Risk Stratification of AF

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Intermountain® Heart Institute

Conflicts of Interest

Boehringer Ingelheim – Institutional Research grant, no personal salary or financial benefits

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The Psychiatrist and the Proctologist

Best friends graduating from medical school at the same time decided that in spite of two different specialties, they would open a practice together to share office space and personnel.

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Dr. Smith was the psychiatrist and Dr. Jones was the proctologist; they put up a sign reading:

Dr. Smith and Dr. Jones: Hysterias and Posteriors

The town council was livid and insisted they change it.

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The docs changed it to read:

Schizoids and Hemorrhoids.

This was also not
acceptable so they again changed the sign to read

Catatonics and High Colonics

– no go. Next they tried

Manic Depressives and Anal Retentives

thumbs down again.

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Then came Minds and Behinds – still no good.

Another attempt resulted in
Lost Souls and Butt Holes – unacceptable again!

So they tried Nuts and Butts – no way.

Freaks and Cheeks – still no good.

Loons and Moons - forget it.

Almost at their wit's end, the docs finally came up with:

Dr. Smith and Dr. Jones – Specializing in Odds and Ends.

Everybody loved it

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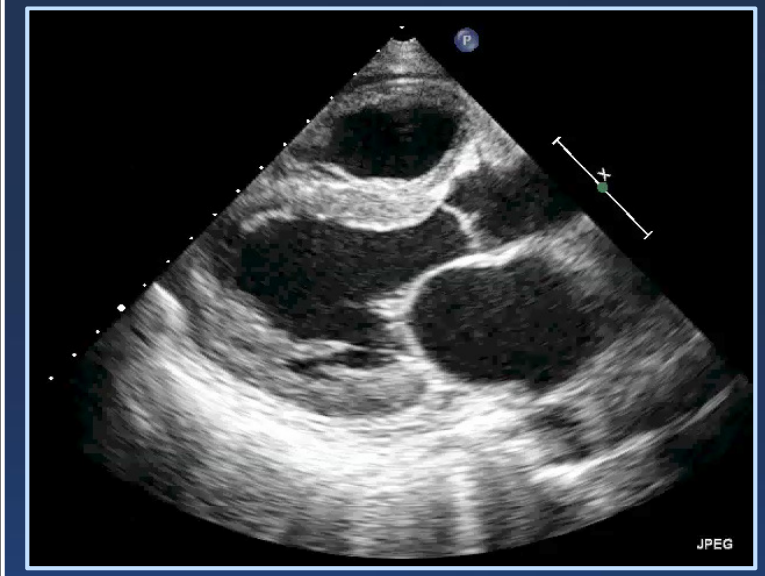
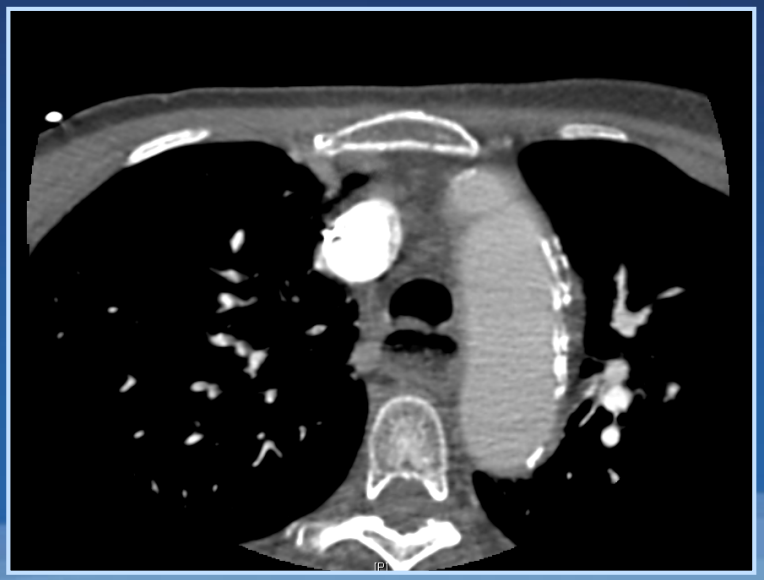
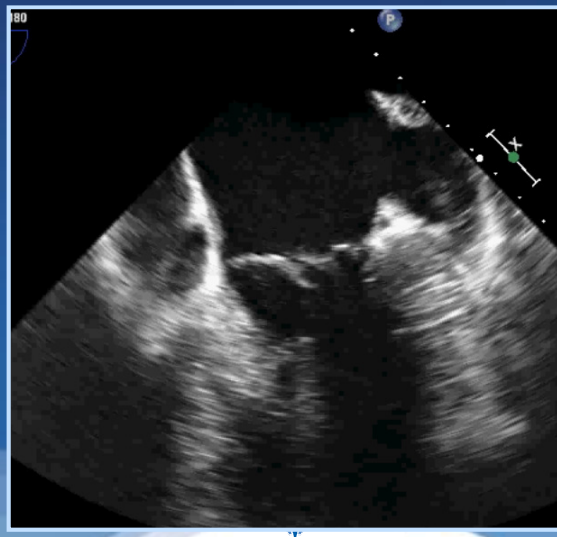
AF is often a part of a systemic disease state of aging







86 yo Female Acute Stroke with AF when Anticoagulation Held for Surgery

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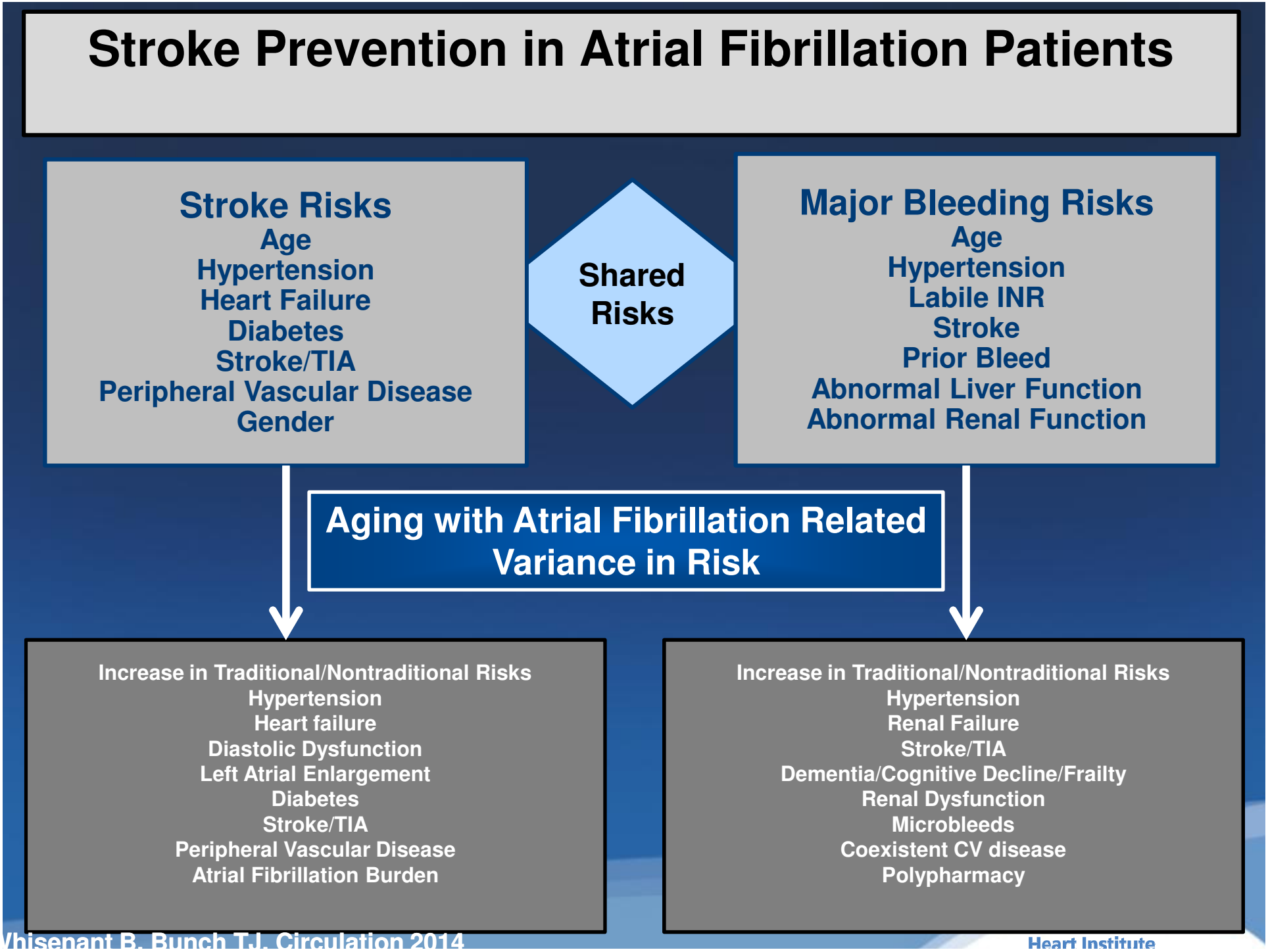
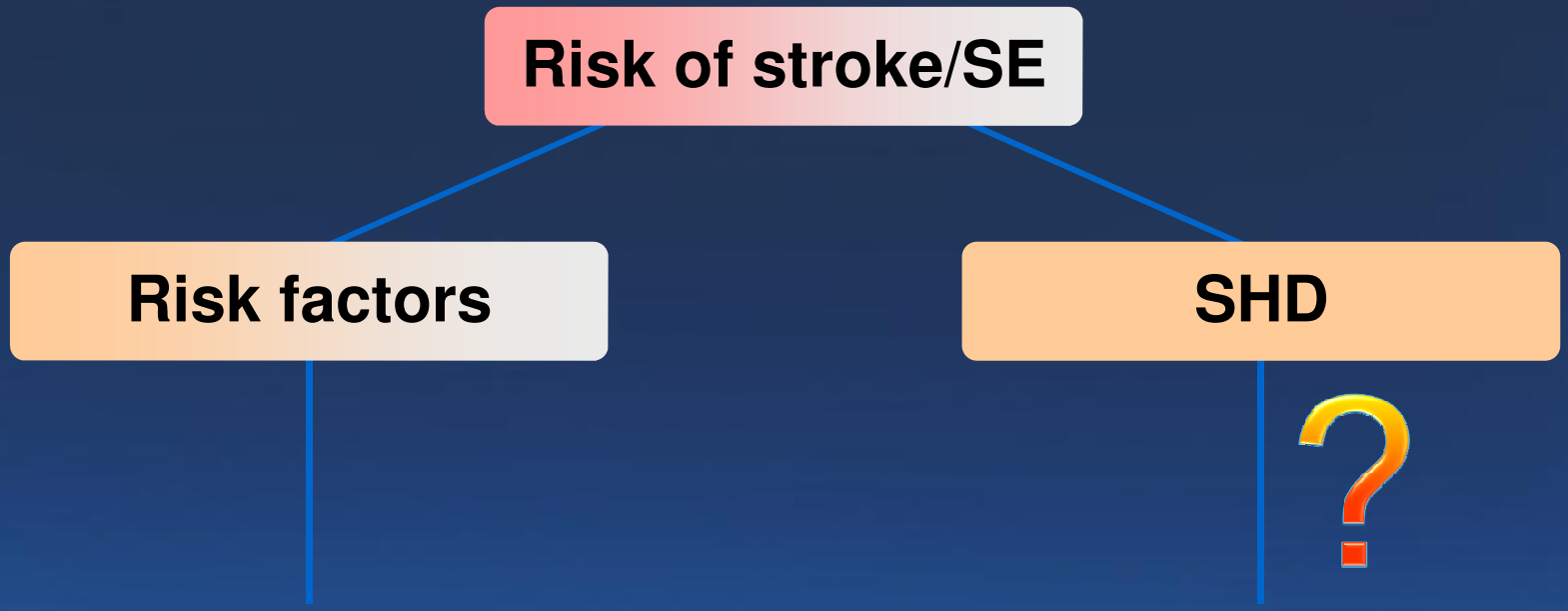
Stroke Prevention in Atrial Fibrillation Patients

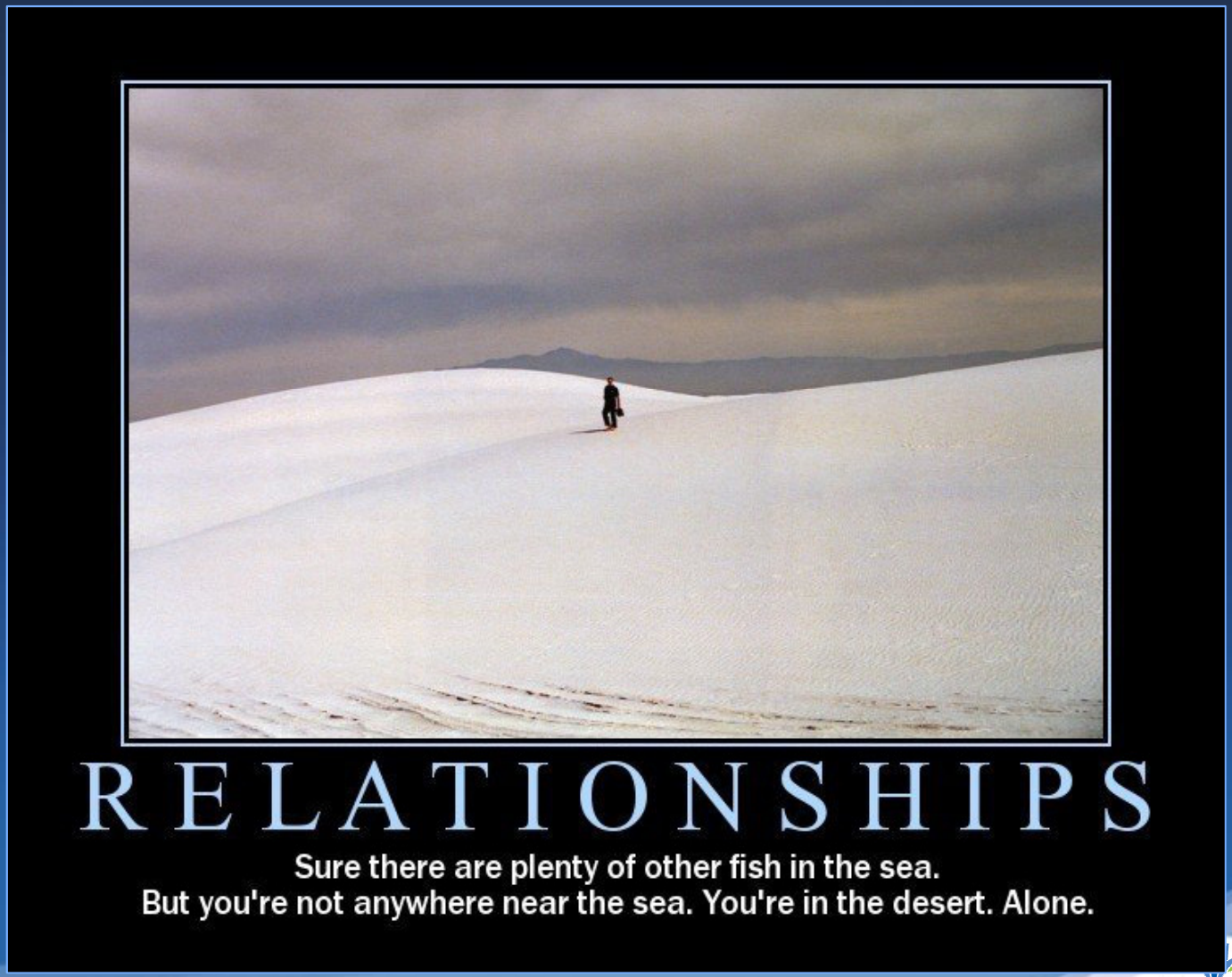


Whisenant B, Bunch TJ. Circulation 2014

Atrial Fibrillation: Impact of Risk Factors and Structural Heart Disease (SHD)



Risk and Our Long Relationship with the CHADS2 (CHADS2 – Vasc) Score



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ORIGINAL ARTICLE

MAYO CLINIC

Clinical Predictors of Risk for Atrial Fibrillation: Implications for Diagnosis and Monitoring

Kyle J. Brunner, MBA; T. Jared Bunch, MD; Christopher M. Mullin, MS; Heidi T. May, PhD; Tami L. Bair, BS; David W. Elliot, MBA; Jeffrey L. Anderson, MD; and Srijoy Mahapatra, MD

TABLE 1. Risk Factor Meta-analysis Summary

Risk factor	No. of patients included in analysis
Heart failure[10-19]	65,074
Valvular disease[10,11,20,21]	14,880
Coronary artery disease[10-12,14,16,18-21]	57,516
Age (per 10 years)[10,12-14,16-18,20]	44,690
Hypertension[10-23]	112,364
Diabetes mellitus[10,12-16,18,19,21,22,24]	69,739
Sex (male)[10,12-16,18,19,21,24,25]	63,164

[a]$P<.001$ for all.

Risks Factors for AF Risk Associations also Drive AF Incidence

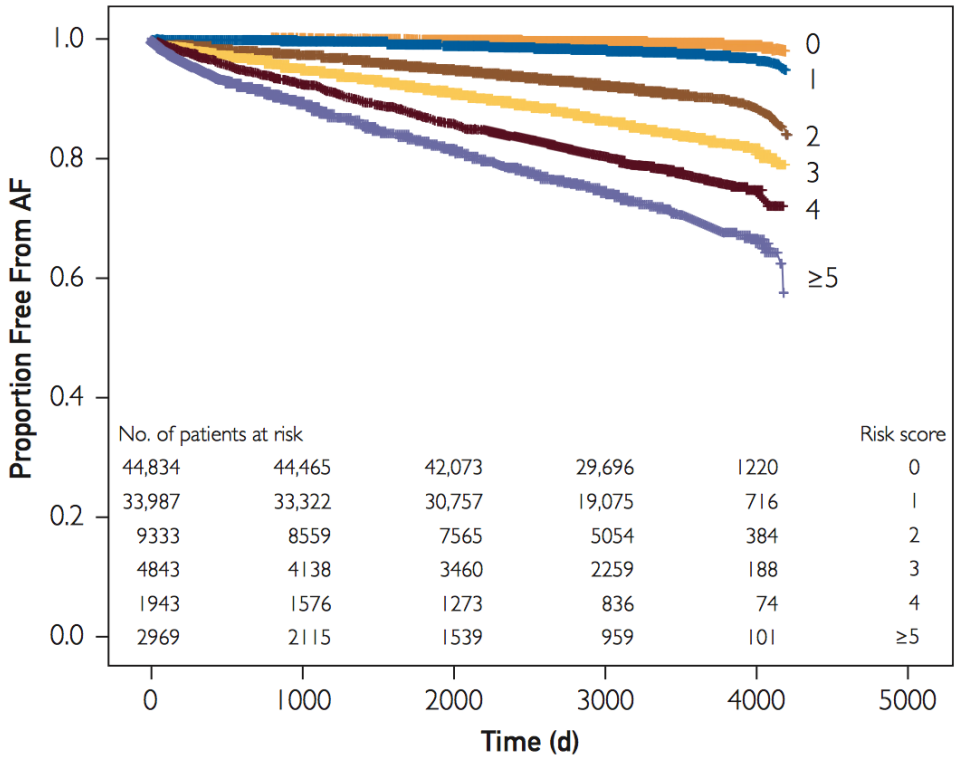
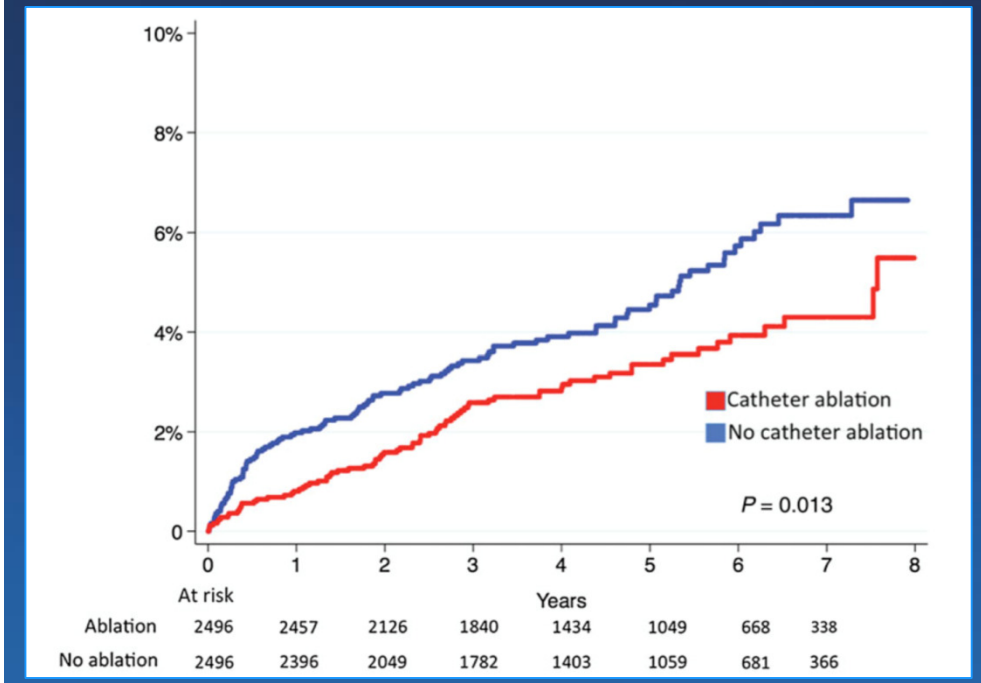


FIGURE. The Kaplan-Meier survival analysis reveals the incidence of atrial fibrillation (AF) over time for the respective subgroups on the basis of risk score. The number at risk for each subgroup for the respective time point is displayed below the curve.

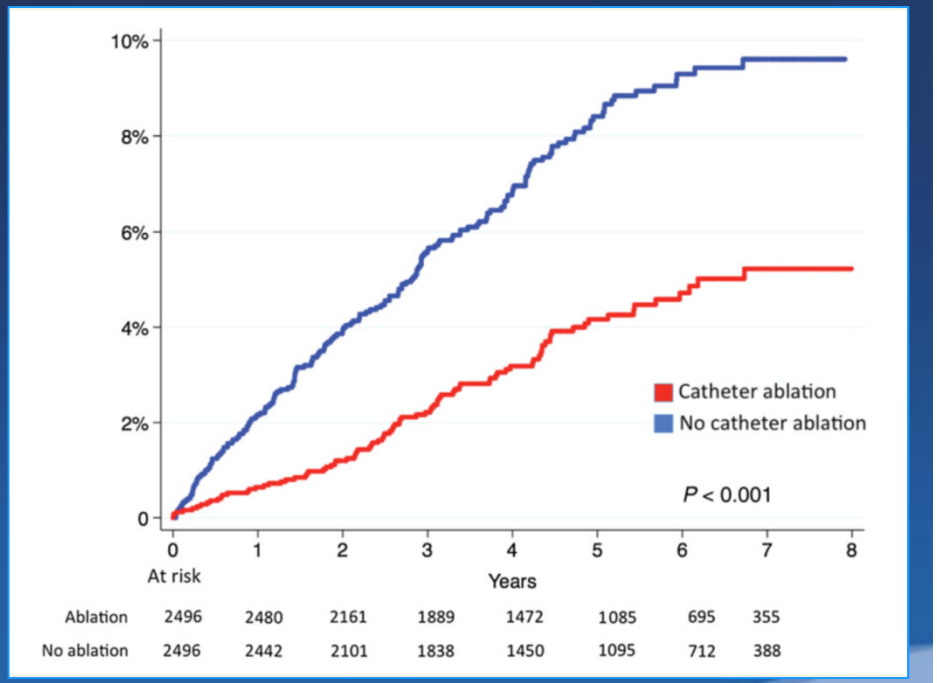
Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries

Leif Friberg[1,2*], Fariborz Tabrizi[3,4], and Anders Englund[3,4]

Stroke/Tia



Mortality



Long-term Mortality Rates are Higher Than Stroke Rates in AF Pts
CHADS2 Score Predicts Mortality>CVA

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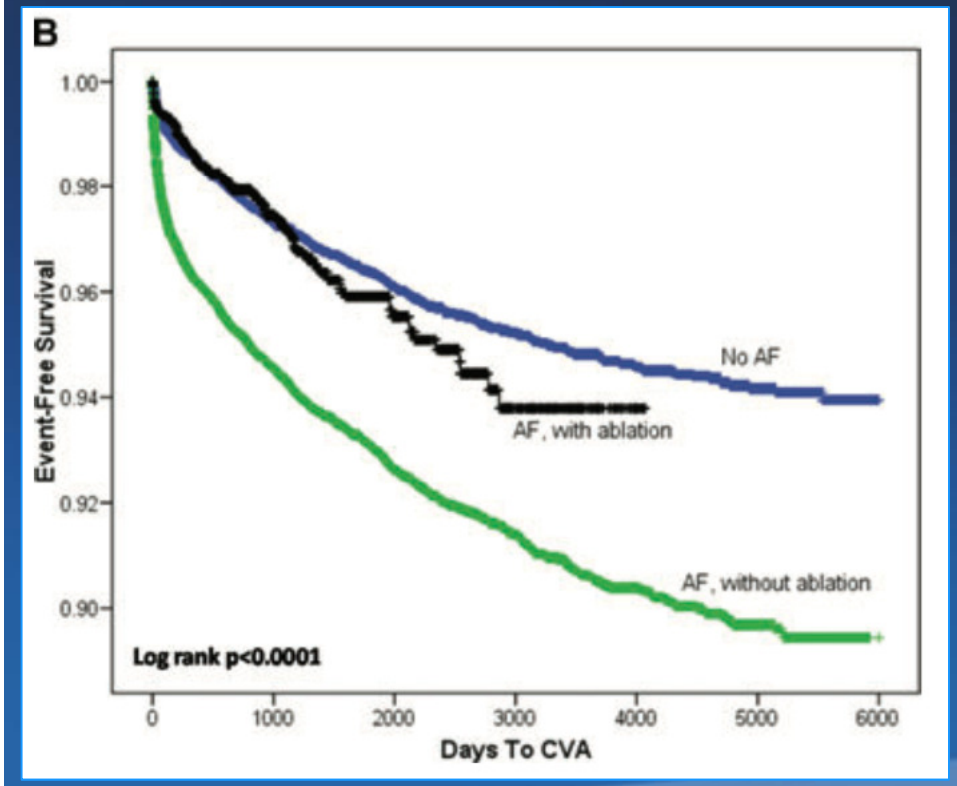
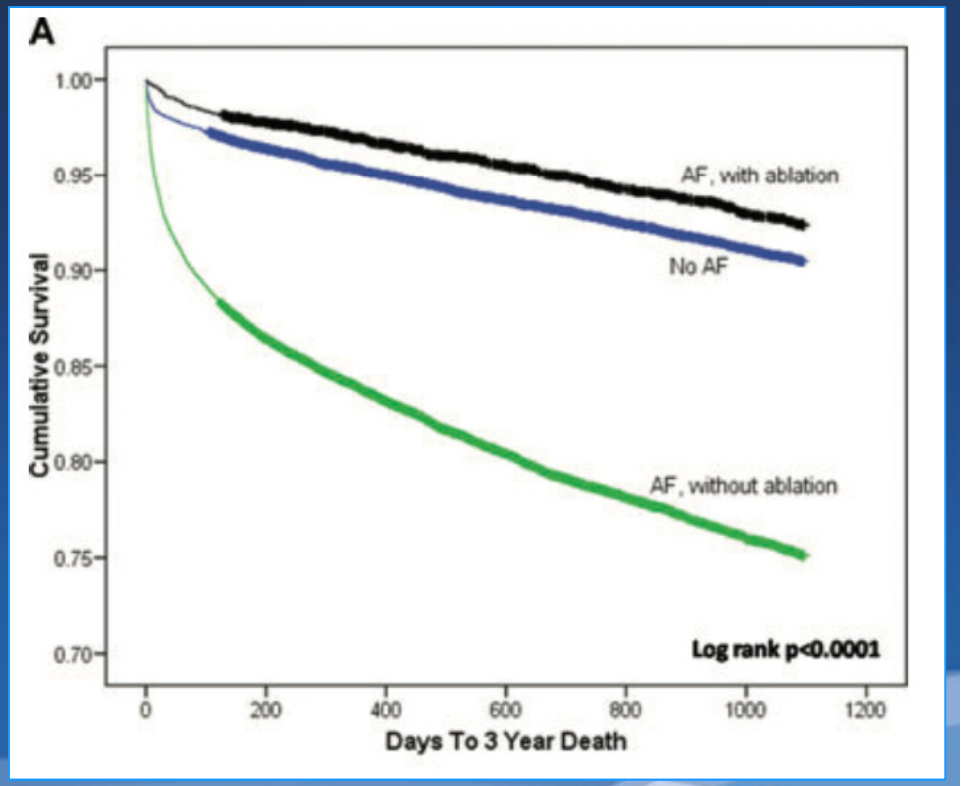
Patients Treated with Catheter Ablation for Atrial Fibrillation Have Long-Term Rates of Death, Stroke, and Dementia Similar to Patients Without Atrial Fibrillation

T. JARED BUNCH, M.D.,*,† BRIAN G. CRANDALL, M.D.,*,† J. PETER WEISS,*,†
HEIDI T. MAY, PH.D., M.S.P.H.,† TAMI L. BAIR,† JEFFREY S. OSBORN, M.D.,*,†
JEFFREY L. ANDERSON, M.D.,† JOSEPH B. MUHLESTEIN, M.D.,†
BENJAMIN D. HORNE, PH.D., M.P.H.,† DONALD L. LAPPE, M.D.,† and JOHN D. DAY, M.D.*,†





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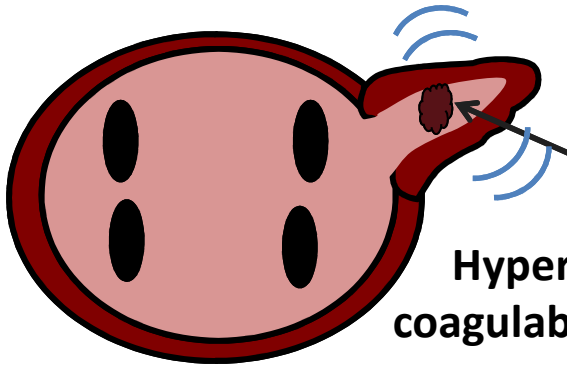
Atrial Fibrillation and Stroke

Focal Electrical Disease

Risk Factor

Reduced LA/LA Appendage Velocities

Atrial Dilitation/Myopathy≈Arrhythmia Burden



Focal Disease

Hyper-coagulability

Stasis

Endothelial Dysfunction

Temporal Association AF & Stroke
As needed Anticoagulation Plausible
Focal Therapy -> Lower Risk
Rhythm Treatments -> Lower Risk

Systemic Disease Symptom

Risk Marker

Obesity

Vascular Disease

Sedentary Lifestyle

Metabolic Syndrome

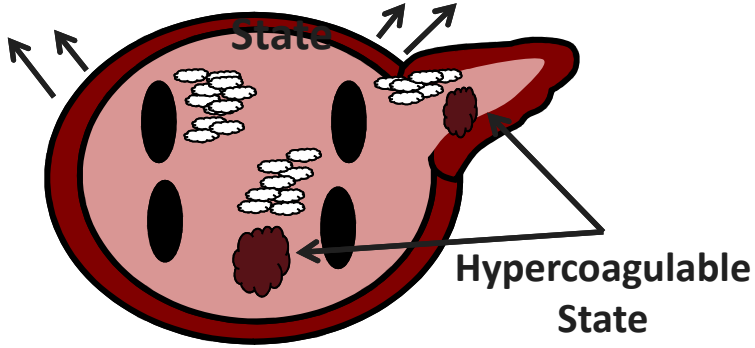
Sleep Apnea

Diabetes

Hypertension

Arterial Stiffness
Microvascular Dysfunction
Diastolic Dysfunction

Atrial Dilatation/Fibrosis/Myopathy≈Disease



Hypercoagulable State

Poor Temporal Association AF & Stroke
Systemic Therapy-> Lower Risk
Risk Persists Despite Rhythm Treatment

Bunch TJ – Eur Heart J 2016

Performance of Contemporary Risk Stratification Schemes

Lip: Chest, 2010

MAYO CLINIC

Gersh BJ, Mayo

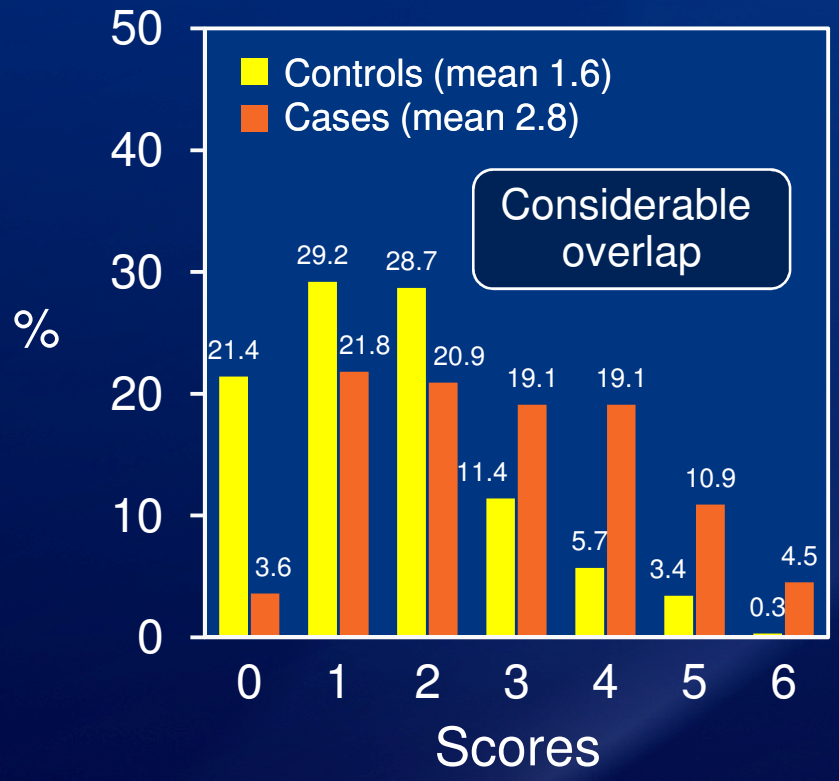
$CHADS_2$ Score and Left Atrial Thrombi in AF

- Case control study

Cases

- 110 pt
- NVAF
- LAA thrombus
- TEE

Distribution of Scores



Wysosinski: AHJ, 2010

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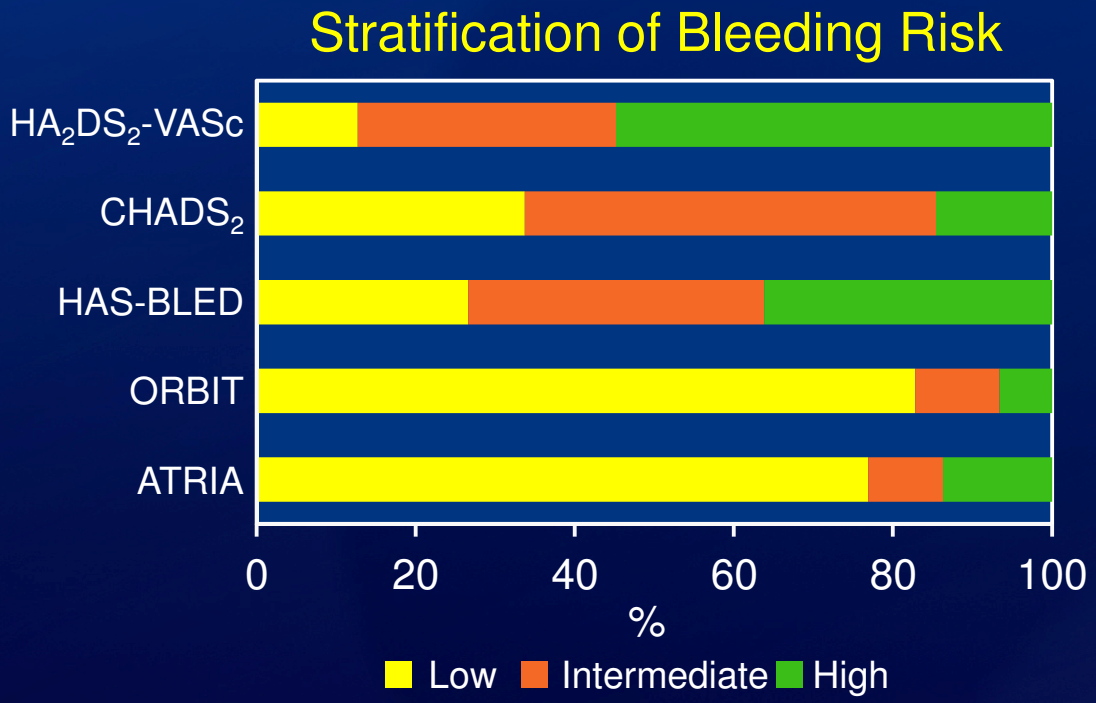
Gersh BJ, Mayo

Comparison of Stroke and Bleeding Scores in Patients on NOACS

- 39,539 patients
- U.S. commercial insurance database



C-statistic

Major bleeding	Intracranial bleeding
0.65	0.61
0.64	0.66
0.64	0.63
0.60	0.55
0.60	0.55

Yao and Noseworthy in press

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Gersh BJ, Mayo

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3511528-7

The Challenge of Change In Electrophysiology

The first testicular guard, the "cup" was used in Hockey in 1874…

….and the first helmet was used in 1974

That means it only took 100 years for men to realize that their brain is also important

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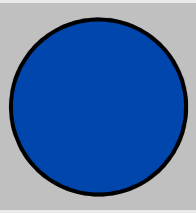
Risk Factors for Thromboembolic Events in Atrial Fibrillation Patients

Not All One-Pointers Are Equal

Risk Factor	Hazard ratio estimates	CHA_2DS_2-VASc Points
Age ≥75 years (reference <65 years)		2
Age 65-74 years (reference <65 years)		1
Previous Ischemic Stroke		2
Female Gender		1
Vascular Disease		1
Hypertension		1
Diabetes Mellitus		1
History of heart failure		1
History of intracranial bleeding		0
Reference		

Argulian: Am J Med, 2015

Value of Static or Point of Care Risk Factors?

HTN
DM
Diastolic HF
Sleep Apnea
Low Activity
Morbid Obesity
Inflammation

Many Risk Factors are Reversible with Life Style Changes

HTN
DM
Diastolic HF
Sleep Apnea
Low Activity
Morbid Obesity
Inflammation

HTN
DM
Diastolic HF
Sleep Apnea
Low Activity
Morbid Obesity
Inflammation

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Frequency: 3-5 days/wk

Intensity: ≤95% peak HR

Time: 120 to 200 Min/Wk

Type : Aerobic Exercise +/- Resistance Training

Short-Term (<6 months)
Reduced AF Burden
Reduced Symptom Severity
(Malmo et al, 2015)

Long-Term (>4 years)
Increased AF freedom
Reduced Symptom Severity
(Pathak et al., 2015)

Potential Mechanisms
Reversed atrial remodeling
Weight loss
Improved BP control
Improved glycemic control
Reduced Inflammation
Improved autonomic tone

Elliott AD, Mahajan R, Pathak RK, Lau DH, Sanders P. Circulation 2016

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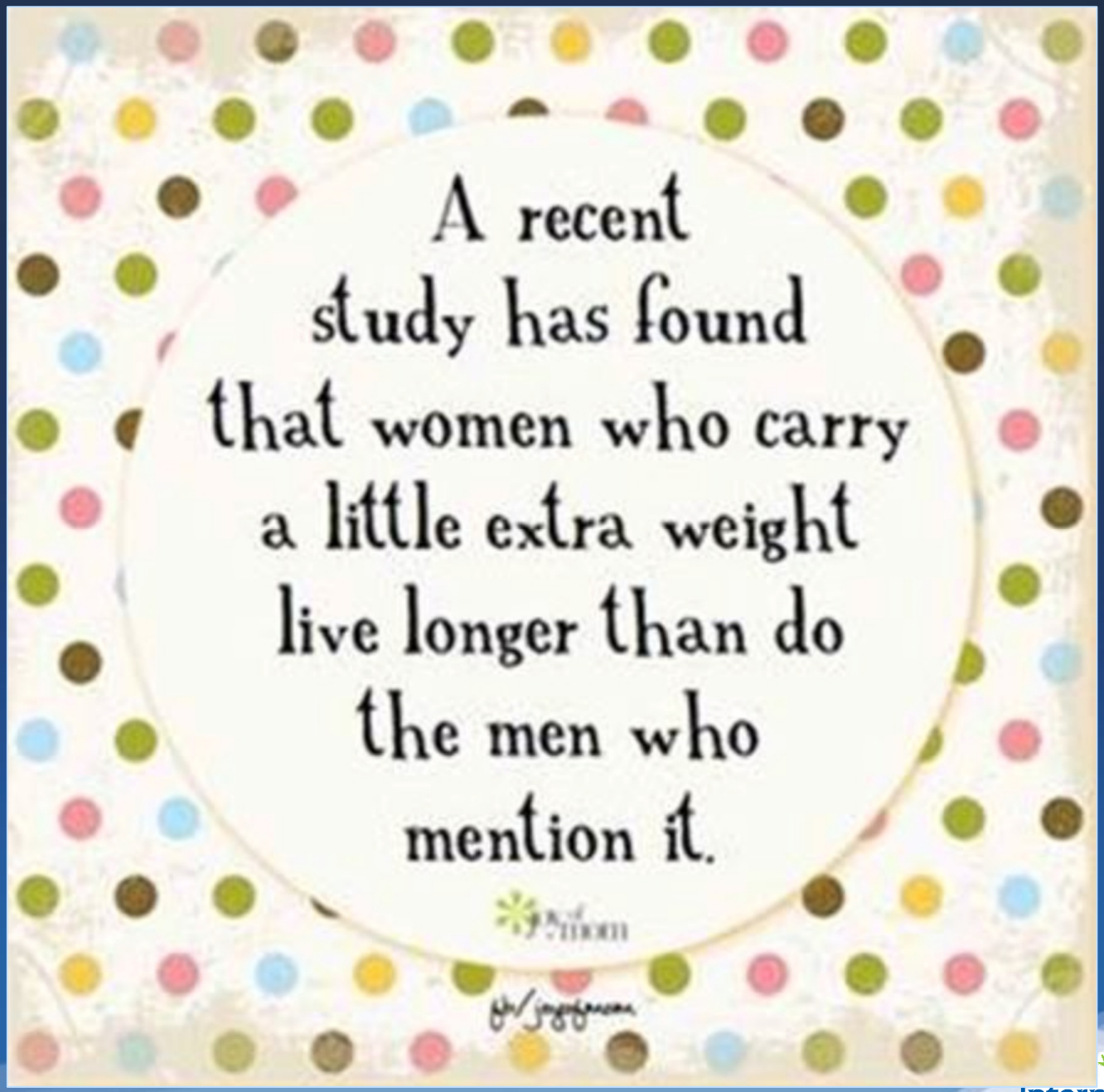
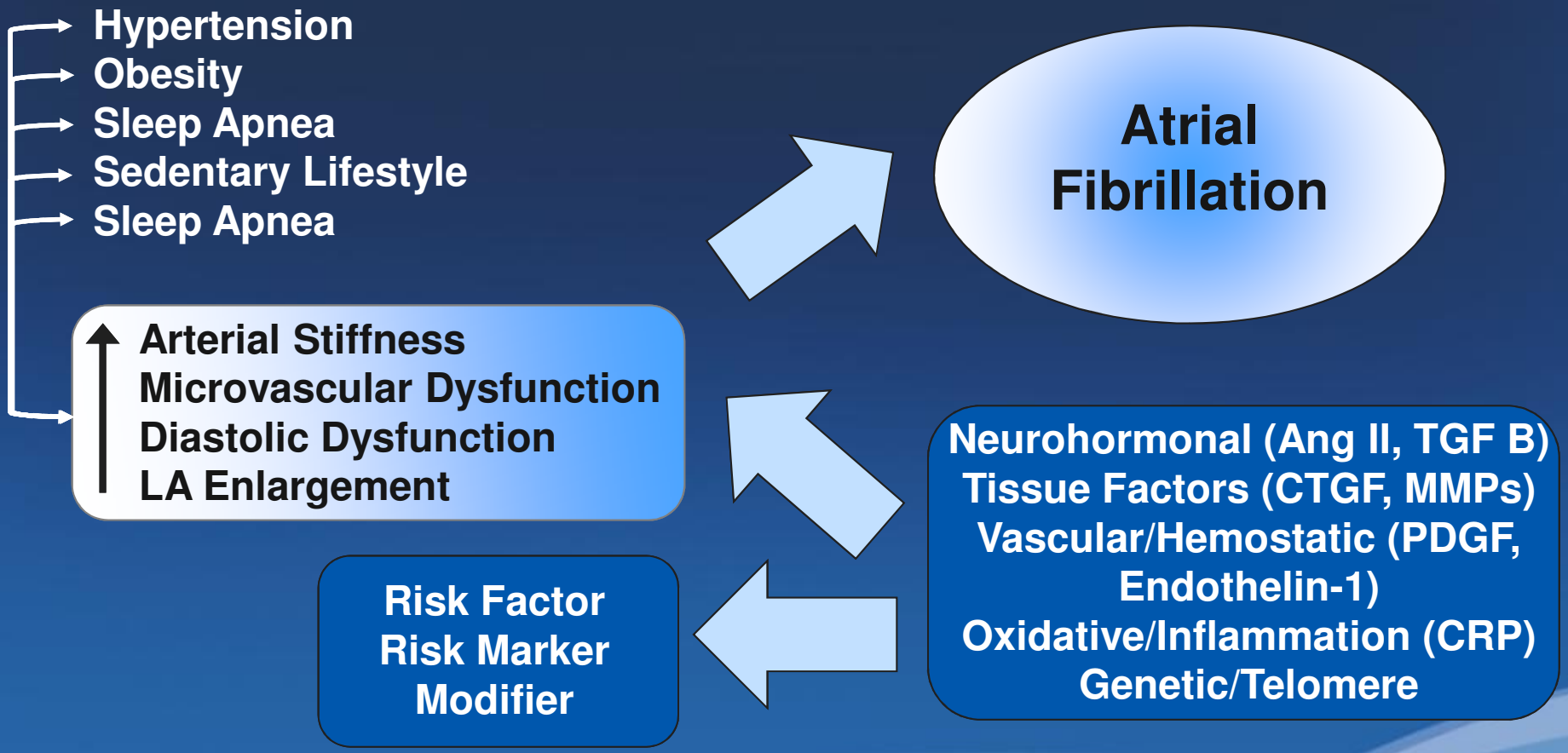

A recent
study has found
that women who carry
a little extra weight
live longer than do
the men who
mention it.

Linking – Diastolic Function, Left Atrial Size, and Left Atrial Appendage Size and Function

Atrial Fibrillation as a Result of Vascular Systemic Disease



Gersh BJ, Mayo

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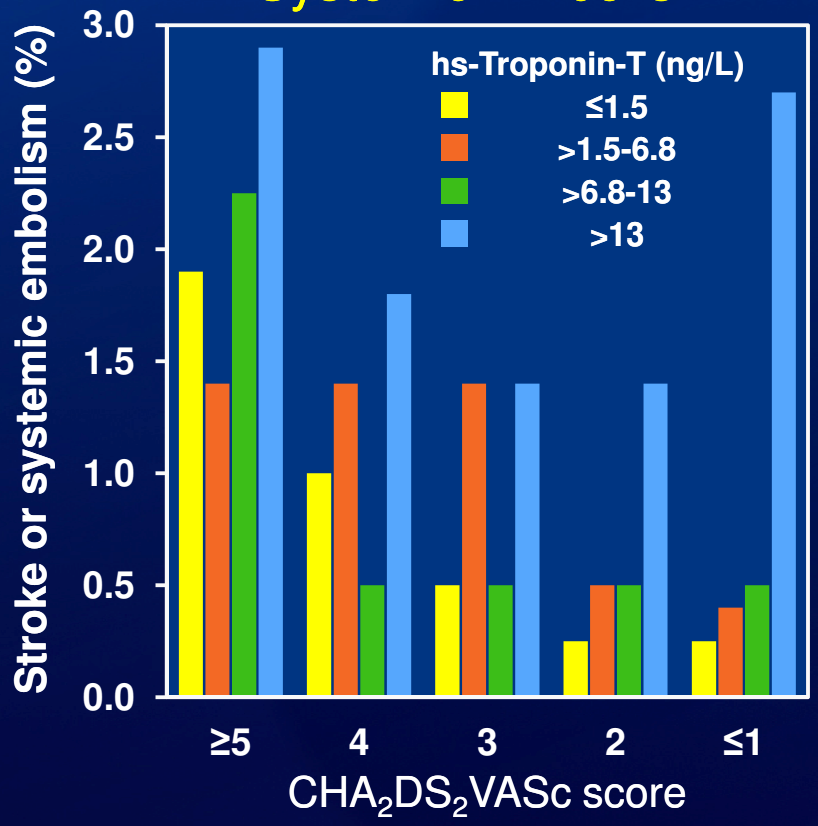
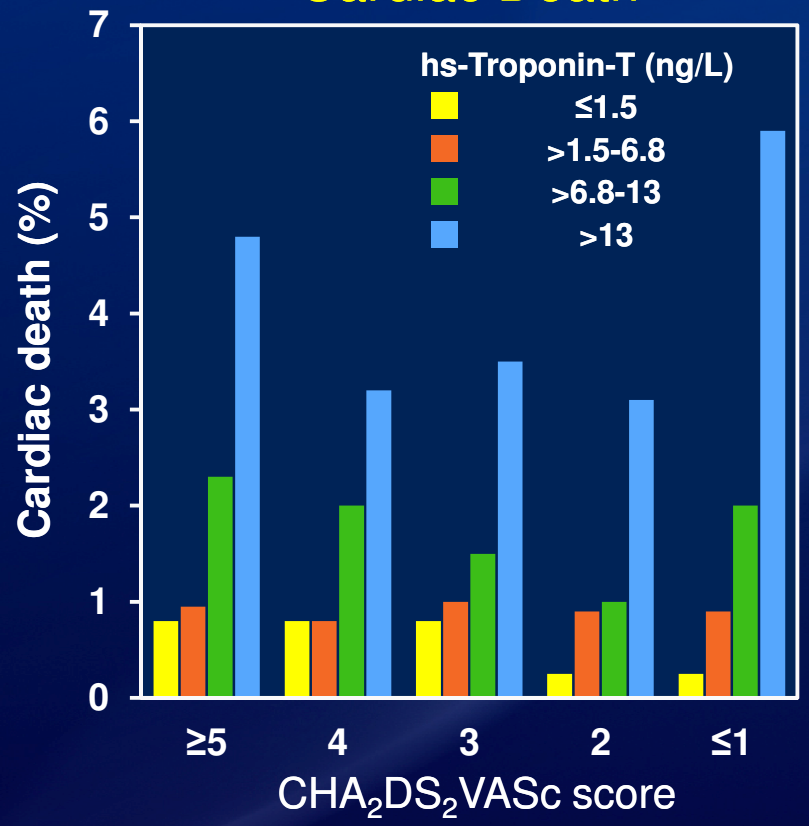
Outcomes in Patients With AF Stratified by CHA_2DS_2-VASc Score and hs-TnT

12,892 Patients ARISTOTLE Trial

Stroke and Systemic Embolism



Cardiac Death



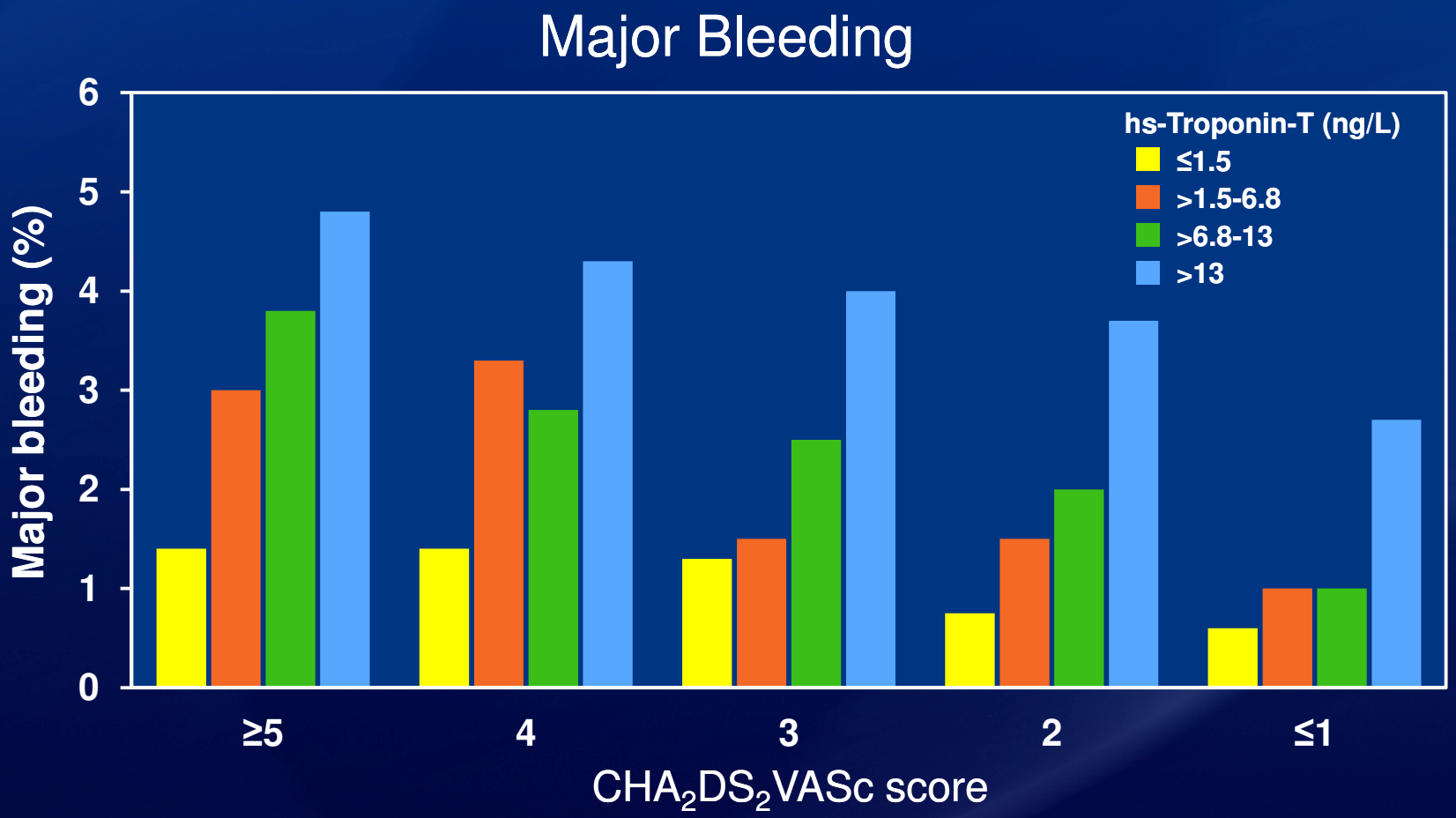
Hijazi: JACC

MAYO CLINIC

Gersh BJ, Mayo

Outcomes in Patients With AF Stratified by CHA_2DS_2-VASc Score and hs-TnT

12,892 Patients ARISTOTLE Trial



Hijazi JACC 2013

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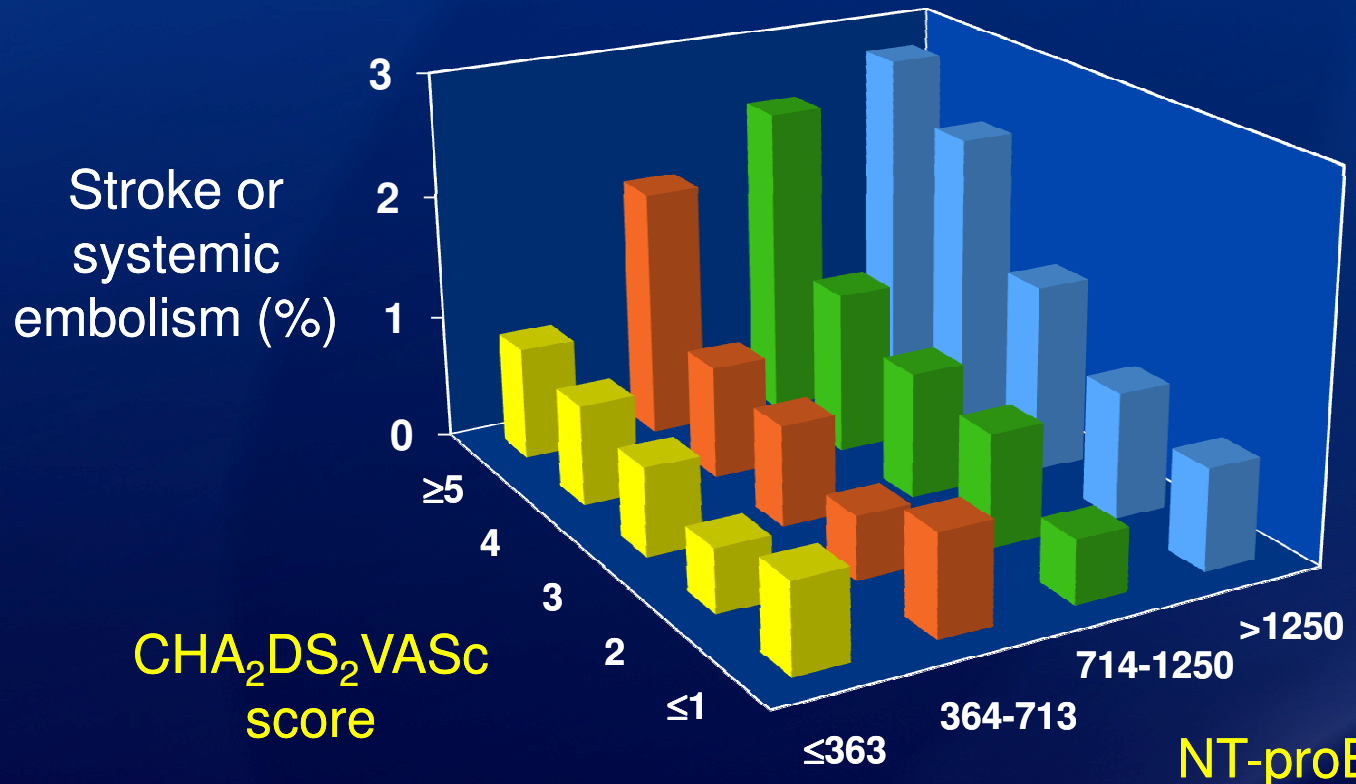
Gersh BJ, Mayo

Stroke and Systemic TE and NT-proBNP in Patients With AFib

18,201 Patients – ARISTOTLE Trial

Stratified by $CHAD_2$ VASc Score



Hijazi: JACC,I 2013

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Gersh BJ, Mayo

Refining Stroke Prediction Using CHA_2DS_2-VASc Score and African-American Ethnicity

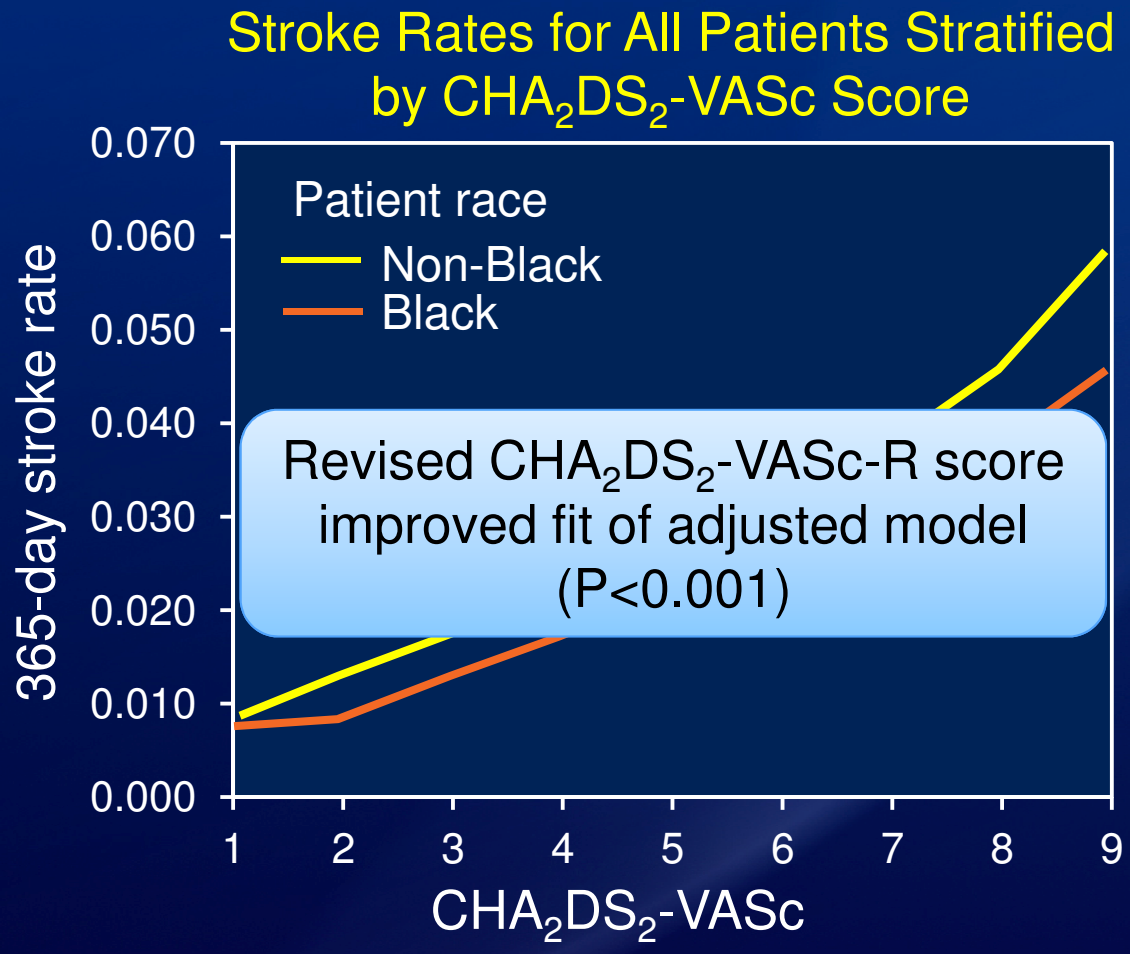
- Medicare claims database
- Newly diagnosed AF
- 460,417 patients

|

Non-Hispanic African-Americans

|

7%



Kabra et al: JACC, 2016

MAYO CLINIC

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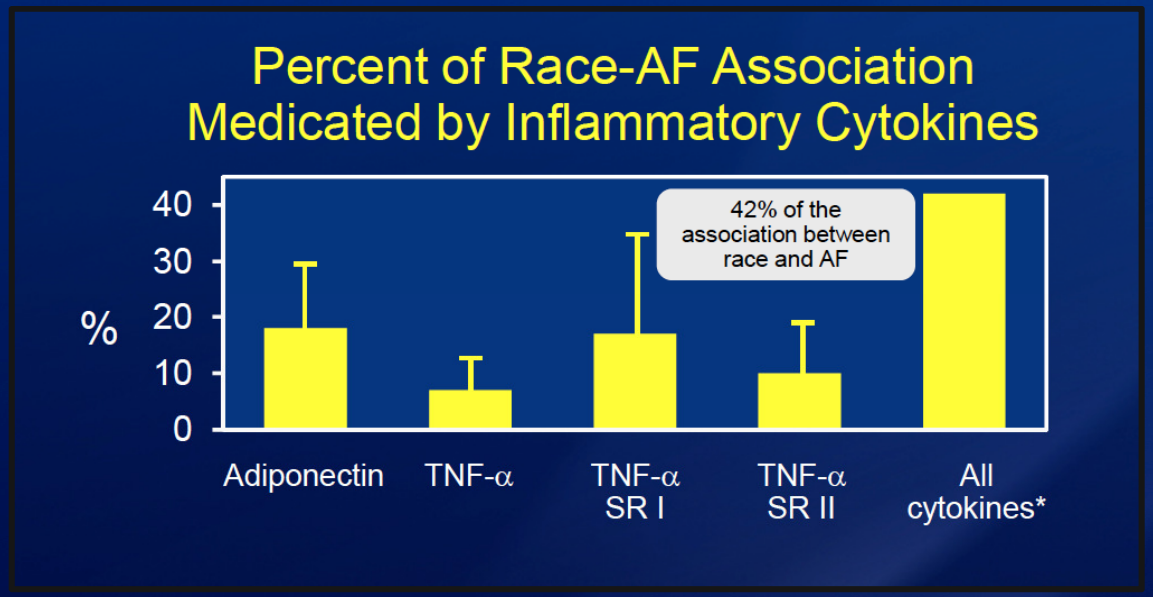
3557507-02

Inflammation as a Mediator of the Association Between Race and aF

Background	Despite a lower prevalence of established AF risk factors, whites have substantially higher rates of AF than Blacks

- 2,768 Participants AF (10.9 yrs mean)
- Adjusted risk: White vs Black (P<0.0001)



Conclusions	Systemic inflammatory pathways significantly mediate the heightened risk of AF among whites

MAYO CLINIC

Dewland JACC EP, 2015

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Association of CRP and CHADS2 Scores in all patients

Crandall MA, Bunch TJ. PACE 2009

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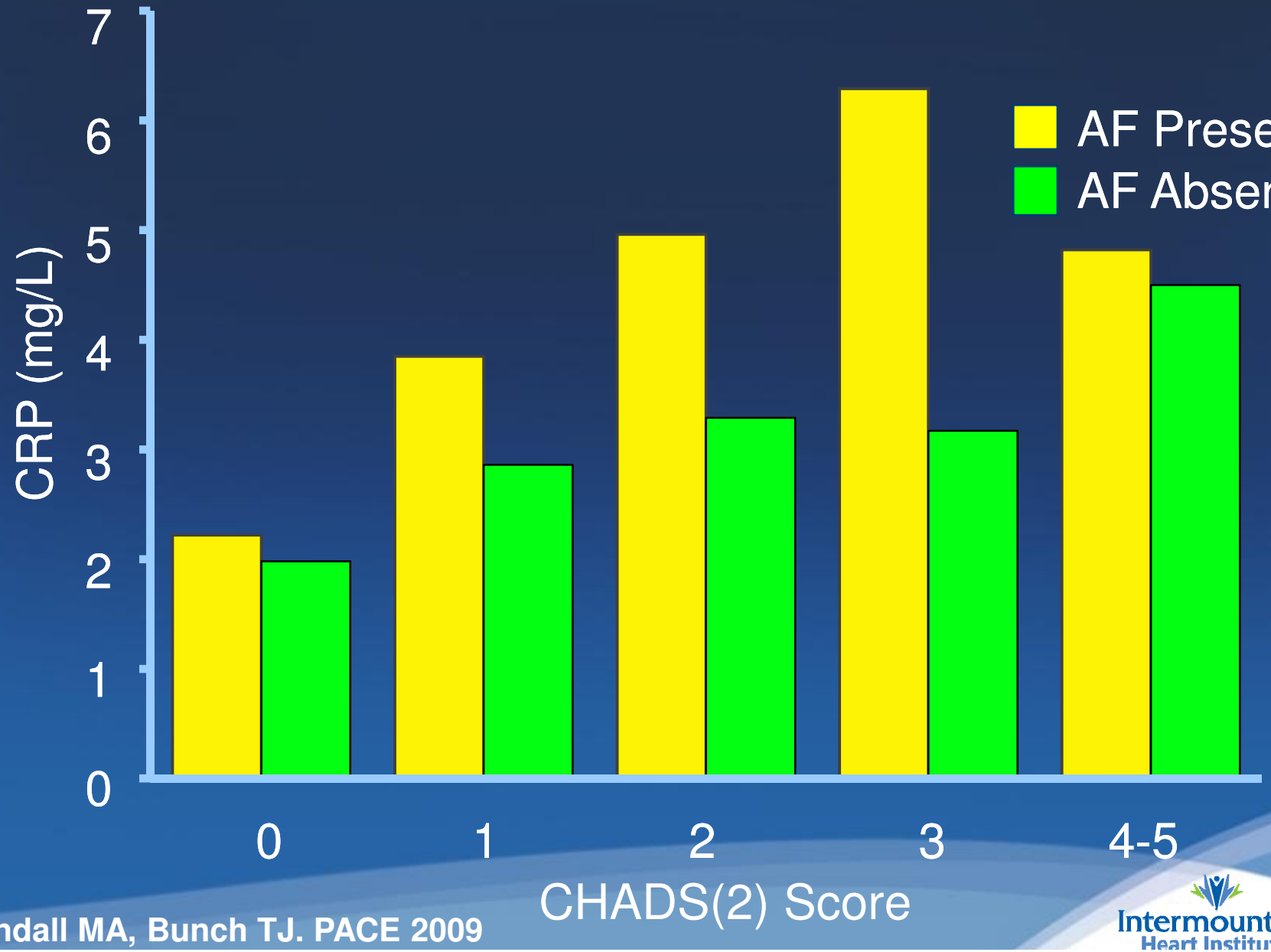
CRP and CHADS2 Scores in patients with and without AF



Crandall MA, Bunch TJ. PACE 2009

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Intermountain Medical Center Risk Score

The Intermountain Mortality Risk Scores (IMRS) are sex-specific tools for risk stratification composed of RDW and other Complete Blood Count (CBC) and/or basic metabolic profile (BMP) components

MAWDS
(All)
No
Yes

PRIOR NUMBER OF DAYS
2

and who were diagnosed with HF in the past, or had a BNP>200 in the past 48 hours, or had Diuretics ordered in the past 48 hours. This report
heart failure nor is it intended to give *any indication of the patient's current condition.*

SYMPTOM	BNP > 200	DIURETIC LAST 24 HRS	EF <= 40	PRIOR CMS HF	KEY WORD	HSPTLZTN PRIOR 30-DAYS	MAWDS	HF DX1 Risk	Readmission Risk	Mortality Risk
HYPOKALEMIA,HYPOMAGN..	Yes	0	0	0	0	0	No	MED	HIGH	LOW
RESP FAILURE, ELEV TROP	Yes	0	Yes	0	0	Yes	No	MED	HIGH	LOW
SEPSIS,PNA	Yes	0	Yes	0	0	0	No	MED	HIGH	LOW
HYPOXIA, RESP FAILURE	0	0	Yes	Yes	Yes	0	No	HIGH	HIGH	MED
PULM HTN WITH RIGHT HEART FAILURE	0	0	0	0	Yes	0	No	MED	LOW	LOW
NEURO	0	Yes	0	0	0	0	No	LOW	LOW	LOW
PANCREATITIS,ANEMIA	0	0	0	0	Yes	0	Yes	MED	MED	LOW
FULL ARREST	0	0	Yes	0	0	0	No	LOW	HIGH	LOW
715.15	0	Yes	0	0	0	0	No	LOW	HIGH	LOW
HYPERKALEMIA	0	Yes	0	0	0	0	No	LOW	HIGH	LOW
CHOLECYSTTIS	0	0	Yes	0	0	Yes	No	LOW	LOW	LOW
UTI RENAL FAILURE	0	0	0	0	0	Yes	No	LOW	HIGH	HIGH
GENERALIZED WEAKNESS	Yes	Yes	Yes	0	Yes	0	No	HIGH	HIGH	MED
CMV; S/P LTP 2015	0	0	Yes	0	0	0	No	LOW	HIGH	HIGH

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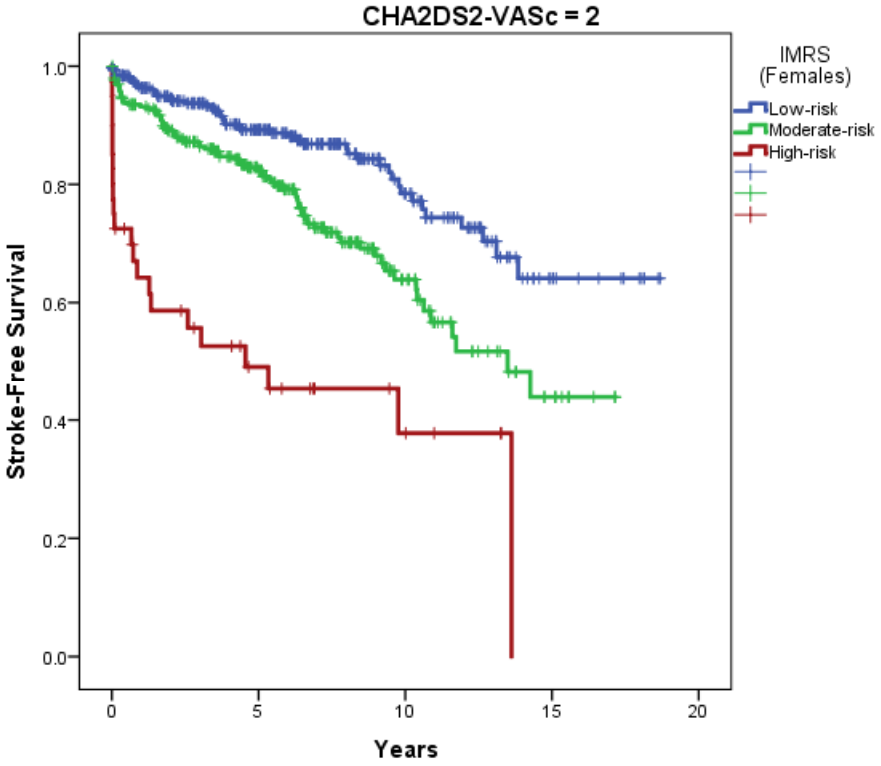
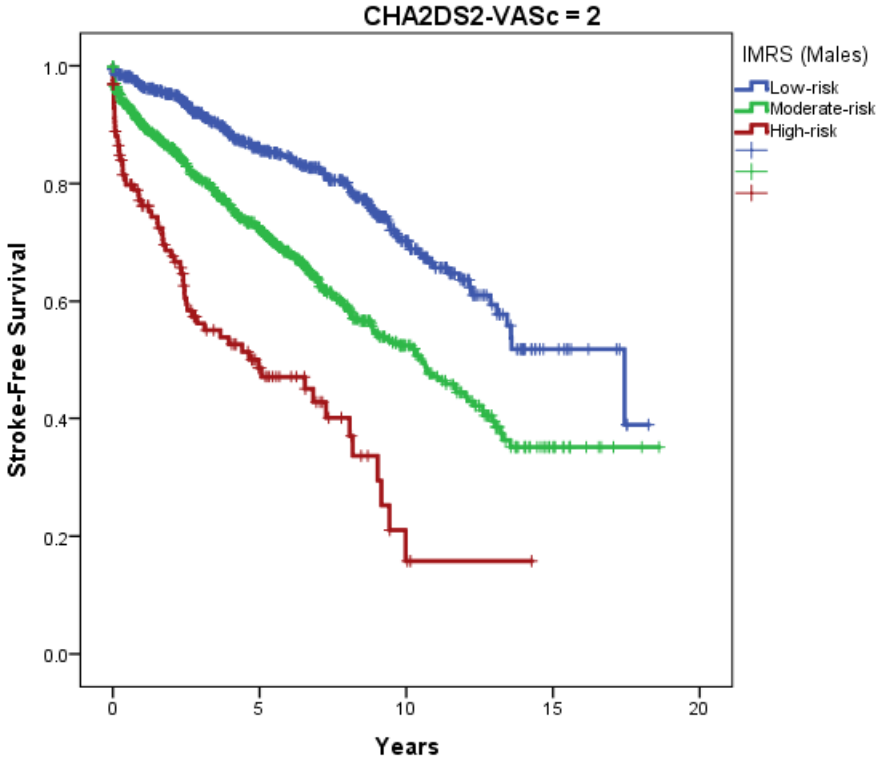
Intermountain Medical Center Risk Score (Low-Medium Risk Pts)





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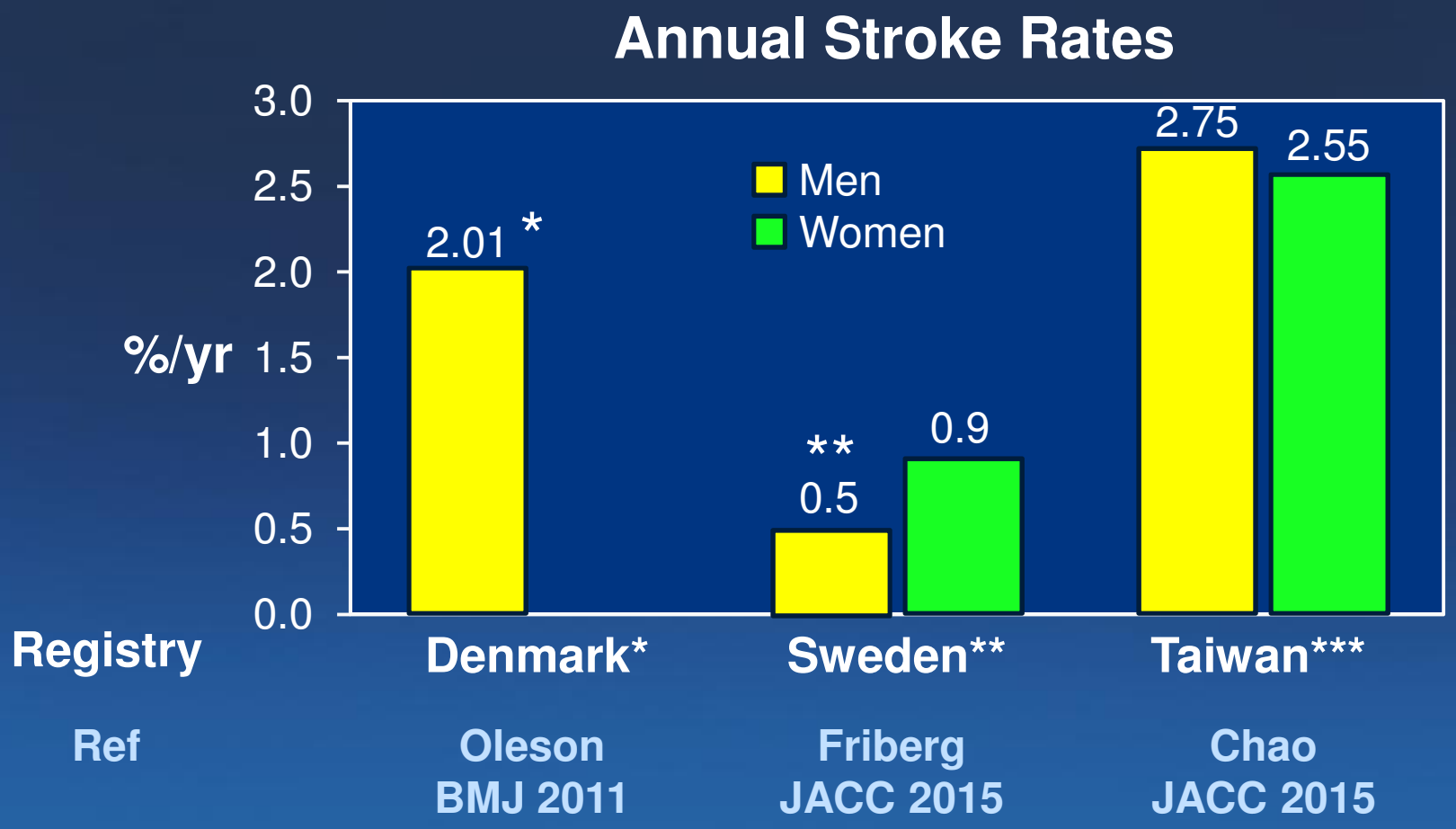
Annual Stroke Rates in Different Cohort Studies

Patients With $CHADS_2$-VASc of 1



*Hospital admission and death due to TE

** Ischemic stroke only

*** Other thromboembolic events and TIA

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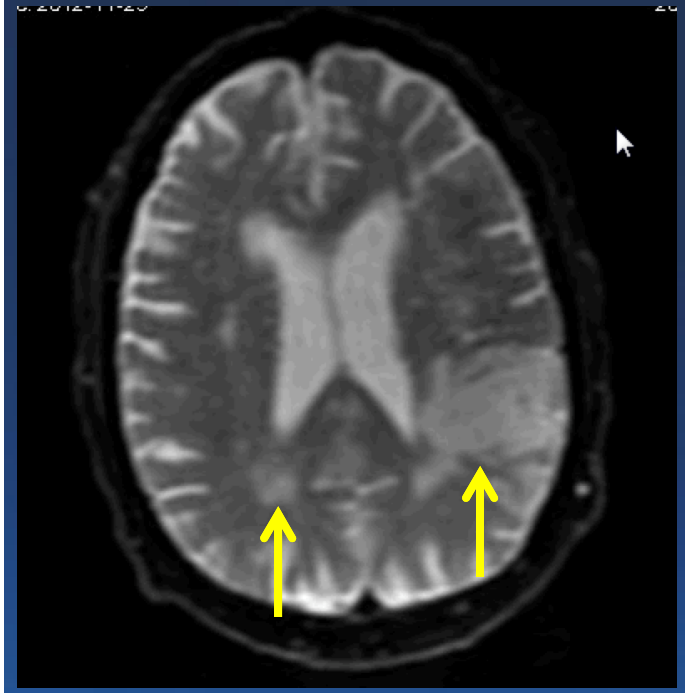
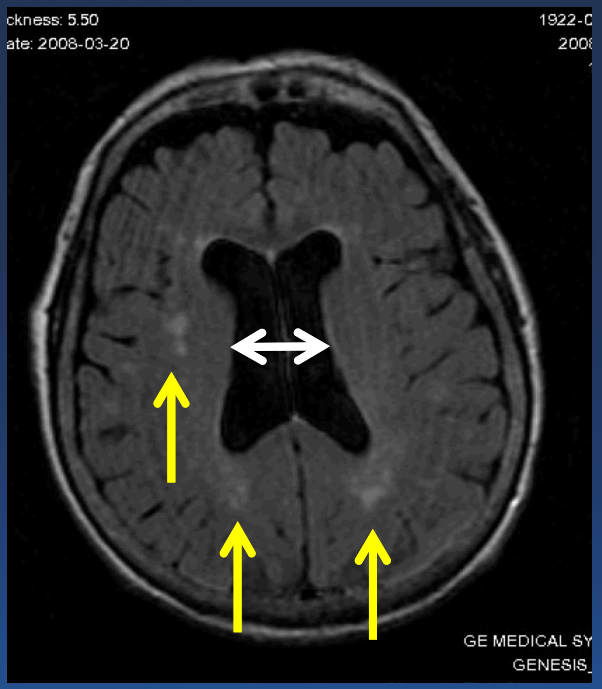
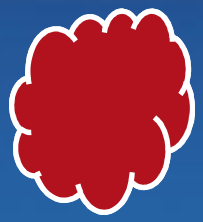
Spectrum of Cerebral Injuries from Atrial Fibrillation and Atrial Fibrillation Management

AF Brain Risk is More than Stroke







Macro Emboli

Micro Emboli ± Micro Bleed

Macro Bleed

acobs V, Bunch TJ. Trends in CV Med 2014

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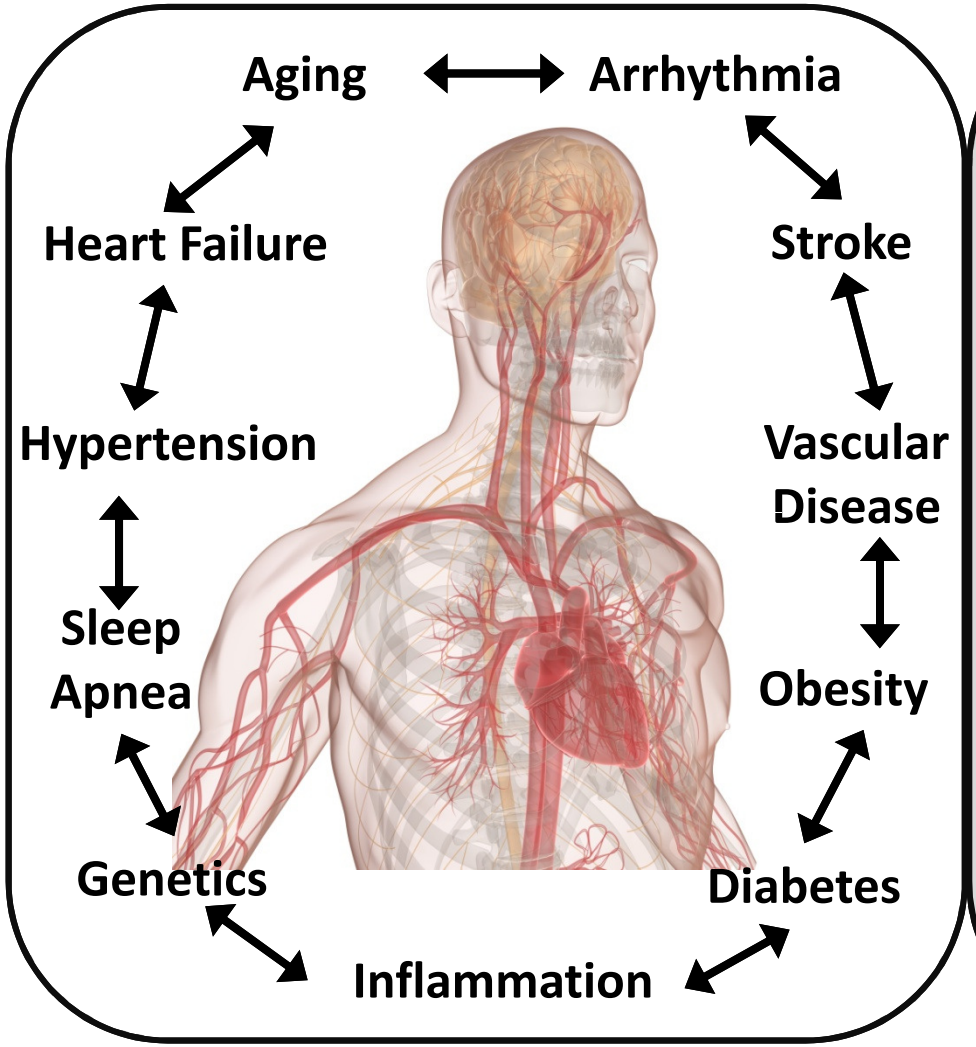
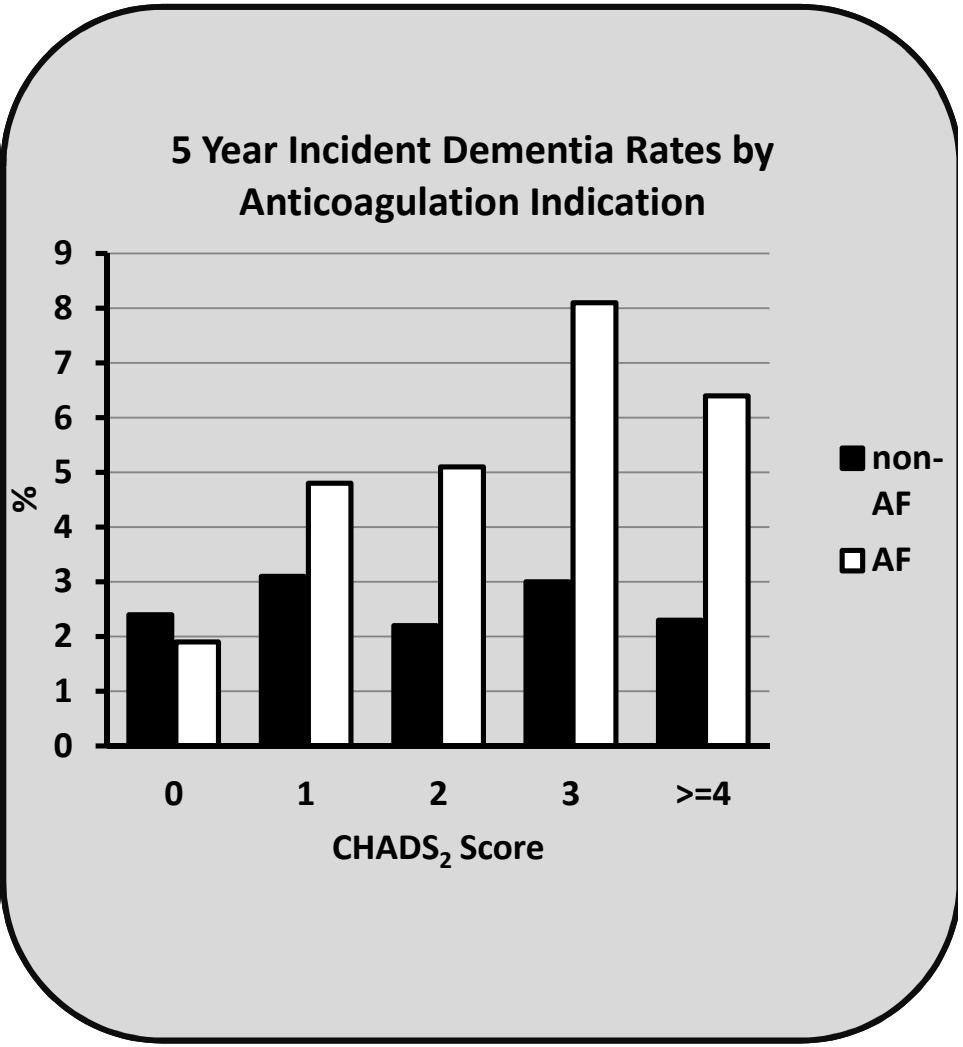
Linking Heart and Brain Disease



Risk of Dementia from Systemic Disease and Atrial Fibrillation



Graves K, Bunch TJ. AHJ (submitted w revisions)

Dementia Risk in Low, Medium, High Risk AF Patients Adjusted for IMRS

	Females	Males
CHADS2Vasc=0		
Moderate vs. Low IMRS	---	HR=1.40, p=0.28
High vs. Low IMRS	---	HR=3.69, p=0.03
CHADS2Vasc=1		
Moderate vs. Low IMRS	HR=1.71, p=0.04	HR=1.75, <0.0001
High vs. Low IMRS	HR=4.15, p=0.02	HR=0.95, p=0.90
CHADS2Vasc=2		
Moderate vs. Low IMRS	HR=1.67, p<0.0001	HR=1.92, p<0.0001
High vs. Low IMRS	HR=1.74, p=0.03	HR=3.33, p<0.0001
CHADS2Vasc≥3		
Moderate vs. Low IMRS	HR=1.77, p<0.0001	HR=1.76, p<0.0001
High vs. Low IMRS	HR=3.12, p<0.0001	HR=2.41, p<0.0001

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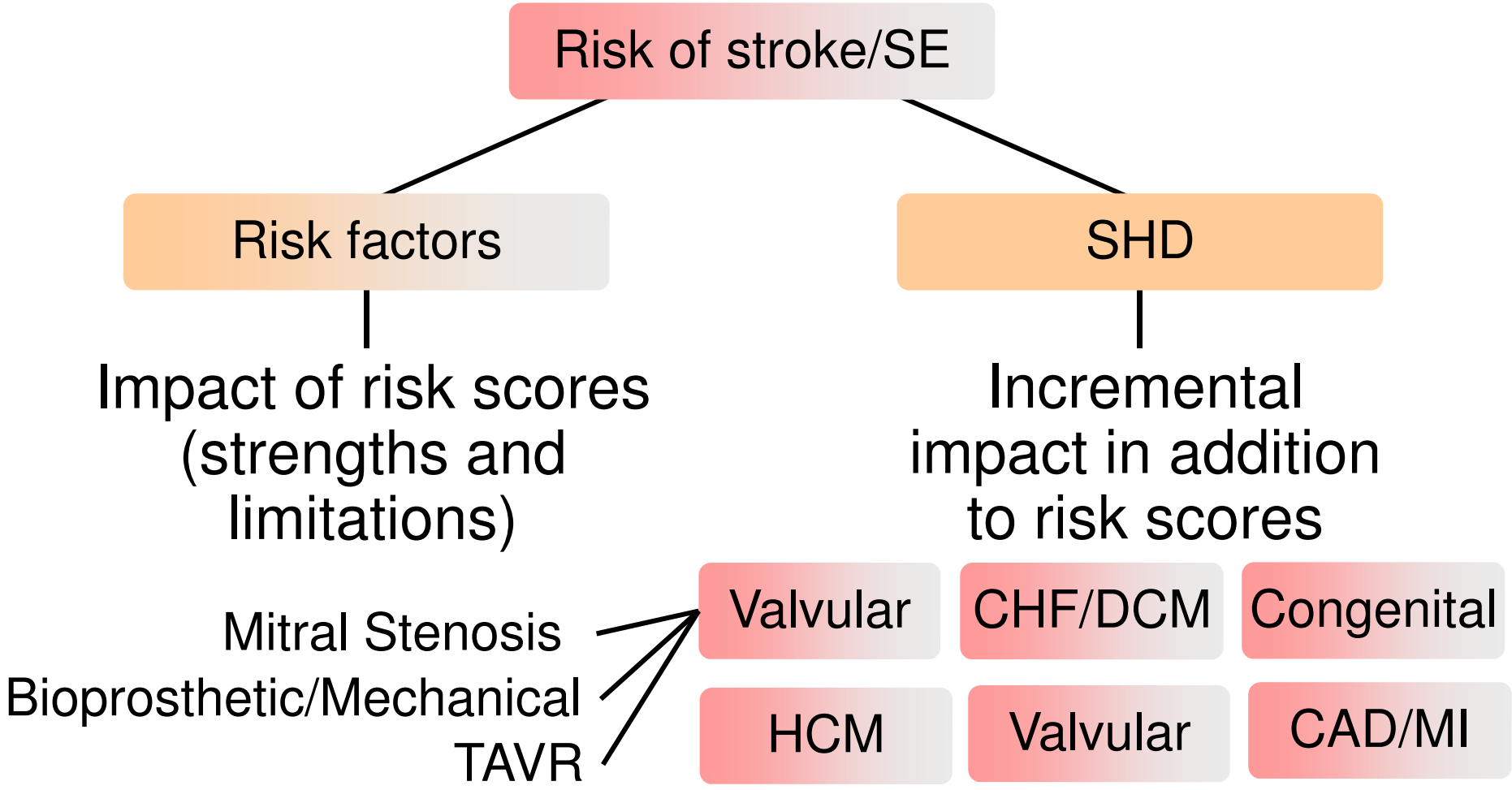
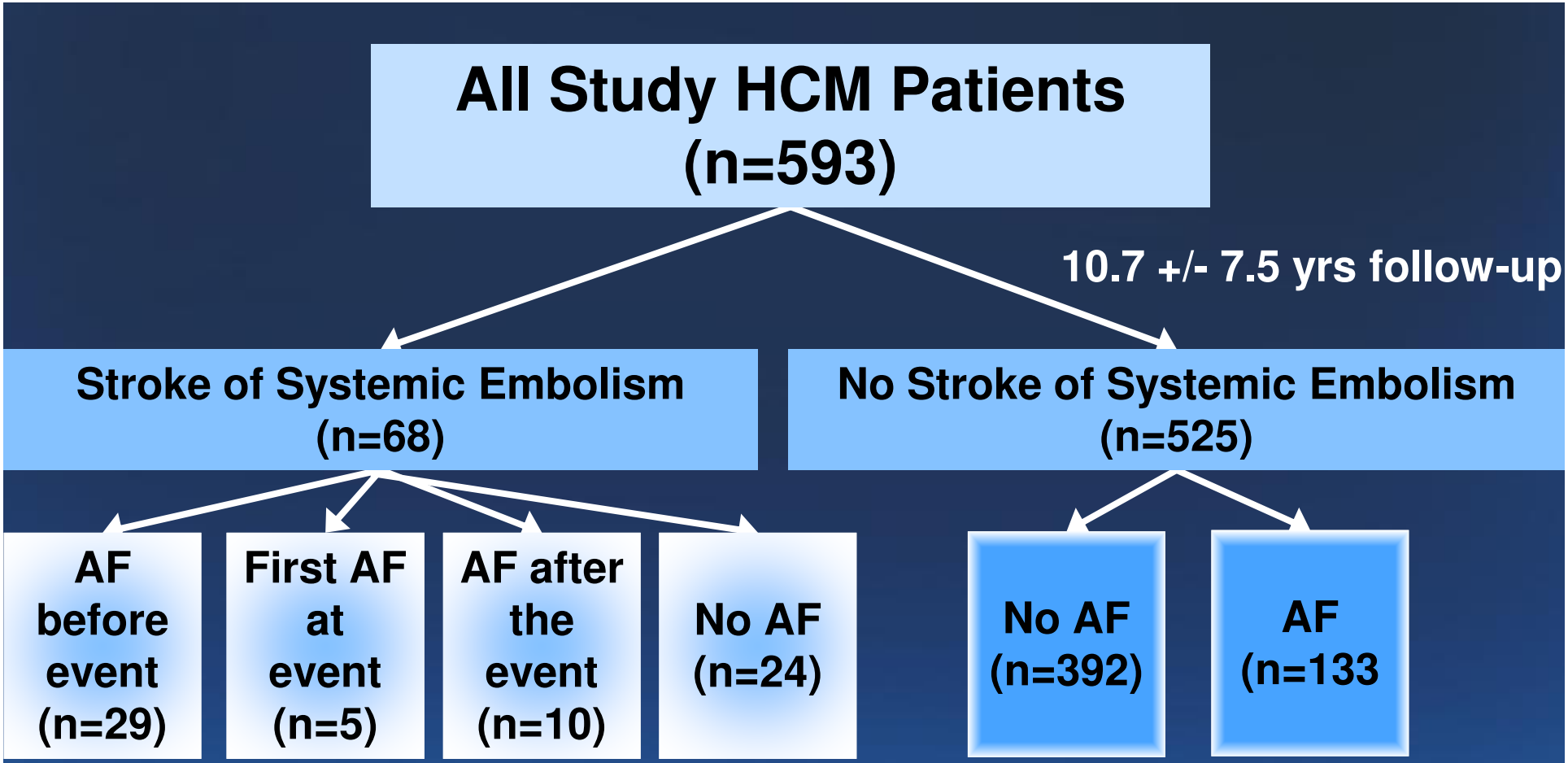
Atrial Fibrillation: Impact of Risk Factors and Structural Heart Disease (SHD)



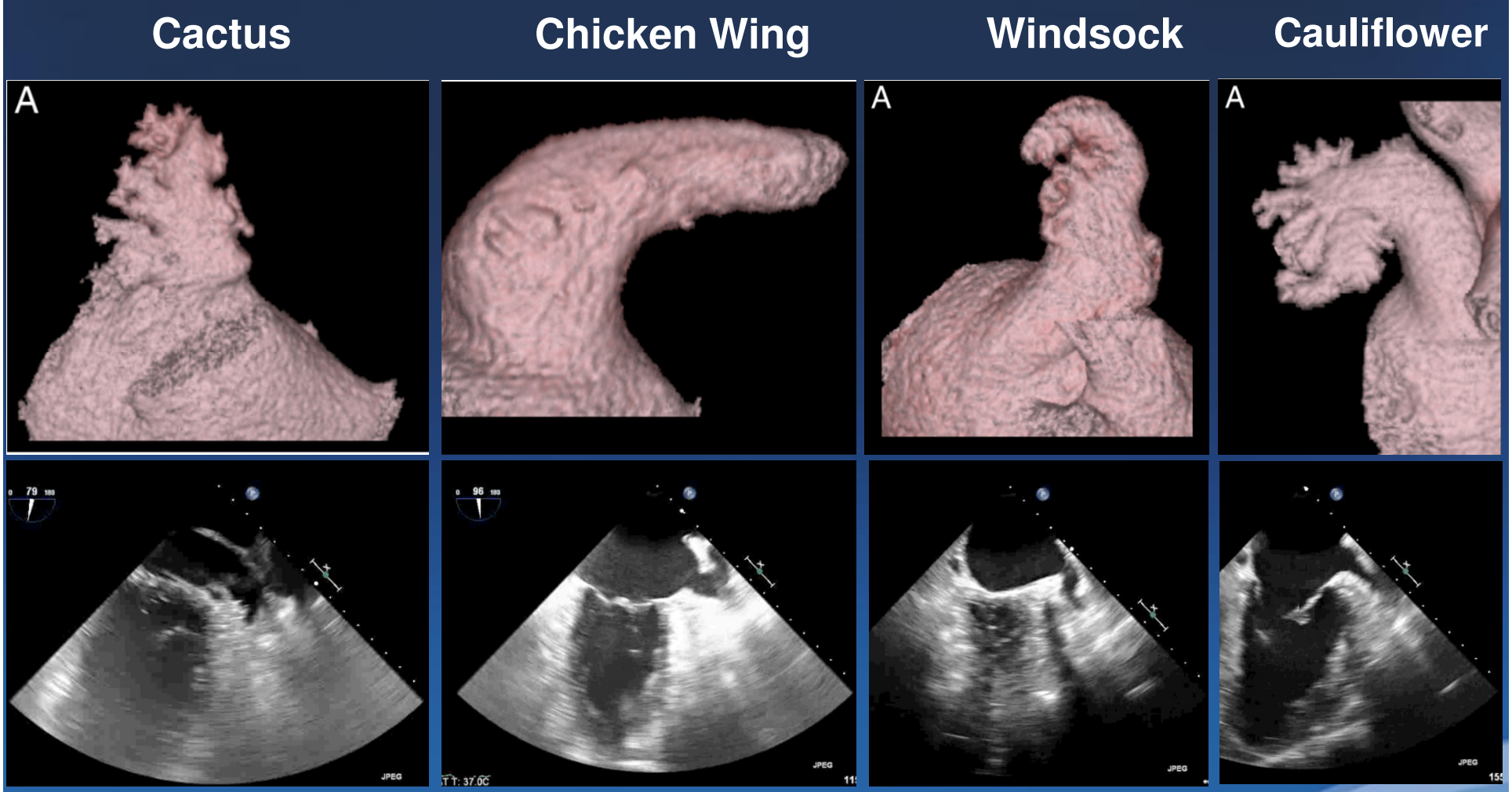


- AF: 17.9 % event rate versus 9.0% without AF
- 57% in the cohort that developed embolic events on anticoagulation with warfarin (risk factors: older age, larger LA dimensions)

Haruki, et al. Stroke 2016

Intermountain® Heart Institute

Left Atrial Appendage Morphologies



Di Biase L, et al. JACC 2012

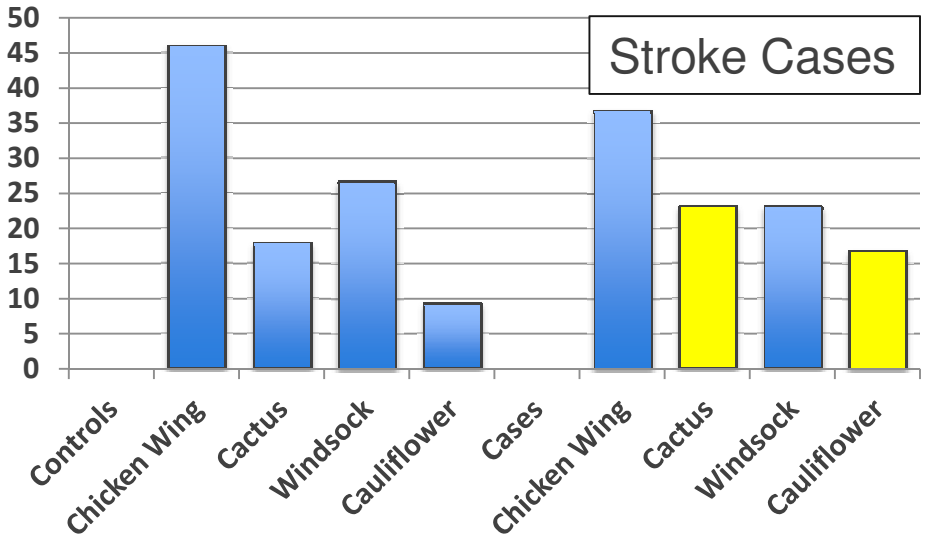
Intermountain® Heart Institute

Relationship between left atrial appendage morphology and stroke in patients with atrial fibrillation

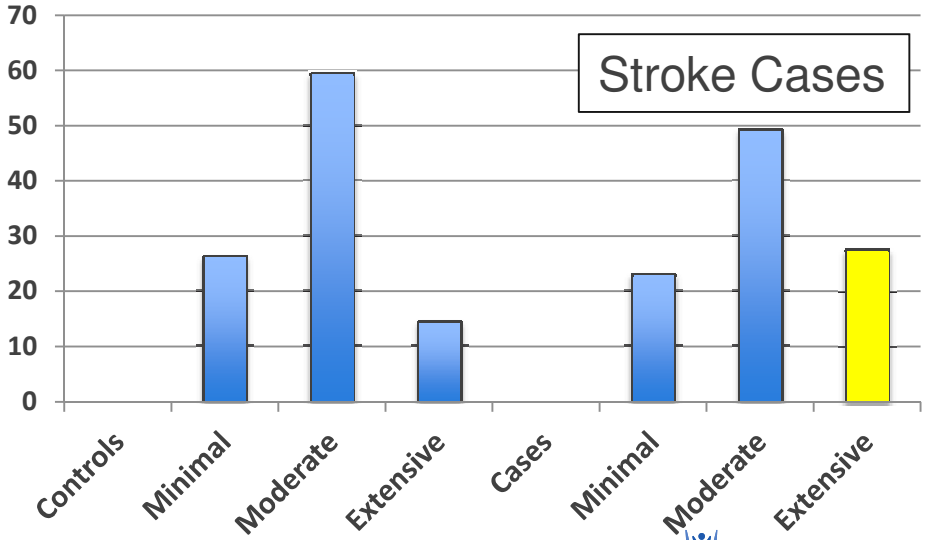
Irfan M. Khurram, MD,[*] Jane Dewire, BA,[*] Michael Mager, RT (R) (MR),[†] Farhan Maqbool, MD,[*] Stefan L. Zimmerman, MD,[†] Vadim Zipunnikov, PhD,[‡] Roy Beinart, MD,[*] Joseph E. Marine, MD, FHRS,[*] David D. Spragg, MD, FHRS,[*] Ronald D. Berger, MD, PhD, FHRS,[*] Hiroshi Ashikaga, MD, PhD,[*] Saman Nazarian, MD, PhD, FHRS,[*] Hugh Calkins, MD, FHRS[*]

From the [*]Department of Medicine/Cardiology, [†]Department of Radiology, and [‡]Department of Biostatistics, Johns Hopkins University, Baltimore, Maryland.

LAA Morphology and Stroke (Cases)



LAA Trabeculations and Stroke (Cases)



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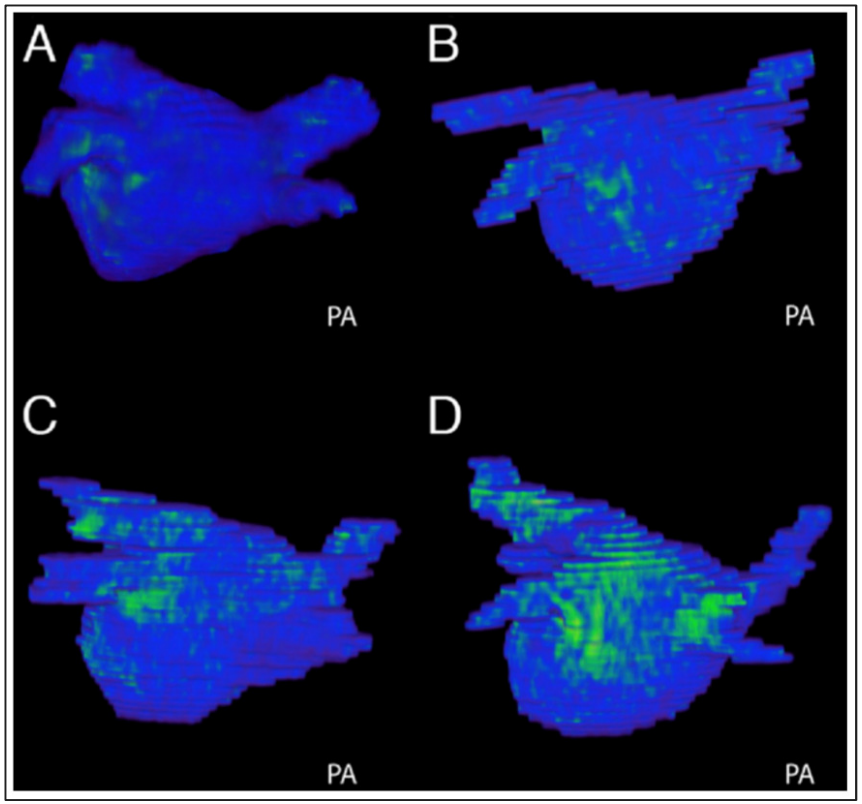
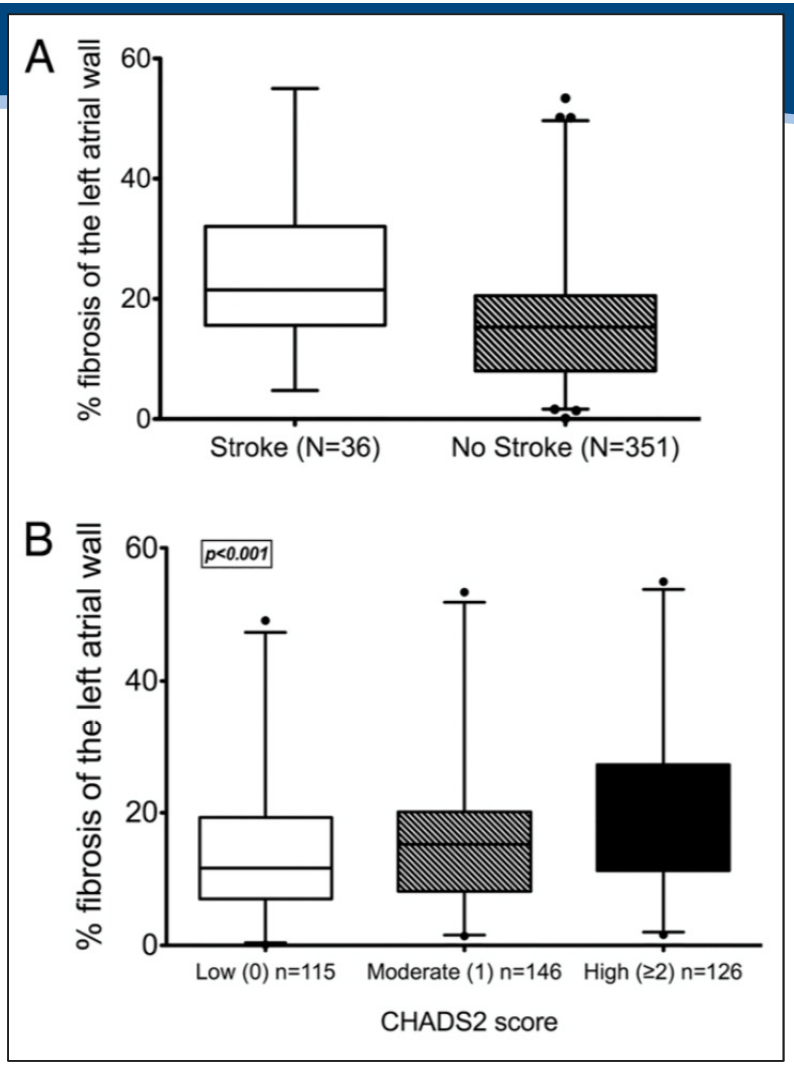
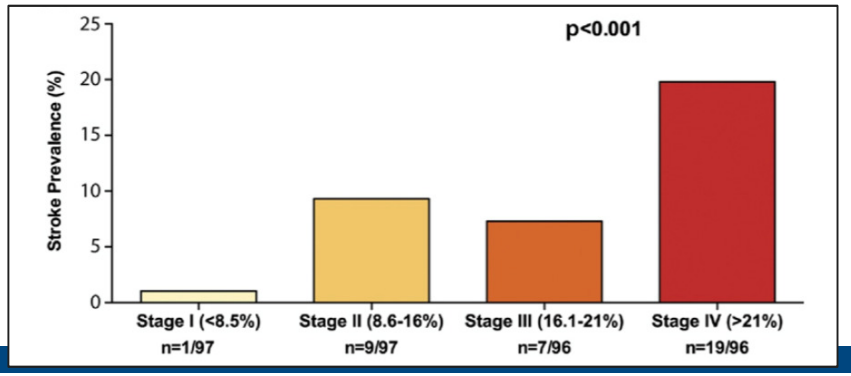
Association of Left Atrial Fibrosis Detected by Delayed-Enhancement Magnetic Resonance Imaging and the Risk of Stroke in Patients With Atrial Fibrillation

Marcos Daccarett, MD, MSc,* Troy J. Badger, MD,* Nazem Akoum, MD,* Nathan S. Burgon, BSc,* Christian Mahnkopf, MD,*† Gaston Vergara, MD,* Eugene Kholmovski, PhD,* Christopher J. McGann, MD,* Dennis Parker, PhD,* Johannes Brachmann, MD, PhD,† Rob S. MacLeod, PhD,* Nassir F. Marrouche, MD*

Salt Lake City, Utah; and Coburg, Germany







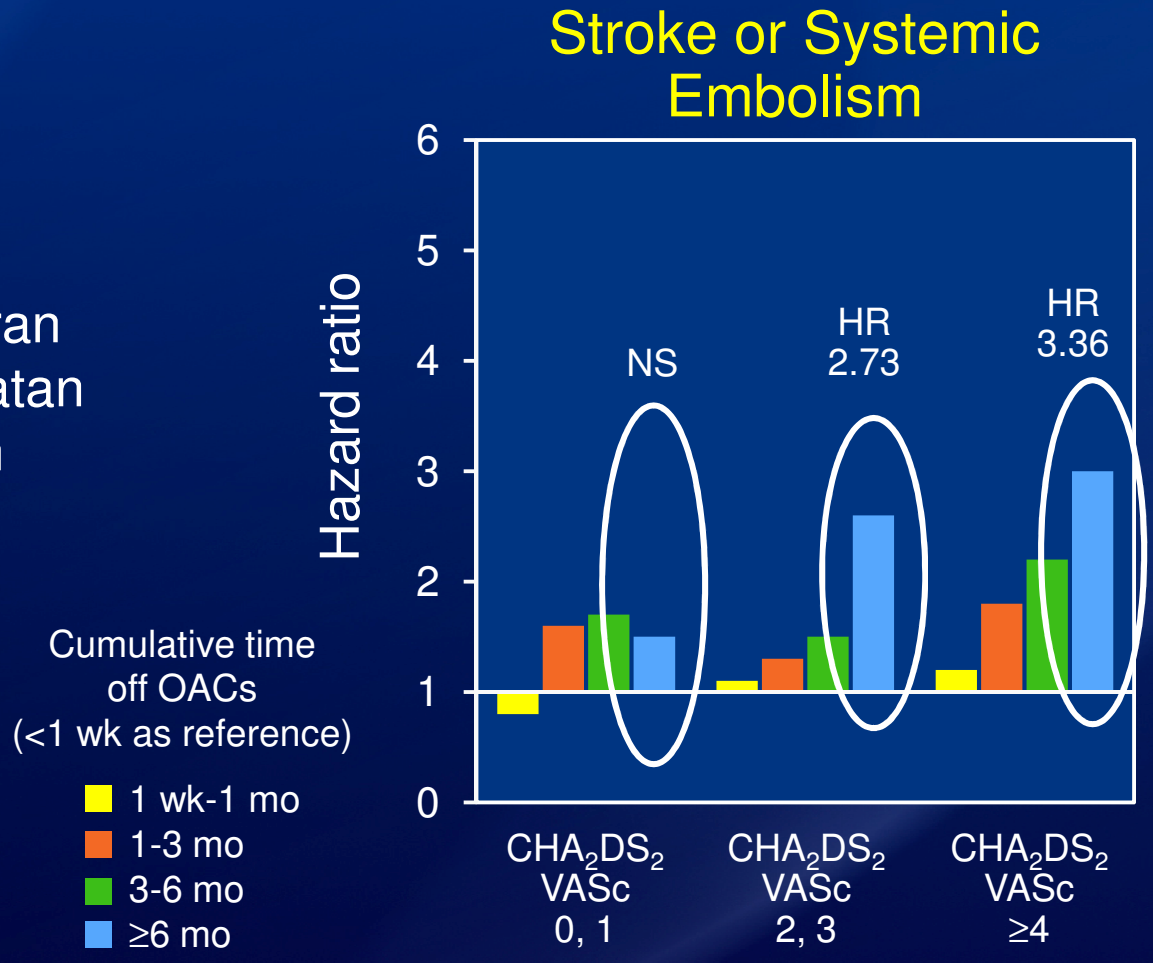
Adherence to Warfarin and NOAC – Clinical Outcomes

Insurance Administrative Claims Database (USA – 100 Million Enrollees Over 20 Yr Period)

- 64,661 pt
- 2000-2014
- AF (OAC)
  - Warfarin
  - Dabigatran
  - Rivaroxatan
  - Apixiban

Adherence (≥80 days covered by OAC)

43.2%



Noseworthy P (In Press)

MAYO CLINIC

Taking on New Risk with Old and Limited Treatments

That should fix it

MAYO CLINIC

Promotes Active Lifestyles

Boosts Personality

Gives Body Essential Sugars

Effect of Yoga on Arrhythmia Burden, Anxiety, Depression, and Quality of Life in Paroxysmal Atrial Fibrillation

The YOGA My Heart Study

Dhanunjaya Lakkireddy, MD,* Donita Atkins, RN,* Jayasree Pillarisetti, MD,* Kay Ryschon, MS,† Sudharani Bommana, MPHIL,* Jeanne Drisko, MD,‡ Subbareddy Vanga, MBBS, MS,§ Buddhadeb Dawn, MD*

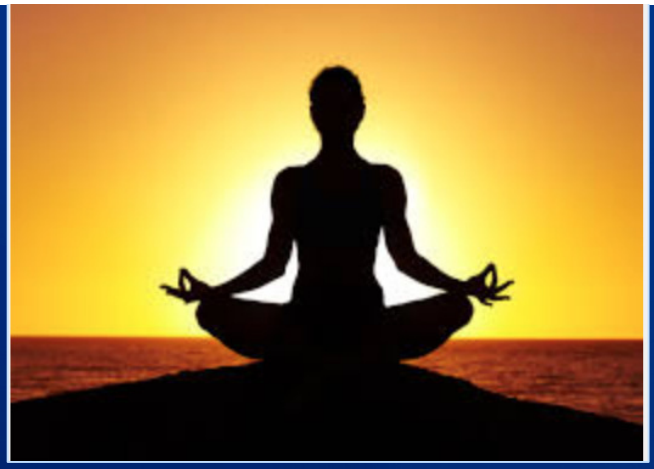
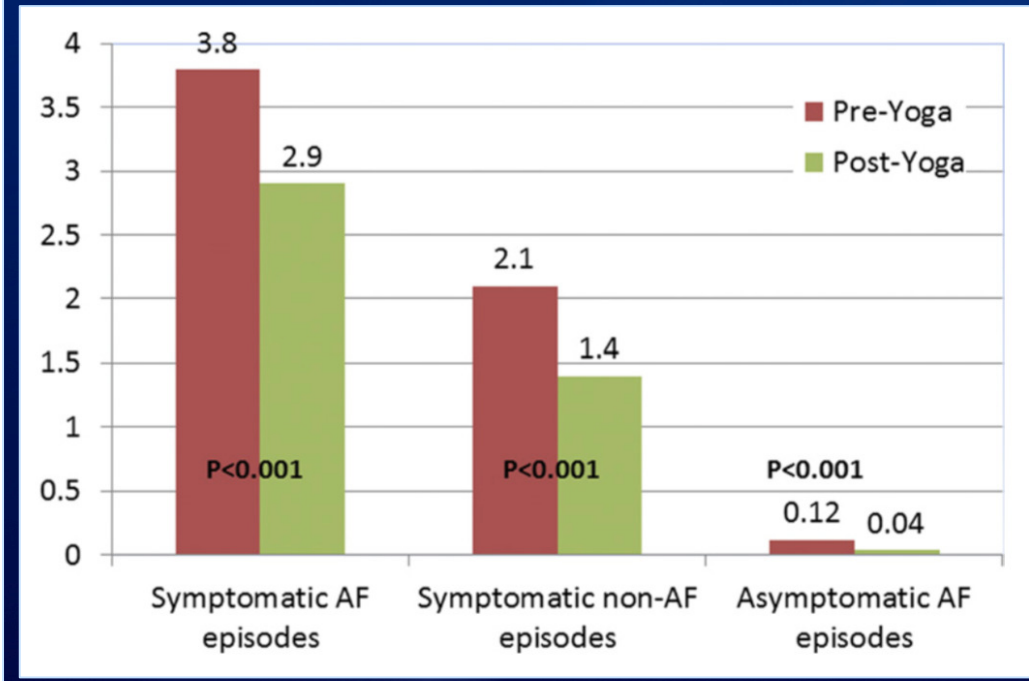


Table 1 Baseline Characteristics of Participants

Clinical characteristics	
Gender (M/F)	23 (46.9)/26 (53.1)
Age, yrs	60.6 ± 11.5
BMI, kg/m^2	28.0 ± 5.9
Duration of AF, months	63.9 ± 71.9
Symptomatic AF	43 (87.7)
LV ejection fraction, %	58.5 ± 6.3
LA size, cm	4.01 ± 0.50
Comorbid conditions	
Coronary artery disease	9 (18.4)
Diabetes mellitus	1 (2.0)
Hypertension	19 (38.8)
Hyperlipidemia	20 (40.8)
Obstructive sleep apnea	11 (22.4)
Prior revascularization (PCI/CABG)	4 (8.2)
Medication use	
Aspirin	28 (57.1)
Beta-blockers	31 (63.3)
ACE-I/ARB	10 (20.4)
Statins	16 (32.7)
Antiarrhythmic medications	38 (77.6)



Summarizing Risks Markers of Stroke in Atrial Fibrillation Patients

Risk Scores That Dynamically Assess Severity of Systemic Disease State are Needed

CHADS2 and CHADS2 Vasc Persist due to ease of Use

New Risk Factors May More Accurately Reflect Disease State

- **Structural Heart Disease**
  - HCM
  - DCM
  - Non Compaction
- **Biomarkers**
  - TnT
  - CRP
  - D-Dimer
  - Nt-ProBNP
  - vWF
- **Heart Imaging**
  - LAA Size/Function /Morphology
  - LA fibrosis
- Other
  - Renal
  - Sleep Apnea

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Thank You

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