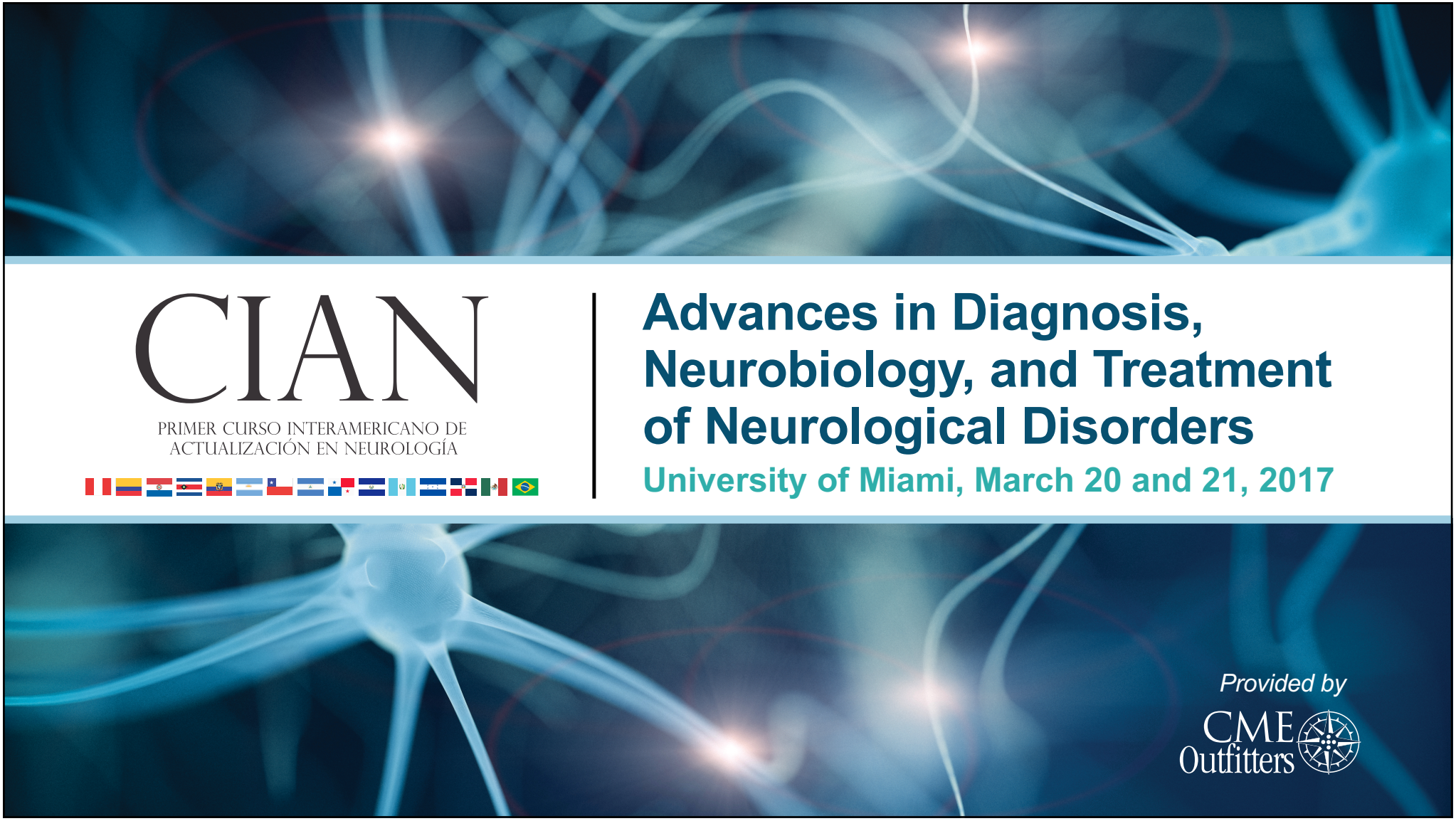


CIAN

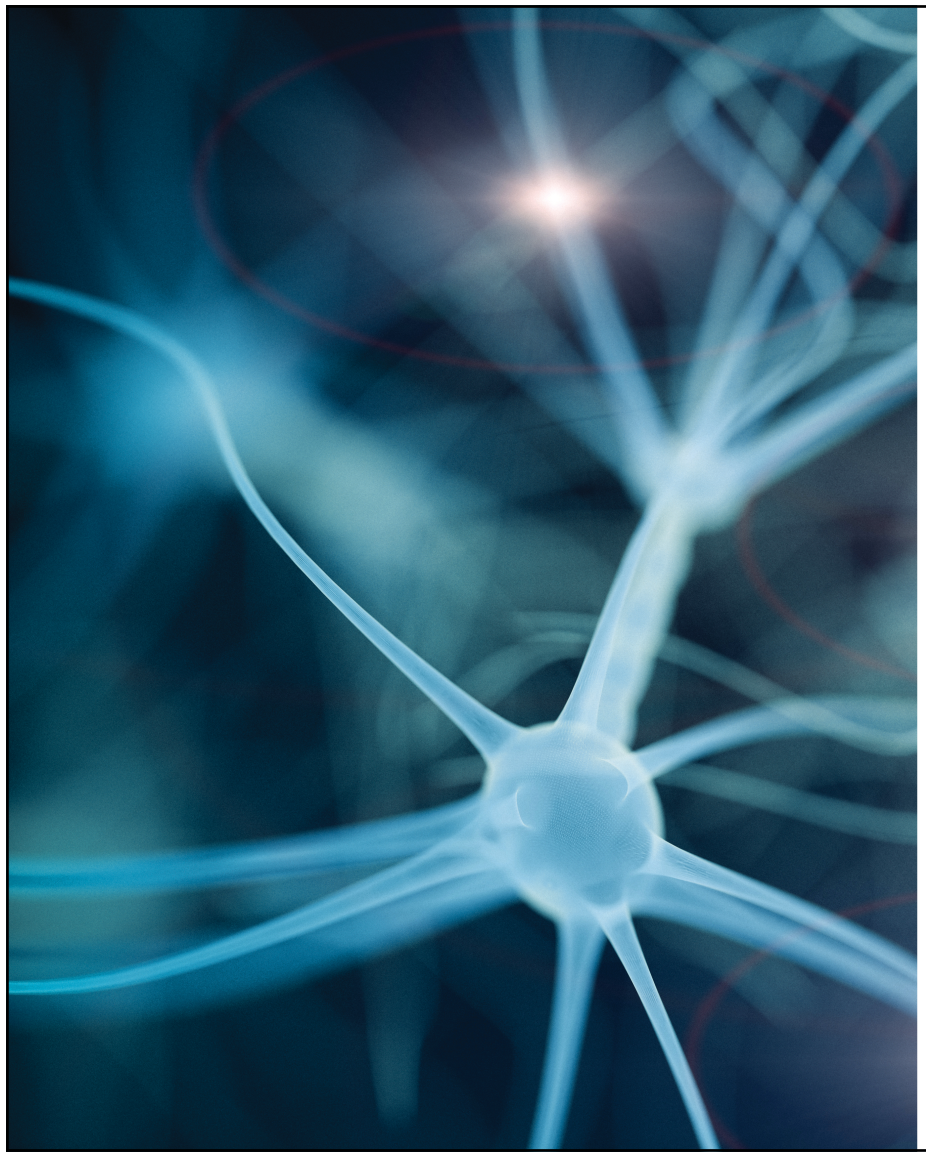
PRIMER CURSO INTERAMERICANO DE ACTUALIZACIÓN EN NEUROLOGÍA

Advances in Diagnosis, Neurobiology, and Treatment of Neurological Disorders

University of Miami, March 20 and 21, 2017

Provided by

CME Outfitters



Ralph L. Sacco, MD, MS, FAHA, FAAN

Clinical and Translational Science Institute
University of Miami
Miller School of Medicine
Miami, FL

Ralph L. Sacco, MS, MD, FAAN, FAHA

Disclosures

- ***Research/Grants***: Boehringer Ingelheim

Stroke: Clinical Update and Best Practices for Improved Outcomes

Learning Objective 1

Discuss primary prevention and lifestyle modification with all patients at risk for stroke.

Learning Objective 2

Integrate all medical therapy options into your care of patients with stroke.

Stroke

- Stroke Facts, Burden, and Outlook
- Subtypes and Diagnostic Evaluations
- Primary Stroke Prevention
  - Promoting Ideal Cardiovascular Health
- Secondary Prevention
  - Carotid Interventions
  - Oral Anticoagulants: Warfarin and NOACs
  - Anti-platelets
- Global NCD Approaches

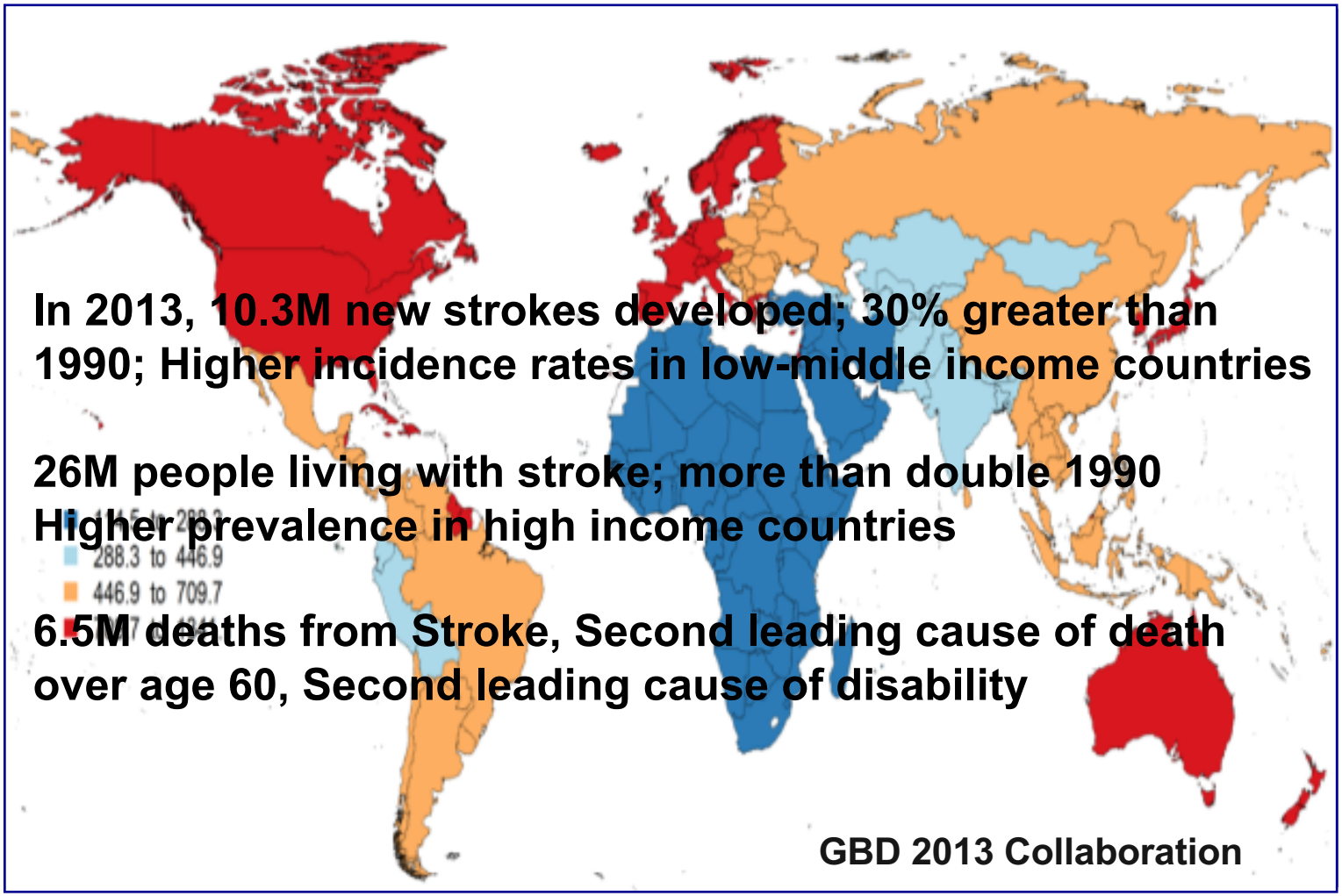
Global Vascular Risk Burden

VASCULAR DISEASE
STROKE, MI, PAD, VASCULAR DEATH

2002: 16.7 MILLION DEATHS
2005: 17.4 MILLION DEATHS
2010: 18.1 MILLION DEATHS

5.9M deaths from Stroke
Second leading cause of death over age 60
Second leading cause of disability after dementia

Worldwide Stroke Burden



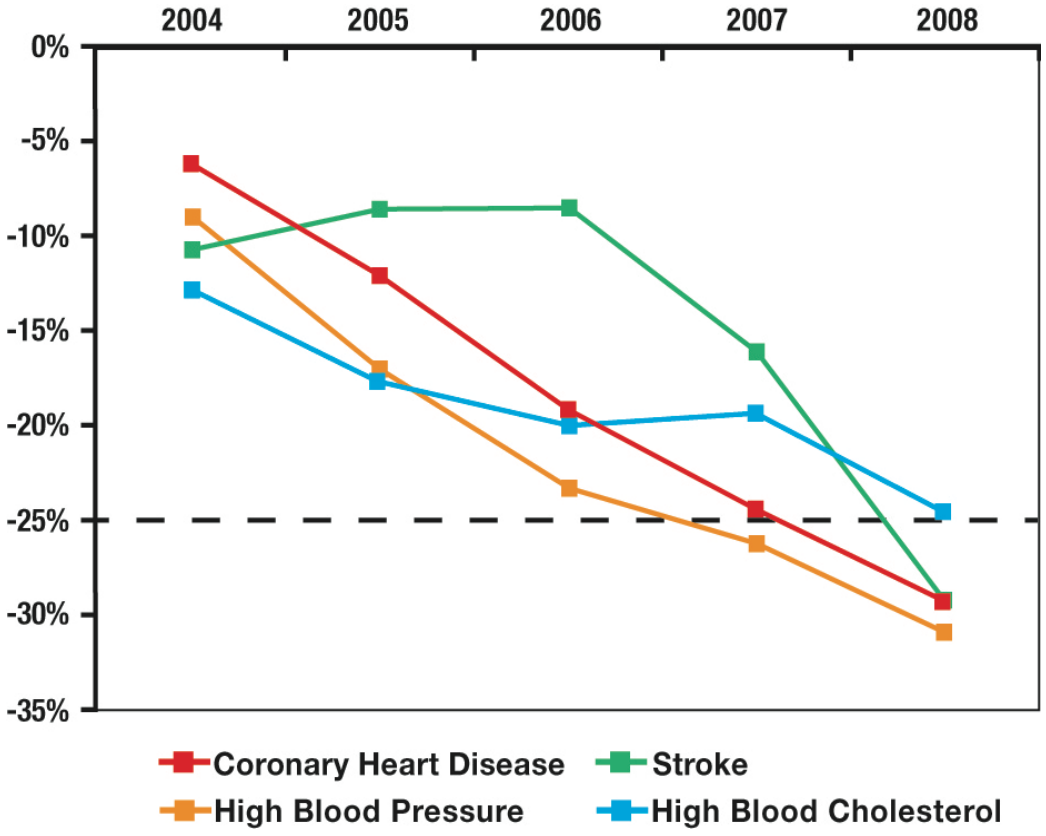
In 2013, 10.3M new strokes developed; 30% greater than 1990; Higher incidence rates in low-middle income countries

26M people living with stroke; more than double 1990 Higher prevalence in high income countries

6.5M deaths from Stroke, Second leading cause of death over age 60, Second leading cause of disability

GBD 2013 Collaboration

Declining US Stroke Mortality



Stroke -32.5%
CHD -35.7%

HTN -27.7%
CHOL -22.1%

STROKE DROPPED TO 5th LEADING CAUSE OF DEATH

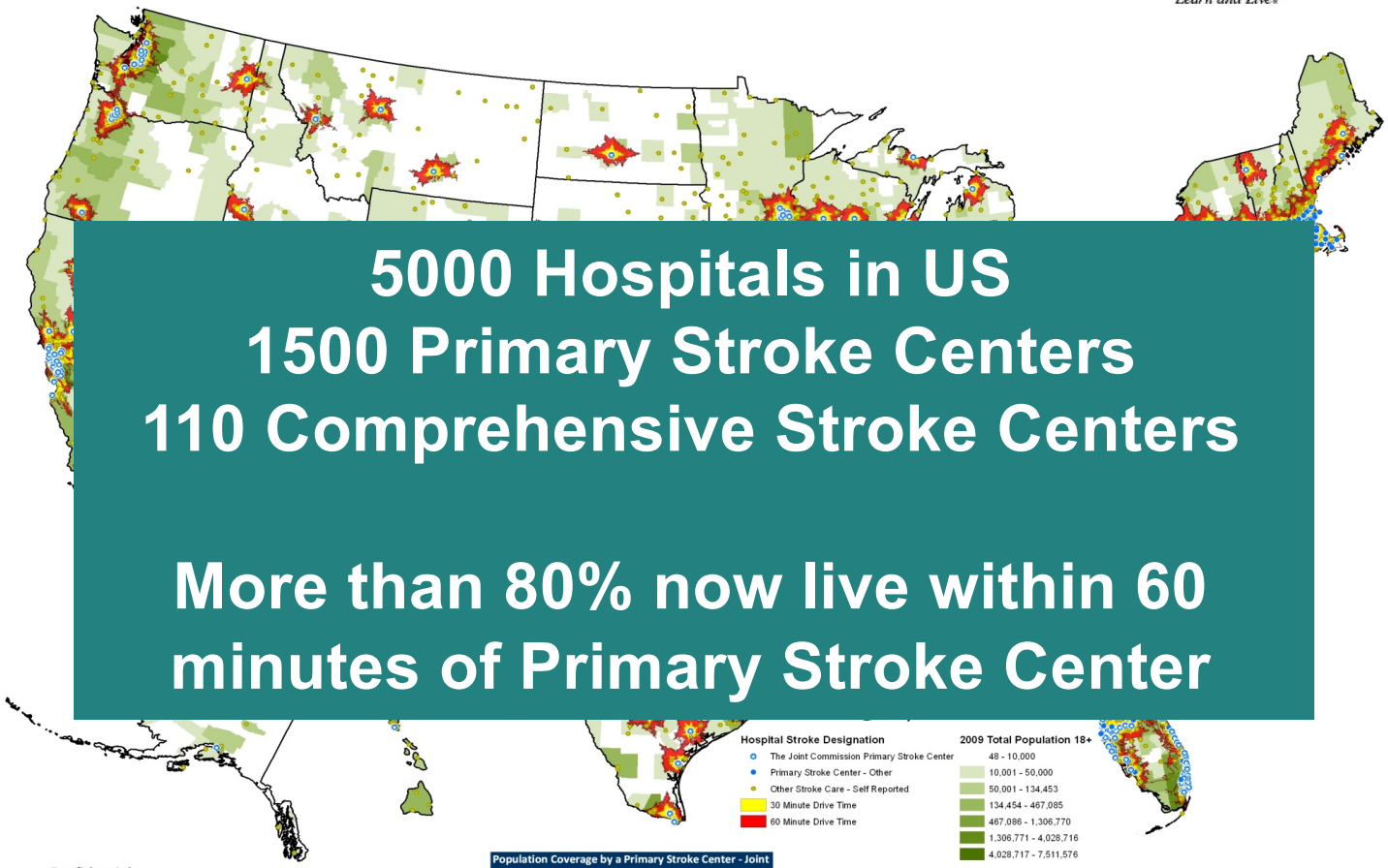
www.cdc.gov

Stroke Systems of Care - Hospitals

USA: Total Population 18+ by County

30 & 60 Minute Drive Times from Primary Stroke Centers

American Heart Association. | American Stroke Association.
Learn and Live.



5000 Hospitals in US
1500 Primary Stroke Centers
110 Comprehensive Stroke Centers

More than 80% now live within 60 minutes of Primary Stroke Center

Population Coverage by a Primary Stroke Center - Joint Commission and Others		
Drive Time	Population	Percentage
30 Min	215,876,490	69.7%
60 min	258,695,506	83.5%

Population Data Source: ESRI 2009

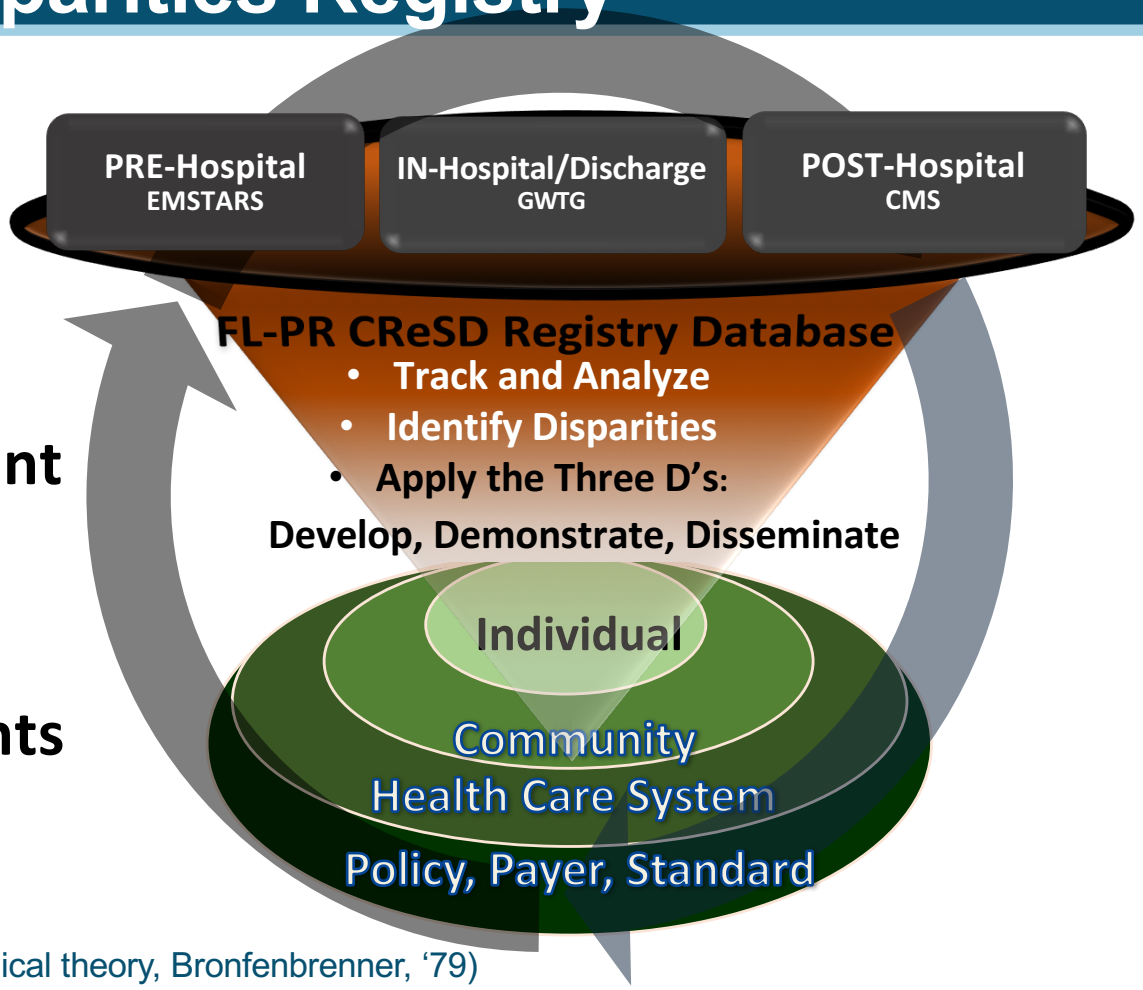
Joint Commission Primary Stroke Centers & State Designated Stroke Centers as publicly reported on 6/13/10

Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Registry

Data

Quality Improvement Program

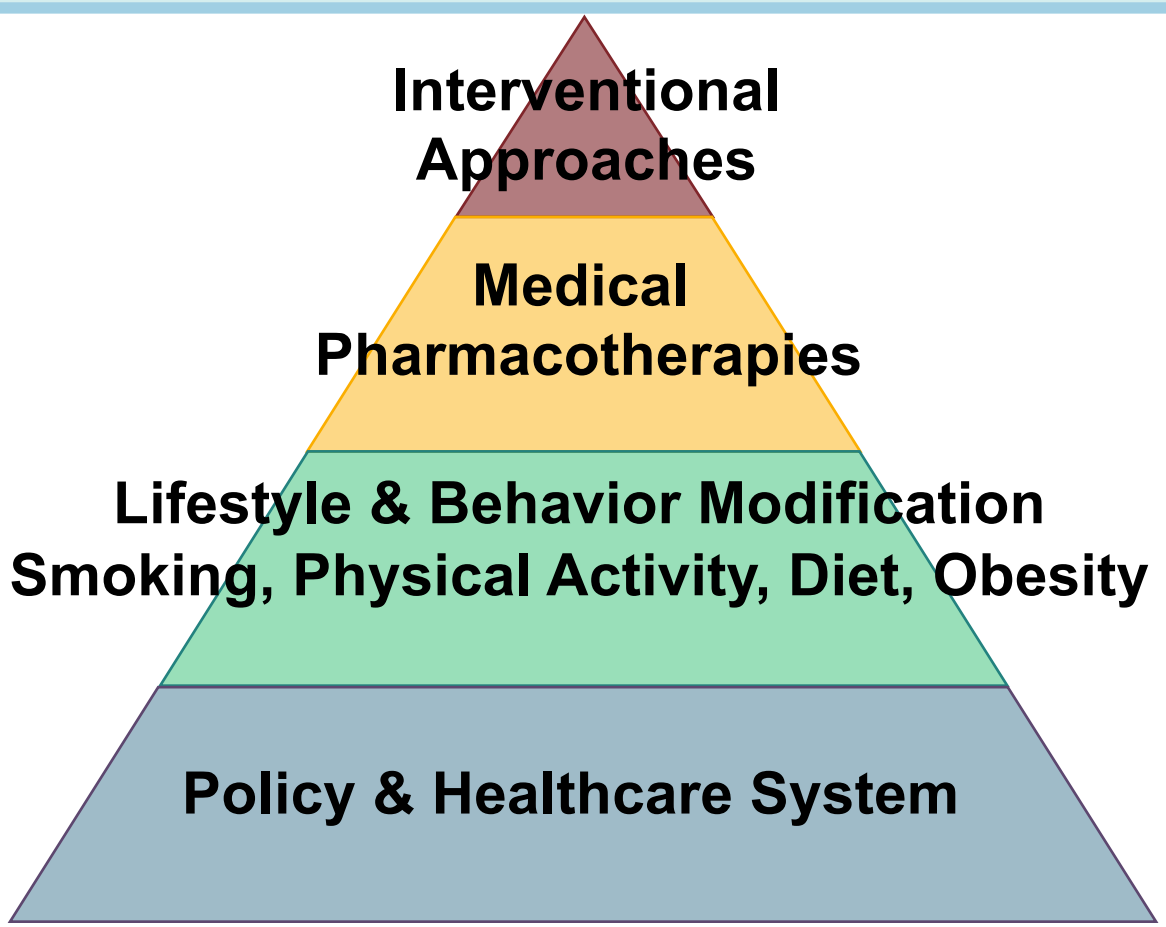
Multilevel Determinants of Health



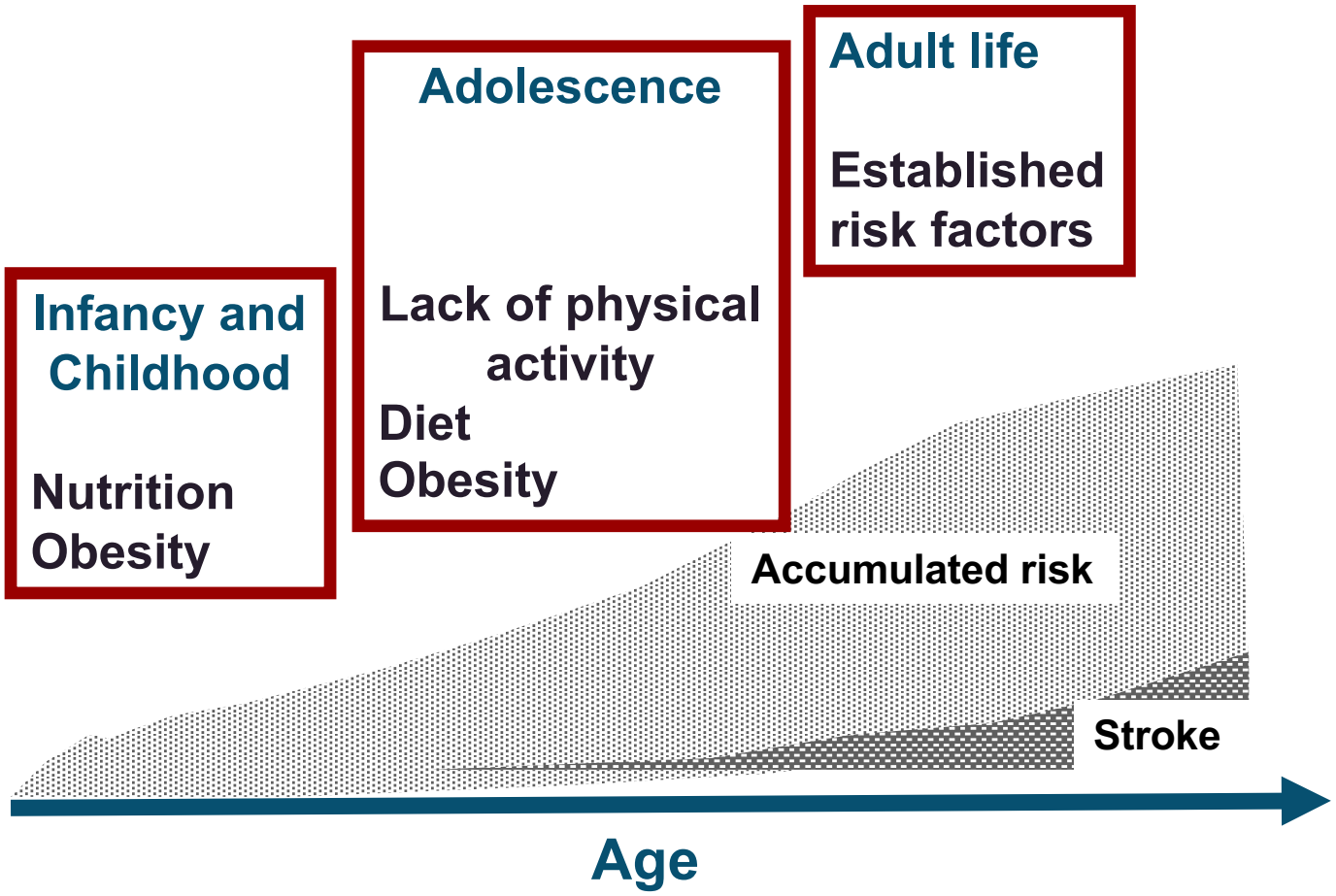
NINDS U54 NS-081763

(Derived from socio-ecological theory, Bronfenbrenner, '79)

Stroke Prevention 2017



Stroke Prevention A Life Course Approach



Risk Factors for Stroke

Northern Manhattan Study

Alcohol, Physical Activity, Obesity, Homocysteine

Diet: Mediterranean Pattern, Salt, Fat, Diet Soda

HDL, LDL, Lp(a), Metabolic Syndrome, HOMA Index, GFR

Social Factors: Isolation, SES, Depression

Cardiac

- Patent Foramen Ovale
- Aortic Arch Atheroma
- Left Ventricular Hypertrophy
- Left Ventricular Mass
- Left Atrial Size

Inflammation & Infection

- Chlamydia Pneumoniae
- Periodontal Disease
- White Blood Cell Count
- TNF alpha Receptor levels
- CRP, Cytokines

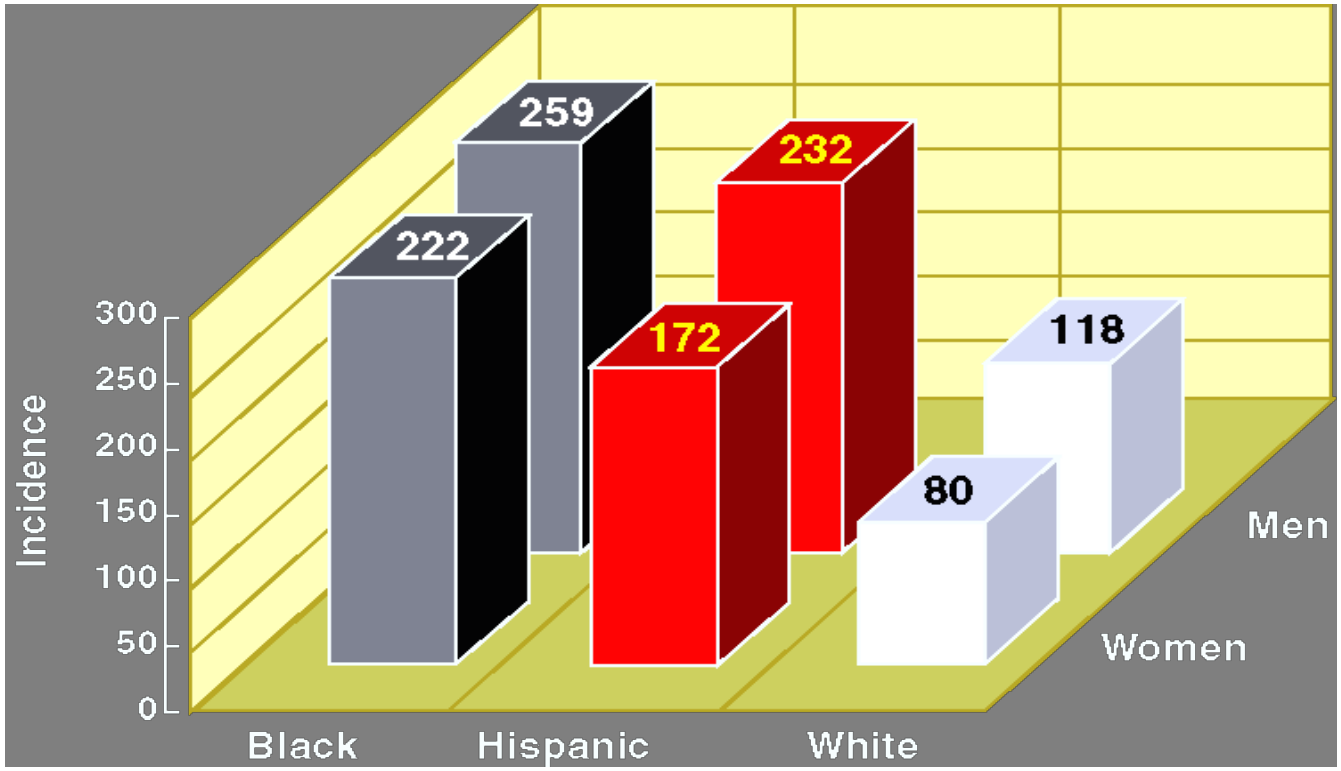
http://columbianomas.org/publications.html

Classification of Cardiovascular Health

Life's Simple 7

	Ideal	Intermediate	Poor
Smoking	Never or quit > 1 year	Quit < 1 year	Current
BMI	< 25 kg/m^2	25 - <30 kg/m^2	≥ 30 kg/m^2
Physical activity	≥ 75 min/wk vigorous or ≥ 150 min/wk moderate or equivalent combination	1-74 min/wk vigorous or 1-149 min/wk moderate or equivalent combination	No moderate or vigorous activity
Diet	4-5 healthy components	2-3 healthy components	0-1 healthy components
Blood pressure	Untreated & SBP < 120 & DBP < 80 mmHg	Treated to <120/<80 or 120-139/80-89 mmHg	SBP ≥ 140 mmHg or DBP ≥ 90 mmHg
Fasting glucose	Untreated & < 100 mg/dL	Treated to <100 mg/dL or 100-125 mg/dL	>125mg/dL
Total cholesterol	Untreated & < 200 mg/dL	Treated to < 200 mg/dL or 200-239 mg/dL	≥ 240 mg/dL

Annual Stroke Incidence
Northern Manhattan Stroke Study



Age-adjusted stroke incidence for white, black, and Hispanic northern Manhattan residents over age 20

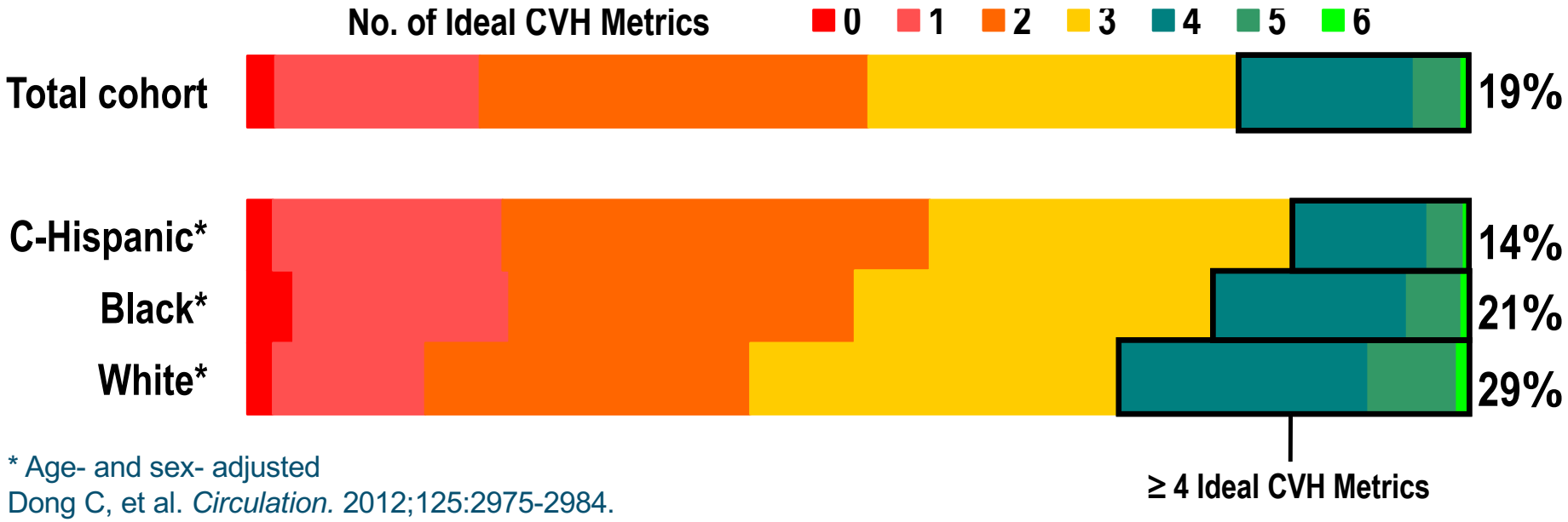
Sacco RL, et al. *Am J Epidemiol* 1998;147(3):259-268.

Cardiovascular Heath at Baseline in NOMAS Total Cohort (n = 2,981, 21% white, 25% black, 54% Hispanics)

Ideal Cardiovascular Health Predicts Lower Risks of Myocardial Infarction, Stroke, and Vascular Death Across Whites, Blacks, and Hispanics

The Northern Manhattan Study

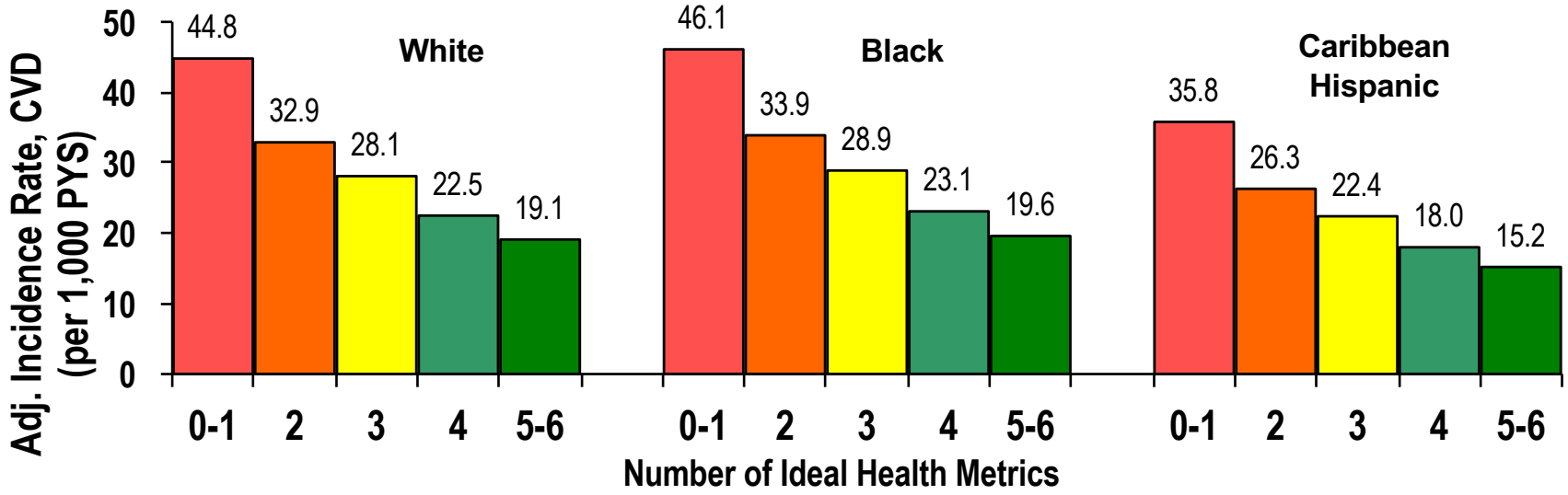
Chuanhui Dong, PhD; Tatjana Rundek, MD, PhD; Clinton B. Wright, MD, MS; Zane Anwar; Mitchell S.V. Elkind, MD, MS; Ralph L. Sacco, MD, MS

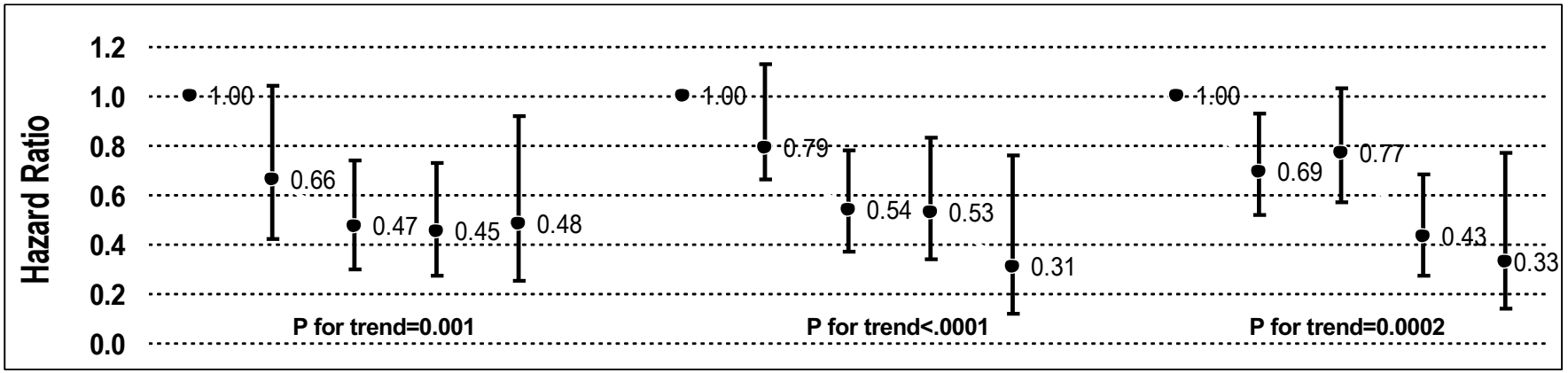


* Age- and sex- adjusted

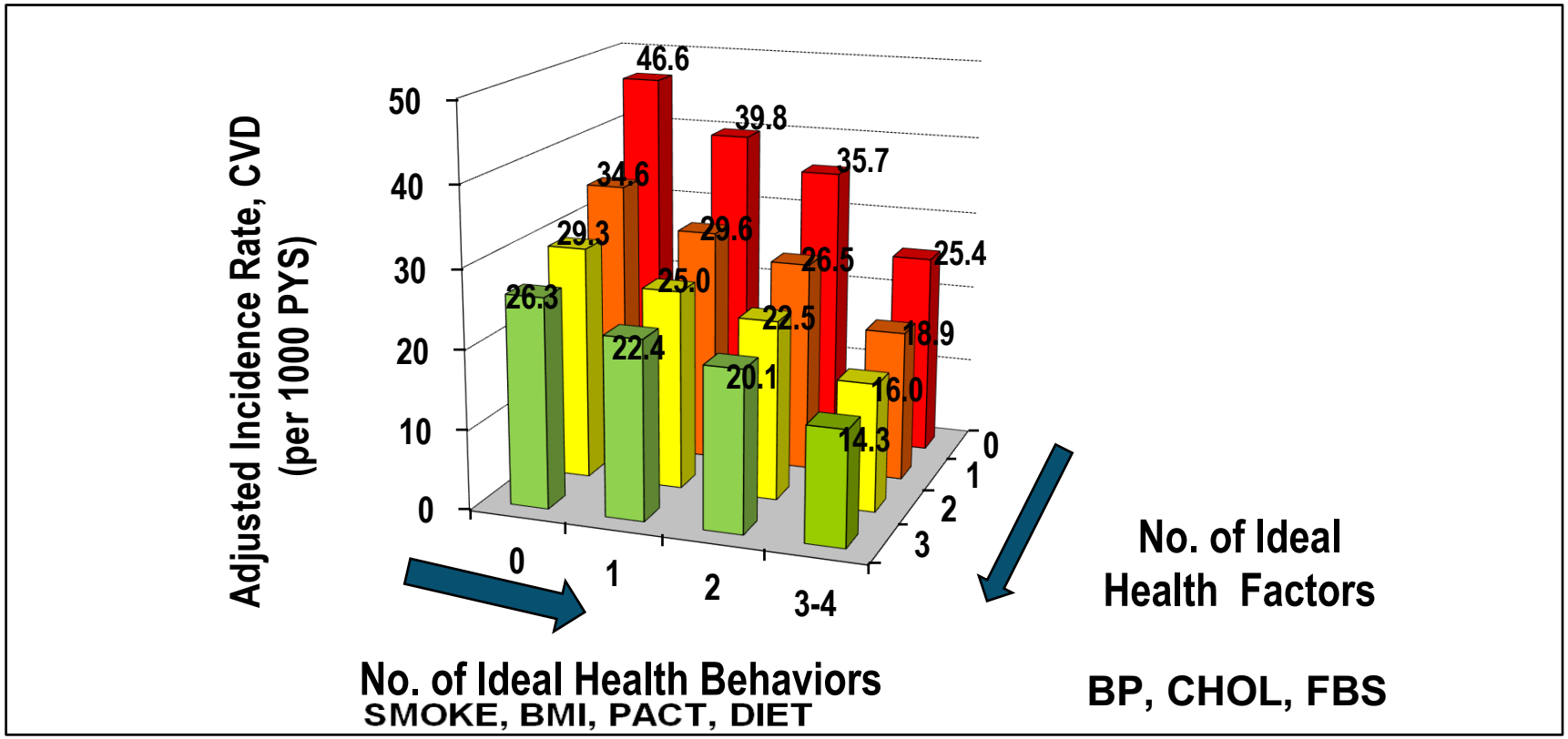
Dong C, et al. *Circulation.* 2012;125:2975-2984.

Ideal CVH and Risk of MI, Stroke, or Vascular Death by Race-Ethnicity in NOMAS Cohort





Numbers of Ideal Health Factors and Behaviors and Incidence of MI, Stroke or Vascular Death in NOMAS



Dong C, et al. *Circulation*. 2012;125:2975-2978.

AHA/ASA Guidelines

Guidelines for the Primary Prevention of Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

James F. Meschia, Cheryl Bushnell, Bernadette Boden-Albala, Lynne T. Braun, Dawn M. Bravata, Seemant Chaturvedi, Mark A. Creager, Robert H. Eckel, Mitchell S.V. Elkind, Myriam Fornage, Larry B. Goldstein, Steven M. Greenberg, Susanna E. Horvath, Costantino Iadecola, Edward C. Jauch, Wesley S. Moore and John A. Wilson

Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

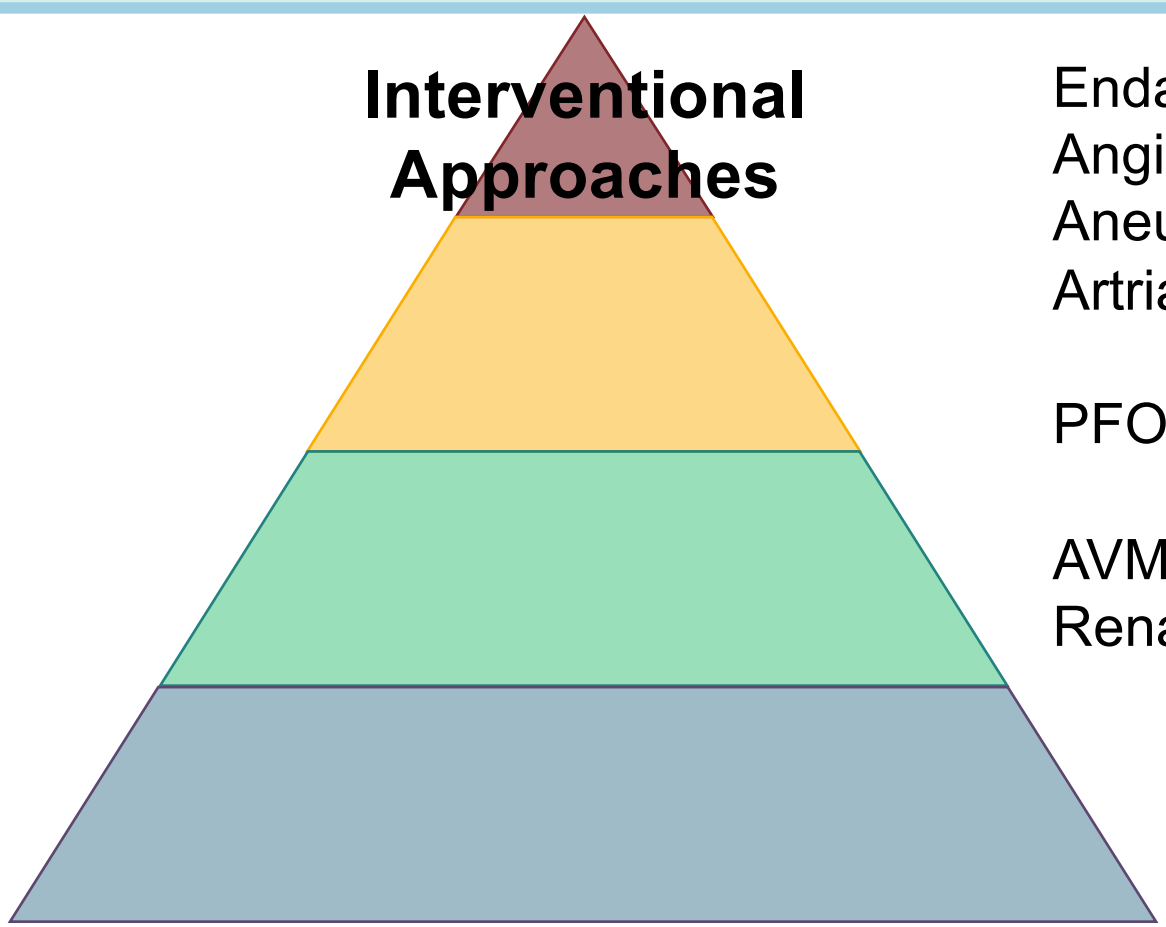
Walter N. Kernan, Bruce Ovbiagele, Henry R. Black, Dawn M. Bravata, Marc I. Chimowitz, Michael D. Ezekowitz, Margaret C. Fang, Marc Fisher, Karen L. Furie, Donald V. Heck, S. Claiborne (Clay) Johnston, Scott E. Kasner, Steven J. Kittner, Pamela H. Mitchell, Michael W. Rich, DeJuran Richardson, Lee H. Schwamm and John A. Wilson

Meschia J, et al. *Stroke*. 2014;45:3754-832.
Kernan W, et al. *Stroke*. 2014;45:2160-236.

Get With The Guidelines -Stroke

- 7 Predefined Performance Measures
  1. IV t-PA 2 Hour
  2. Early Antithrombotics (2 days)
  3. VTE Prophylaxis
  4. Antithrombotics at discharge
  5. Anticoagulation for AF at discharge
  6. LDL < 100 or ND-Statin
  7. Smoking Cessation Counseling
- & Defect-Free Care Measure

Stroke Prevention 2017



Endarterectomy
Angioplasty
Aneurysm Coiling
Artrial Appendage Occulders
PFO Closure Devices
AVM Embolization
Renal Denervation

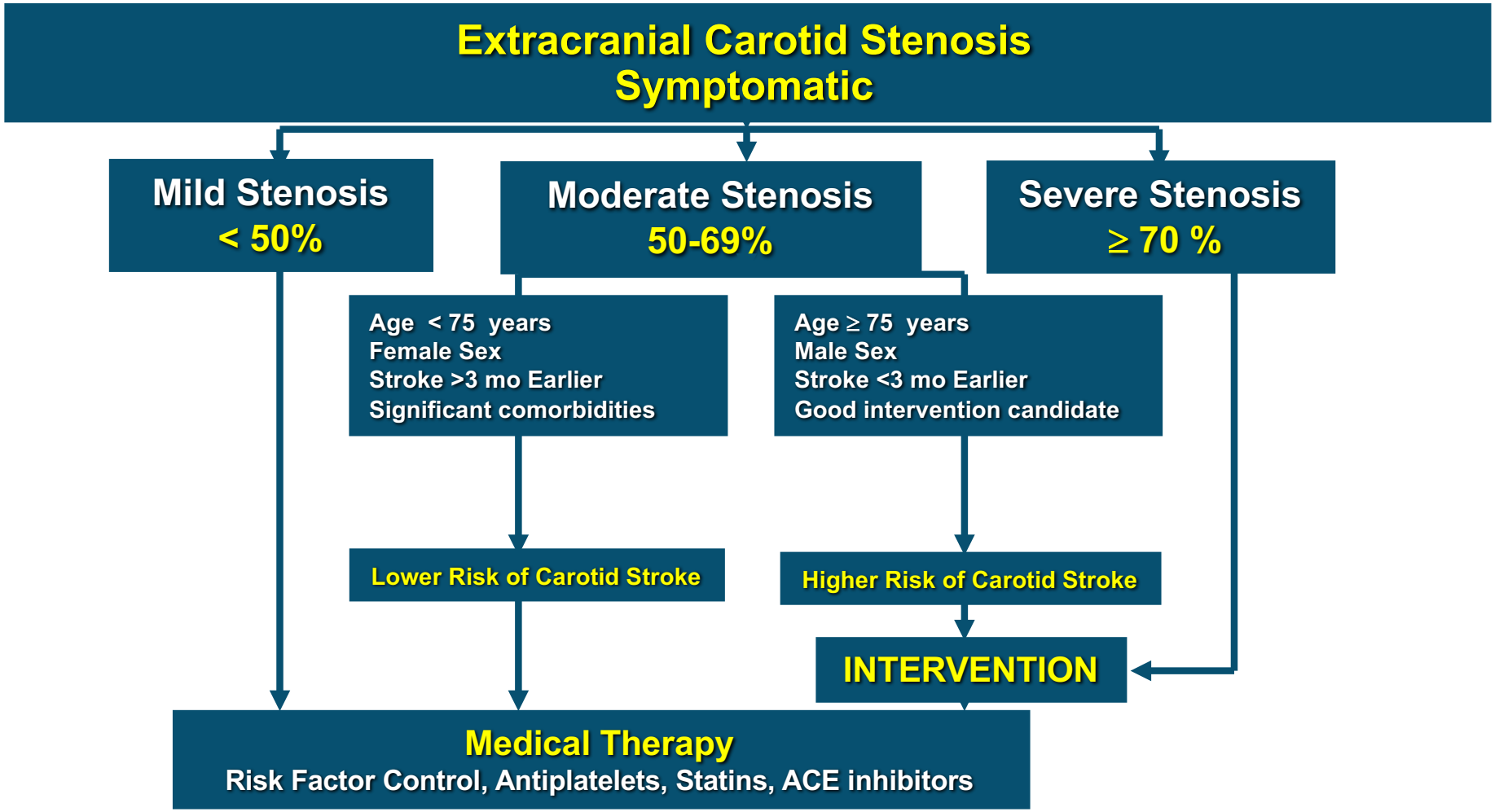
Case

- A 64-year-old woman has sudden, transient loss of vision in her L eye.
- She reports a prior episode of difficulty speaking and mild weakness of the R hand
- PMH: smoking and hypercholesterolemia
- EXAM: Normal except for a L neck bruit
- WORK-UP: CT and MRI negative, L carotid artery stenosis of 80-99% on carotid Doppler confirmed by MRA

MRA = magnetic resonance angiography

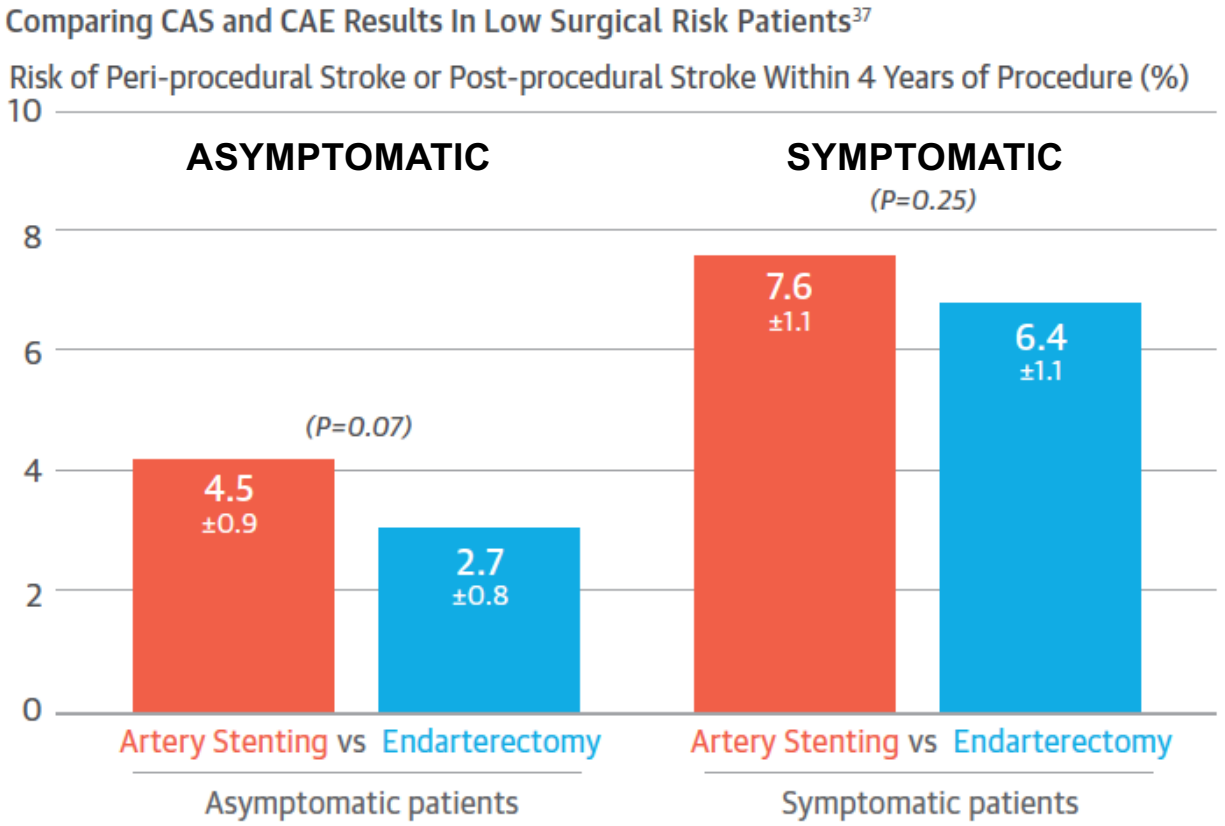
Definition of TIA

- Tissue-based definition of transient ischemic attack (TIA):
  - A transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.



Chaturvedi S, Sacco RL. *J Am Coll Cardiol* 2015;65:1134-43.

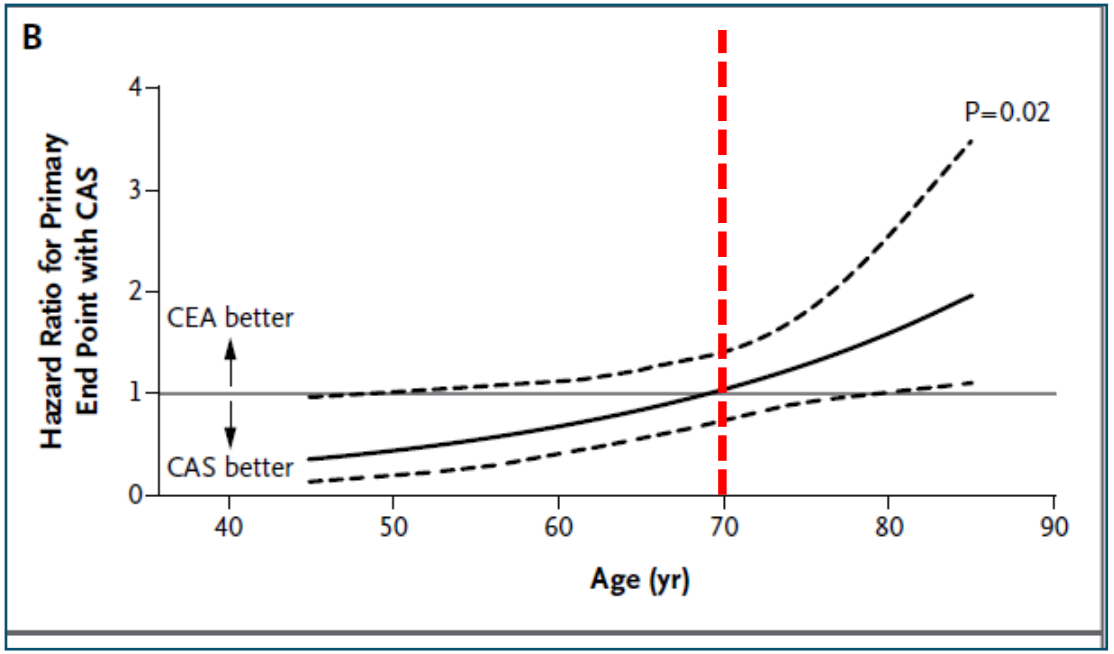
CREST Results
Asymptomatic vs. Symptomatic



White CJ, *J Am Coll Cardiol* 2014;64:722–31. Brott TJ, *NEJM.* 2010; 363:11-23.

NINDS Carotid Revascularization Endarterectomy vs. Stenting Trial

Interaction with Age: < 70: CAS, > 70: CEA



CAS = carotid-artery stenosis, CEA = carotid endarterectomy

Brott TJ, *N Eng J Med*. 2010; 363:11-23.

Discriminant Factors in Choosing Between CEA and CAS

- Favors CEA
  - Age >70 years
  - Recently symptomatic patient (< 2 weeks)
  - Tortuous or heavily calcified aorta
  - Long lesion, heavily calcified lesion
- Favors CAS
  - Contralateral carotid occlusion
  - Recurrent carotid stenosis
  - Presence of significant cardiac disease
  - Presence of significant lung disease

Symptomatic Carotid Disease
ASA 2014 2ndary Stroke Recommendations

- CAS is an alternative to CEA for symptomatic patients at average or low risk of complications with stenosis >70% by noninvasive imaging or >50% by angiography
  - Class IIa, Evidence B
- It is reasonable to consider patient age in choosing between CAS and CEA.
  - Patients > 70 y.o., CEA may be associated with improved outcome compared with CAS
  - Younger patients, CAS is equivalent to CEA
  - Class IIa; Level of Evidence B

Symptomatic Carotid Disease
ASA 2014 2ndary Stroke Recommendations

- Optimal Medical Therapy should include antiplatelet, statin, and risk factor modification recommended for all patients with carotid artery stenosis and a TIA or stroke
  - Class I, Evidence A
- ICAE – aspirin 81-325mg
- CAS – clopidogrel + ASA x 3 months, ASA

http://stroke.ahajournals.org/content/strokeaha/early/2014/04/30/STR.0000000000000024.full.pdf

Intracranial Atherosclerosis SAMMPRIS Trial

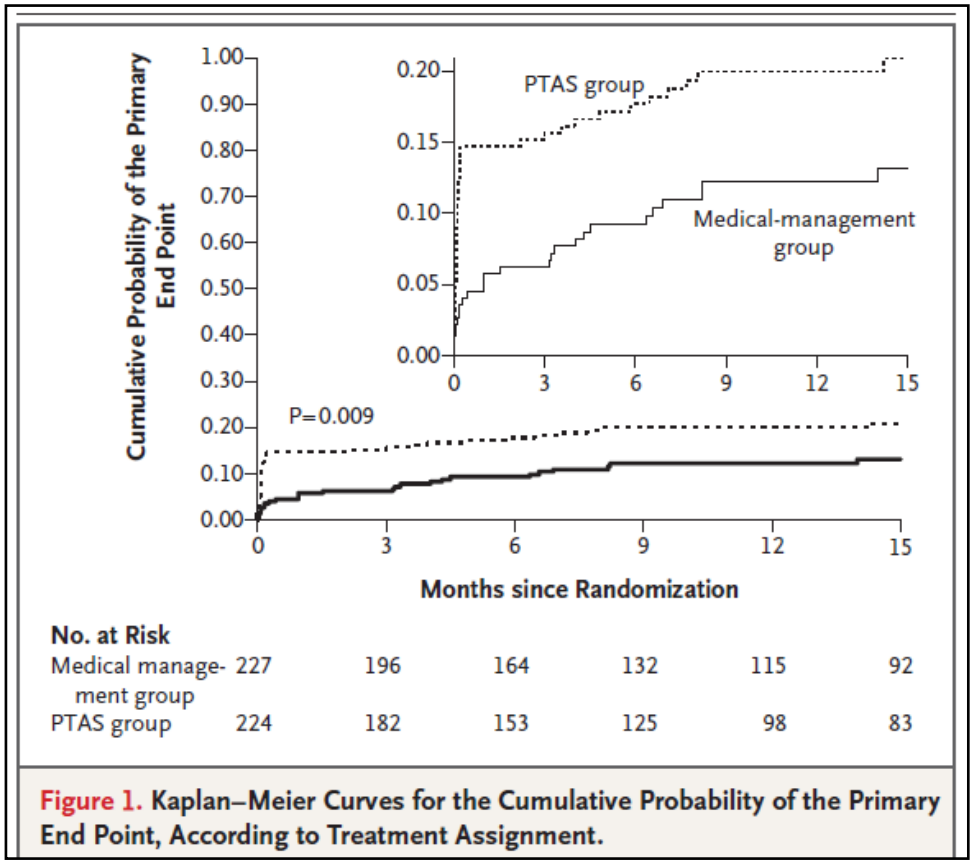


Figure 1. Kaplan–Meier Curves for the Cumulative Probability of the Primary End Point, According to Treatment Assignment.

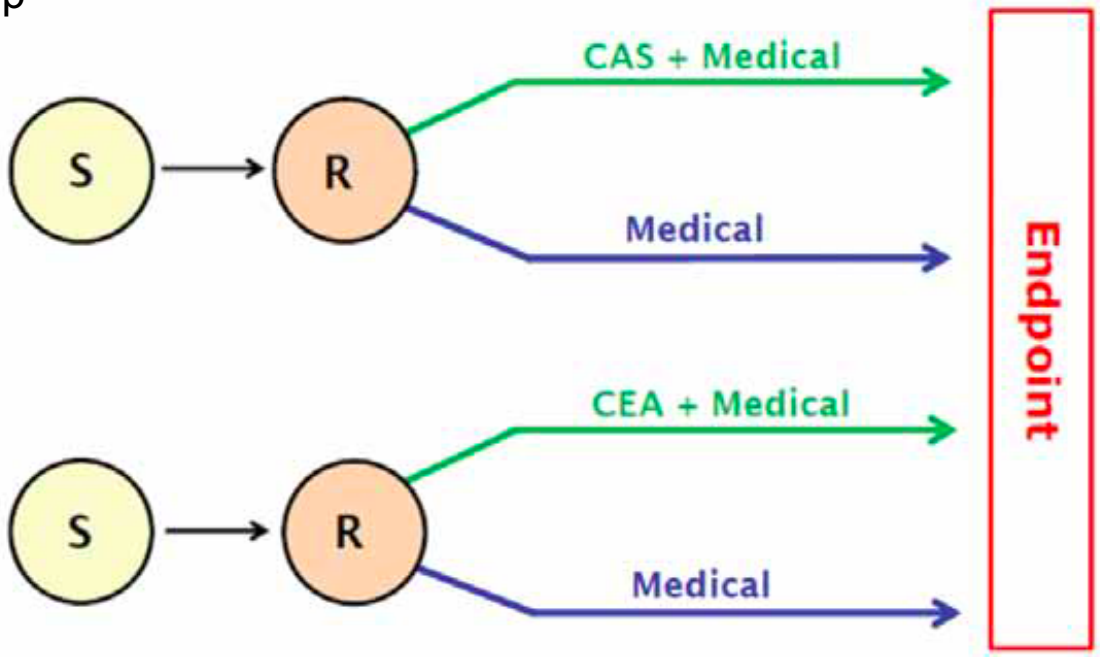
Medical Management:
Aspirin 325mg/day
+ Clopidogrel 75mg/day x 90 days

Chimowitz MI, et al. *N Eng J Med*. 2011;365:993-100.

NINDS - CREST 2

Asymptomatic Carotid Stenosis ≥ 70% by Doppler & one confirmatory study (MRA or CTA)

Primary Endpoint - any periprocedural stroke or death and ipsilateral stroke thereafter, out to 4 years of follow-up



Moore WS, et al. *J Vasc Surg*. 2016;63:851-857.

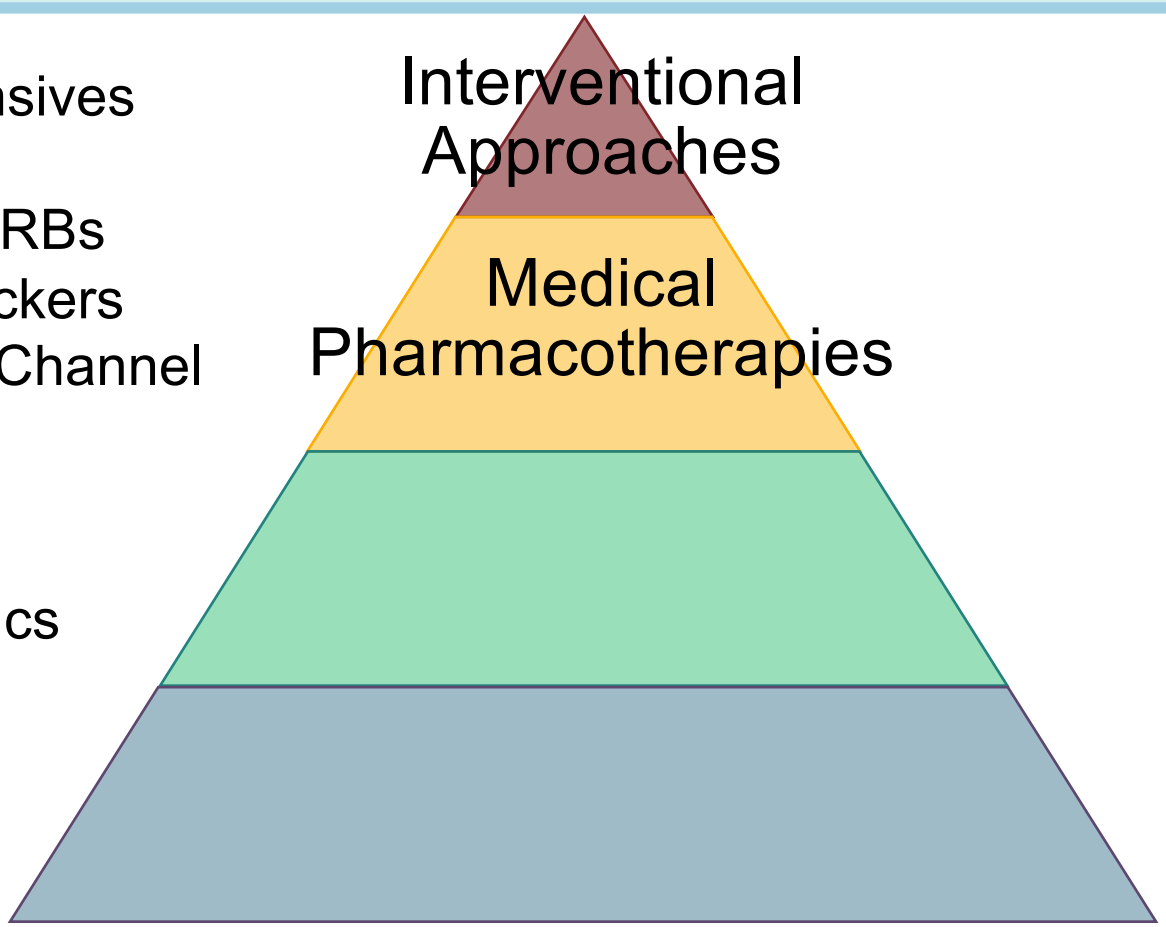
Stroke Prevention 2017

Anti-hypertensives
- Diuretics
- ACEIs, ARBs
- Beta-Blockers
- Calcium Channel

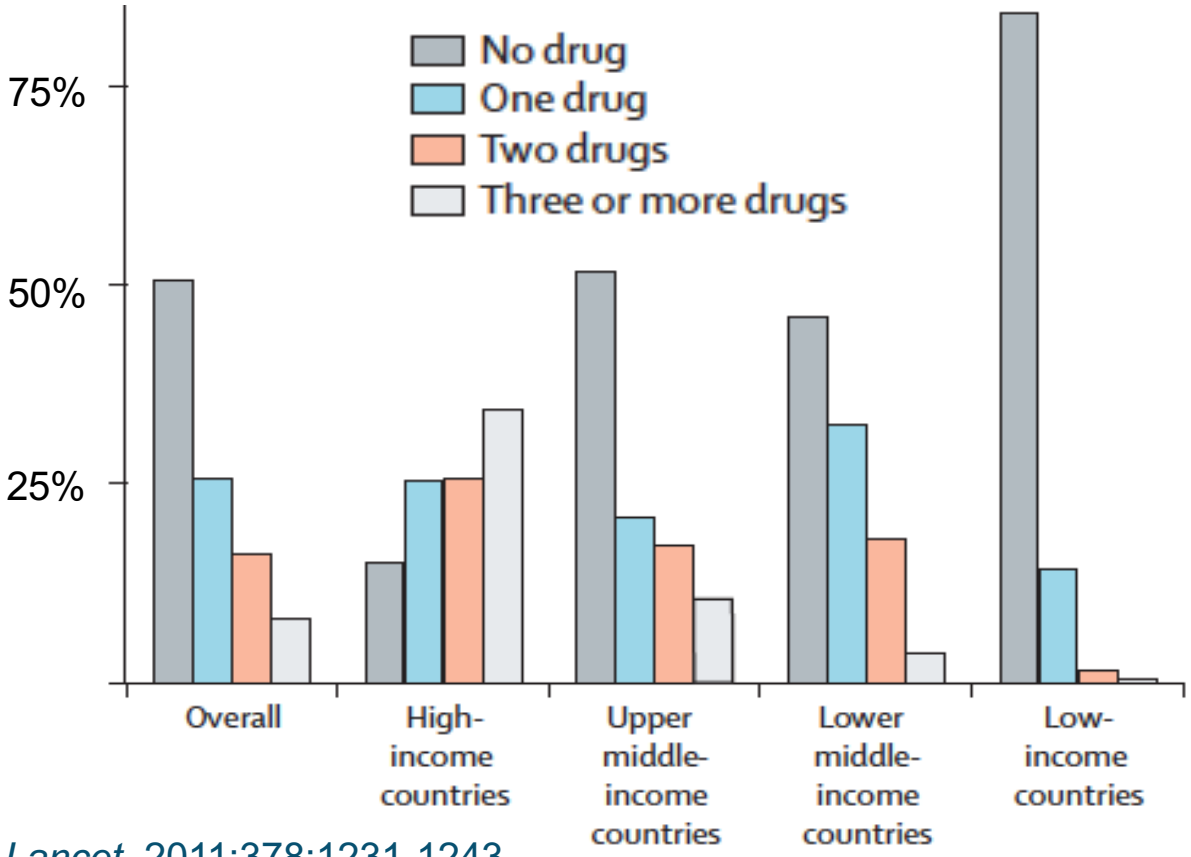
DM Meds

Statins

Antithrombotics



Use of Medications Post Stroke in the PURE Study

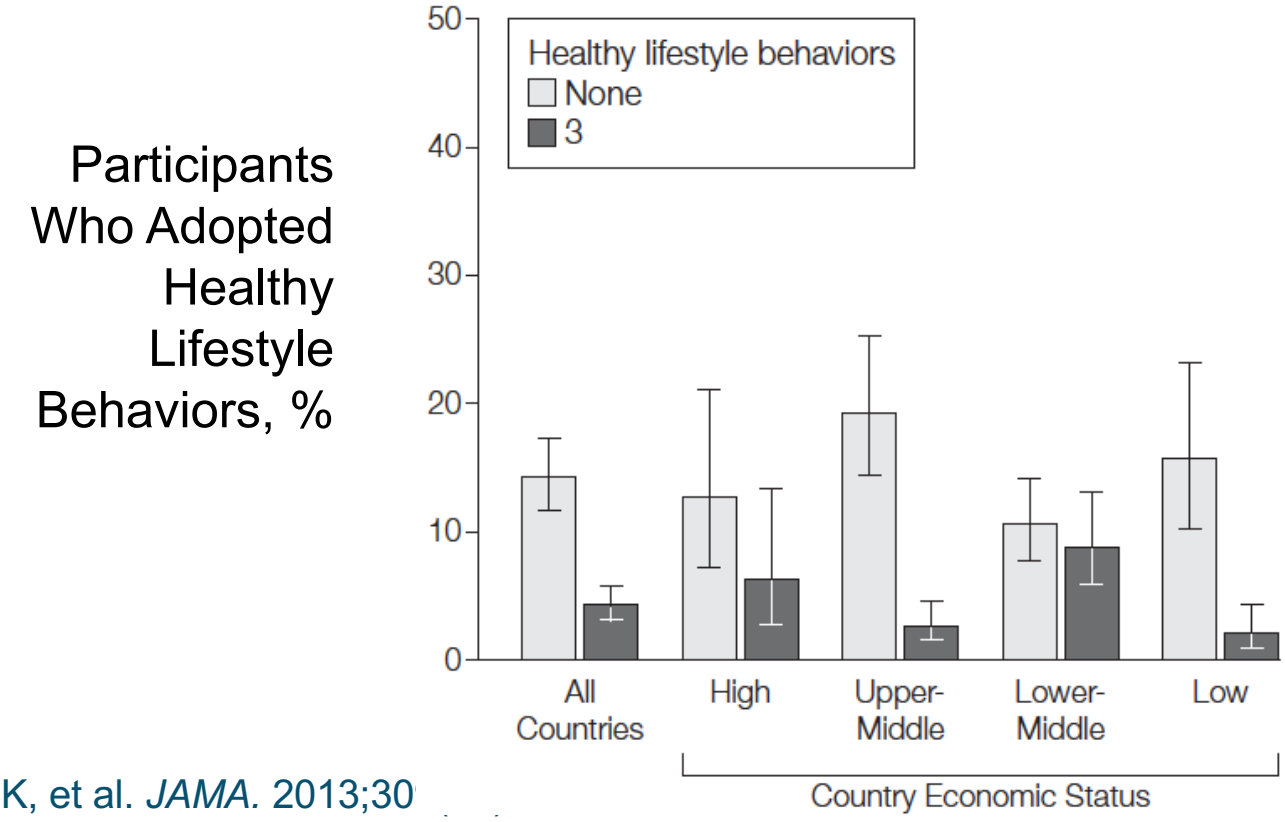


Yusuf, S. et al. *Lancet.* 2011;378:1231-1243.

Prevalence of Healthy Lifestyle Factors in CVD Patients

Country Economic Status

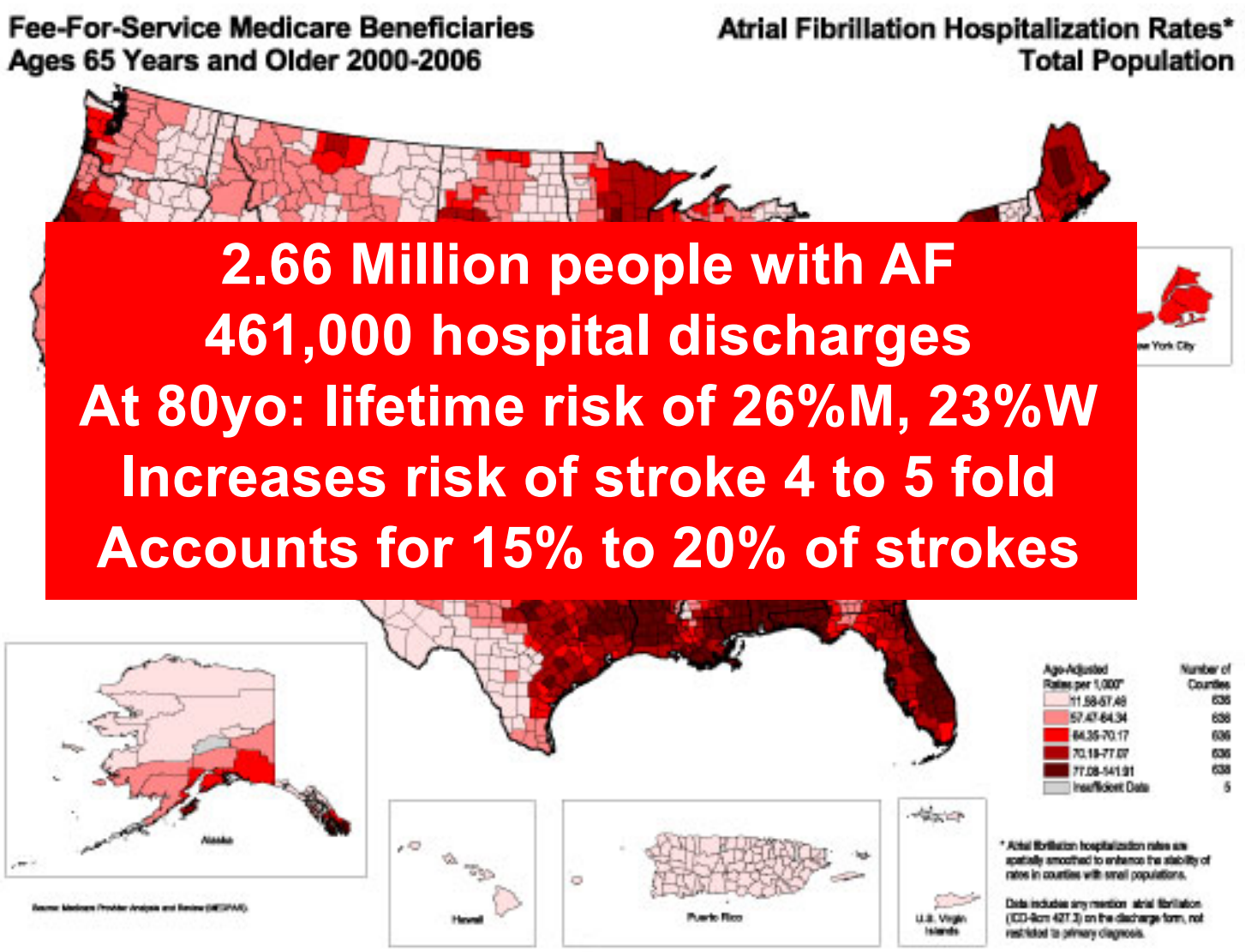
PURE STUDY



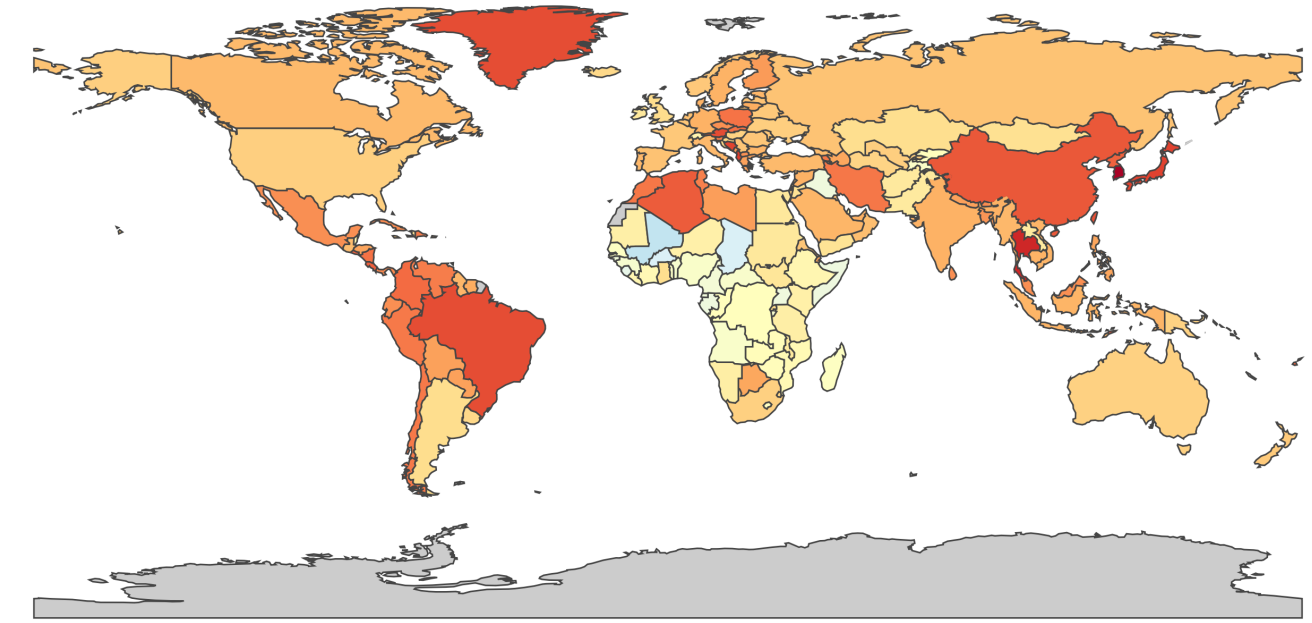
Teo K, et al. *JAMA.* 2013;30

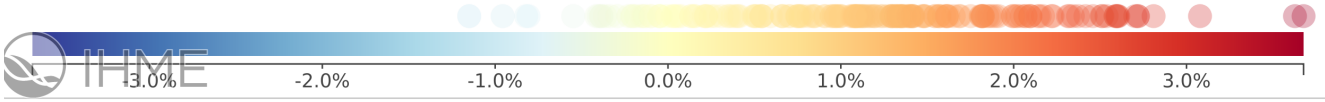
Ischemic Stroke Case

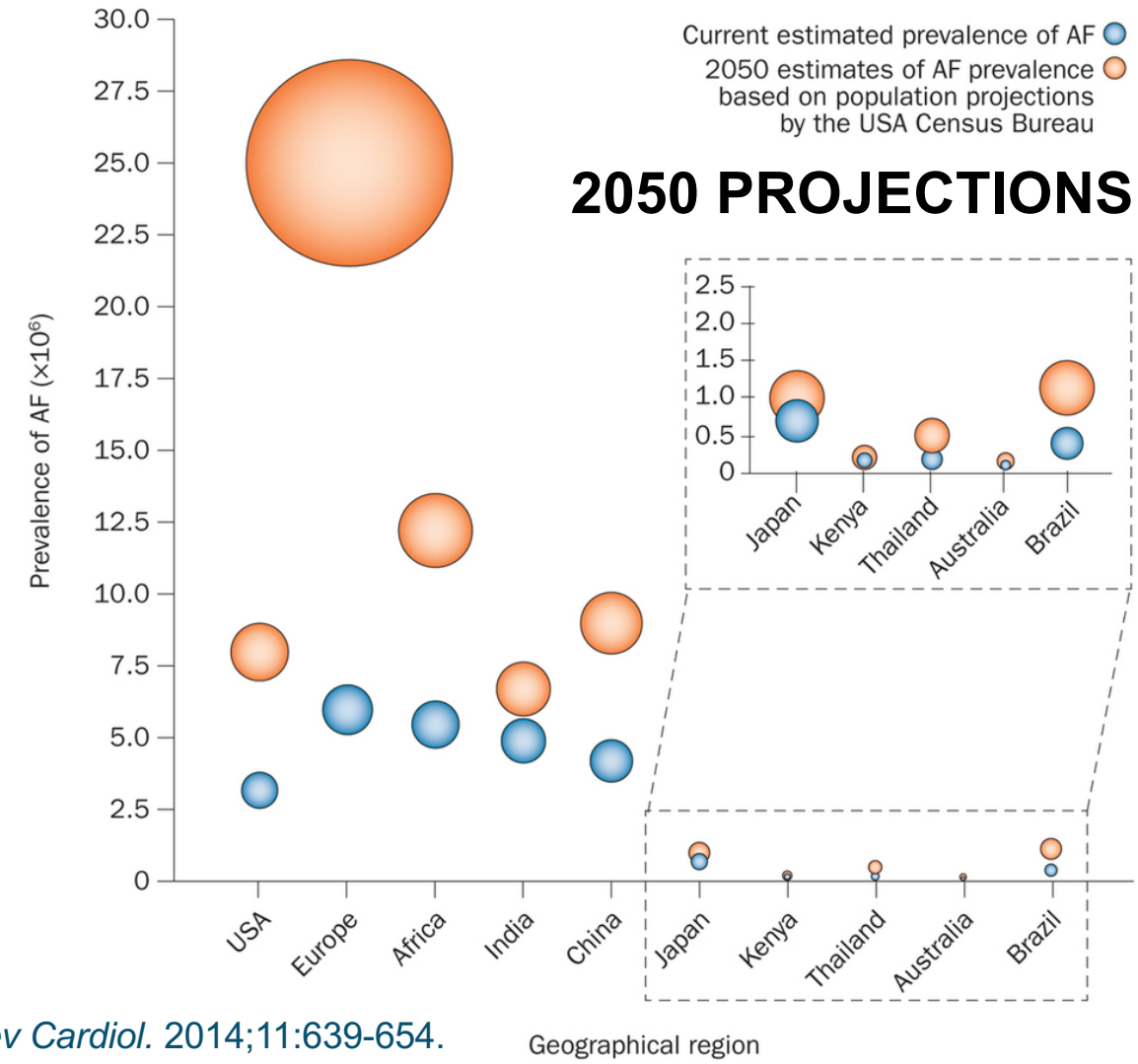
- 78 yo right-handed woman with sudden difficulty speaking and R arm drift
- Prior history of palpitations
- Past medical history: hypertension, diabetes
- Exam: Irregularly irregular heart rate
- Wernicke's type aphasia and mild R hemiparesis
- CT: Wedge-shaped lucency in the L temporal parietal cortex
- EKG: Atrial Fibrillation


Fee-For-Service Medicare Beneficiaries
Ages 65 Years and Older 2000-2006
Atrial Fibrillation Hospitalization Rates*
Total Population
2.66 Million people with AF
461,000 hospital discharges
At 80yo: lifetime risk of 26%M, 23%W
Increases risk of stroke 4 to 5 fold
Accounts for 15% to 20% of strokes
Age-Adjusted Rates per 1,000*
Number of Counties
11.58-57.46
57.47-64.34
64.35-70.17
70.18-77.07
77.08-141.91
Insufficient Data
Alaska
Hawaii
Puerto Rico
U.S. Virgin Islands
* Atrial fibrillation hospitalization rates are spatially smoothed to enhance the stability of rates in counties with small populations.
Data includes any mention atrial fibrillation (ICD-9cm 427.3) on the discharge form, not restricted to primary diagnosis.

Atrial Fibrillation Prevalence
Annual % Change, 1990-2015, GBD

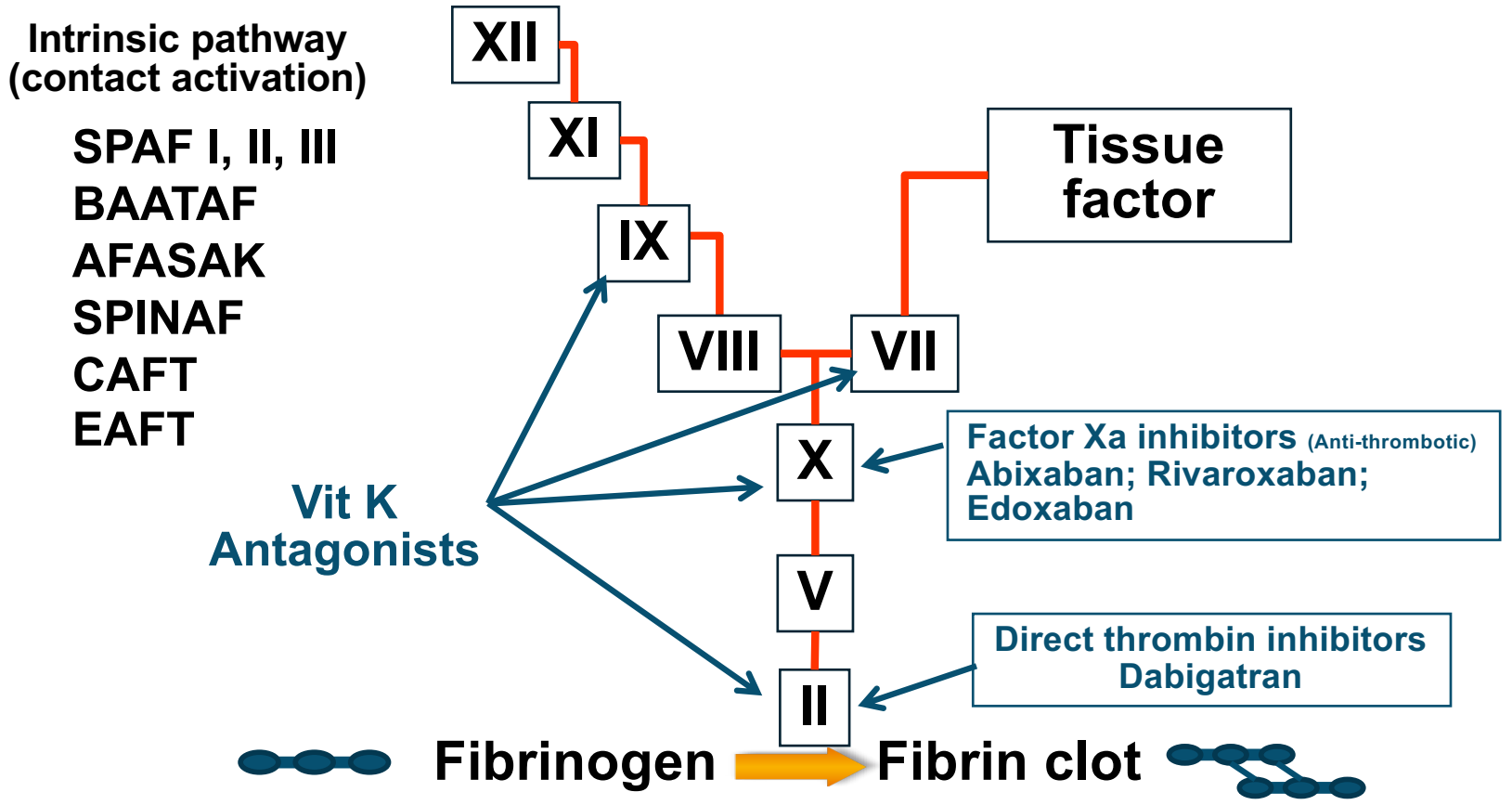






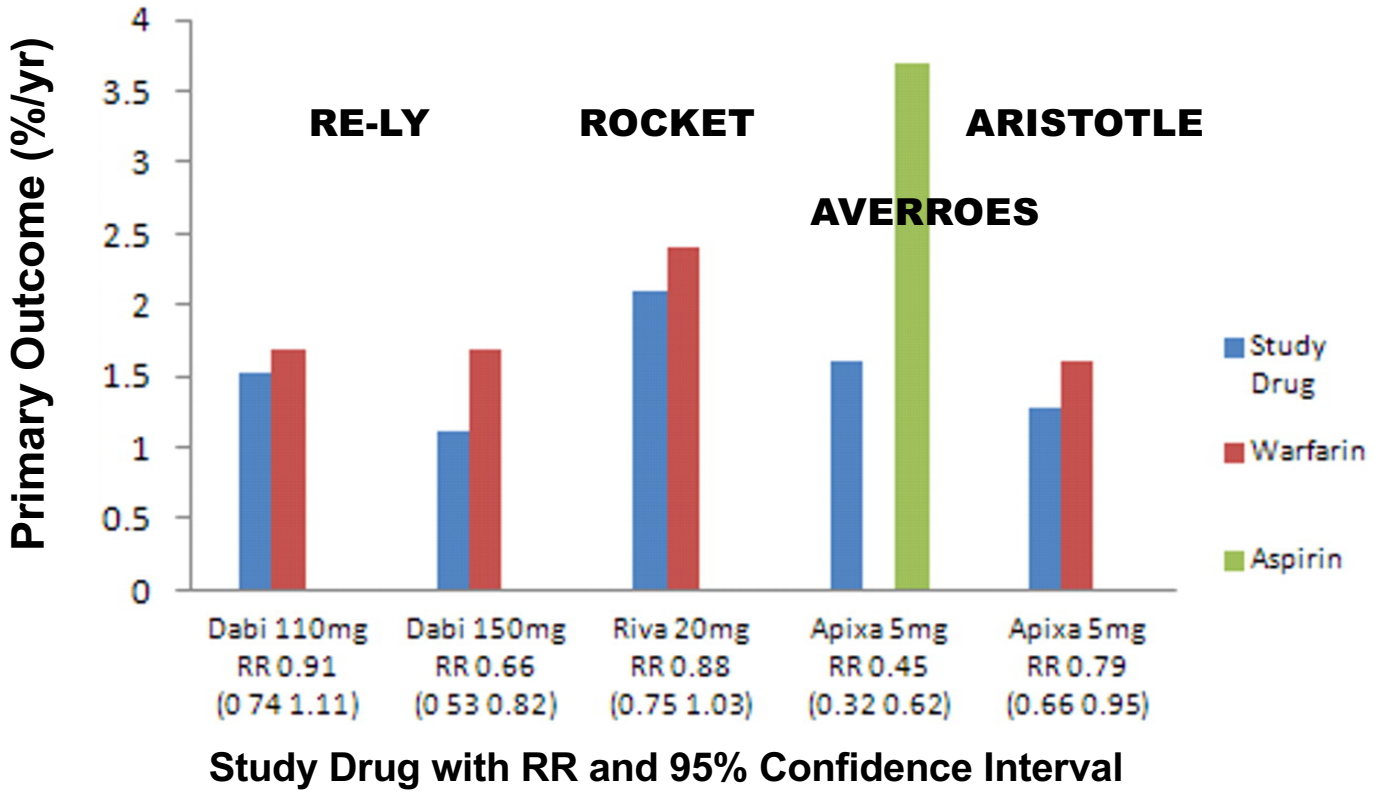
Rahman F, et al. *Nat Rev Cardiol.* 2014;11:639-654.

Targets in Coagulation Pathways



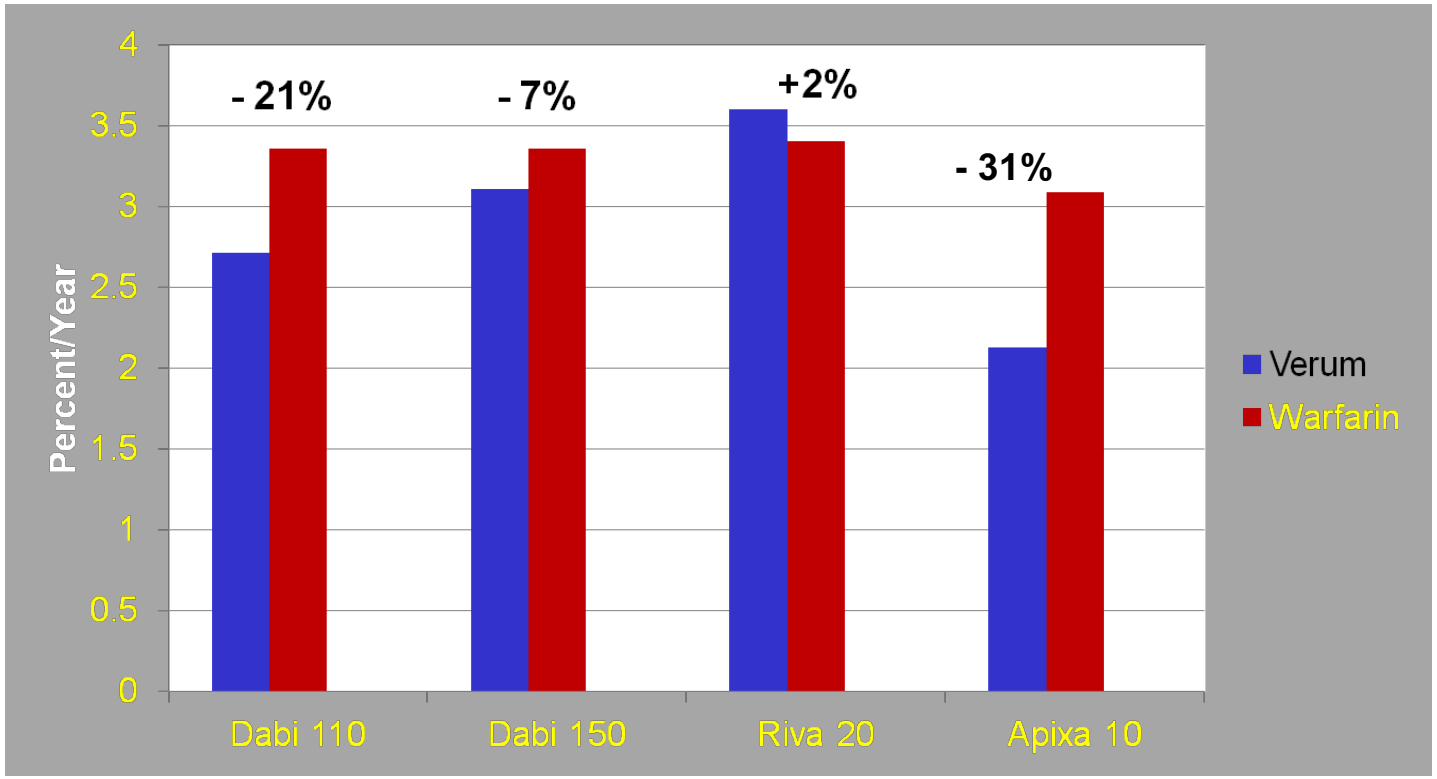
Nutescu EA, et al. *Cleve Clin J Med.* 2005;72:S1;S2-6.

Comparison of Primary Outcomes Stroke of Systemic Embolism



Katsnelson M, et al. *Stroke.* 2012;43:1179-1185.

Major Bleeding
RE-LY, ROCKET and ARISTOTLE



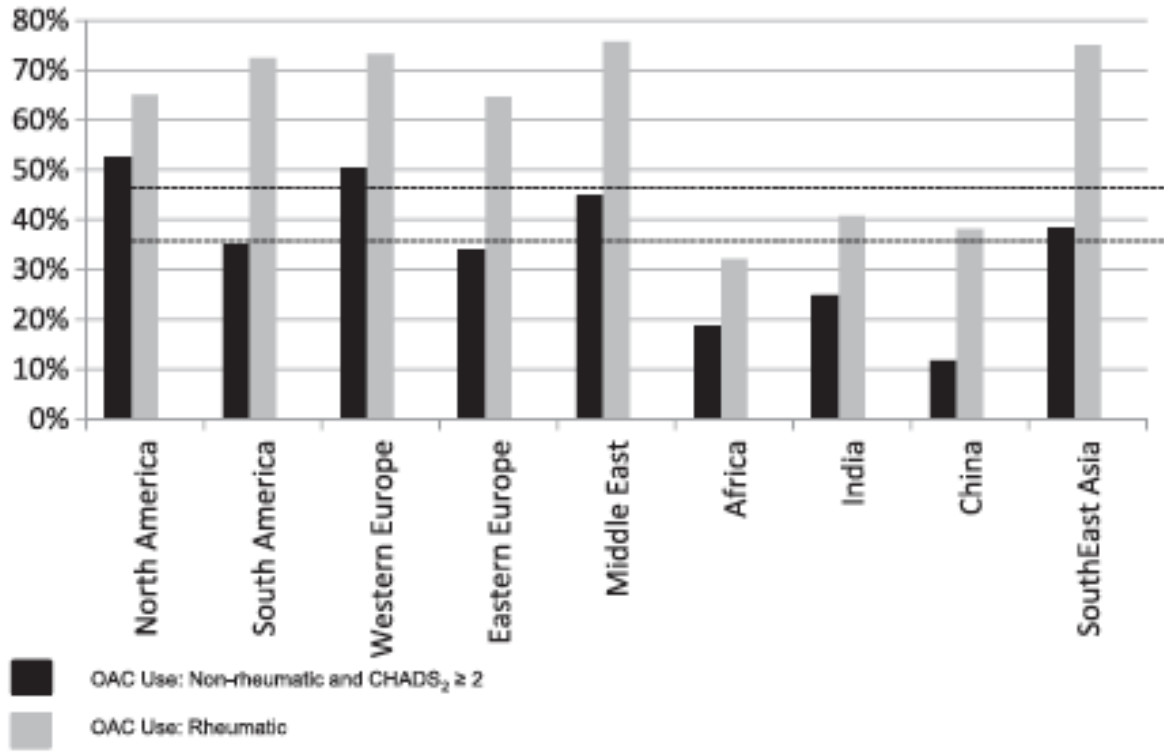
Katsnelson M, et al. *Stroke* 2012;43:1179-1185.

Stroke Prevention - Cardioembolic ASA 2014 Recommendations

- Vitamin K antagonist therapy (Class I, LOE A), apixaban (Class I, LOE A), and dabigatran (Class I, LOE B) are all indicated in patients with NVAF, paroxysmal or permanent AF
- Rivaroxaban is reasonable for patients with NVAF (Class IIa, LOE B)
- Combination of OAC with antiplatelets is not recommended but is reasonable in patients with clinically apparent CAD (Class IIb, LOE C)
- The selection of agents should be individualized

http://stroke.ahajournals.org/content/early/2014/04/30/STR.0000000000000024

Use of OAC Among Patients with a CHADS2 ≥ 2 Greatest in NA



Rheumatic
Global average 45.4%

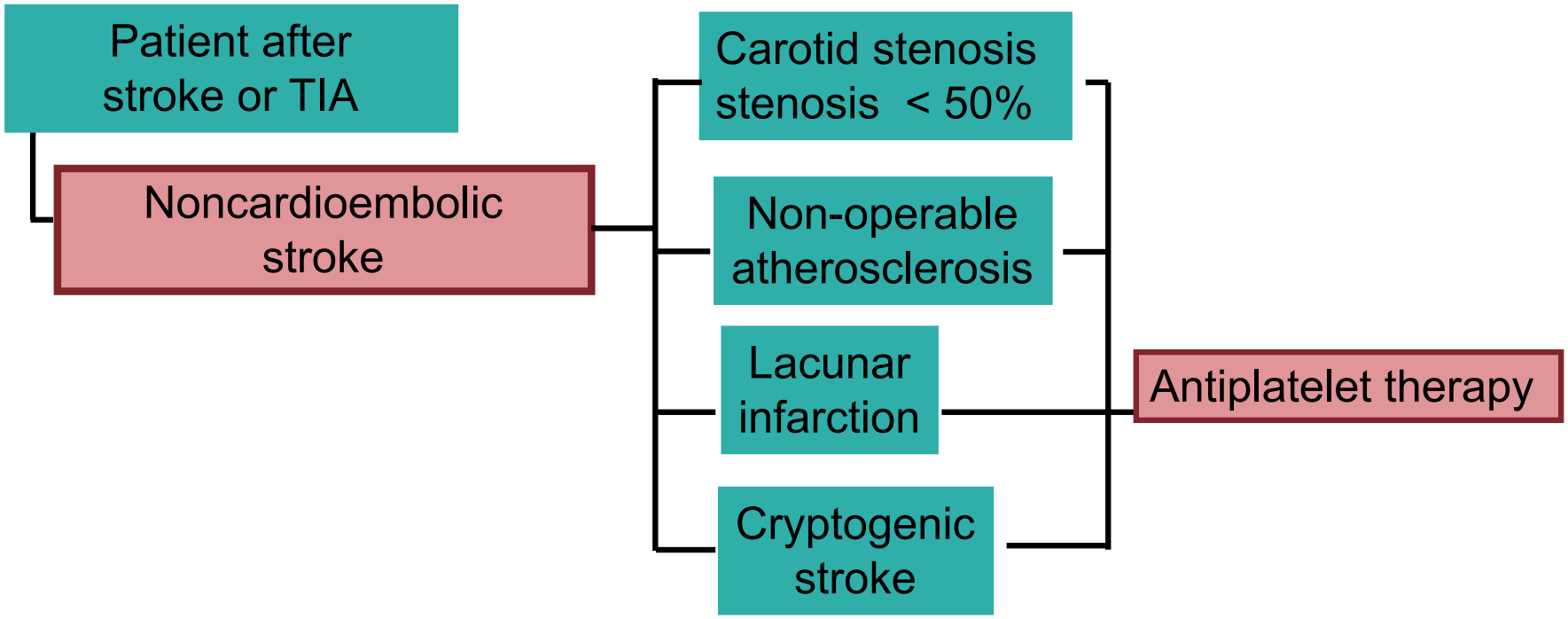
Non-rheumatic
CHADS, ≥2
Global average 34.4%

Oldgren J et al. *Circulation*. 2014;129:1568-1576

Ischemic Stroke Case

- 78 yo RH woman with sudden difficulty speaking and R arm drift
- Prior history of palpitations
- Past medical history: hypertension, diabetes
- Exam: Wernicke's type aphasia and mild R hemiparesis
- CT: Wedge-shaped lucency in the L temporal parietal cortex
- EKG: Normal Sinus Rhythm

Ischemic Stroke Prevention
Non-cardioembolic Stroke



Embolic Stroke of Undetermined Source
RE-SPECT ESUS™

Randomized Evaluation in Secondary Stroke Prevention Comparing Dabigatran vs. ASA

- To evaluate the efficacy and safety of dabigatran for secondary stroke prevention in patients with an embolic stroke of undetermined source (ESUS)
- 6,000 patients who had an ESUS within six months prior to enrollment
- ASA 100 mg vs dabigatran 150 mg BID or 110 mg BID for pts older than 75 or who have reduced renal function

Stroke Prevention - Non-cardioembolic ASA Recommendations

- Antiplatelet agents are recommended rather than oral anticoagulation (Class I, LOE A).
- Acceptable options for initial therapy
  - Aspirin (50-325 mg qd) (Class I, LOE A)
  - The combination of aspirin and extended-release dipyridamole (25/200 mg bid) (Class I, LOE B)
  - Clopidogrel (75 mg qd) (Class IIa, LOE B)

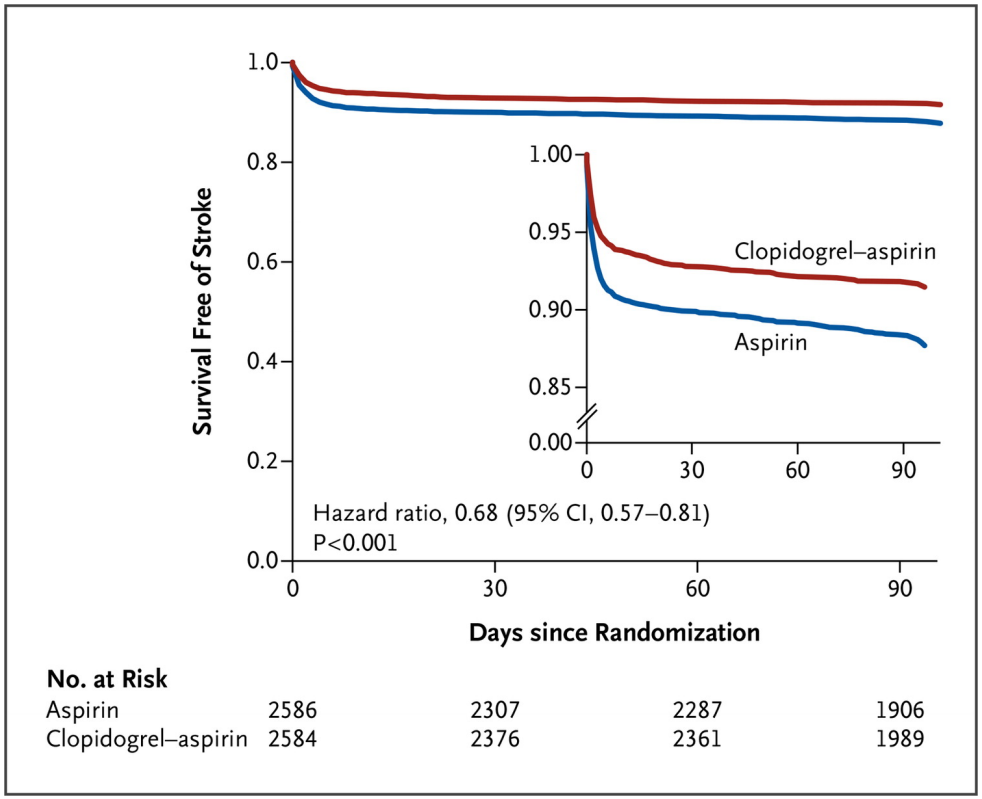
Kernan WN, et al. *Stroke.* 2014;45(7):2160-236.

Clopidogrel + Aspirin

- Definite benefits for acute coronary syndrome and post cardiac angioplasty and stent
- Less evidence of benefit for stroke
  - MATCH (high risk stroke)
    - CP+ASA vs CP: no benefit, incr bleeding
  - CHARISMA (MI, stroke, PAD, and asx)
    - CP+ASA vs ASA: no benefit
  - SPS3 (Small Subcortical Strokes)
    - CP+ASA vs ASA: no benefit

Albers GW, et al. *Chest.* 2001;119:300S-320S.

CHANCE TRIAL
Clopidogrel + ASA in Acute TIA/stroke



At 90 days:

Any stroke Reduced with CP+ASA

HR 0.68, 0.57-0.81

Stroke, MI, VD reduced

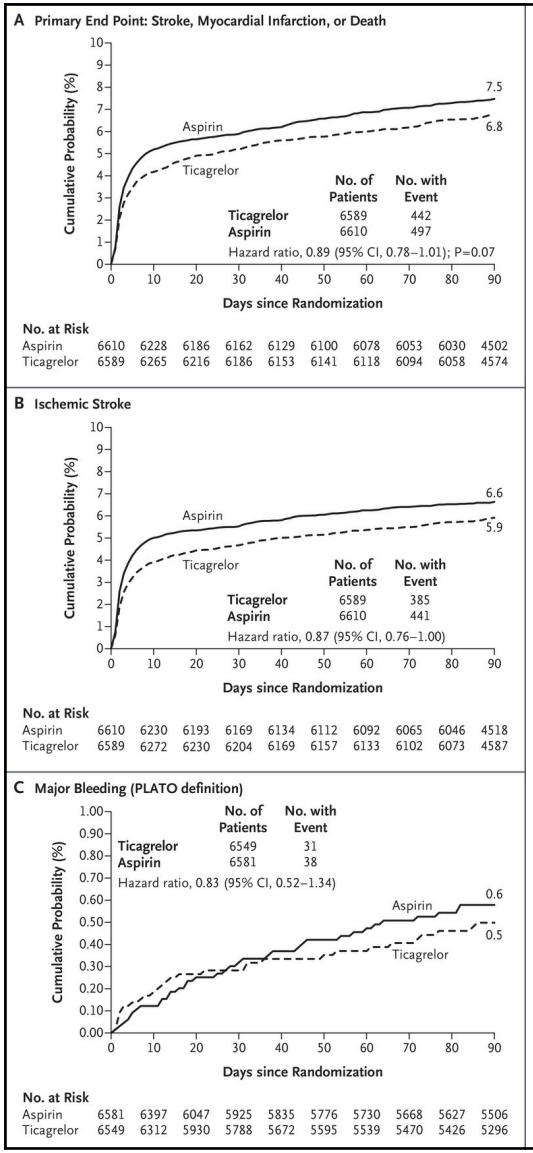
HR 0.69, 0.58-0.82

Hemorrhagic stroke no different (0.3%)

Wang Y, et al. *NEJM*. 2013;369:11-19.

Stroke Prevention - Non-cardioembolic ASA Recommendations

- Combination of aspirin and clopidogrel might be considered for initiation within 24 hours of a minor ischemic stroke or TIA for 90 days (Class IIb; LOE B) → POINT, SOCRATES
- Combination of aspirin and clopidogrel, when initiated days to years after a minor stroke or TIA and continued for 2 to 3 years, increases the risk of hemorrhage relative to either agent alone and is not recommended for routine long-term secondary prevention (Class III; LOE A).



SOCRATES

- Double-blind, randomized trial
- Ticagrelor vs. ASA 325mg
- NIHSS score of 5 or lower
- 13,199 patients with ischemic stroke or TIA
- Randomized within 24 hours after onset
- Not superior to aspirin in reducing the rate of stroke, MI, or death at 90 days
- Risk of IS was 13% lower in ticagrelor group

Johnston SC, et al. *N Engl J Med* 2016;375:35-43.

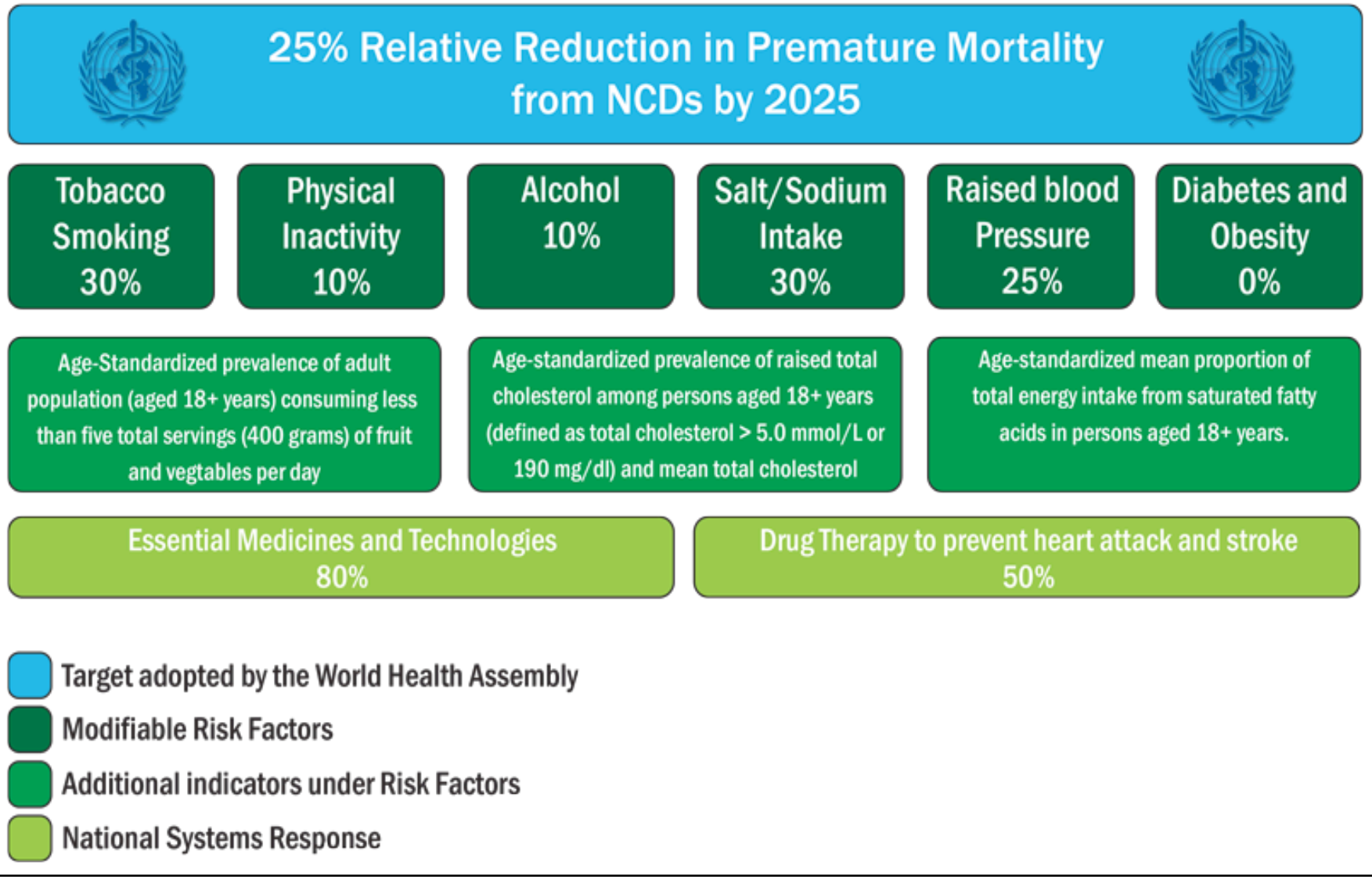
Evolving from Stroke to Brain Health

- Stroke
- Dementia
- Vascular Cognitive Impairment
- Cognitive Aging
- Age-related Memory Loss
- Vascular Functional Impairment
- Subclinical Vascular Disease
  - White matter hyperintensities
  - Brain volumes or atrophy
  - Silent brain infarctions
  - Cerebral Microbleeds

International Strategies and Collaborations

UN High Level Meeting on NCDs Prevention and Control of Non-communicable Diseases

- September 19-20, 2011 at the UN, New York
- Participation of Heads of State and Government
- Led by Caribbean countries
- 130 states co sponsored
- Links NCDs to MDG Review


25% Relative Reduction in Premature Mortality from NCDs by 2025
Tobacco Smoking 30%
Physical Inactivity 10%
Alcohol 10%
Salt/Sodium Intake 30%
Raised blood Pressure 25%
Diabetes and Obesity 0%
Age-Standardized prevalence of adult population (aged 18+ years) consuming less than five total servings (400 grams) of fruit and vegtables per day
Age-standardized prevalence of raised total cholesterol among persons aged 18+ years (defined as total cholesterol > 5.0 mmol/L or 190 mg/dl) and mean total cholesterol
Age-standardized mean proportion of total energy intake from saturated fatty acids in persons aged 18+ years.
Essential Medicines and Technologies 80%
Drug Therapy to prevent heart attack and stroke 50%
Target adopted by the World Health Assembly
Modifiable Risk Factors
Additional indicators under Risk Factors
National Systems Response

Advocacy Efforts to Improve Policies

- Tobacco (excise taxes, clean air, prevention)
- Physical education and nutrition policy in schools
- Transfat, sodium, menu labeling
- Reducing barriers to receipt of antihypertensive medications and statins through subsidies
- Preventive Health Benefits

Stroke: Clinical Update and Best Practices for Improved Outcomes

- Stroke mortality has declined due to adherence to evidence-based prevention guidelines
- Carotid interventions (CAE & CAS) are of definite value for symptomatic ICA disease
- Oral anticoagulants prevent cardioembolic stroke
- Optimal medical therapy includes antithrombotics, BP control, statins, and aggressive lifestyle interventions.
- Promoting ideal cardiovascular health will reduce stroke as well as improve brain health

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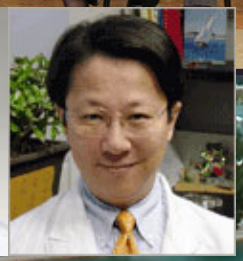
Mitch Elkind, MD
Bernadette Boden-Albala, DrPH

Tanja Rundek, MD PhD Clinton Wright, MD MS
Chuanhui Dong, MD PhD; Susan Blanton, PhD



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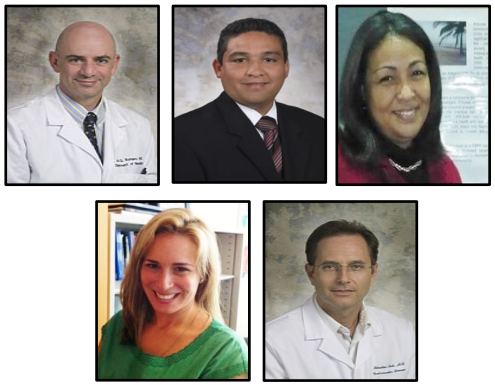
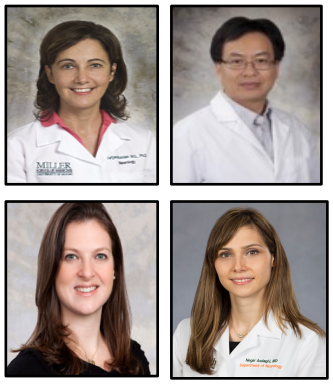
FL-PR CReSD Team

Core A:
Administrative Core

Core B:
Research/Education Training Plan Core



Core C:
Data Management/ Biostatistics Core



AHA Staff:
Julia Mora
Kathy Fenelon
Sandra Diaz-Acosta
Jeffrey Walker

Consultants:

Questions & Answers

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