## Reducing Your Risk For Stroke

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## **Explaining Stroke**







MAY IS
NATIONAL STROKE
AWARENESS MONTH



## May - National Stroke Awareness Month



National Stroke Association encourages everyone to spread awareness about stroke in May about how to:

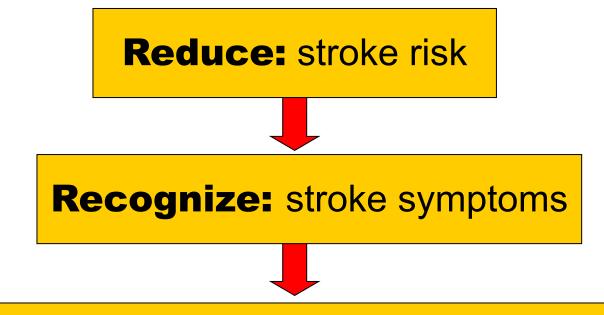


- **STOP** primary and secondary stroke through risk factor management.
- Act F.A.S.T. to increase recognition of and response to stroke symptoms.
- Spread HOPE about recovery from stroke.

Visit www.stroke.org/SAM for free educational resources.

#### Be Stroke Smart





**Respond:** at the first sign of stroke, Call 911 immediately!



#### Stroke Facts



A leading cause of death in the United States



- 795,000 Americans suffer strokes each year
- 134,000 deaths each year
  - From 1996 to 2006, the stroke death rate fell 33.5% and number of deaths fell by 18.4%
- 6,400,000 stroke survivors

### Stroke Facts



A leading cause of adult disability.



- Up to 80% of all strokes are preventable through risk factor management.
- On average, someone suffers a stroke every 40 seconds in America.

#### Women & Stroke



 Stroke kills more than twice as many American women every year as breast cancer.



- More women than men die from stroke and risk is higher for women due to higher life expectancy.
- Women suffer greater disability after stroke then men.
- Women ages 45 to 54 are experiencing a stroke surge, mainly due to increased risk factors and lack of prevention knowledge.

#### African Americans & Stroke



- Incidence is nearly double that of Caucasians
- African Americans suffer more extensive physical impairments
- Twice as likely to die from stroke than Caucasians
- High incidence of risk factors for stroke
  - Hypertension
  - Diabetes
  - Obesity
  - Smoking
  - Sickle cell anemia



## Hispanics & Stroke



 Higher incidence among Mexican Americans than Caucasians.



- Mexican Americans are at increased risk for all types of stroke and TIA at younger ages than Caucasians.
- Spanish-speaking Hispanics are less likely to know stroke symptoms than English-speaking Hispanics, African Americans and Caucasians.

#### Well-known Stroke Survivors



- President Gerald Ford
- Teddy Bruschi
- Sharon Stone
- Della Reese
- Kirk Douglas
- Roy Horn of Siegfried & Roy

- Mary Kay Ash
- Charles Schultz
- Harry Caray
- Charles Dickens
- Ed Koch
- Ted Williams

#### Definition of Stroke

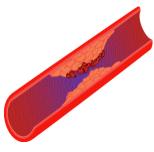


- Sudden brain damage
- Lack of blood flow to the brain caused by a clot or rupture of a blood vessel



Ischemic = Clot (makes up approximately 87% of all strokes)

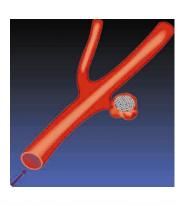


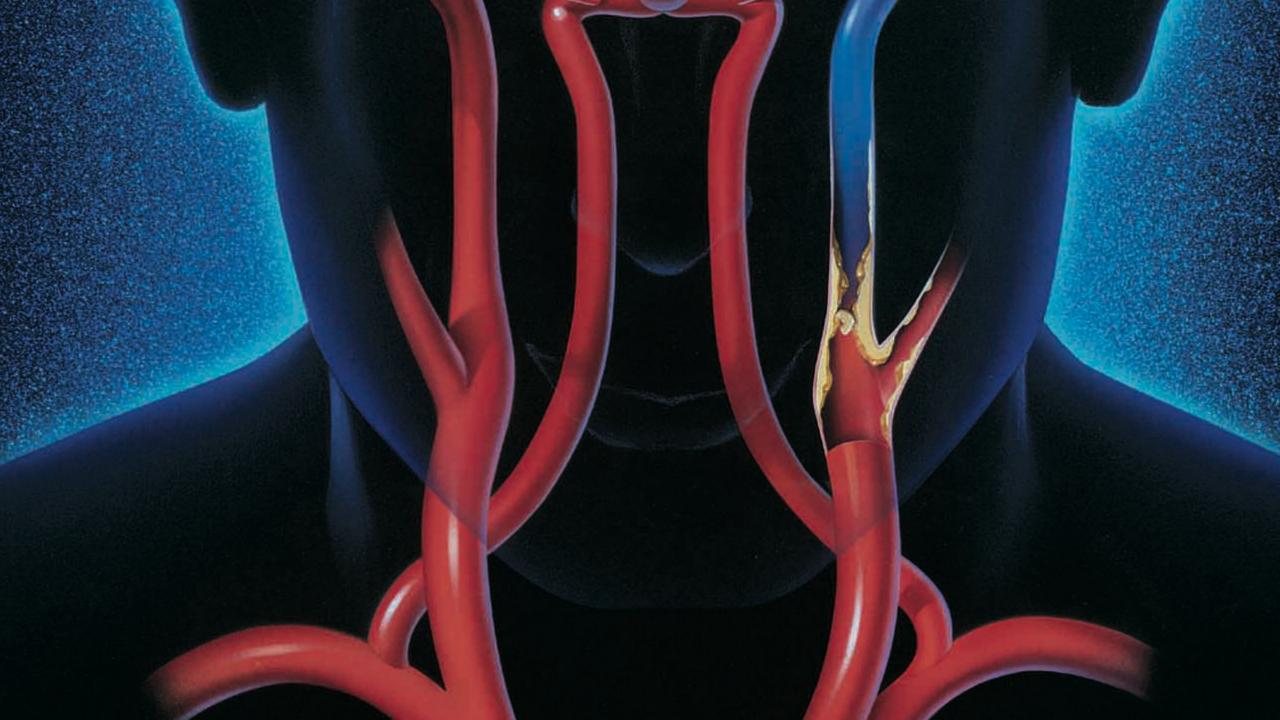


**Thrombotic** 

#### Hemorrhagic = Bleed

- Bleeding around brain
- Bleeding into brain





## Stroke Symptoms





If you observe any of these symptoms, call 911 immediately.

**Every minute matters!** 

## Stroke Strikes F.A.S.T. You Should, Too. Call 9-1-1



• F = Face: ask the person to smile



- A = Arm: ask the person to raise both arms
- S = Speech: ask the person to speak a simple sentence
- T = Time: to call 911

#### Every minute matters!



 Transient ischemic attack (TIA) is a warning sign of a future stroke – up to 40% of TIA patients will have a future stroke.



- Symptoms of TIAs are the same as stroke.
- TIA symptoms can resolve within minutes or hours.
- It is important to seek immediate medical attention if you suspect that you are having or have had a TIA.

## The Perceptions of Stroke



#### Myth:

- Stroke is not preventable
- Stroke cannot be treated
- Stroke only strikes the elderly
- Stroke happens in the heart
- Stroke recovery ends after 6 months

#### **Reality:**

- Up to 80% percent of strokes are preventable
- Stroke requires emergency treatment
- Anyone can have a stroke
- Stroke is a "Brain Attack"
- Stroke recovery can last a lifetime



#### The Cost of Stroke





The estimated direct and indirect cost of stroke was 73.7 billion in 2010.

The mean lifetime cost of ischemic stroke is about \$140,048 in America.

#### How Do You Prevent Stroke?



National Stroke Association recommends that you follow these guidelines to help people reduce their risk for stroke...



#### Stroke Prevention Guidelines



- 1. Know your blood pressure. Have it checked at least annually. If it is elevated, work with your doctor to control it.
- 2. Find out if you have atrial fibrillation (AF) a type of irregular heartbeat. If you have it, work with your doctor to manage it.
- 3. If you smoke, stop.



#### Stroke Prevention Guidelines



National Stroke Association™ www.stroke.org

- 4. If you drink alcohol, do so in moderation.
- 5. Know your cholesterol number. If it is high, work with your doctor to control it.
- 6. If you are diabetic, follow your doctor's recommendations carefully to control your diabetes.

#### Stroke Prevention Guidelines



- 7. Include exercise in your daily routine.
- Enjoy a lower sodium (salt) and lower fat diet.
- If you have circulation problems, work with your doctor to improve your circulation.
- 10. If you experience any stroke symptoms, call 911 immediately. **Every minute matters!**





National Stroke Association recommends that you learn stroke symptoms and how to respond to symptoms by calling 9-1-1.



# Why People Don't Recognize and Respond to Symptoms



- Don't recognize symptoms
- Denial
- Think nothing can be done
- Worry about cost
- Think symptoms will go away
- Fear or don't trust hospitals



#### Acute Stroke Treatments



#### Ischemic stroke (Brain Clot)

Clot busting medication: t-PA (Tissue Plasminogen Activator)

Clot-removing devices: Merci Retriever, Penumbra

#### Hemorrhagic Stroke (Brain Bleed)

Clipping

Coiling



## Stroke Recovery







- 25% recover with minor impairments.
- 40% experience moderate to severe impairments requiring special care.
- 10% require care within either a skilled-care or other long-term care facility.
- 15% die shortly after the stroke.

## Types of Stroke Rehabilitation



### Physical Therapy (PT)

Walking, range of movement

### Occupational Therapy (OT)

Taking care of one's self

#### Speech Language Therapy

Communication skills, swallowing, cognition

#### Recreational Therapy

Cooking, gardening



# Lifestyle Changes for Survivors and Caregivers



- Daily living skills
- Dressing and grooming
- Diet, nutrition and eating difficulties
- Skin care problems
- Pain
- Sexuality/Intimacy

- Behavior
- Depression & Anger
- Emotional Liability
- One-sided Neglect
- Memory Loss
- Communication Problems



## Types of Recovery Services



- Rehabilitation unit in the hospital
- In-patient rehabilitation facility
- Home-bound therapy
- Home with outpatient therapy
- Long-term care facility
- Community-based programs



#### National Stroke Association



#### What we do...



- Reduce the incidence and impact of stroke
- Advocate for prevention and public education
- Provide professional education and training
- Provide recovery resources for stroke survivors and caregivers



## National Stroke Association 1-800-STROKES (787-6537)

www.stroke.org





# Stroke: Straight from the Heart

Srinivas Iyengar, MD Director, Structural Heart Boulder Heart

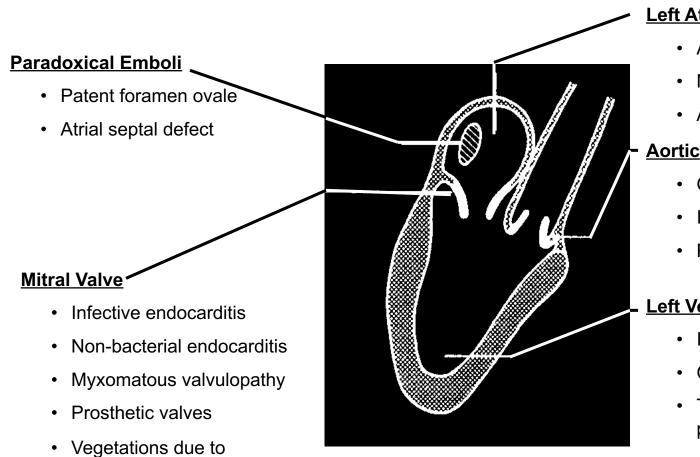
#### What causes stroke?



- Emboli from valves/LV
- Vascular (i.e., carotid/aortic)
- Bleeding
- AF (mainly LAA)
- Cryptogenic (i.e., PFO)
- HTN

## Sources of Cardiogenic Emboli





#### Left Atrium

- Atrial fibrillation
- Myxoma
- Atrial septal aneurysm

#### **Aortic Valve**

- Calcific stenosis
- Infective endocarditis
- Prosthetic valve

#### **Left Ventricle**

- Ischemic dyskinesis
- Cardiomyopathy
- Thrombi due to prothrombotic states

Lowell Satler MD, CRT 2010

prothrombotic states

#### Atrial Fibrillation



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

#### Causes



- 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



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

### Treatment



- 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 AF.
- Ablation (surgically or percutaneously) can also be utilized.

### But what else does AF cause?



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

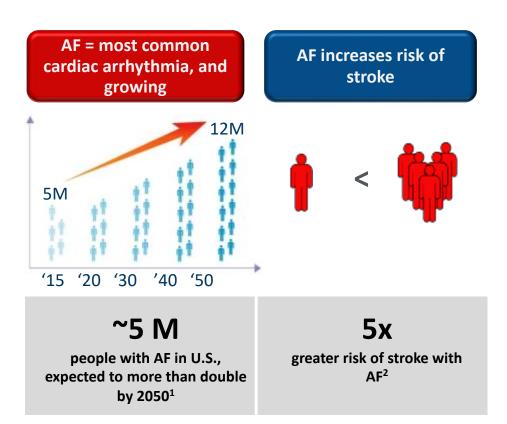
### **Blood Thinners**



- 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.

## AF is a Growing Problem Associated with Greater Morbidity and Mortality





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

<sup>1.</sup> 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.

### AF-related strokes are debilitating



#### **Stroke**

#1

cause of **adult disability** worldwide<sup>1</sup>

#### **AF-related Stroke**

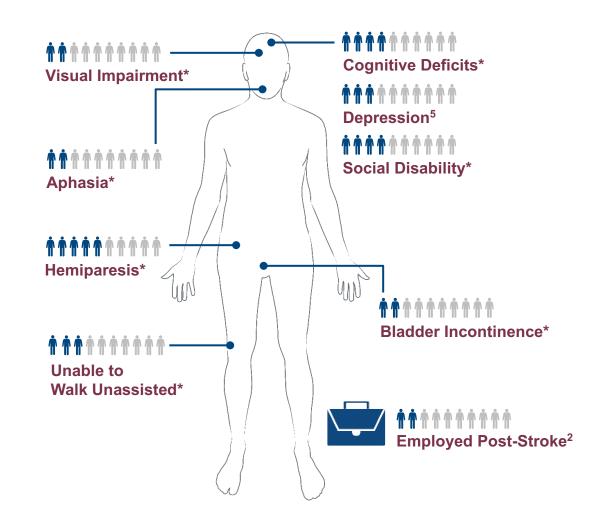
1.5X higher disability<sup>3\*\*</sup>

2X higher mortality<sup>3\*\*</sup>

70% result in death or permanent disability<sup>6</sup>

\*at 6 months post-stroke4

<sup>\*\*</sup>compared with stroke patients without AF



## Anticoagulant Therapy Carries Risk of Intracerebral Hemorrhage or Death





Spontaneous intraparenchymal bleed



Hemorrhagic transformation

### Validated Scoring Systems to Assess Stroke Risks



#### CHA<sub>2</sub>DS<sub>2</sub>VASc Score (Stroke Risk)<sup>3</sup>

|                | Condition                  | Points |
|----------------|----------------------------|--------|
| С              | Congestive heart failure   | 1      |
| Н              | Hypertension (SBP>160)     | 1      |
| A <sub>2</sub> | Age ≥ 75 years             | 2      |
| D              | Diabetes mellitus          | 1      |
| S <sub>2</sub> | Prior stroke, TIA or       | 2      |
|                | thromboembolism            |        |
| V              | Vascular disease (PAD, MI) | 1      |
| Α              | Age 65-74 years            | 1      |
| Sc             | Sex category (Female)      | 1      |
|                | TOTAL POINTS               |        |

| Score | Yearly Stroke Risk (%) |                           |                            |  |
|-------|------------------------|---------------------------|----------------------------|--|
|       | No Warfarin            | With Aspirin <sup>2</sup> | With Warfarin <sup>2</sup> |  |
| 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                        |  |

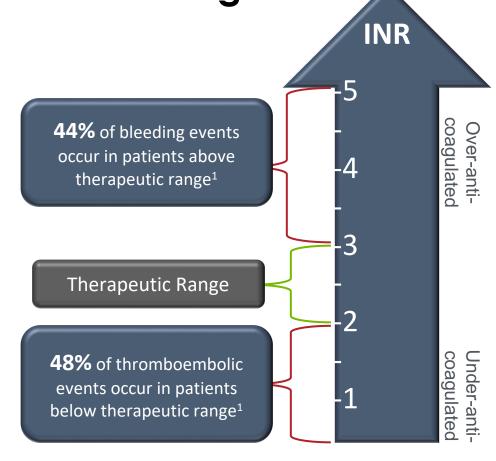
## Stroke Treatment Option: Warfarin



Warfarin is an effective means of stroke reduction in patients with AF 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<sup>2</sup>



<sup>1</sup> 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

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



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

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

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



- AF 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.

## Watchman video

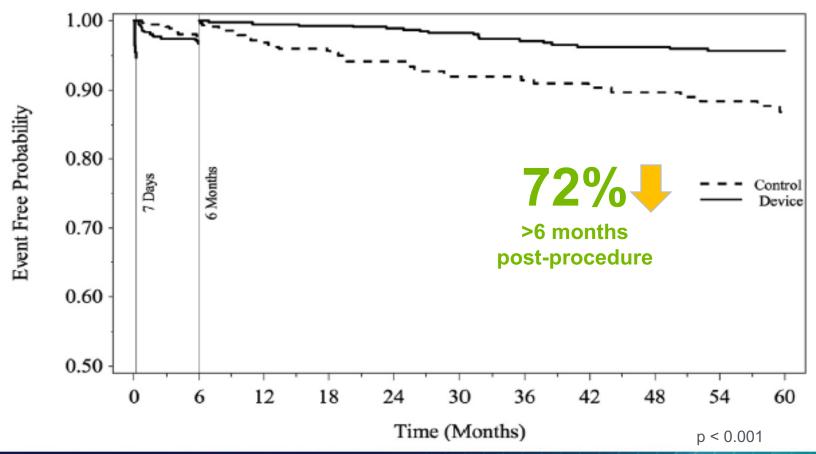
https://www.youtube.com/watch?v=uxER4HMfuP4&t=3s



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



## Freedom of Major Bleeding Over 3 Adjunctive Pharmacotherapy Intervals



## PROTECT AF: WATCHMAN Disabling Stroke Reduction Superior to Warfarin



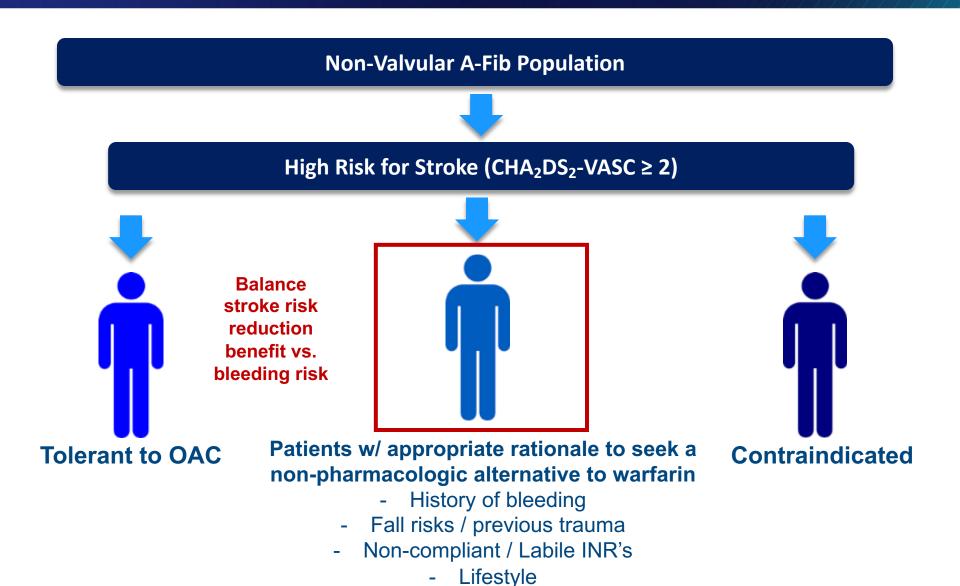
#### Significant Reduction in Disabling Strokes

|               | Event Rate<br>(per 100 pt-yrs) |                          |                          | Posterior Probabilities, % |             |
|---------------|--------------------------------|--------------------------|--------------------------|----------------------------|-------------|
| PROTECT AF    | <b>WATCHMAN</b><br>N=463       | <b>Warfarin</b><br>N=244 | Rate Ratio<br>(95% CrI)  | Non-<br>Inferiority        | Superiority |
| Stroke (all)  | 1.5                            | 2.2                      | <b>0.68</b> (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                      | <b>1.05</b> (0.54, 2.80) | 89                         | 34          |

Disabling stroke defined as Modified Rankin Score 3-6

## Patient Populations





## Patent Foramen Ovale (PFO)

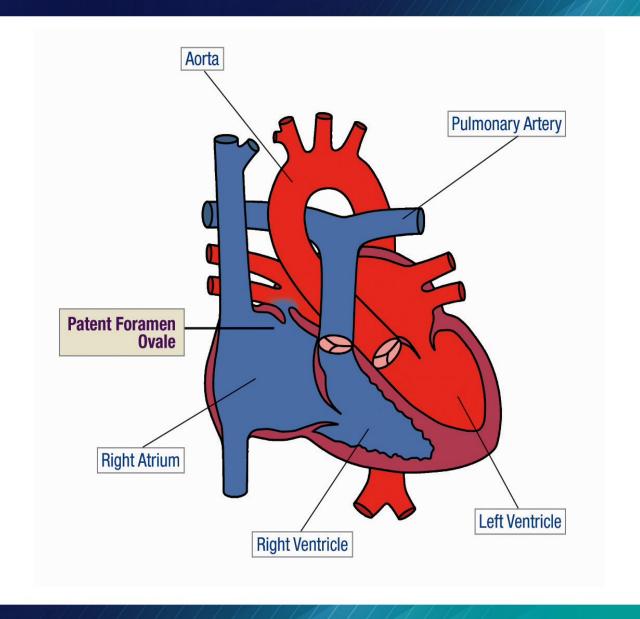


- A patent foramen ovale (PFO) is a persistent, usually flap-like opening between the atrial septum primum and secundum at the location of the fossa ovalis.
- In utero, the foramen ovale serves as a physiologic conduit for right-to-left shunting.
- After birth, with the establishment of pulmonary circulation, the increased left atrial blood flow and pressure results in functional closure of the foramen ovale.
- This functional closure is subsequently followed by anatomical closure of the septum primum and septum secundum.

## Patent Foramen Ovale (PFO)



- Persistent flap-like opening: atrial septum primum and secundum
- In utero, physiologic rightto-left shunting
- After birth, increased left atrial blood flow and pressure closes flap
- Anatomical closure follows



## Patent Foramen Ovale (PFO)



- The association between PFO and cryptogenic stroke has been identified increasingly over the last twenty years.
- Prevalence of PFO in the general population ranges from 15% to 25%.
- In patients with cryptogenic stroke prevalence of PFO is 40% to 60%.
- Evidence is mounting to seek a better alternative than just prescribing anti-platelet medications (i.e., ASA, Plavix).

## Cryptogenic stroke



- Defined as cerebral ischemia of obscure or unknown origin
- The cause of CS remains undetermined because the event is transitory or reversible, investigations did not look for all possible causes, or because some causes truly remain unknown.
- One third of the ischemic strokes is cryptogenic.

## Cryptogenic Stroke



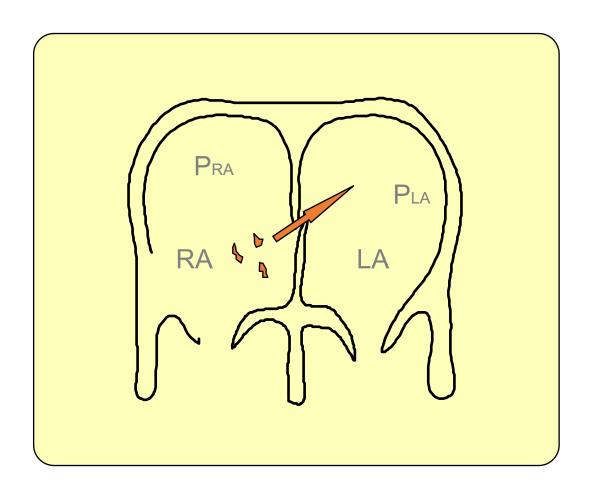
- 700,000 strokes/yr in US
- 80-85% ischemic
- 30-40% of strokes remain defined as cryptogenic
- 40-60% frequency of PFO among cryptogenic strokes
- ~100,000 strokes/yr with PFO as only identified potential etiology

## Presumed Mechanism of Stroke with PFO



#### Pressure in RA > Pressure in LA:

- Early systole
- Valsalva
- Coughing
- Pulmonary hypertension
- COPD
- Pregnancy
- Asthmatics
- Wind instruments
- Decompression sickness (diving)
- High altitude flying
- Obstructive sleep patterns



### PFO closure studies



- Historically, a number of trials had not shown a major benefit from PFO closure for stroke reduction compared to medical therapy.
- However, a number of these studies had "signals" of a positive benefit with device utilization.



# The NEW ENGLAND JOURNAL of MEDICINE

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## Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism

Bernhard Meier, M.D., Bindu Kalesan, Ph.D., Heinrich P. Mattle, M.D., Ahmed A. Khattab, M.D., David Hildick-Smith, M.D., Dariusz Dudek, M.D., Grethe Andersen, M.D., Reda Ibrahim, M.D., Gerhard Schuler, M.D., Antony S. Walton, M.D., Andreas Wahl, M.D., Stephan Windecker, M.D., and Peter Jüni, M.D., for the PC Trial Investigators\*

## PC Trial: Percutaneous Closure of Patent Foramen Ovale (PFO) in Cryptogenic Embolism

414 patients with PFO and prior ischemic stroke, TIA, or peripheral thrombotic event.

| 4-Year Follow-up  | Closure<br>(n = 214) | Medical<br>Therapy<br>(n = 210) | <i>P</i> Value |  |
|---|----------------------|---------------------------------|----------------|--|
| Primary Composite <sup>a</sup>                                    | 3.4%                 | 5.2%                            | 0.34           |  |
| Nonfatal Stroke   | 0.5%                 | 2.4%                            | 0.14           |  |
| TIA   | 2.5%                 | 3.3%                            | 0.56           |  |
| <sup>a</sup> Death, nonfatal stroke, TIA, or peripheral embolism. |                      |                                 |                |  |

**Conclusion:** Percutaneous PFO closure does not reduce the risk of subsequent events in patients with cryptogenic thromboembolism.



Meier B, et al. *N Engl J Med*. 2013;368:1083-1091.

#### ORIGINAL ARTICLE

### Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke

John D. Carroll, M.D., Jeffrey L. Saver, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Scott Berry, Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D., for the RESPECT Investigators\*

N Engl J Med 2013;368:1092-100. DOI: 10.1056/NEJMoa1301440

#### CONCLUSIONS

In the primary intention-to-treat analysis, there was no significant benefit associated with closure of a patent foramen ovale in adults who had had a cryptogenic ischemic stroke. However, closure was superior to medical therapy alone in the prespecified per-protocol and as-treated analyses, with a low rate of associated risks. (Funded by St. Jude Medical; RESPECT ClinicalTrials.gov number, NCT00465270.)

## RESPECT: Closure of Patent Foramen Ovale (PFO) vs. Medical Therapy After Cryptogenic Stroke

980 pts randomized to medical therapy (warfarin or ≥1 antiplatelet) or closure using the Amplatzer PFO Occluder.

| Recurrent Strokes per<br>100-Pt Yrs | Closure | Medical<br>Therapy | <i>P</i> Value |
|-------------------------------------|---------|--------------------|----------------|
| Intention to Treat <sup>a</sup>     | 0.66    | 1.38               | 0.08           |
| Per Protocol                        | 0.46    | 1.30               | 0.03           |
| As Treated                          | 0.39    | 1.45               | 0.007          |
| <sup>a</sup> Primary analysis.      |         |                    |                |

Conclusion: In patients with cryptogenic stroke, percutaneous PFO closure does not appear to prevent recurrent stroke, although secondary analyses suggest possible efficacy.







#### ORIGINAL ARTICLE

# Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke

Jean-Louis Mas, M.D., Geneviève Derumeaux, M.D., Benoît Guillon, M.D., Evelyne Massardier, M.D., Hassan Hosseini, M.D., Ph.D., Laura Mechtouff, M.D., Caroline Arquizan, M.D., Yannick Béjot, M.D., Ph.D., Fabrice Vuillier, M.D., Olivier Detante, M.D., Ph.D., Céline Guidoux, M.D., Sandrine Canaple, M.D., et al., for the CLOSE Investigators\*

#### Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke

Lars Søndergaard, M.D., Scott E. Kasner, M.D., John F. Rhodes, M.D., Grethe Andersen, M.D., D.M.Sc., Helle K. Iversen, M.D., D.M.Sc., Jens E. Nielsen-Kudsk, M.D., D.M.Sc., Magnus Settergren, M.D., Ph.D., Christina Sjöstrand, M.D., Ph.D., Risto O. Roine, M.D., David Hildick-Smith, M.D., J. David Spence, M.D., and Lars Thomassen, M.D.

### **CLOSE trial**

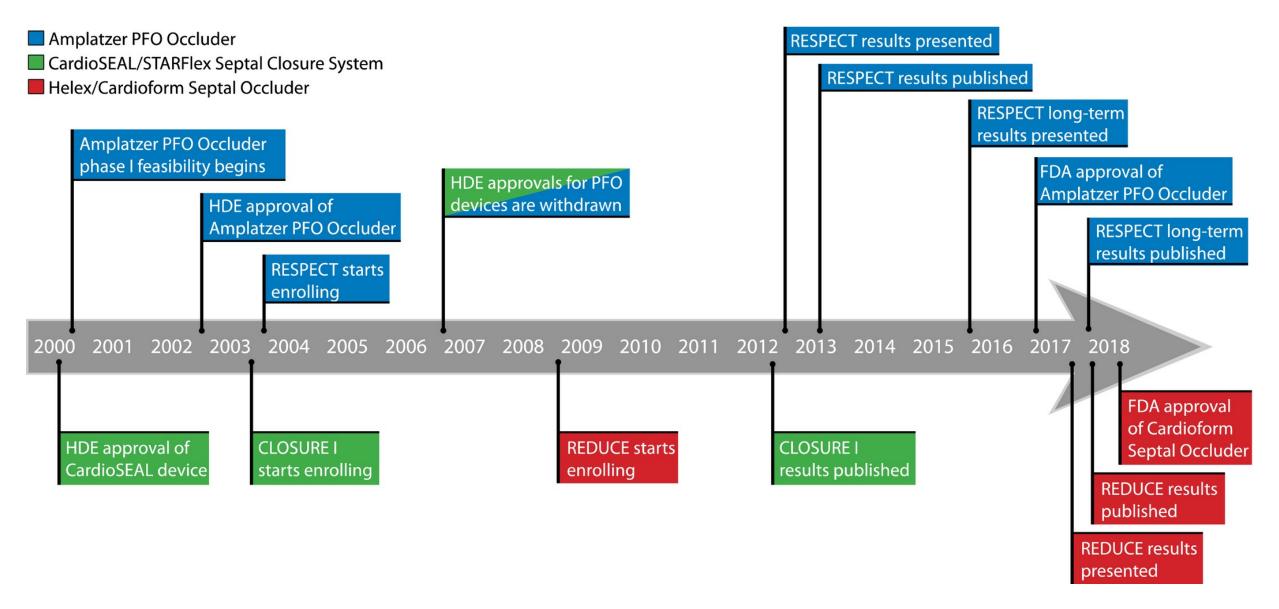


- Randomized 663 patients with cryptogenic stroke to PFO closure, antiplatelet therapy alone, or oral anticoagulation
- PFO closure (plus long-term antiplatelet therapy) bested the antiplatelet therapy group
- No strokes occurred over a mean of 5.3 years among those randomized to PFO, whereas 14 strokes occurred in the antiplatelet-only group (HR 0.03; 95% CI 0-0.12).
- Three strokes occurred in the anticoagulation group, but there was inadequate statistical power to compare these outcomes with the other two groups.
- Conclusion: Among patients 16 to 60 years of age who had had a recent cryptogenic stroke attributed to PFO with an associated atrial septal aneurysm or large interatrial shunt, the rate of stroke was lower with PFO closure plus long-term antiplatelet therapy than with antiplatelet therapy alone.

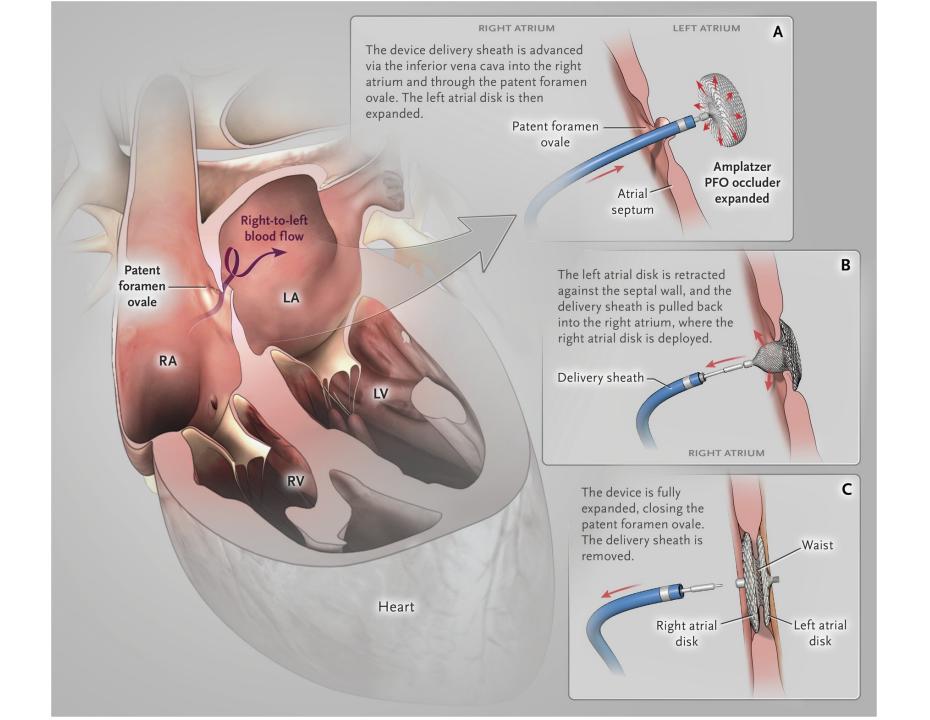
### REDUCE trial



- Gore Helex Septal Occluder or the Gore Cardioform Septal Occluder (both WL Gore & Associates) against medical therapy alone, 2:1, in 664 patients
- Medical therapy consisted of aspirin alone, aspirin plus dipyridamole, or clopidogrel, with use of other antiplatelet agents or anticoagulants prohibited
- PFO closure was associated with significantly lower incidence of clinical ischemic stroke at 1.4% versus 5.4% (HR 0.23; 95% CI 0.09-0.62)
- Incidence of new brain infarctions was also significantly lower in the PFO closure group, although silent brain infarctions were no different.



Patent Foramen Ovale Closure for Stroke Prevention and Other Disorders, Volume: 7, Issue: 12, DOI: (10.1161/JAHA.117.007146)



## PFO video

https://www.youtube.com/watch?v=b0aEAFd6i0U



## Where do we go now?



- Every patient who has a history of TIA/CVA needs a professional neurologic evaluation.
- If a PFO is found, alternate reasons for CVA need to be evaluated first (i.e., AF, carotid).
- If a patient indeed has a documented neurologic event and has no other viable explanation other than a PFO, then closure can be considered.

### Future Directions



- But what about anti-coagulation therapy (i.e., Coumadin, NOACs) when compared to closure?
- Trials are ongoing.
- If a patient has an alternate reason to be on AC tx (i.e., mechanical valves, hypercoagulable state) that would not push to close.

### Conclusions



- Stroke can occur from a number of different avenues.
- Therapies to reduce stroke burden are essential to reduce morbidity/mortality associated with this condition.
- It's exciting to see future technologies develop.

## Thank You!



Boulder Community Health

## Reducing Your Risk For Stroke

Alan Zacharias, MD Associated Neurologists, 303-578-3807

> Srinivas Iyengar, MD Boulder Heart, 303-747-3874

