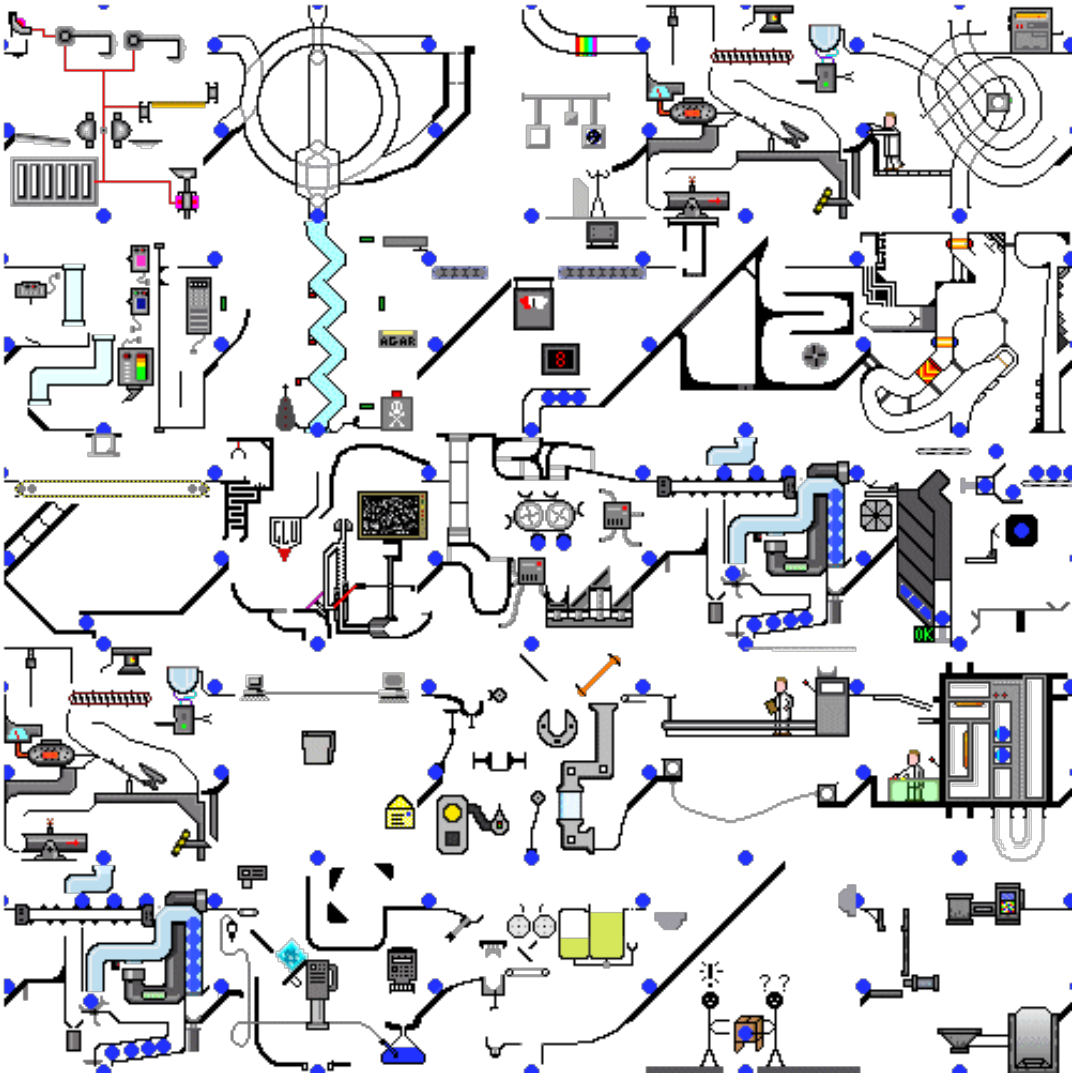
- Pregnancy factors
  - Pre-clampsia
- Hormonal exposure
  - Oral contraceptives, postmenopausal hormone therapy
- Changes in hormone status across the lifespan
- Menarche, menopause an oophorectomy
- Depression
- Atrial fibrillation in the elderly

Summary

- Review epidemiology
- Review polyvascular disease
- Discuss new definitions of TIA
- Review medical interventions
  - Thrombolysis
  - Antihypertensives
  - Statin therapy
  - Anticoagulants
  - Antiplatelet therapy
- Review barriers to improve outcomes
- Discuss promotion of stroke centers
- Review stroke workup

I have no conflicts of interest

Thank you for your Attention



Question 1

Mr. Jones has 3 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 A.**
- **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 2 hours with a neg. CT

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

Answer to Question 3

- **The answer is C.**
- **In giving IV TPA within 3 hours, there is no age cutoff.**
- **ASA or Clopedigril 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. Aspririn
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 and to evaluate ejection fraction.
- EKG and Holter to r/o Afib.
- We always need brain imaging and neurovascular imaging