Innovative Treatments for Atrial Fibrillation

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AFib Clinic

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BOULDER COMMUNITY HEALTH'S AFib Clinic at Boulder Heart

Our Passions

- Our Community
- Evidence-based care
- Quality of life
- Education and shared decision-making
- Cutting edge technology and resources

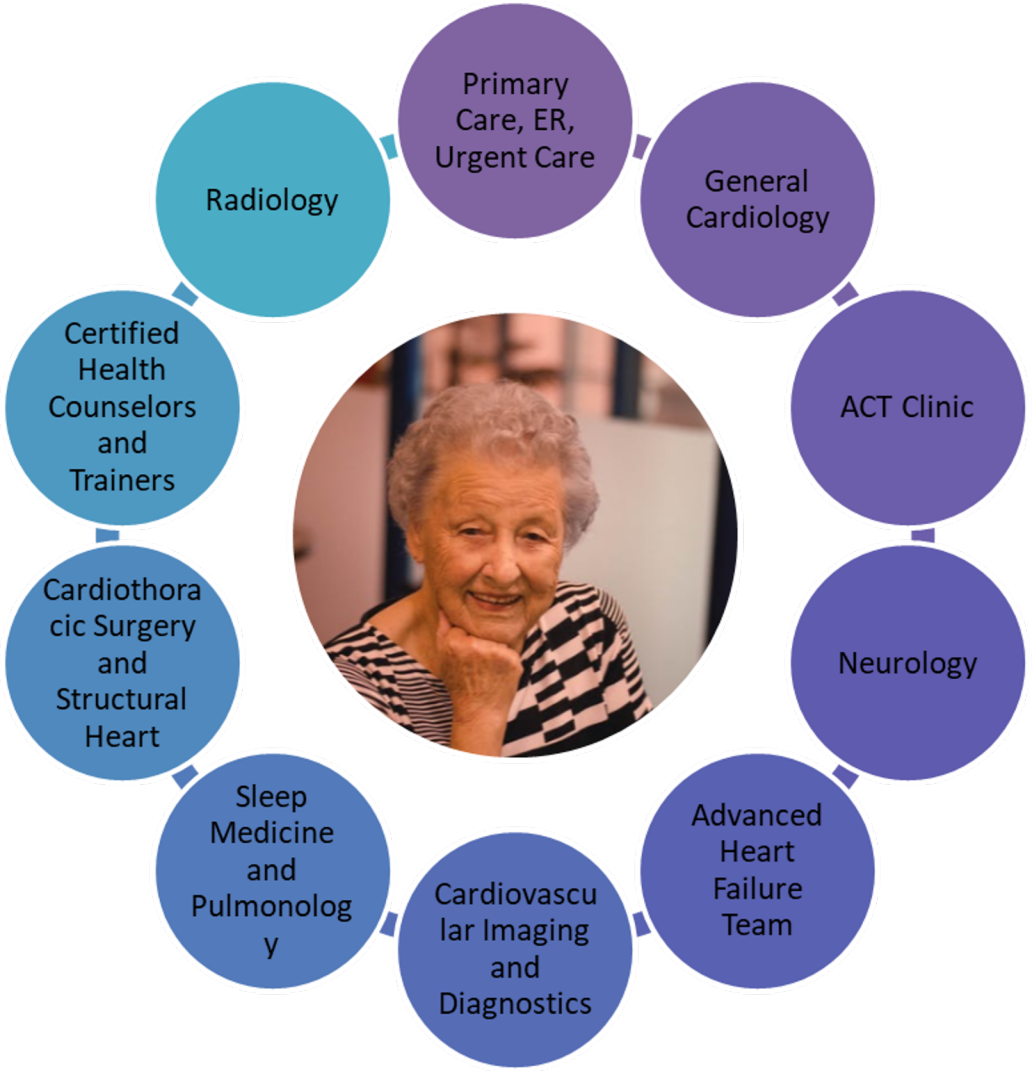
Our Approach

- Whole patient care
- Multispecialty team approach
- Collaborative decision-making
- Full spectrum of care
- Emphasis on comprehensive evaluation, individualized care planning, listening, education, and support

Our Goals

- Best possible outcomes (our 1st priority)
- Fewer ER visits
- Aggressive stroke prevention
- Streamlined, efficient access to care
- Lower costs for patients and families
- Supportive, connected care

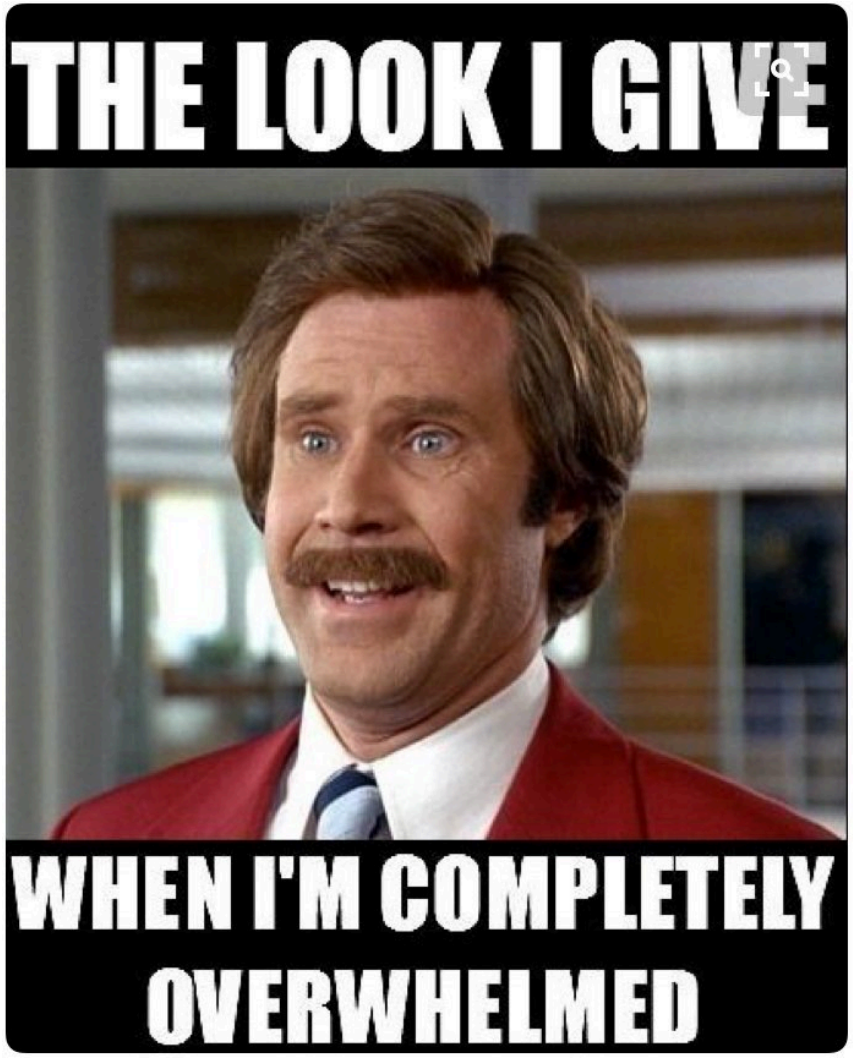
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What Can I Do About My Atrial Fibrillation?

Maria Anderson, MD
Cardiac electrophysiologist
Boulder Heart


THE LOOK I GIVE
WHEN I'M COMPLETELY OVERWHELMED

Lifestyle Measures Are Critical!

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- You have the power to improve your AFib!
- Lifestyle measures
  - Improve freedom from AFib
  - Prevent AFib from progressing from paroxysmal (episodic) to persistent (staying in AFib)
  - Make ablation more effective
  - Decrease risk of stroke

Lifestyle modifications for treatment of atrial fibrillation

Melissa E Middeldorp,[1,2] Jonathan Ariyaratnam,[1,2] Dennis Lau,[1,2] Prashanthan Sanders [1,2]

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/heartjnl-2019-315327).

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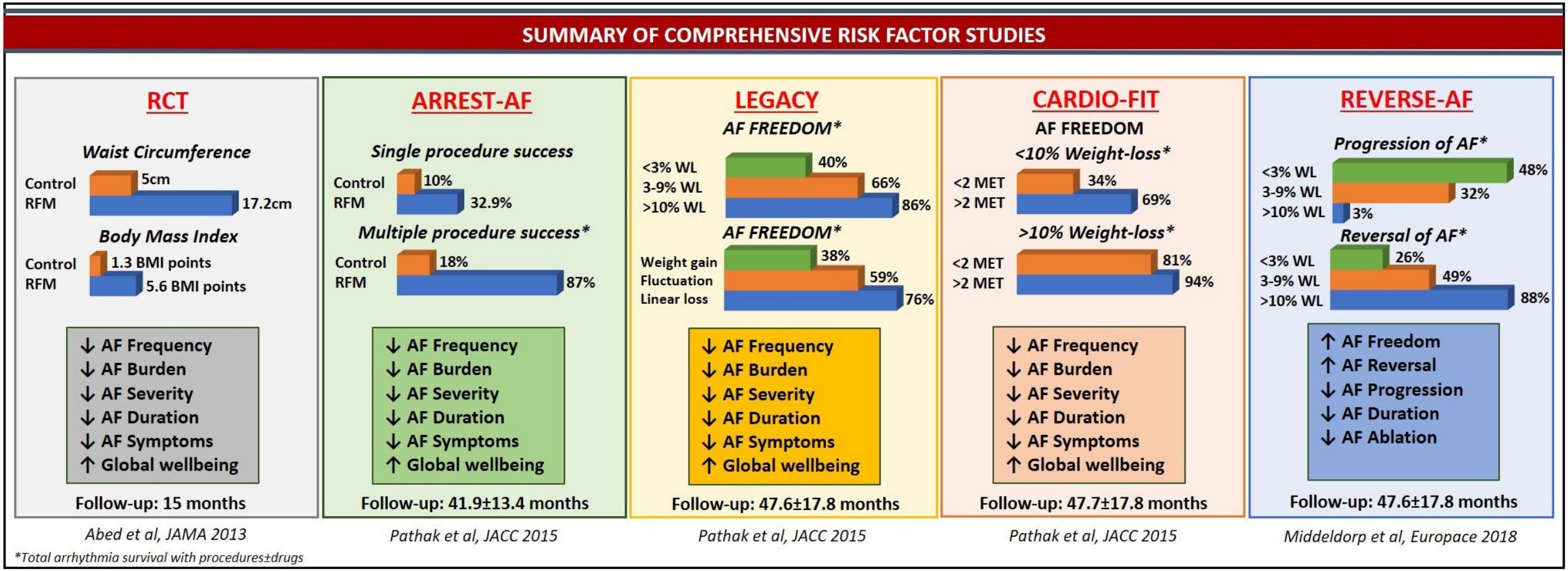
ABSTRACT

The management of atrial fibrillation (AF) has focused on anticoagulation, rhythm control and ventricular rate control. Recently, a fourth pillar of AF management has been incorporated recognising the importance of risk factor management (RFM). There are several risk factors that contribute to the development and progression of AF, these include traditional risk factors such as age, hypertension, heart failure, diabetes and valvular heart disease. However, increasingly it is recognised that obesity, sleep apnoea, hyperlipidaemia, smoking, alcohol, physical inactivity, genetics, aortic stiffness are associated with the development of AF. Importantly, several of these risk factors are modifiable. We have seen the evolution of RFM programmes which have demonstrated promising results. Indeed, the evidence is now so compelling that major clinical guidelines strongly advocate that aggressive treatment of these risk factors as a key component of AF management. Patients with

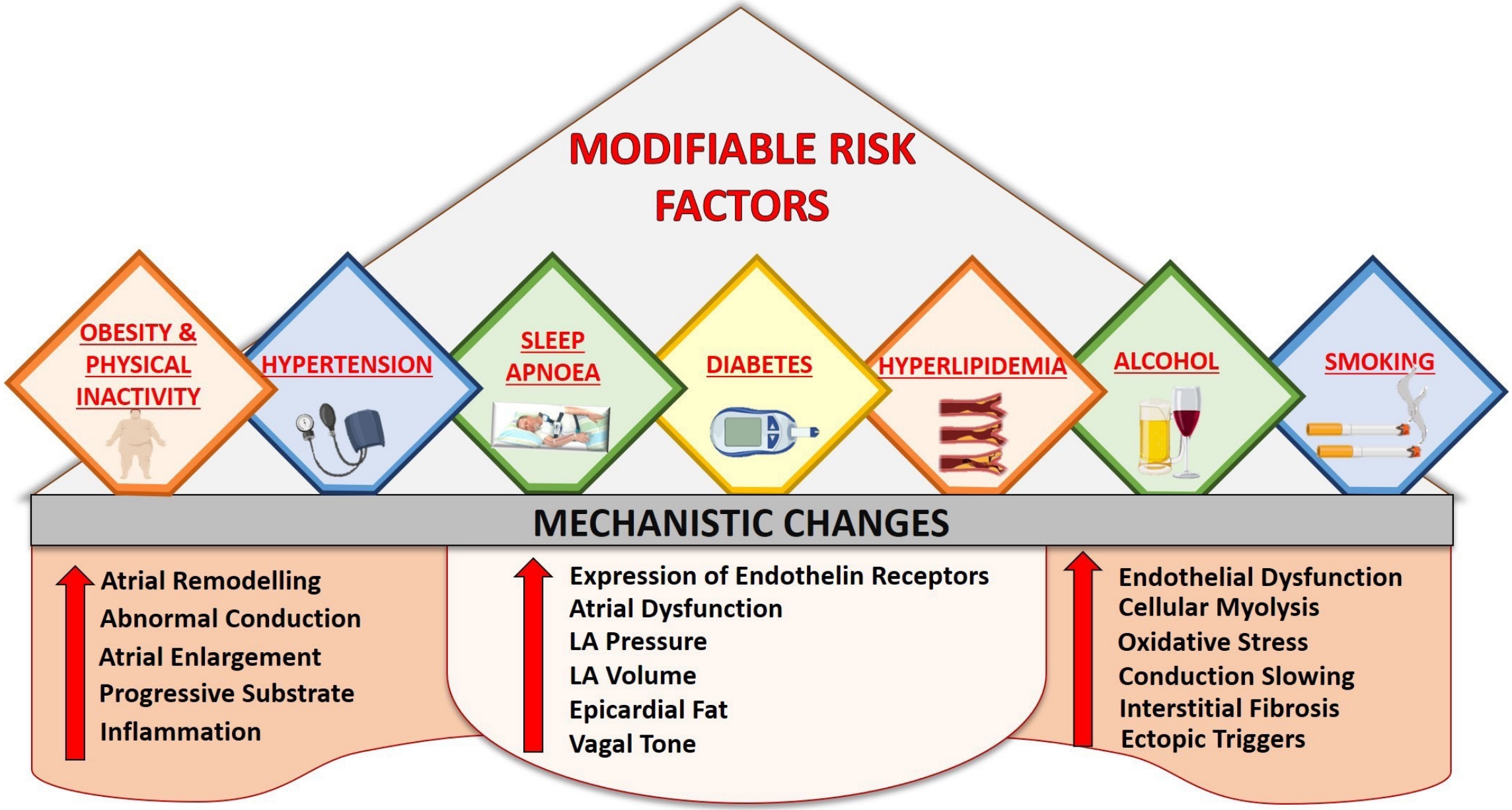
OBESITY

Epidemiological studies have demonstrated a clear correlation between obesity and AF. Risk of incident AF has been shown to increase up to 29% with every 5-point increase in body mass index (BMI).[2] Significant weight loss is associated with a much reduced risk of incident AF development.[3]

The link between obesity and AF is likely multifactorial. Animal studies have revealed that the atria demonstrate significant conduction slowing, increased conduction heterogeneity and electrogram fractionation, all of which create the electrophysiological milieu for AF.[4 5] In the clinical setting, obese individuals have been demonstrated to have significantly increased left atrial (LA) pressure and volume,[6] and altered electroanatomic features in areas contiguous with pericardial fat.[7] Obesity is also known to significantly alter circulatory haemodynamics, creating a high cardiac



Middeldorp ME, *et al*. *Heart* 2020;**106**:325–332.
doi:10.1136/heartjnl-2019-315327



Middeldorp ME, *et al*. *Heart* 2020;**106**:325–332.
doi:10.1136/heartjnl-2019-315327

Dietary Pattern and AFib

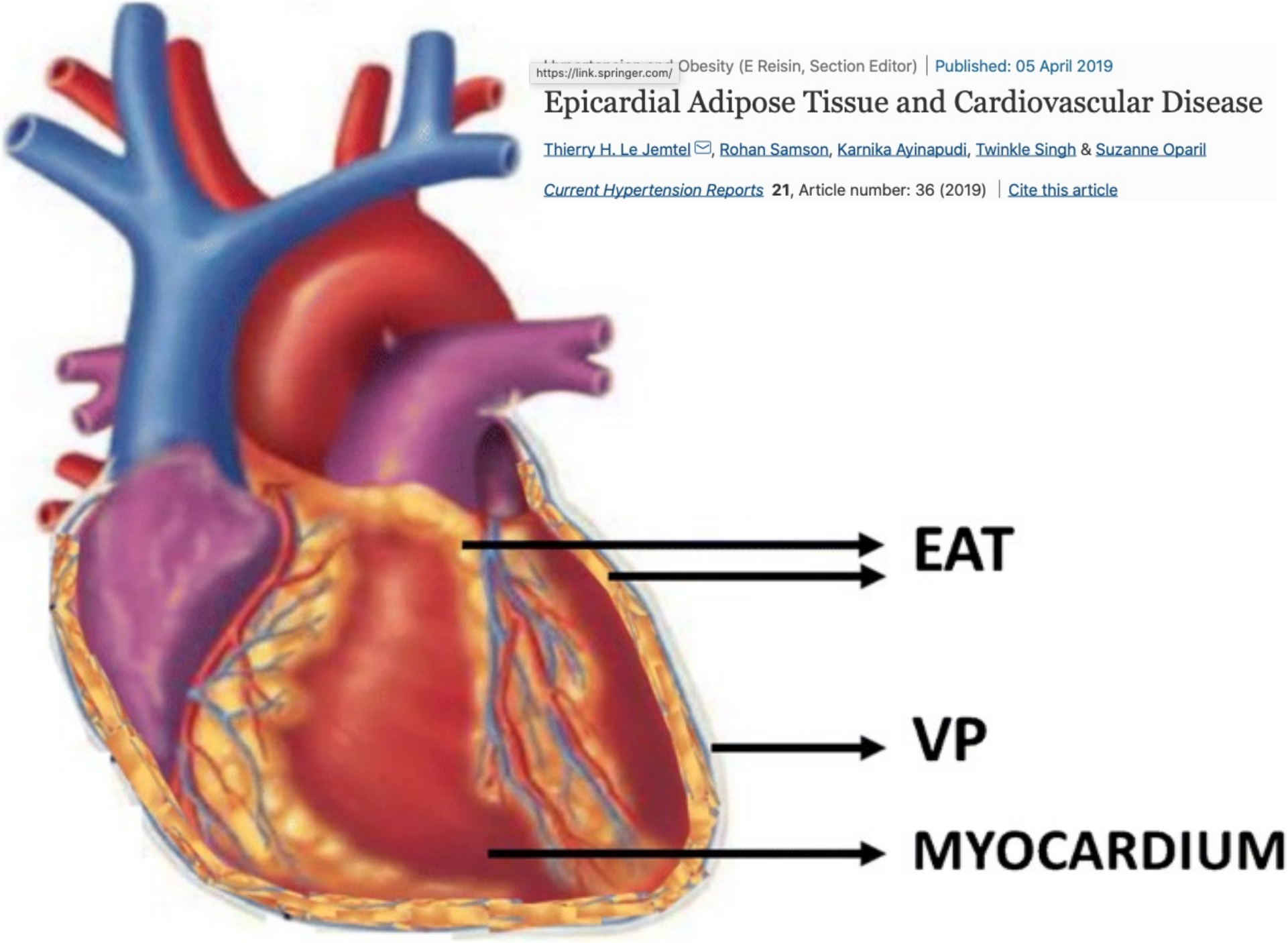
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- Standard western diet increases AFib
  - Inflammation, blood vessel damage, high glucose
- Whole food, plant-based diet improves AFib
  - Less inflammation, heals blood vessels
  - Regulates blood sugar
  - Lower amount of fat on surface of the heart

Weight and AFib

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- Excess weight increases AFib
  - Epicardial adipose: fat that sits on the heart
  - Inflammation and damage to heart cells
  - Increases other risks factors for AFib and stroke
    - Sleep apnea
    - High blood pressure
  - Losing 10% weight when needed improves AFib



https://link.springer.com/

Obesity (E Reisin, Section Editor) | Published: 05 April 2019

Epicardial Adipose Tissue and Cardiovascular Disease

Thierry H. Le Jemtel, Rohan Samson, Karnika Ayinapudi, Twinkle Singh & Suzanne Oparil

Current Hypertension Reports **21**, Article number: 36 (2019) | Cite this article

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HeartRhythm Heart Rhythm Society

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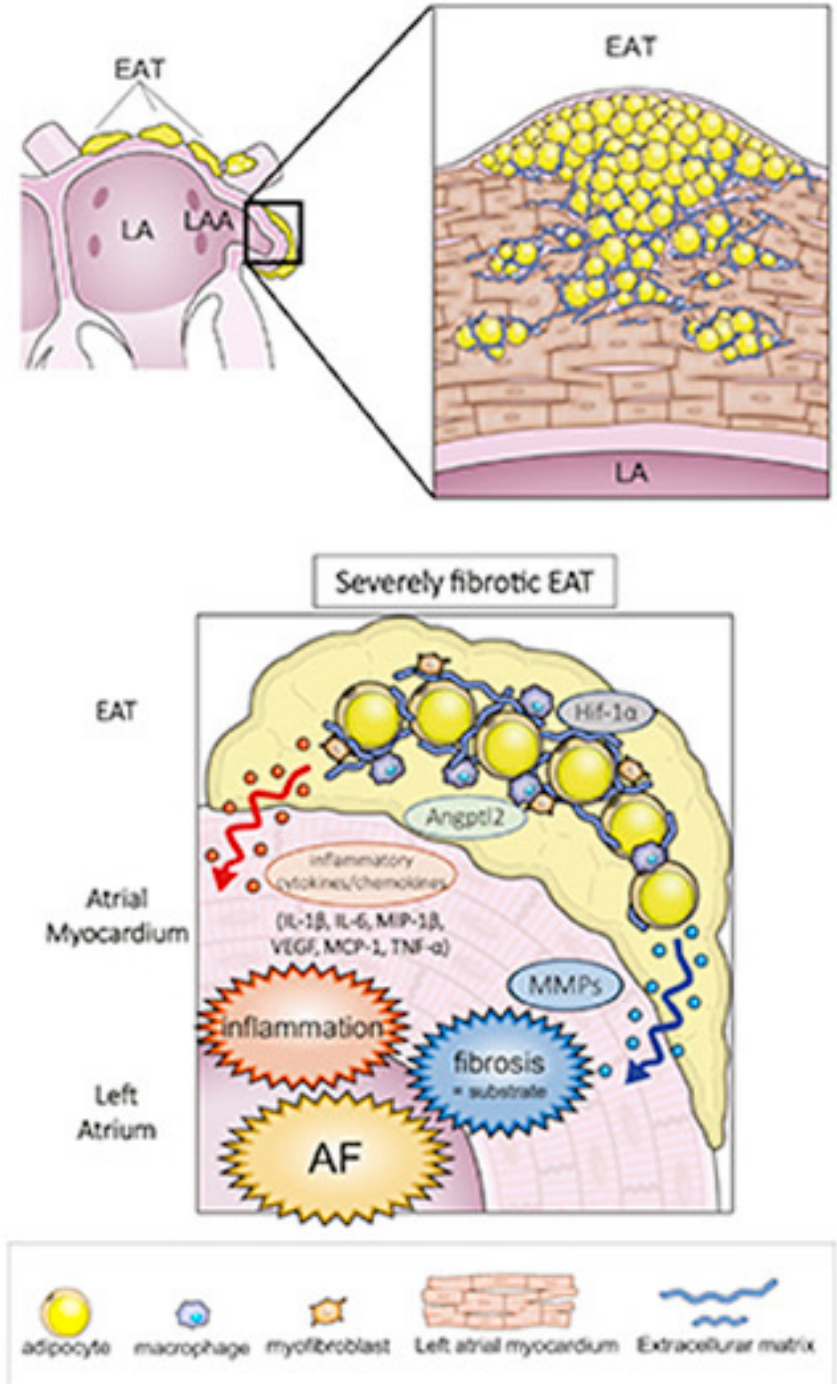
EXPERIMENTAL | VOLUME 15, ISSUE 11, P1717-1727, NOVEMBER 01, 2018

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Association of fibrotic remodeling and cytokines/chemokines content in epicardial adipose tissue with atrial myocardial fibrosis in patients with atrial fibrillation

Ichitaro Abe, MD • Yasushi Teshima, MD, PhD • Hidekazu Kondo, MD, PhD • ... Tatsuo Shimada, PhD • Shinji Miyamoto, MD, PhD • Naohiko Takahashi, MD, PhD • Show all authors

Published: June 13, 2018 • DOI: https://doi.org/10.1016/j.hrthm.2018.06.025 • Check for updates


EAT
LA
LAA
EAT
LA
Severely fibrotic EAT
EAT
Atrial Myocardium
Left Atrium
Hif-1α
Angptl2
inflammatory cytokines/chemokines
(IL-1β, IL-6, MIP-1β, VEGF, MCP-1, TNF-α)
MMPs
inflammation
fibrosis
= substrate
AF
adipocyte
macrophage
myofibroblast
Left atrial myocardium
Extracellular matrix



Smoking and AFib

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- Makes AFib 5x more likely
- Increases risk of stroke
- Damage to heart cells and blood vessels
- Inflammation

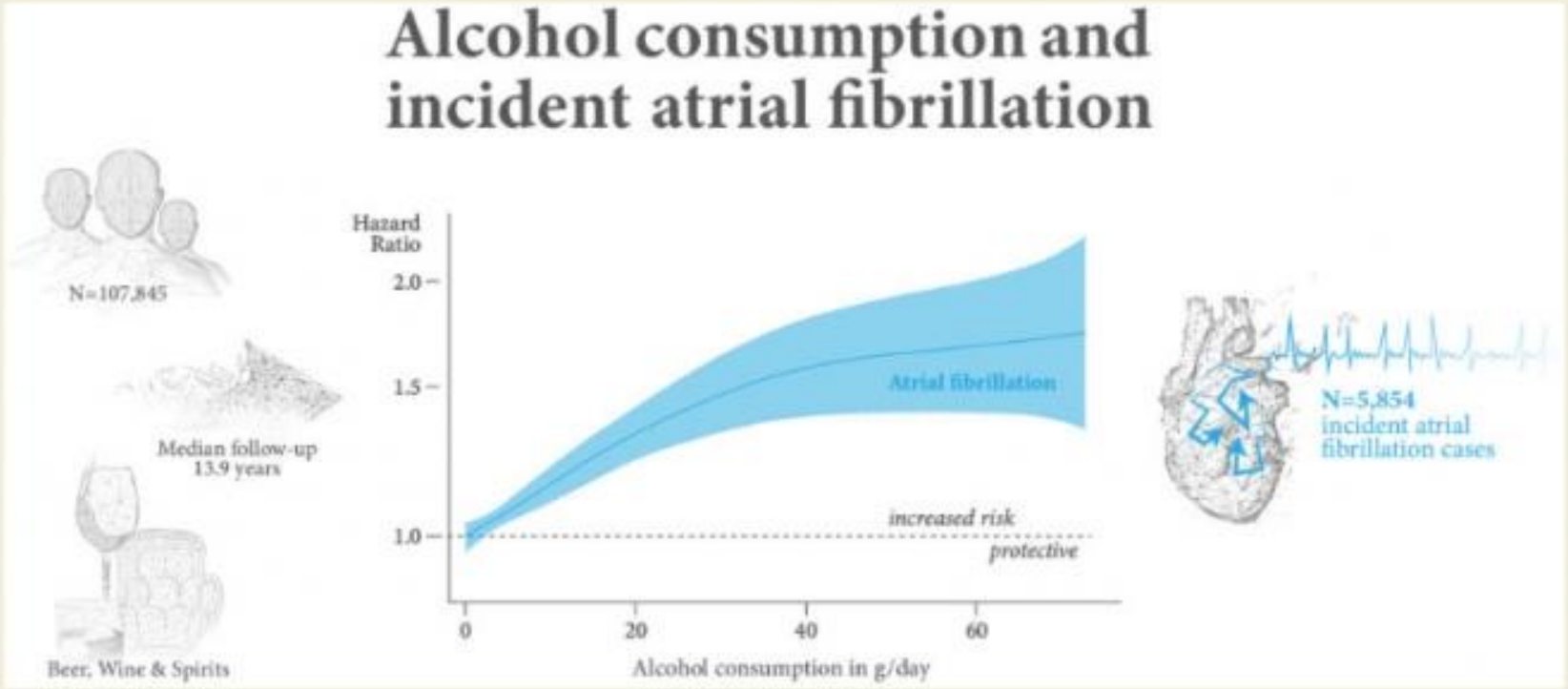


Alcohol and AFib

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- Even one drink per day increases AFib.

Graphical Abstract



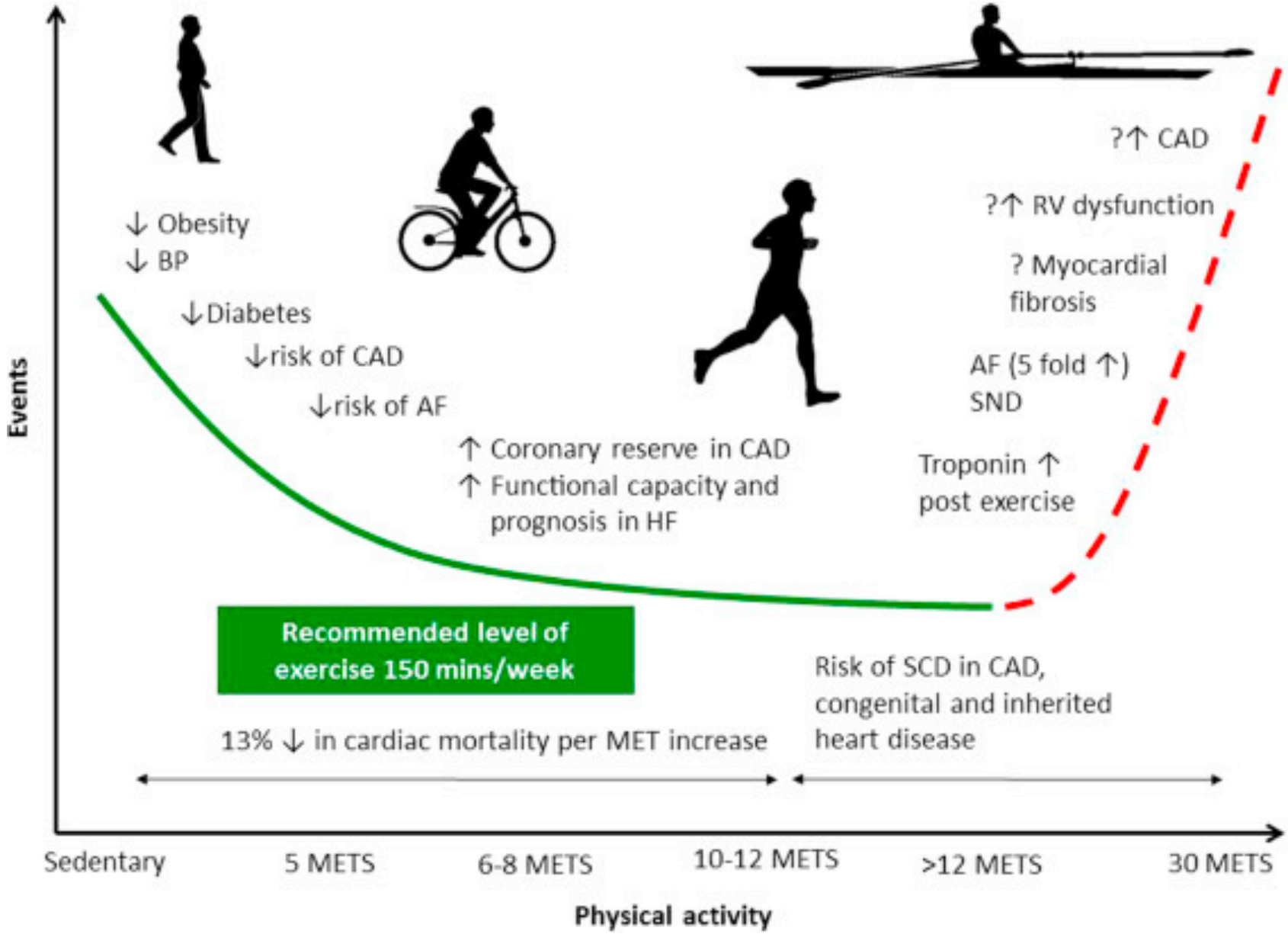
ESC European Society of Cardiology
European Heart Journal (2021) 42, 1170–1177
doi:10.1093/eurheartj/ehaa953
CLINICAL RESEARCH
Epidemiology and prevention

Alcohol consumption, cardiac biomarkers, and risk of atrial fibrillation and adverse outcomes

Exercise and AFib

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- Between 150-300 minutes per week is least associated with AFib
- Baby Bear zone: not too little, not too much
- “U-shaped curve” relationship



Trends in Cardiovascular Medicine
Volume 26, Issue 3, April 2016, Pages 232-240

Stress and AFib

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- Vicious cycle
- Physical and emotional stress triggers AFib
- AFib causes physical and emotional stress
- Stress reduction improves AFib
- Walk, hike, various forms of meditation

Sleep and AFib

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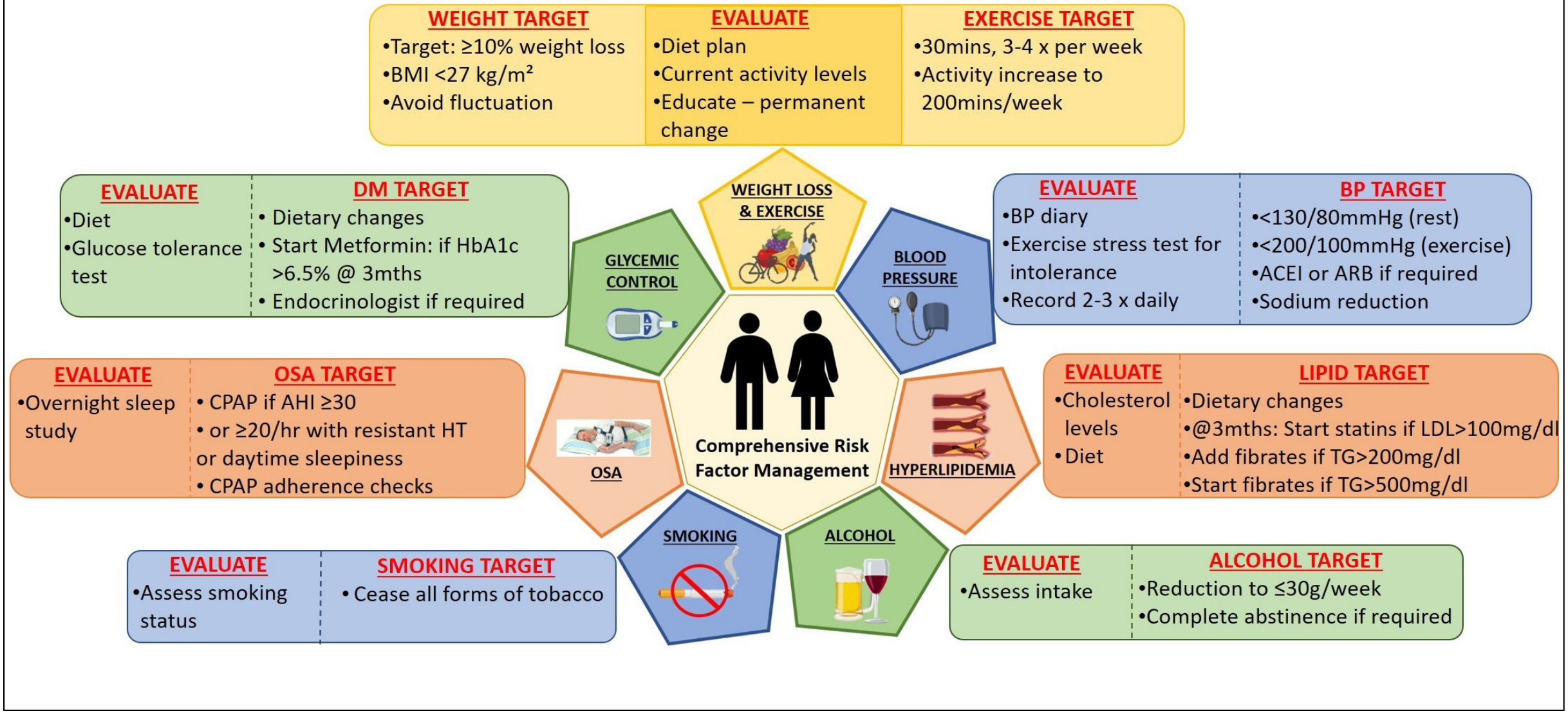
- Sleep and other lifestyle factors are interconnected
- 7-8 hours of sleep associated with least AFib
- Poor sleep quality increases AFib
- Alcohol, excess weight, and stress worsen sleep

Sleep and AFib

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- Sleep apnea is a major cause of AFib
  - 85% of those in AFib clinic have sleep apnea
- If sleep apnea is present but not treated
  - AFib ablation success drops from 70% to 50%
  - AFib progresses from paroxysmal to persistent
- Treatments for sleep apnea
  - Weight loss if needed
  - CPAP

AGGRESSIVE RISK FACTOR MANAGEMENT



Middeldorp ME, *et al*. *Heart* 2020;**106**:325–332.
doi:10.1136/heartjnl-2019-315327

Lifestyle and AFib Conclusions

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- Many things *you* can do can improve AFib!
- Reach weight where waist smaller than hips
- Eat a diet high in whole plant foods and low in processed foods
- Quit smoking
- Avoid alcohol
- Reduce stress, consider meditation
- Moderate exercise - ideally 5 hours per week



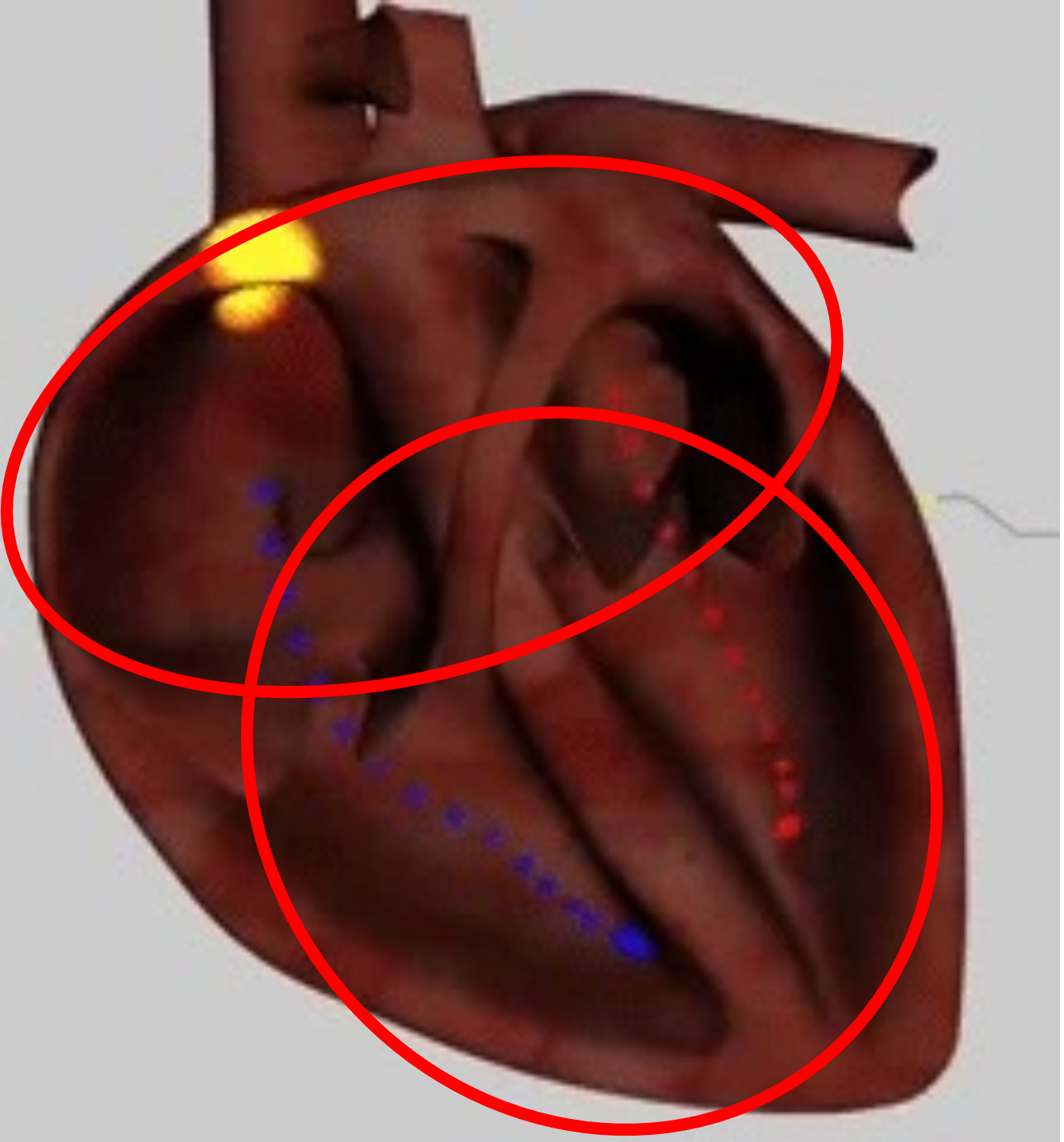
Atrial Fibrillation:
Options for Rate and Rhythm Control

Objectives

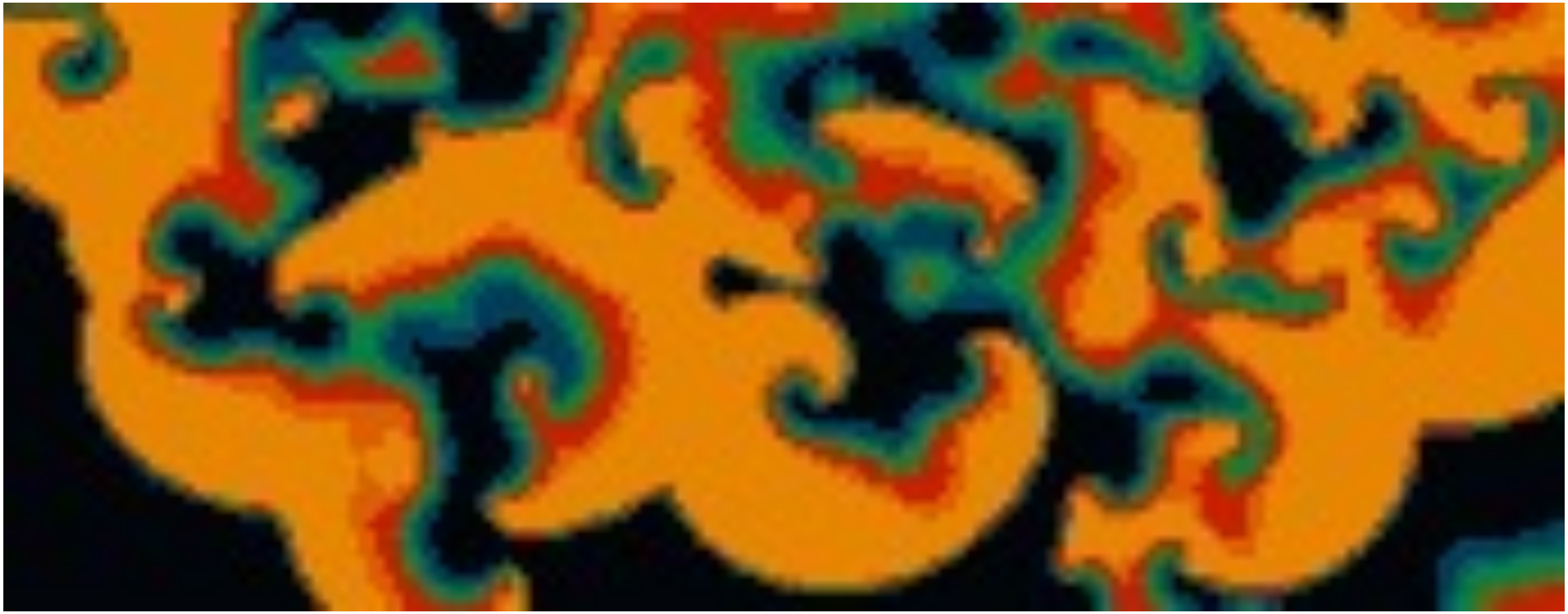
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- AFib basics
  - Definitions, risk factors, “the AFib timeline”
- Rhythm control and rate control
- Medical vs procedural rhythm control options

What is Atrial Fibrillation?



- Ventricles:
  - Lower chambers of the heart
  - Pump function
  - **Critical** to the heart's function
- Atria:
  - Upper chambers of the heart
  - **Support** function
    - Blood reservoir
    - Regulation of filling pressures
    - Blood volume regulation
    - Coordinate **timing** of the heart's chambers

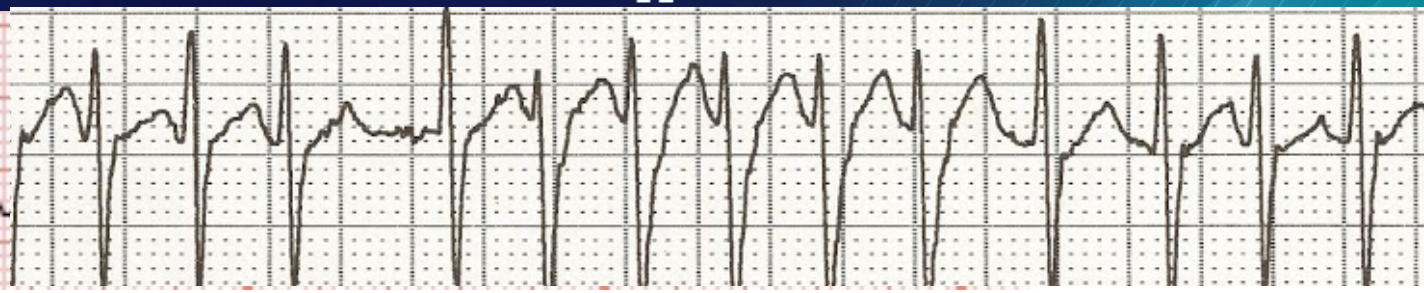


- Chaotic, disorganized electrical rhythm
- Loss of atrial timing / reservoir / pressure optimization
  - Loss of heart efficiency
- NOT immediately life-threatening

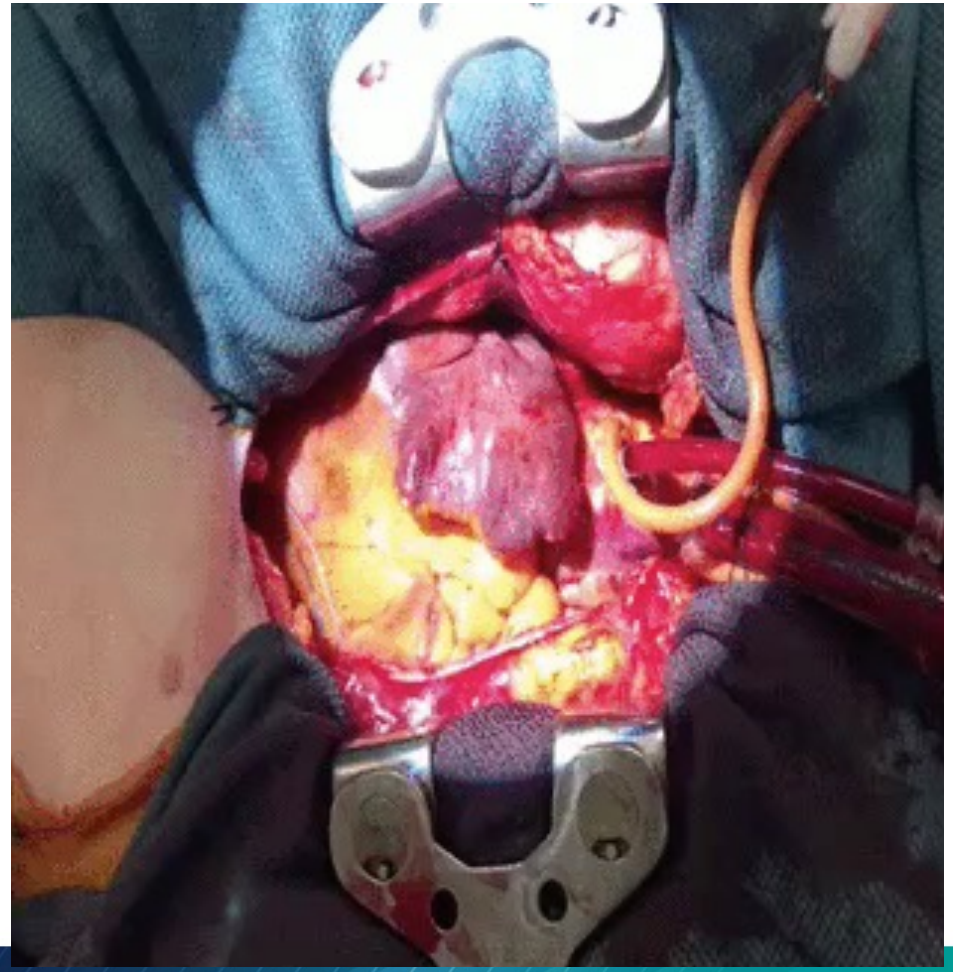
Consequences of AFib

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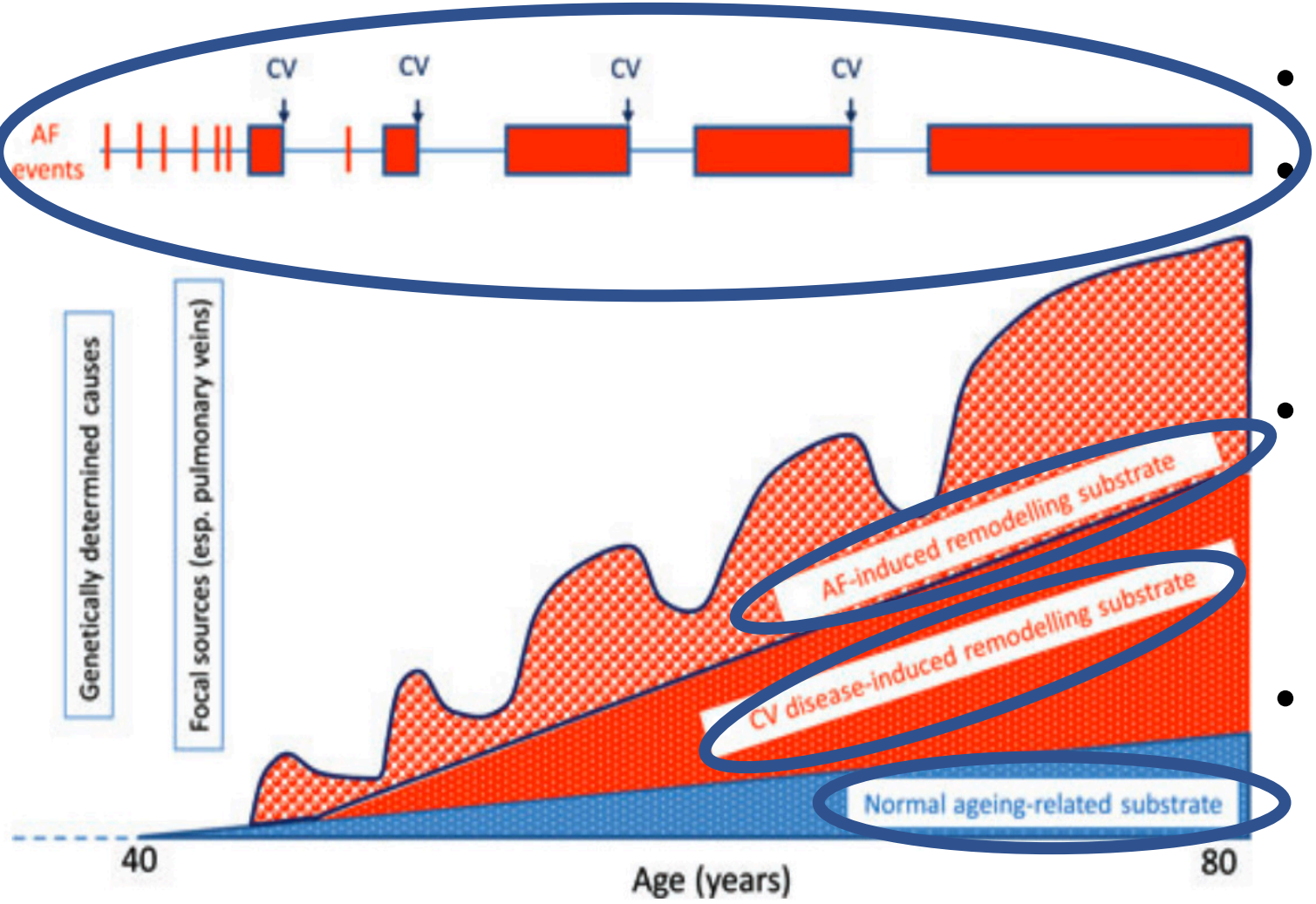


- Rapid heart rates
  - Palpitations
- Loss of heart efficiency
  - Shortness of breath, fatigue, chest pain
  - Risk of **heart failure** over the long term
- Risk of stroke!



The AFib Timeline

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- **<u>Progressive disease</u>**
- Risk factors for AFib accumulate over time
  - More “wear and tear”
- AFib begets AFib
  - Burden of disease tends to **<u>accelerate</u>**
  - Especially if not treated appropriately
- Later-stage AFib is more difficult to treat
  - Requires more aggressive measures to achieve the same result

Risk Factors for Atrial Fibrillation

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- **STRUCTURAL HEART DISEASE**
  - Heart failure
  - Valvular heart disease
  - Heart attack
- **CARDIAC RISK FACTORS**
  - Hypertension (high blood pressure)
  - Diabetes
  - Sleep apnea
- **NON-CARDIAC CONDITIONS**
  - Thyroid imbalance
  - Lung disease (COPD / emphysema)
  - Substance use – alcohol, cocaine, ?caffeine
- **ACUTE / SELF-LIMITED PRECIPITANTS**
  - Severe trauma
  - Sepsis
  - Respiratory failure
  - Post-surgical (pain / blood loss)
  - Electrolyte disturbances (primary / kidney failure / others)

Rate control vs rhythm control

RATE CONTROL

- Addresses the rapid heart rates associated with atrial fibrillation
- The AFib itself is not affected
- Least complicated option
  - *Very* early-stage AFib
  - Medically frail patients
- Least effective
  - Doesn't control symptoms of AFib itself
  - Doesn’t slow the **progression** of AFib

RHYTHM CONTROL

- Directly addresses AFib
  - Prevents AFib **progression** over time
  - Treats the symptoms of AFib itself
  - Prevents consequences of AFib over time
    - Reduced heart failure
    - Reduced stroke risk (not enough to stop blood thinners!)
    - Longer survival??
- Medications – anti-arrhythmic drugs
- Procedures – ablation
- Both designed to **suppress triggers** of AFib

How to Choose Between Rate vs Rhythm Control?

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- Not mutually exclusive!
  - Generally use both as complementary tools

- Rhythm control helpful for:
  - Symptomatic patients – **fatigue**, palpitations, lightheadedness, chest pain, short of breath
  - Earlier (but progressive) AFib
  - When rate control isn't working
  - With Afib-related heart failure

- Rate control (only) helpful for:
  - Patients who are unable to tolerate more aggressive treatments
  - Patients in permanent AFib

Rhythm Control Options

Anti-arrrhythmic Drugs

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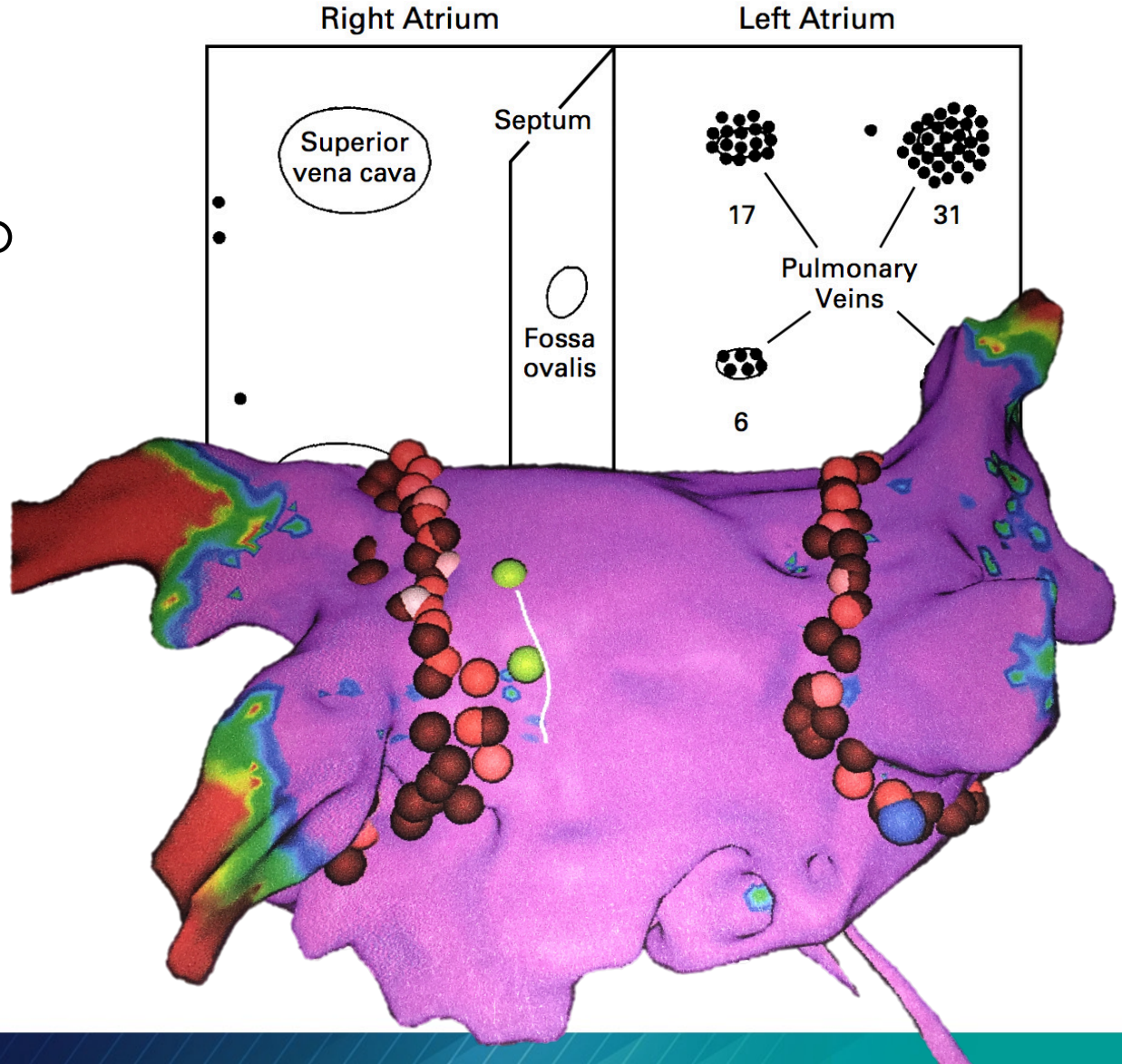
- No perfect option
  - Most effective drugs also have the most side effects
- Amiodarone – the best (and worst) anti-arrhythmic
  - LOTS of long-term side effects
    - Lung disease, liver disease, thyroid gland imbalance, neuropathy
  - Very well tolerated in the **short term**
- Several mid-range options that have minimal long-term side effects
  - May be **pro-arrhythmic** – serious arrhythmias in subset of patients
  - Require prior testing or monitored loading in the hospital
- Dronedarone – the worst (and best) anti-arrhythmic
  - Less side effects / no pro-arrhythmic properties
  - Easier to use
  - Least effective for control of AFib



Ablation Procedure

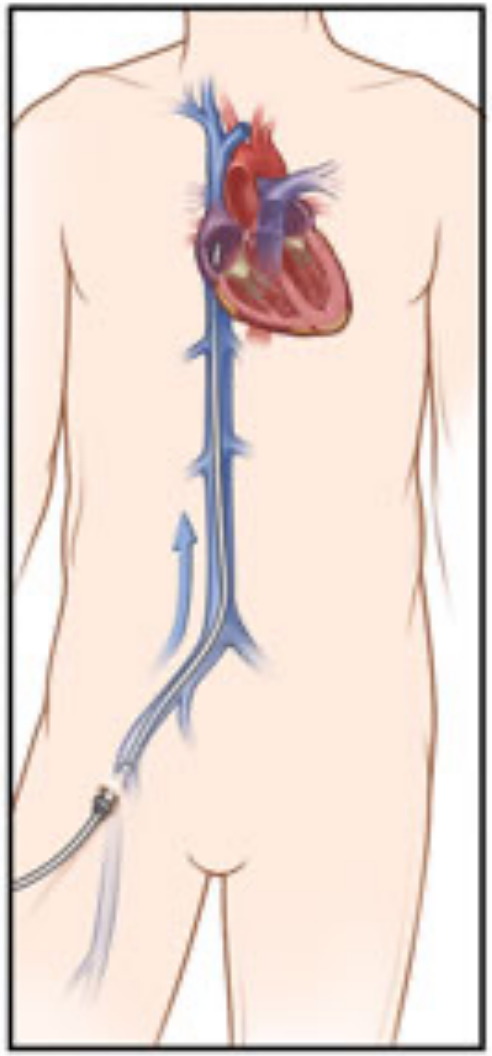
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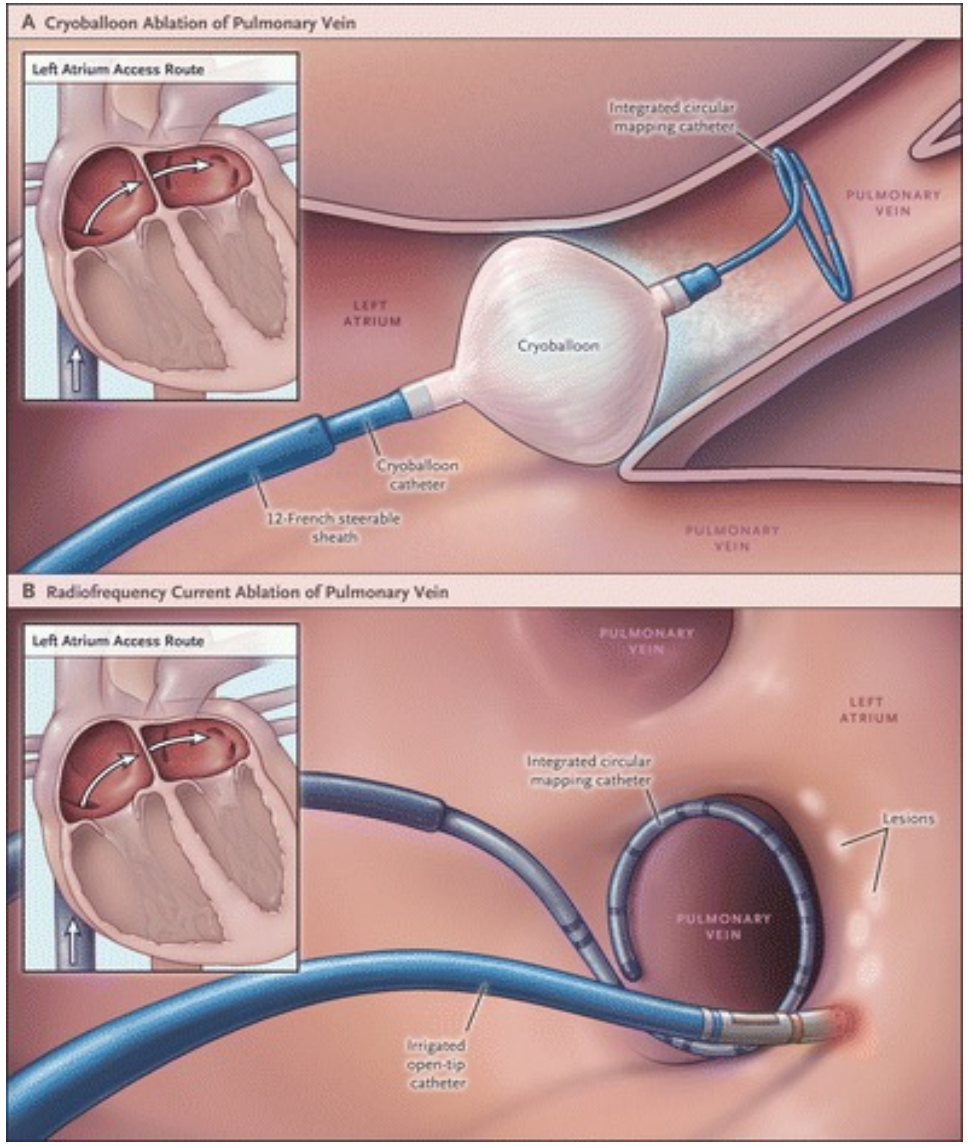
- Triggers of atrial fibrillation reside in the pulmonary veins.
- The ablation procedure is designed to **electrically silence these triggers.**
- As AFib progresses, these triggers migrate into the left atrium proper.
  - Ablation in late-stage AFib requires **more extensive** trigger modification, has less favorable AFib control
- **Upfront risks** related to the invasive nature of the procedure
- Full benefit of the procedure takes **several months** to achieve.



How is Ablation Performed?

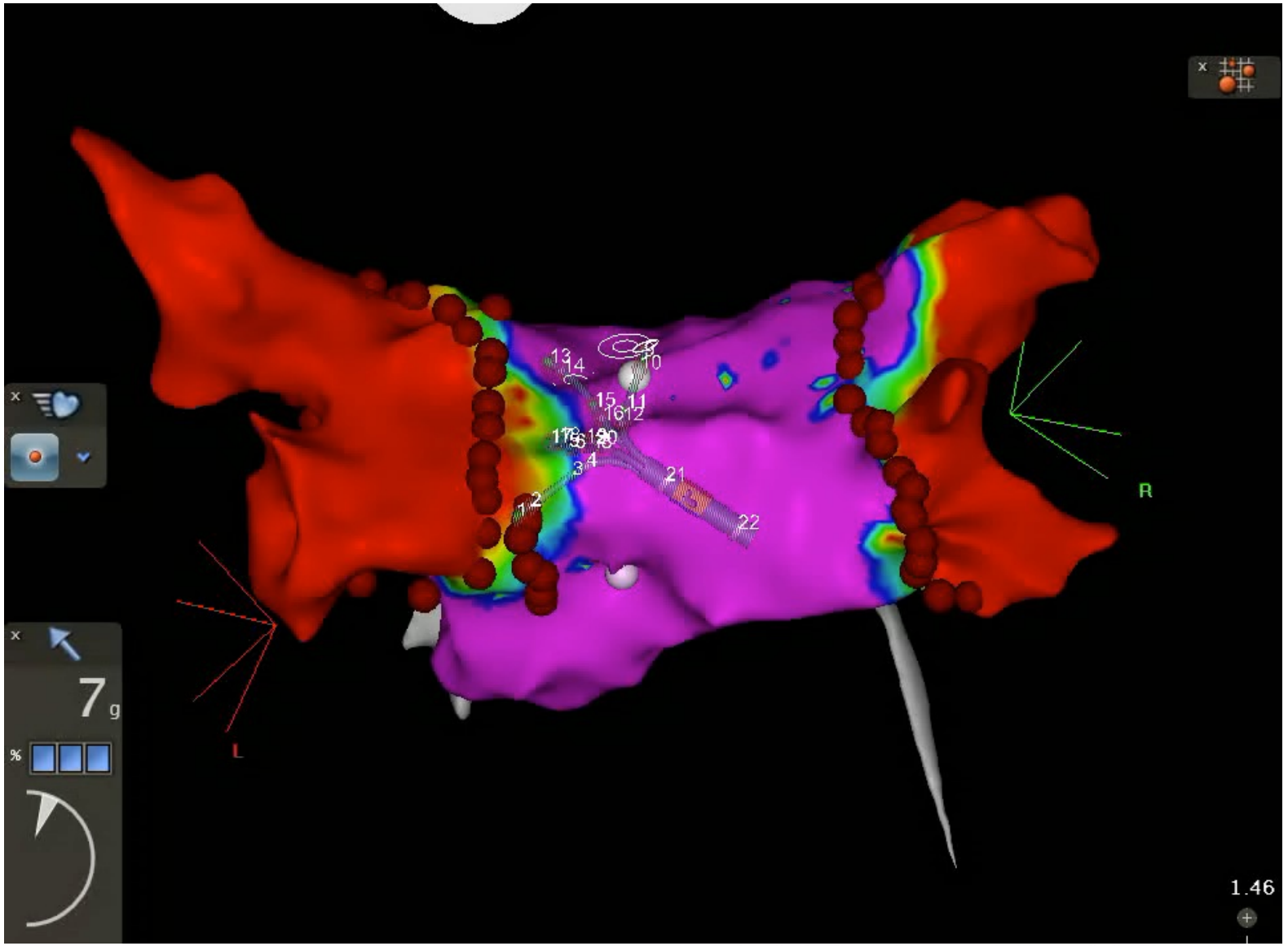
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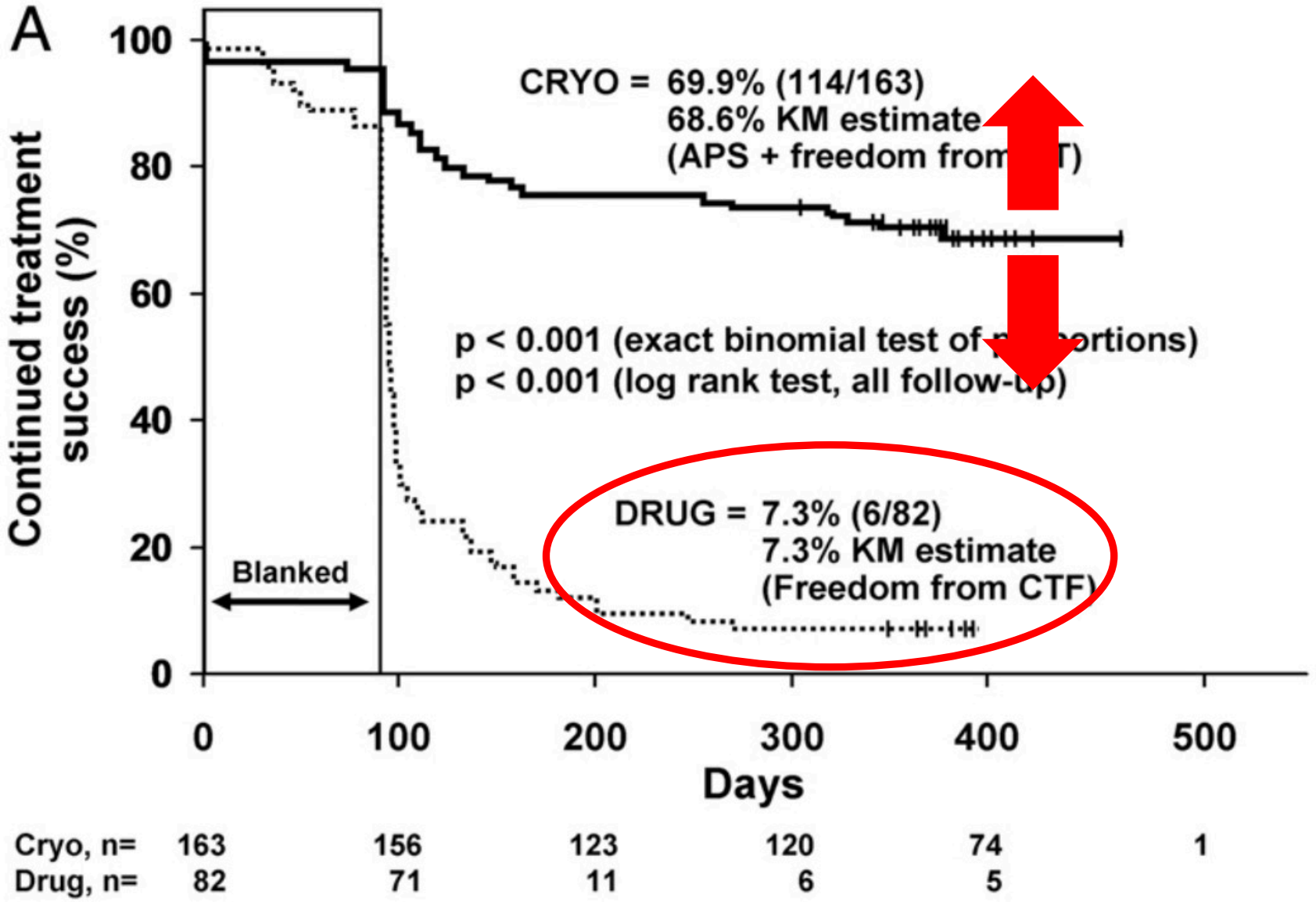
How is Ablation Performed?

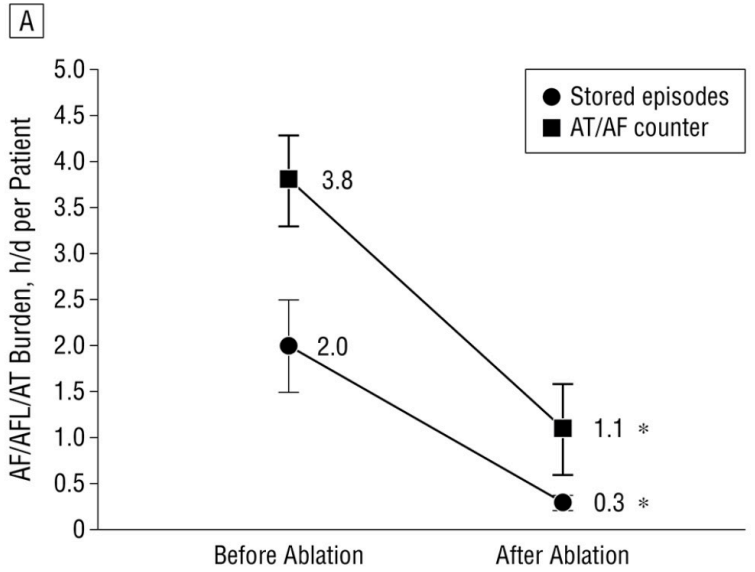
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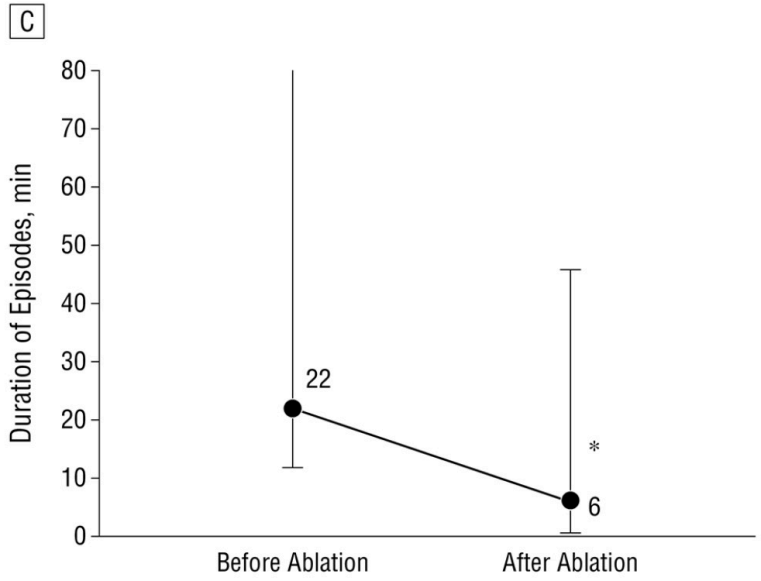


How Effective Are These Options?

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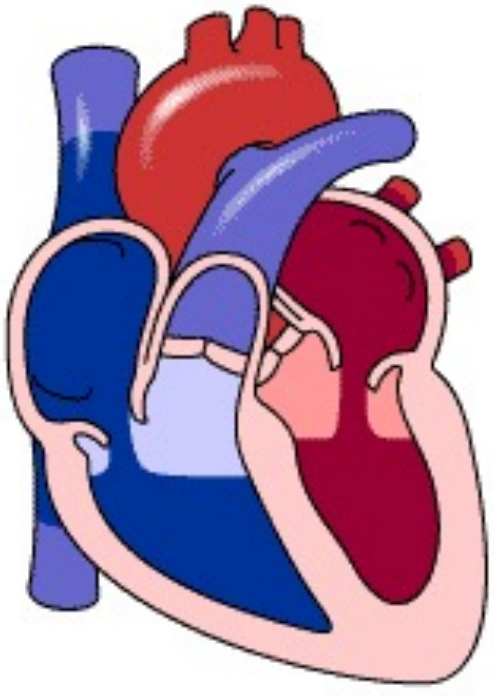




Thank you

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- Community awareness of cardiac disease
  - If you know about it, your family/friends/neighbors will know about it through you.
  - You may save a life when you're not even in the room.
- Don't live in denial
  - If you ignore your symptoms, it won't solve the problem.
  - Degenerative diseases are always *easier to prevent than to treat*.



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Atrial Fibrillation: Stroke and Blood Thinning Medications…What else is available?

Srinivas Iyengar, MD
Interventional Cardiologist
Structural Heart Director, Boulder Heart

Atrial Fibrillation

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- Irregular heart rhythm
- Basically, the top parts of the heart ("atria") don't communicate electrically with the bottom ("ventricles")
- Results in symptoms of SOB, light-headedness, and palpitations

Causes

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- High blood pressure
- Heart attacks
- CAD
- Abnormal heart valves
- Heart defects you're born with (congenital)
- An overactive thyroid gland or other metabolic imbalance
- Exposure to caffeine, tobacco or alcohol

Diagnosis

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- ECG is mandatory
- Not every “irregular heart rhythm” is AFib!
- PVCs, APCs, skipped beats can all mimic feelings of AFib
- AFib does not have to be chronic, it can be short-lasting or come/go (i.e., PAF)

Treatment

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- Medications to control HR (i.e., beta-blockers, Ca-channel blockers) are first line.
- Anti-arrhythmic medications can be used to control rhythm.
- Cardioversion (either electrically or chemically) can be utilized for symptomatic AFib.
- Ablation (surgically or percutaneously) can also be utilized.

But What Else Does AFib Cause?

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- Stroke!!
- The left atrial appendage (LAA), which is in the left atrium, can collect blood and form clots that can break free in patients with AFib.
- That's why we place patients with AFib who have elevated risks for stroke on blood thinners.

Blood Thinners

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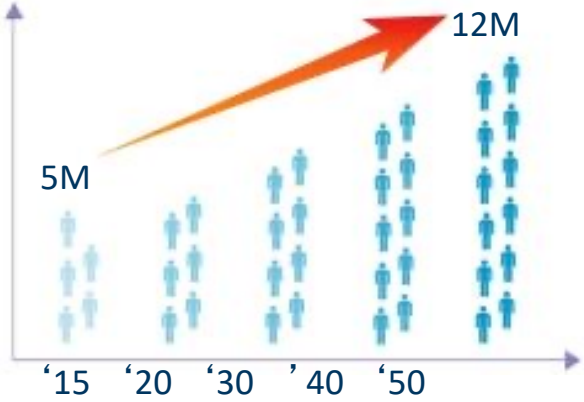
- Work very well as long as compliance is maintained and no side effects seen.
- Warfarin - cheap but compliance with diet/testing an issue as well maintaining adequate levels.
- NOACs - Costly, lack readily available reversal agents.
- All the above can exacerbate bleeding.

AFib is a Growing Problem Associated with Greater Morbidity and Mortality

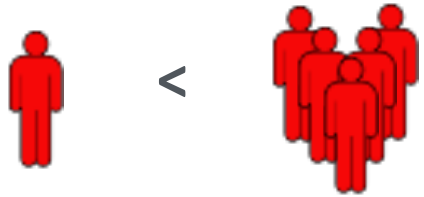
WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

- Higher stroke risk for older patients and those with prior stroke or TIA
- 15-20% of all strokes are AFib-related
- AFib results in greater disability compared to non-AFib-related stroke

AF = most common cardiac arrhythmia, and growing



AF increases risk of stroke



~5 M
people with AF in U.S., expected to more than double by 2050[1]

5x
greater risk of stroke with AF[2]

1. Go AS. et al, Heart Disease and Stroke Statistics—2013 Update: A Report From the American Heart Association. Circulation. 2013; 127: e6-e245.
2. Holmes DR, *Seminars in Neurology* 2010;30:528–536.
Wolf PA et al, Duration of Atrial Fibrillation and the Imminence of Stroke: The Framingham Study, Stroke 1983; 14:664-667

AFib-related Strokes are Debilitating

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Stroke

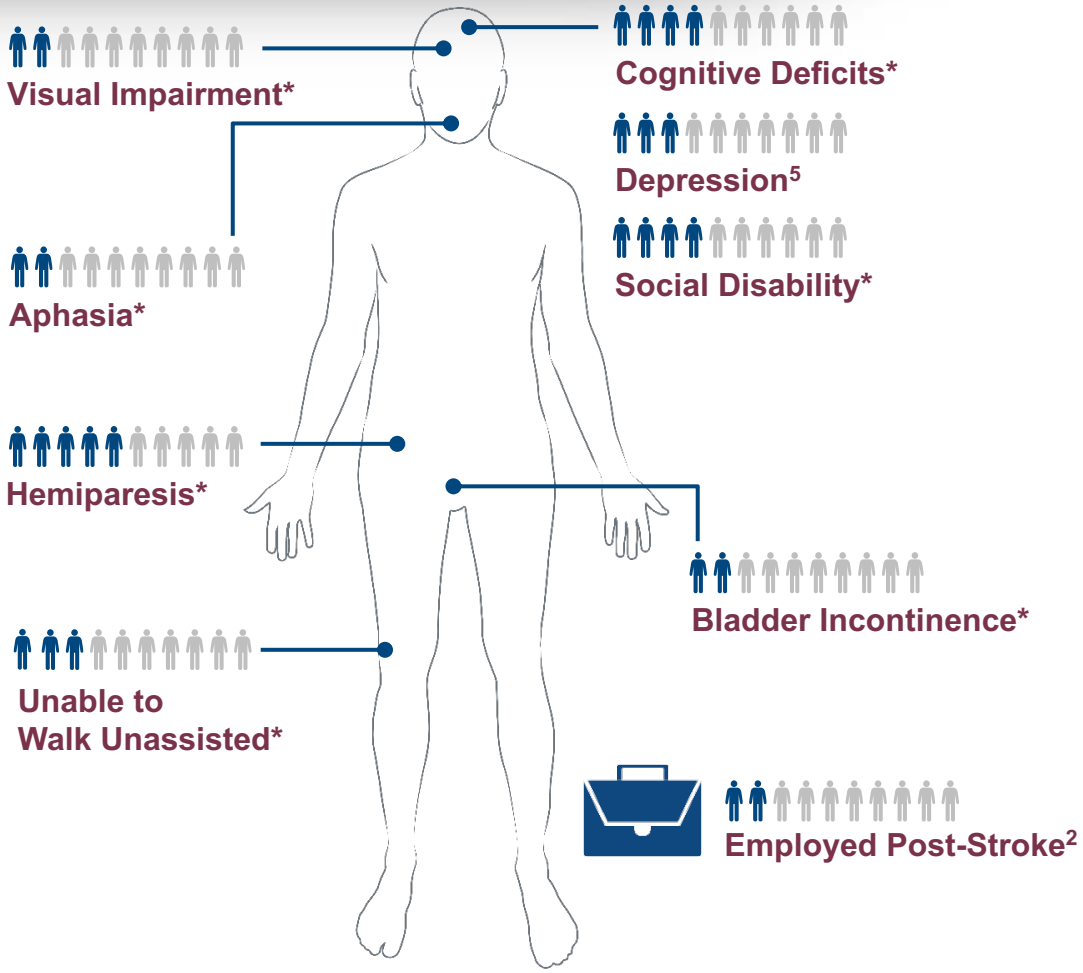
#1 cause of **adult disability** worldwide[1]

AF-related Stroke

1.5X higher **disability**[3**]

2X higher **mortality**[3**]

70% result in **death or permanent disability**[6]



*at 6 months post-stroke[4]

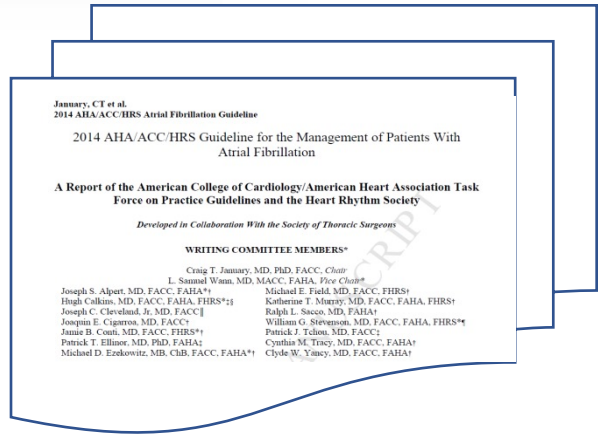
**compared with stroke patients without AF

[1]Chee and Tan. *Med J Malaysia* 69.3 (2014): 119-23. [2]Sreedharan et al. *Journ of the neurological sciences* 332.1 (2013): 97-101. [3]Lamassa et al. *Stroke* 32.2 (2001): 392-398.[4]Kelly-Hayes et al. *Journ of Stroke and Cerebrovascular Diseases* 12.3 (2003): 119-126. [5]Loo and Gan. *International Journ of Stroke* 7.2 (2012): 165-167. [6]Holmes DR, *Seminars in Neurology* 2010;30:528–536.

2014 ACC/AHA/HRS Treatment Guidelines to Prevent Thromboembolism in Patients with AF

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

- Assess stroke risk with CHA_2DS_2-VASc score
  - Score 1: Annual stroke risk 1%, oral anticoagulants or aspirin may be considered
  - Score ≥2: Annual stroke risk 2%-15%, **oral anticoagulants are recommended**
- **Balance stroke risk reduction benefit vs. bleeding risk**


January, CT et al.
2014 AHA/ACC/HRS Atrial Fibrillation Guideline

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Developed in Collaboration With the Society of Thoracic Surgeons

WRITING COMMITTEE MEMBERS*

2014 AHA/ACC/HRS Guideline for the Management of Patients with AF

CHA_2DS_2 VASc Score	Recommendation
0	No anticoagulant
1	Aspirin (81-325 mg daily) or warfarin (INR 2-3)
≥2	Oral anticoagulants are recommended (warfarin (INR 2-3), dabigatran, rivaroxaban or apixaban

January, CT. et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. JACC. 2014; doi: 10.1016/j.jacc.2014.03.022

Anticoagulant Therapy Carries Risk of Intracerebral Hemorrhage or Death



Spontaneous intra-parenchymal bleed



Hemorrhagic transformation

Validated Scoring Systems to Assess Stroke Risks



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

CHA_2DS_2VASc Score (Stroke Risk)[3]

	Condition	Points
C	Congestive heart failure	1
H	Hypertension (SBP>160)	1
A_2	Age ≥ 75 years	2
D	Diabetes mellitus	1
S_2	Prior stroke, TIA or thromboembolism	2
V	Vascular disease (PAD, MI)	1
A	Age 65-74 years	1
Sc	Sex category (Female)	1
	TOTAL POINTS	

Score	Yearly Stroke Risk (%)		
	No Warfarin	With Aspirin[2]	With Warfarin[2]
0	0	0	0
1	1.3	1.0	0.5
2	2.2	1.8	0.8
3	3.2	2.6	1.1
4	4.0	3.2	1.4
5	6.7	5.4	2.3
6	9.8	7.8	3.4

3. *Chest*. 2010 Feb;137(2):263-72.

Validated Scoring Systems to Assess Bleeding Risks



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

HAS-BLED Score (Bleeding risk with warfarin)[4]

	Condition	Points
H	Hypertension	1
A	Abnormal renal/liver function (1 pt each)	1 or 2
S	Hemorrhagic Stroke	1
B	Bleeding history or disposition [4]	1
L	Labile INRs	1
E	Elderly	1
D	Current drugs (medication) or alcohol use (1pt each)	1 or 2
	TOTAL POINTS	

Score	Yearly Major Bleeding Risk %
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5+	Not well validated

4. *Chest*. 2010 Nov;138(5):1093-100.

Bleeding Risk Increases Over Patients' Lifetime



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

HAS-BLED Score	Annual % Bleed Risk*	10-Year Bleeding Risk (%)**
0	0.9	8.6
1	3.4	29.2
2	4.1	34.2
3	5.8	45.0
4	8.9	60.6
5	9.1	61.5

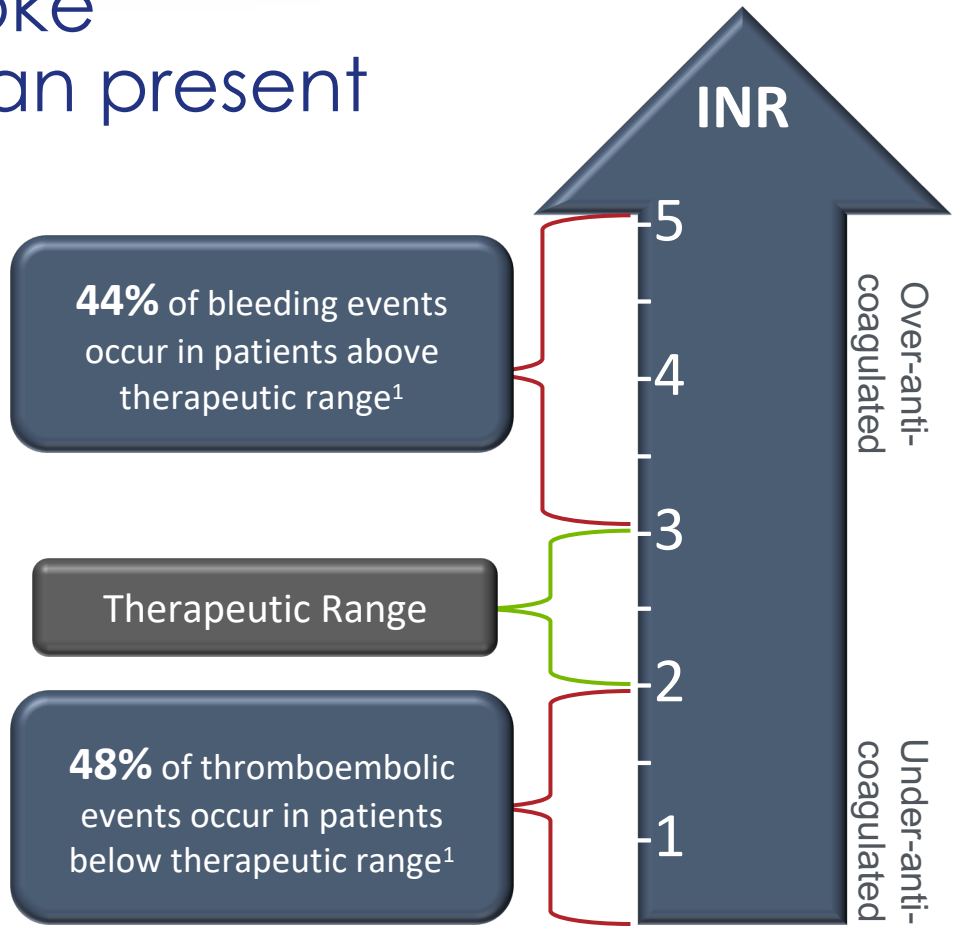
** Assumes constant risk despite increasing age and bleeding risk is independent from bleeding risk in previous years

* Lip. JACC (2011)

Stroke Treatment Option: Warfarin

Warfarin is an effective means of stroke reduction in patients with AFib but can present challenges.

- Many patients spend a significant amount of time outside of the therapeutic range.
- Warfarin tops the list for emergency hospitalizations for adverse drug events in older Americans[2]

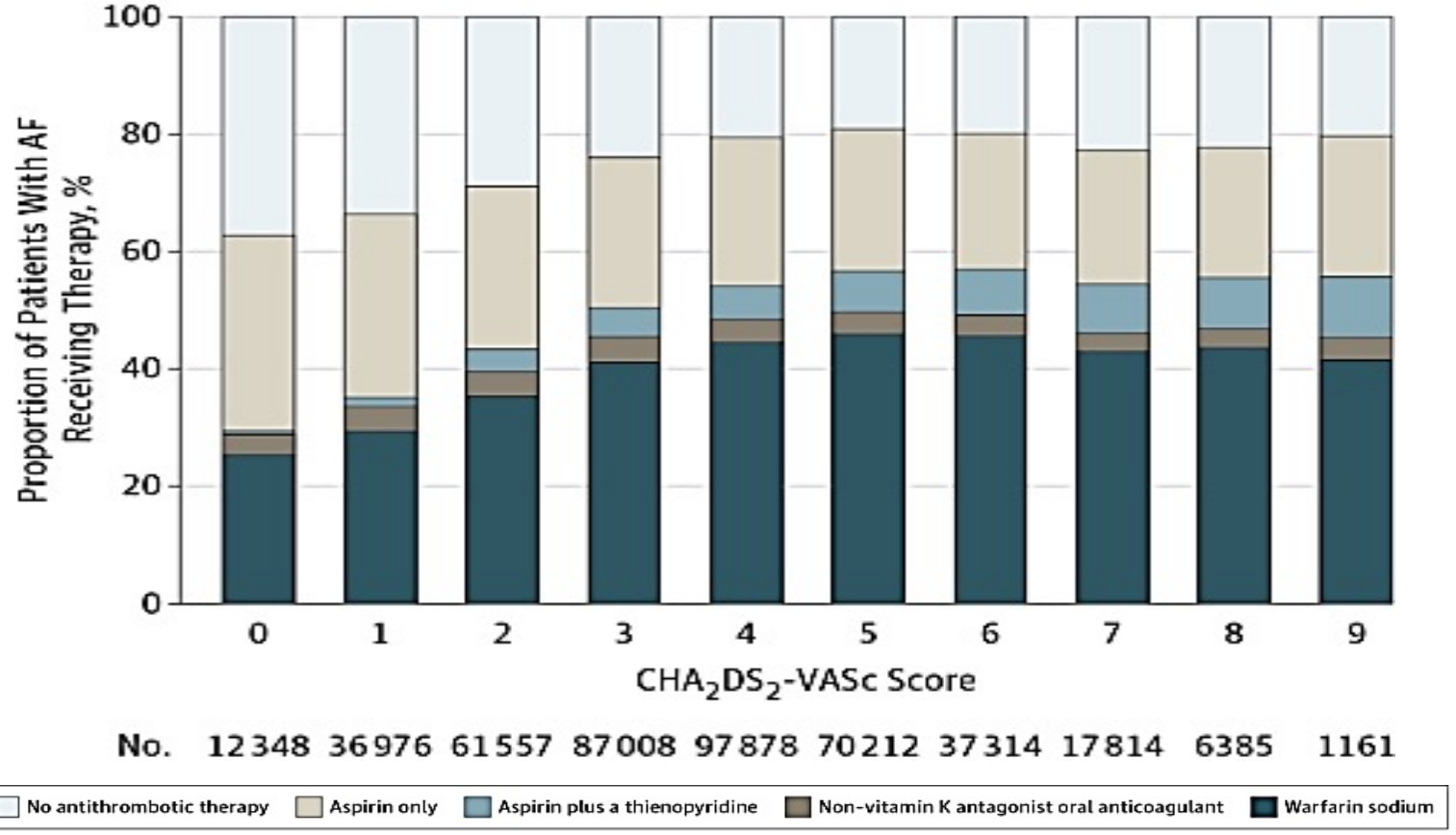


1 Oake N, et al. *Can Med Assoc J.* 2007:176(11);1589−1594
2 Budnitz, MD, MPH. et al. *Annals of Internal Medicine*. 2007:147(11); 229

Oral Anticoagulation is Standard of Care, but Compliance a Challenge

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

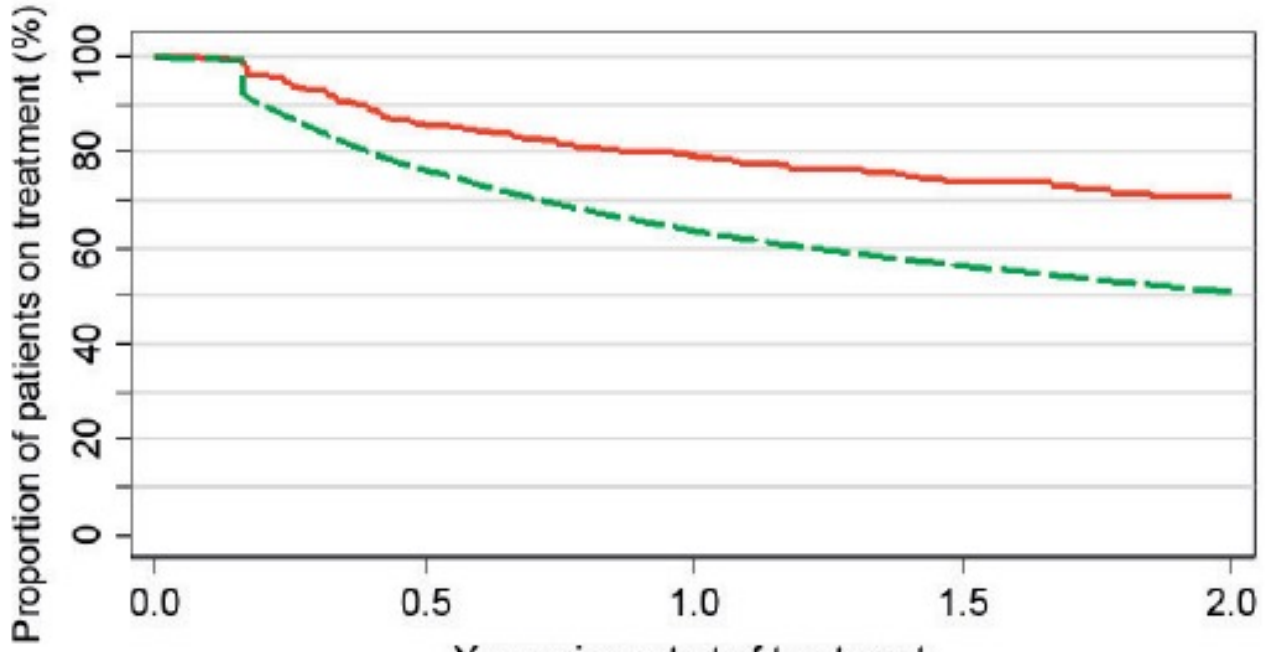
Use of OACs in AF Patients peaks at ~50%, use declines with increasing risk



1. Hsu, J et al. *JAMA Cardiol*. Published online March 16, 2016. doi:10.1001/jamacardio.2015.0374

Despite NOAC Adoption and Ability to Switch NOACs, Adherence to Anticoagulation Remains a Challenge

~30% of NOAC patients stop taking any drug at 2 years



NOAC	914	651	342	139	41
VKA	12307	8453	5762	3915	2506

Martinez C, et al. *Thromb Haemost.* 2015 Dec 22,[illegible].

Challenge: Adherence and Major bleed rates with Novel Oral Anticoagulants (NOACs)

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Treatment	Study Drug Discontinuation Rate	Major Bleeding (rate/year)
Rivaroxaban[1]	24%	3.6%
Apixaban[2]	25%	2.1%
Dabigatran[3] (150 mg)	21%	3.3%
Edoxaban[4] (60 mg / 30 mg)	33 % / 34%	2.8% / 1.6%
Warfarin[1-4]	17 – 28%	3.1 – 3.6%

For those that remain adherent, there is an annual compounding bleeding risk.

1Connolly, S. NEJM 2009; 361:1139-1151 – 2 yrs follow-up (Corrected) 2Patel, M. NEJM 2011; 365:883-891 – 1.9 yrs follow-up, ITT 3Granger, C NEJM 2011; 365:981-992 – 1.8 yrs follow-up, 4Giugliano, R. NEJM 2013; 369(22): 2093-2104 – 2.8 yrs follow-up.

Results from different clinical investigations are not directly comparable.
Information provided for educational purposes only.

Non-Valvular Atrial Fibrillation (NVAF), Stroke, and Current Treatment Options



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

- AFib is a growing problem associated with greater morbidity and mortality
  - 5x increased risk of stroke
  - 90% of clots formed in LA come from LAA
- Current treatments with warfarin or NOACS are effective, but many patients stop taking the medications
  - ~1 in 4 patients discontinue blood thinners after 2 years
- Anti-coagulation bleeding risk compounds over time; may not be viable as a long-term solution for some patients

Connection Between NVAF-Related Stroke and the Left Atrial Appendage

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

AF Creates Environment for Thrombus Formation in Left Atrium

- Stasis-related LA thrombus is a predictor of TIA[1] and ischemic stroke[2].
- In non-valvular AFib, >90% of stroke-causing clots that come from the left atrium are formed in the LAA[3].

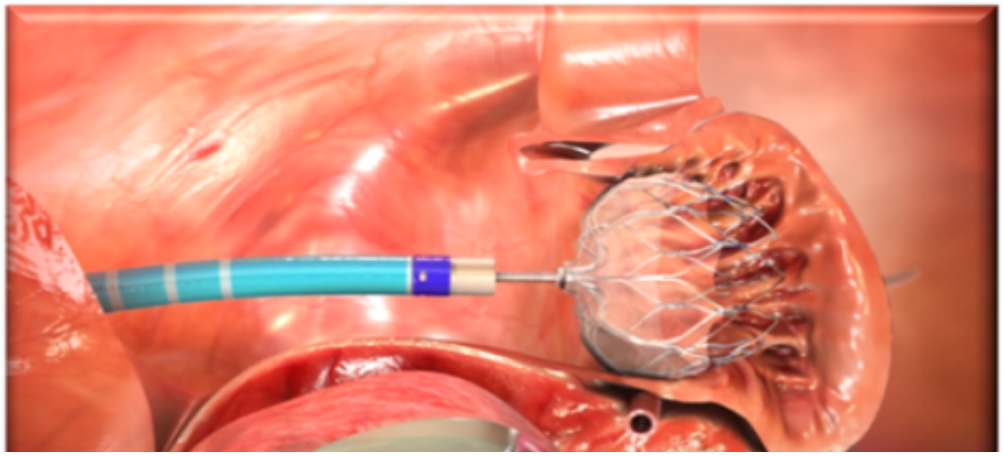


1. Stoddard et al. Am Heart J. (2003); 2. Goldman et al. *J Am Soc Echocardiogr* (1999)
3 Blackshear JL. Odell JA., *Annals of Thoracic Surg* (1996)

WATCHMAN LAAC Device: A One-Time Procedure

Boulder Community Health

- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite by a Heart Team
- Transfemoral Access:
  - Catheter advanced to the LAA via the femoral vein
  - Does not require open heart surgery
- General anesthesia (typical)
- 1 hour procedure (typical)
- 1-2 day hospital stay (typical)



Boulder Community Health

WATCHMAN FLX™

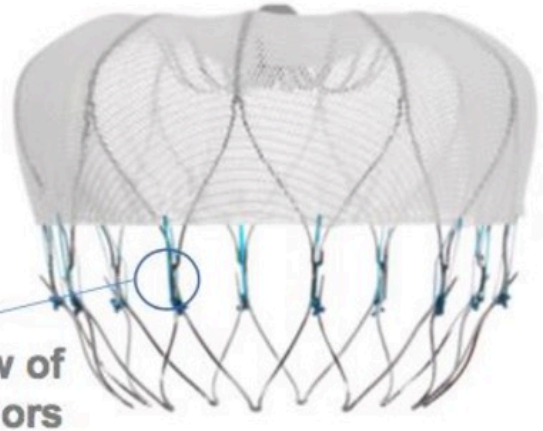
LEFT ATRIAL APPENDAGE CLOSURE DEVICE



Caution: The WATCHMAN FLX™ Left Atrial Appendage Closure Device is an investigational device and is not available for sale in the U.S. or Europe.

10 Strut Frame
Partial Recapture
Minimum LAA Depth = Ostium Diameter

WATCHMAN™



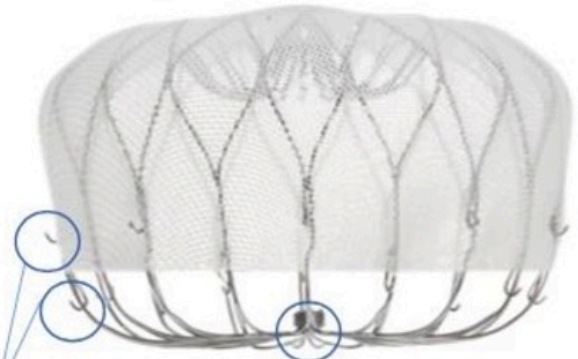
One row of
10 Anchors



'Straight' anchor

18 Strut Frame
Full or Partial Recapture
Minimum LAA Depth = ½ Device Size
PET fabric extended more distally

WATCHMAN FLX™



Two Rows
of 18



'J' anchor



Closed Distal End
Controlled Deployment

WATCHMAN is the Most Studied LAAC Device - Most Patients and Only One with Long-term Clinical Data



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Key Trials	N	Highlights
PROTECT AF[1] (2005-2008)	707	Prospective, randomized 2:1, non-inferiority trial of LAA closure vs. warfarin.
CAP[2] (2008-2010)	566	Prospective registry allowing continued access to the WATCHMAN Device and gain further information prior to PMA approval.
PREVAIL[3] (2010-2012)	407	Prospective, randomized 2:1, non-inferiority trial to collect additional information on the WATCHMAN Device.
CAP2 (2012-2014)	579	Prospective registry allowing continued access to the WATCHMAN Device prior to PMA approval.
Total patients	>2,000	~6,000 Patient-Years of Follow-up

1 Reddy, et al. JAMA. 2014 ;312(19): 1988-1998.; 2 Reddy VY et al. Circulation. 2011; 123:417-424.
3 Holmes et al., JACC 2014,;4(1): 1-11.

PROTECT AFib: WATCHMAN Disabling Stroke Reduction Superior to Warfarin



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Significant Reduction in Disabling Strokes

	Event Rate (per 100 pt-yrs)			Posterior Probabilities, %	
PROTECT AF	WATCHMAN N=463	Warfarin N=244	Rate Ratio (95% CrI)	Non-Inferiority	Superiority
Stroke (all)	1.5	2.2	**0.68** (0.42, 1.37)	>99	83
Disabling	0.5	1.2	**0.37** (0.15, 1.00)	>99	98
Non-disabling	1.0	1.0	**1.05** (0.54, 2.80)	89	34

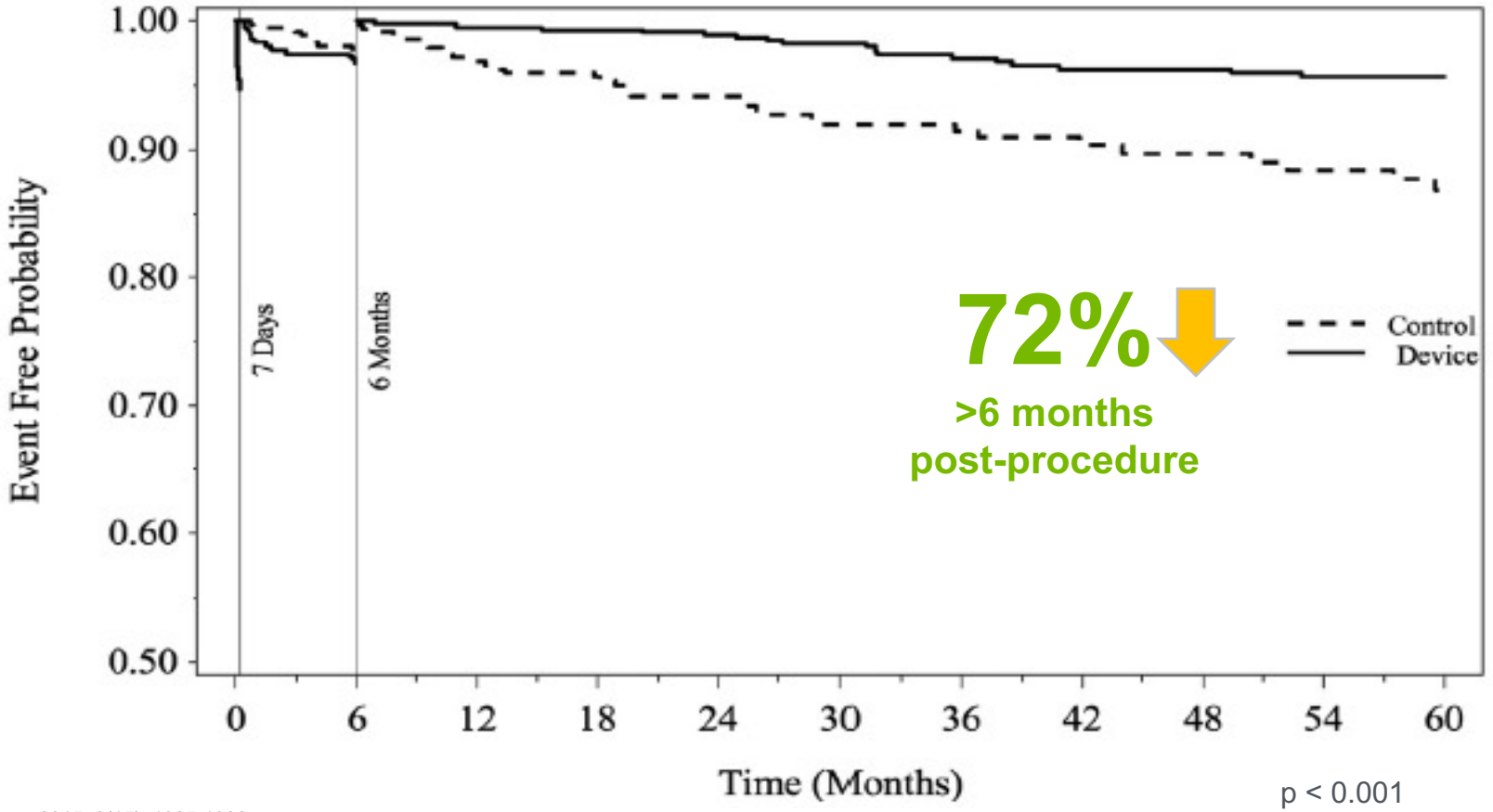
Disabling stroke defined as Modified Rankin Score 3-6

Bayesian – Posterior prob for NI must be ≥97.5%; Posterior Prob for Superiority must be >95%
Reddy, et al. JAMA. 2014

WATCHMAN Major Bleeding Reduction Superior to Warfarin 6-months Post Procedure

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Freedom of Major Bleeding Over 3 Adjunctive Pharmacotherapy Intervals

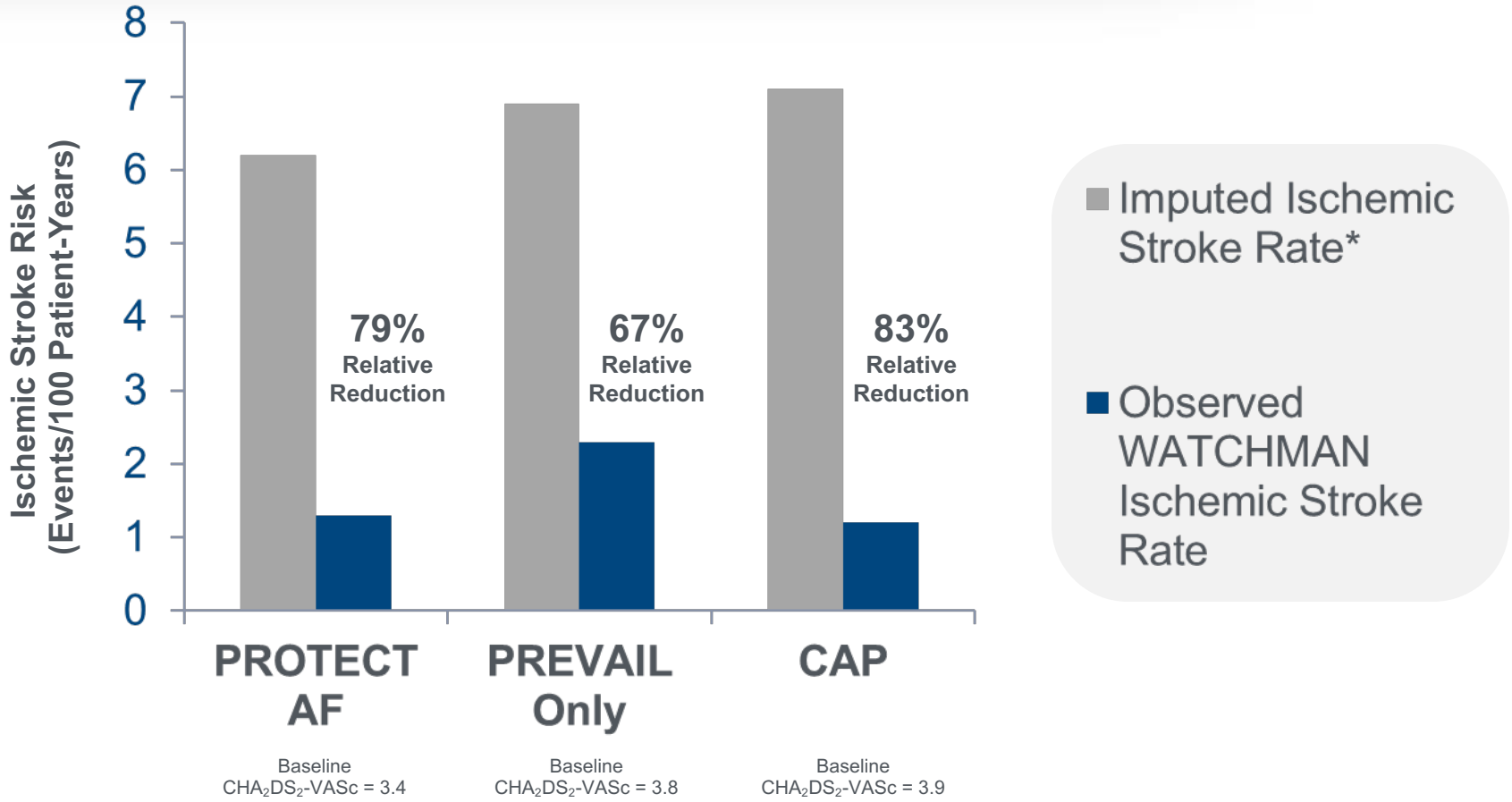


p < 0.001

Price, M. J., V. Y. Reddy, et al. JACC: CV Interv 2015; 8(15): 1925-1932

WATCHMAN Reduced Ischemic Stroke Compared to No Therapy

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE



* Imputation based on published rate with adjustment for CHA_2DS_2-VASc score (3.0); Olesen JB. Thromb Haemost (2011)

FDA Oct 2014 Panel Sponsor Presentation. Hanzel G, et al. TCT 2014 (abstract)

Results from different clinical investigations are not directly comparable. Information provided for educational purposes only.

WATCHMAN is the Most Studied LAAC Device with Long-term Clinical Data



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

		Results
Safety	WATCHMAN procedure is **safe**	95% implant success; ~4% complication rates[1]
Primary Efficacy	WATCHMAN **comparable** to warfarin	21% reduction in events (p=0.22)[3]
All-Stroke	WATCHMAN **comparable** to warfarin	67% reduction in disabling strokes (P_s=98%)[2]; 78% reduction in hemorrhagic strokes (p=0.004)[3]
CV / Unexp death	WATCHMAN **superior** to warfarin	52% reduction in events (p=0.006)[3]
Major Bleeding	WATCHMAN **comparable** to warfarin; **superior** to warfarin **post-procedure**	52% reduction post-procedure (p=0.002); 72% reduction after 6-months (p=0.001)[4]
Warfarin	WATCHMAN allows the **majority** of patients to **discontinue warfarin**	92% of patients discontinue after 45-days; 99% of patients discontinue after 1 year[5]

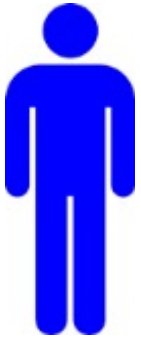
1. WATCHMAN FDA Panel Sponsor Presentation. Oct 2014.; 2 Reddy, et al. JAMA. 2014 ;312(19): 1988-1998.
3 Holmes, DR et al. JACC. 2015;65(24):2614-2623.; 4 Price, M. J., V. Y. Reddy, et al. JACC: CV Interv 2015; 8(15): 1925-1932; 5.Holmes, DR et al. JACC 2014; 64(1): 1-12.

Patient Populations

WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

Non-Valvular A-Fib Population

High Risk for Stroke (CHA_2DS_2-VASC ≥ 2)



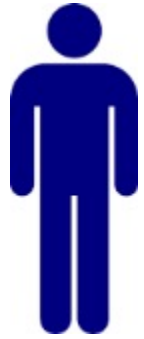
Tolerant to OAC

Balance stroke risk reduction benefit vs. bleeding risk



Patients w/ appropriate rationale to seek a non-pharmacologic alternative to warfarin

-History of bleeding
-Fall risks / previous trauma
-Non-compliant / Labile INR's
-Lifestyle



Contraindicated

WATCHMAN™ Device Patient Selection



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

"Have an appropriate rationale to seek a non-pharmacologic alternative to Warfarin, taking into account the safety and effectiveness of the device compared to Warfarin"

- History of major bleeding while taking anticoagulation therapy
- Patient's prior experience with OAC (if applicable):
  - *inability to maintain stable INR*
  - *inability to comply with regular INR monitoring and unavailability of an approved alternative OAC*
- Medical condition, occupation, or lifestyle placing patient at high risk of major bleeding secondary to trauma

* Please refer to product DFU for more specific details on patient selection

CMS National Coverage Decision Criteria for Coverage



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

CMS will cover percutaneous LAAC implants when specific criteria are met:

Documented in medical record

- Eligible patients must have a $CHADS_2$ score ≥ 2 or a **CHA_2DS_2-VASc score ≥ 3**
- Patients must be **suitable for short-term warfarin**, but deemed **unable to take long-term oral anticoagulation**
- **Documented evidence of a formal shared decision interaction between the patient and an independent non-interventional physician** using an OAC evidence-based decision tool

- *LAA Registry*: Patients must be enrolled in a prospective national registry

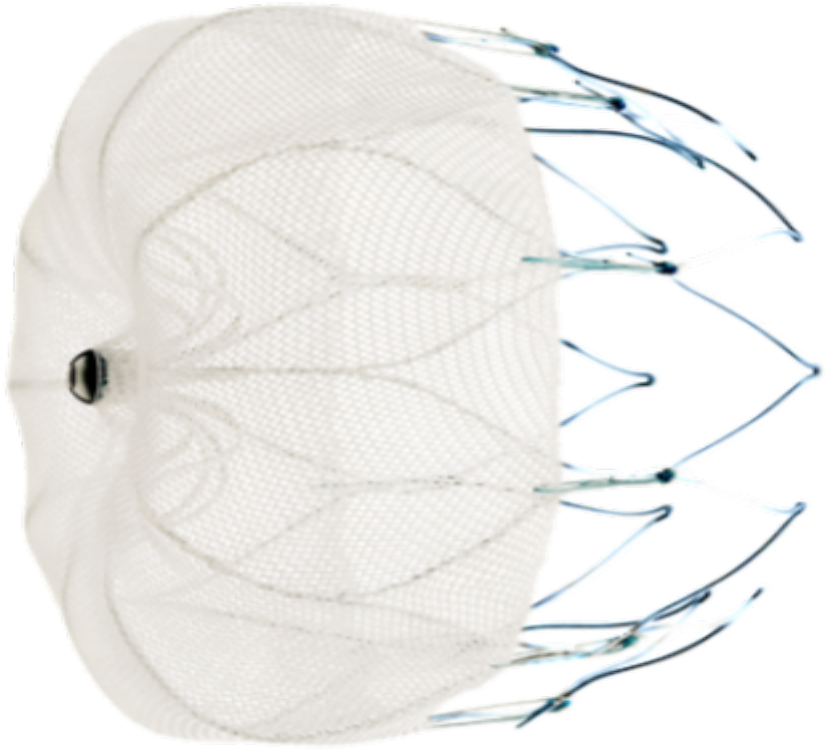
- *Operator requirements*: IC or EP or cardiovascular surgeon must have performed at least 25 transseptal punctures (TSP) through intact septum
  - Must maintain at least 25 TSP over a two year period (at least 12 are LAAC)

- *Facility Requirements*: The procedure must be furnished in a hospital with an established structural heart disease (SHD) and/or electrophysiology (EP) program

WATCHMAN Is A Safe, Effective, One-time Procedure for Appropriate NVAF Patients

Boulder Community Health

- The WATCHMAN Implant has been proven to be a safe and effective alternative to long-term oral anticoagulants (OACs)[1]
- Left atrial appendage closure (LAAC) with WATCHMAN may eliminate the need for long-term warfarin use in patients with non-valvular atrial fibrillation (NVAF) who have a reason to seek an alternative to OACs
- The WATCHMAN Implant has been proven to offer stroke risk reduction comparable to Warfarin—and also reduces the long-term risk of bleeding associated with Warfarin use.[2]



1. Holmes DR . *JACC* 2014;64(1):1-12. 2. Holmes DR. *JACC* 2015;65(24):2614-2623.

Thank You!

Boulder Community Health

Questions?

Innovative Treatments for Atrial Fibrillation

Maria Anderson, MD
Srini Iyengar, MD

Boulder Heart, 303-963-9220

Boulder Community Health