# Status of LAA Occlusion in 2023

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**Director of Electrophysiology**
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**Professor of Medicine**
**Johns Hopkins Medical Institutions**

# Relationships with Industry

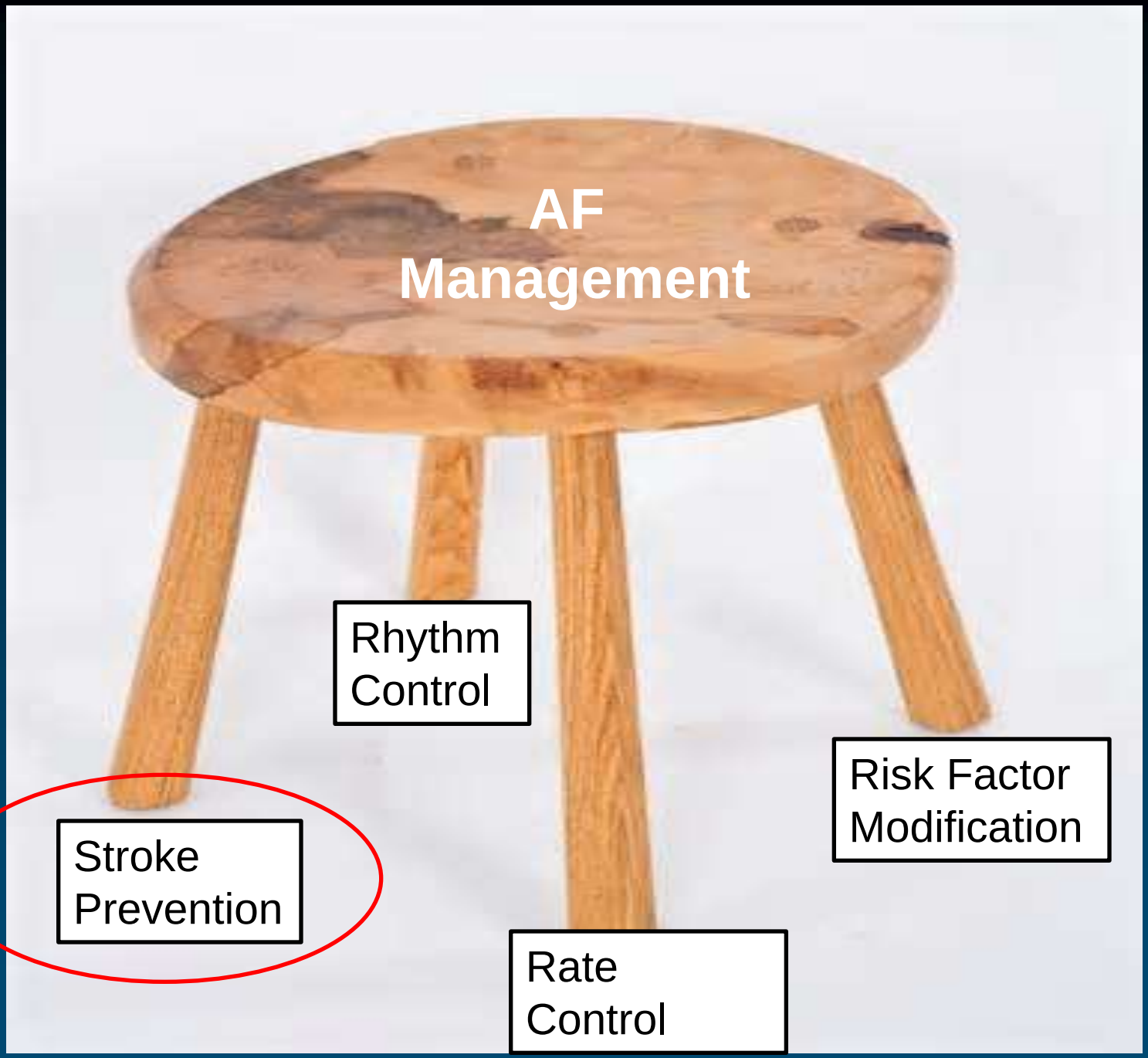
- Consultant/ Lecture Honoraria:  Biosense, Boston Scientific, Medtronic, Abbott Medical, Boehringer Ingelheim, AtriCure

# Case Presentation

- 75 year old man
- Persistent AF
- Echocardiogram reveals 6 cm LA diameter
- Diabetes, Hypertension
- On Eliquis 5 mg bid
- Would like to stop anticoagulation

# What Would You Recommend?

- Continue Eliquis
- Switch to xarelto for increased convenience
- Percutaneous appendage occlusion
- Surgical LAA occlusion


AF
Management
Rhythm
Control
Risk Factor
Modification
Stroke
Prevention
Rate
Control

# 2019 AHA/ACC/HRS Focused Update of the 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 Clinical Practice Guidelines and the Heart Rhythm Society**

***Developed in Collaboration With the Society of Thoracic Surgeons***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# Anticoagulation

- The gender neutral CHADSVasc score is now the metric supported by the 2019 ACC/AFA/HRS AF Guidelines.
- Female gender has been removed from both the ESC and US guidelines.
- Aspirin has been removed from the 2019 US Guidelines
- AF burden is now recognized as a stroke risk factor but it is not incorporated into the guidelines

# Anticoagulation Recommendations
# A Gender Neutral CHADS Vasc is now employed

| | | |
|---|---|---|
| I | A | 1. **For patients with AF and an elevated $CHA_2DS_2$-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended.**<br>**Options include:**<br>■ Warfarin (LOE: A) (S4.1.1-5–S4.1.1-7)<br>■ Dabigatran (LOE: B) (S4.1.1-8)<br>■ Rivaroxaban (LOE: B) (S4.1.1-9)<br>■ Apixaban (LOE: B) (S4.1.1-10), or<br>■ Edoxaban (LOE: B-R) (S4.1.1-11)<br>**MODIFIED:** This recommendation has been updated in response to the approval of edoxaban, a new factor Xa inhibitor. More precision in the use of $CHA_2DS_2$-VASc scores is specified in subsequent recommendations. The LOEs for warfarin, dabigatran, rivaroxaban, and apixaban have not been updated for greater granularity as per the new LOE system. (Section 4.1. in the 2014 AF Guideline) The original text can be found in Section 4.1 of the 2014 AF guideline. Additional information about the comparative effectiveness and bleeding risk of NOACs can be found in Section 4.2.2.2. |
| | B | |
| | B | |
| | B-R | |
| IIa | B | 12. **For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a $CHA_2DS_2$-VASc score of 0 in men or 1 in women, it is reasonable to omit anticoagulant therapy** (S4.1.1-24, S4.1.1-25).<br>**MODIFIED:** Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. (Section 4.1. in the 2014 AF Guideline) |
| IIb | C-LD | 15. **For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a $CHA_2DS_2$-VASc score of 1 in men and 2 in women, prescribing an oral anticoagulant to reduce thromboembolic stroke risk may be considered** (S4.1.1-31–S4.1.1-35).<br>**MODIFIED:** Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and evidence was added to support separate risk scores by sex. LOE was updated from C to C-LD. (Section 4.1. in the 2014 AF Guideline) |

# Anticoagulation Recommendations (cont)

| | | |
|---|---|---|
| I | A | 2. **NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve)** (S4.1.1-8–S4.1.1-11).<br>NEW: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. When the NOAC trials are considered as a group, the direct thrombin inhibitor and factor Xa inhibitors were at least noninferior and, in some trials, superior to warfarin for preventing stroke and systemic embolism and were associated with lower risks of serious bleeding. |

# 4.4. Nonpharmacological Stroke Prevention

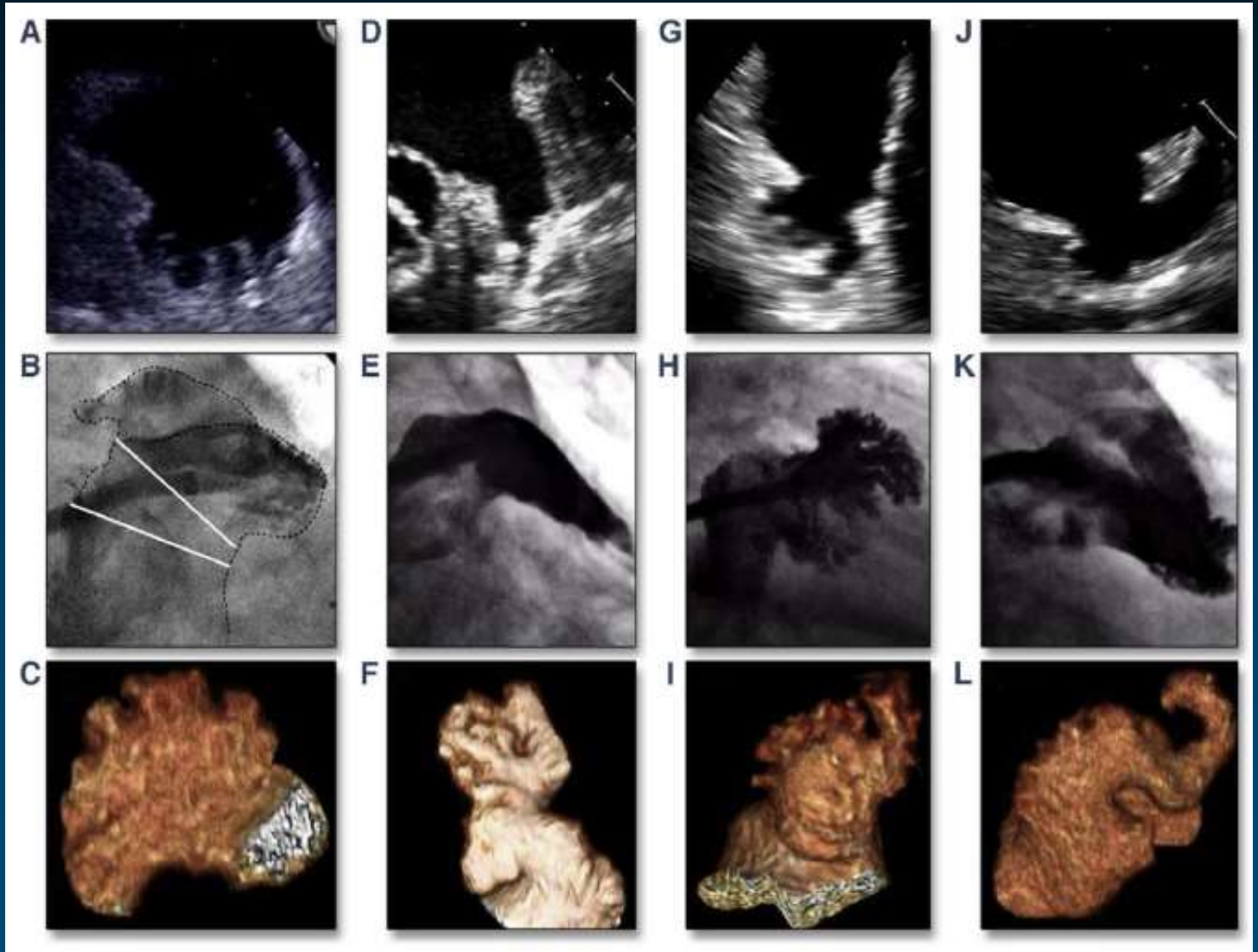
## 4.4.1. Percutaneous Approaches to Occlude the LAA

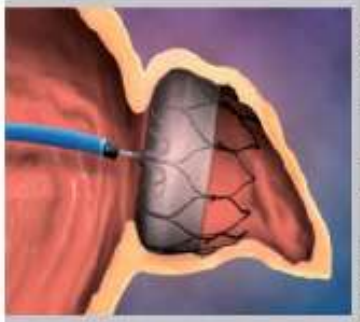
| Recommendation for Percutaneous Approaches to Occlude the LAA<br>Referenced studies that support the new recommendation are summarized in Online Data Supplement 4. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendation** |
| **IIb** | **B-NR** | **1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5).**<br>**NEW**: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation. |

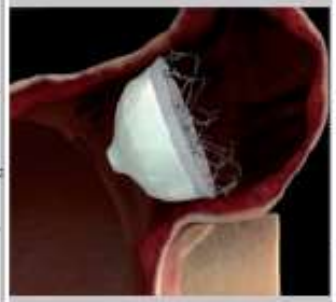
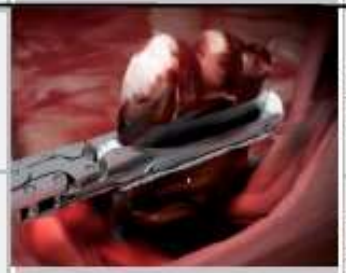
## 4.4.2. Cardiac Surgery—LAA Occlusion/Excision

| Recommendation for Cardiac Surgery—LAA Occlusion/Excision<br>Referenced studies that support the modified recommendation are summarized in Online Data Supplement 5. | | |
|---|---|---|
| **COR** | **LOE** | **Recommendation** |
| **IIb** | **B-NR** | **1. Surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac surgery (S4.4.2-1), as a component of an overall heart team approach to the management of AF.**<br>**MODIFIED**: LOE was updated from C to B-NR because of new evidence. |

# Autopsy and Echocardiographic Studies Have Implicated the Left Atrial Appendage as the Source of Thromboemboli in Most Patients with Nonvalvular AF.



| LAAC Device | Trial design | N | Trial | Trial findings |
|---|---|---|---|---|
|  Watchman | Randomised control trial | 707 | PROTECT AF (Holmes *et al.* 2009) | Procedural success: 90.9%<br>Complications rate[a]: 8.7%<br>Otherr: primary endpoint non-inferiority to warfarin for stroke, systemic embolism or death |
| | Randomised control trial | 1114 | PREVAIL (Holmes *et al.* 2014) | Procedural success: 95.1%<br>Complication rate[a]: 4.2%<br>Other: primary endpoint non-inferiority to warfarin for ischaemic stroke prevention in high risk NVAF: patients. |
| | Prospective multicentre trial | 150 | ASAP (Reddy *et al.* 2013) | Procedural success: 94.7%<br>Complication rate[a]: 8.7%<br>Other: First trial reporting safe LAAO implant without warfarin transition. |
| | Prospective registry | 1021 | EWOLUTION (Boresma *et al.* 2016) | Procedural success: 98.5%<br>Complication rate[a]: 2.8%<br>Other: 30 day mortality rate was 0.7% (0.6% unrelated to device) |
|  Amplatzer Cardiac Plug (ACPI) | Prospective single-centre trial | 59 | Abualsaud *et al.* 2016 | Procedural success:100.%<br>Complication rate[a]: 9.7%<br>Other: Trial compared ACP with AA - similar procedural success between both but, significant reduction in leaks for AA. |
| | Retrospective multicentre registry | 1047 | Tzikas *et al.* 2016 | Procedural success: 97.3%<br>Complication rate[a]: 5.0% |
|  Amplatzer Amulet (AA) | Prospective single-centre trial | 59 | Abualsaud *et al.* 2016 | Procedural success:96.4%<br>Complication rate[a]: 3.6%<br>Other: Trial compared ACP with AA - similar procedural success between both but, significant reduction in leaks for AA. |
| | Retrospective multicentre registry | 1088 | Landmesser *et al.* 2017 | Procedural success : 98.2%<br>Complication rate[a]: 3.2% |

| LAAC device | Trial design | N | Trial | Trial findngs |
|---|---|---|---|---|
|  Wavecrest | Prospective single-centre | 73 | WAVCREST 1 (Reddy *et al.* 2014) | Procedural success: 93.1%<br>Complication rate[a]: 2.7% |
| | | | | |
|  Lariat | Prospective single-centre | 89 | Bartus *et al.* 2013 | Procedural success: 95.5%<br>Complication rate[a]: 9.0% |
| | Retrospective multicentre registry | 154 | Price *et al.* 2014 | Procedural success: 87.0%<br>Complication rate[a]: 9.1% |
|  AtriClip | Prospective single-centre trial | 34 | Salzberg *et al.* 2010 | Procedural success:100%<br>Complication rate[a]: 0%<br>Other: In addition, 30 day mortality rate was 8.8% but not study or device related. |
| | Prospective single-centre trial | 71 | EXCLUDE (Aliawadi *et al.* 2011) | Procedural success: 95.7%<br>Complication rate[a]: 0%<br>Other: significant adverse events[b] was 48.6% though unrelated to the device. |

# Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation

## A Patient-Level Meta-Analysis

David R. Holmes, Jr, MD,* Shephal K. Doshi, MD,† Saibal Kar, MD,‡ Matthew J. Price, MD,§ Jose M. Sanchez, MD,‖ Horst Sievert, MD,¶ Miguel Valderrabano, MD,# Vivek Y. Reddy, MD**

**TABLE 1 PROTECT AF and CAP: Largest Data Sets to Evaluate Totality of Data**

| | PROTECT AF | PREVAIL | CAP | CAP2 | Total |
|---|---|---|---|---|---|
| Enrollment | 2005-2008 | 2010-2012 | 2008-2010 | 2012-2014 | |
| Enrolled | 800 | 461 | 566 | 579 | 2,406 |
| Randomized | 707 | 407 | – | – | 1,114 |
| Watchman:warfarin (2:1) | 463:244 | 269:138 | 566 | 579 | 1,877:382 |
| Mean follow-up, yrs | 4.0 | 2.2 | 3.7 | 0.58 | N/A |
| Patient-years | 2,717 | 860 | 2,022 | 332 | 5,931 |

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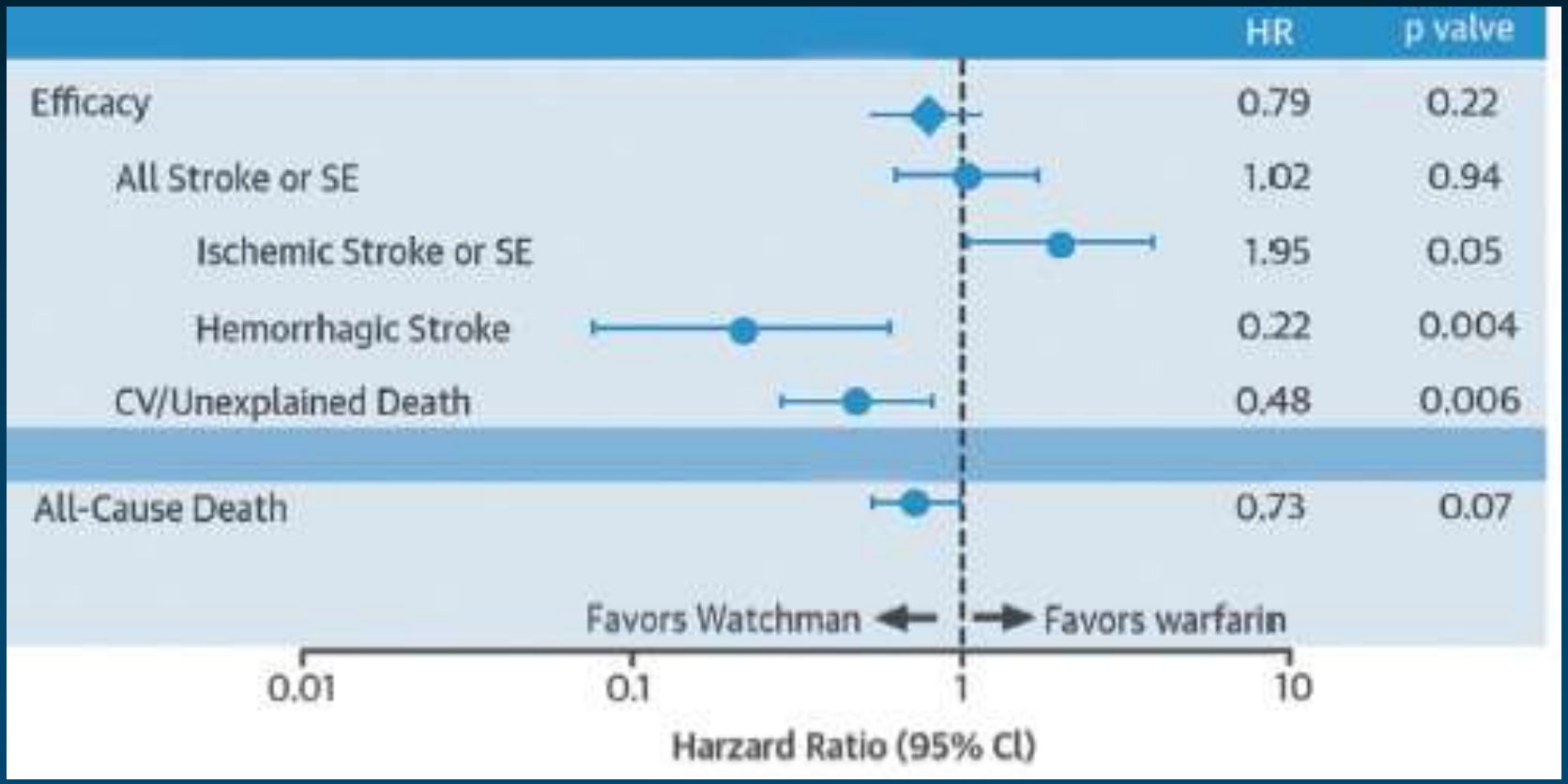

# 5-Year Outcomes After Left Atrial Appendage Closure

## From the PREVAIL and PROTECT AF Trials

Vivek Y. Reddy, MD,[a,b] Shephal K. Doshi, MD,[c] Saibal Kar, MD,[d] Douglas N. Gibson, MD,[e] Matthew J. Price, MD,[e] Kenneth Huber, MD,[f] Rodney P. Horton, MD,[g] Maurice Buchbinder, MD,[h] Petr Neuzil, MD, PhD,[b] Nicole T. Gordon, BSEE,[i] David R. Holmes, Jr, MD,[j] on behalf of the PREVAIL and PROTECT AF Investigators

PROTECT and PREVAIL Clinical trials are both Prospective randomized clinical trials with patients randomized 2:1 to LAAC or warfarin.

1114 patients with 4343 years follow-up were enrolled.

This study reports their five year outcomes.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 70, NO. 24, 2017

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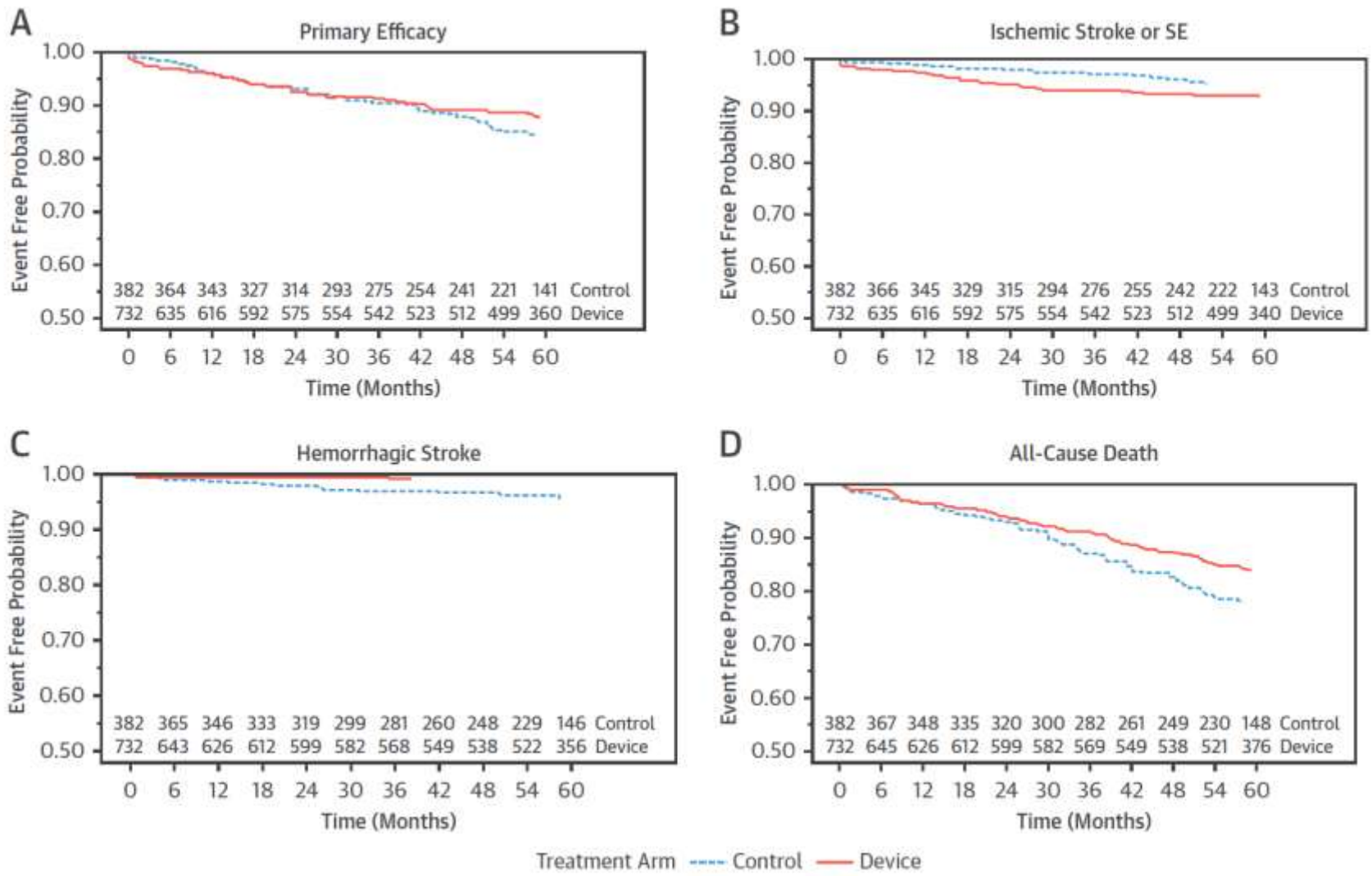
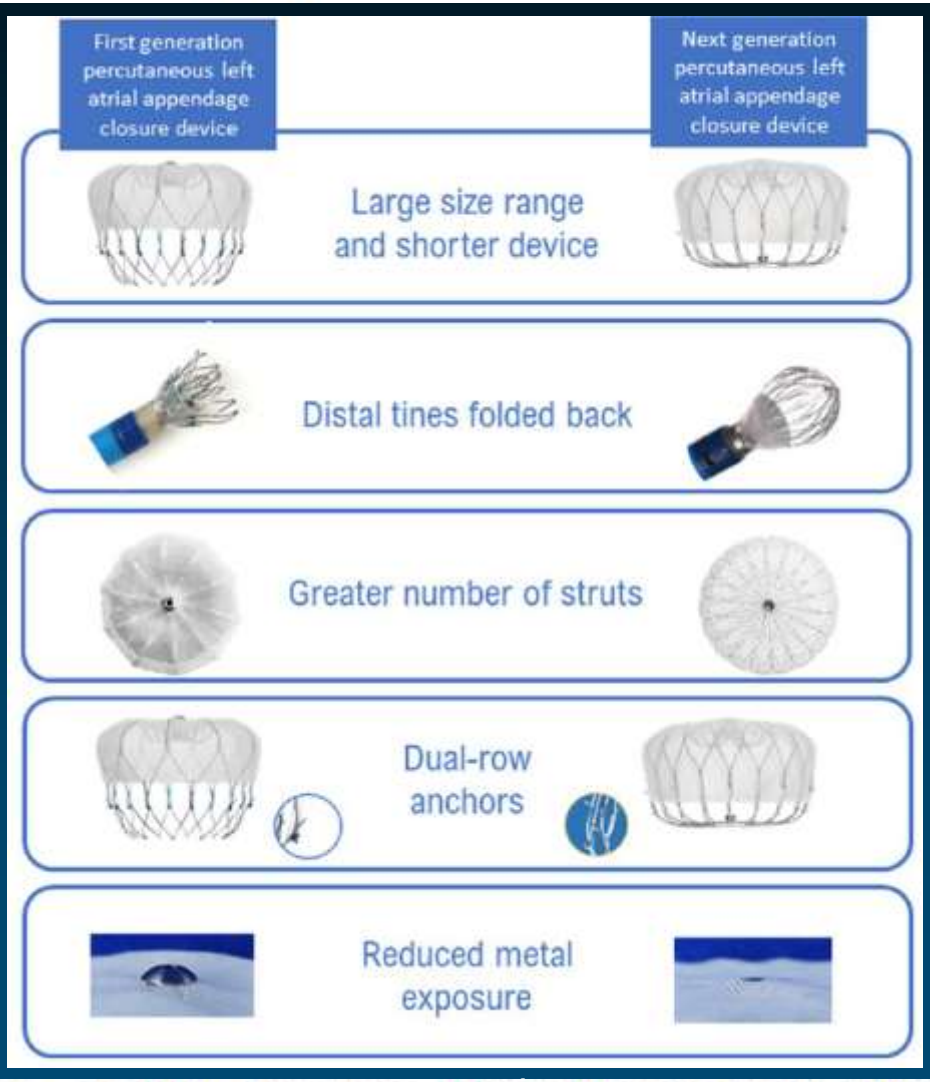
**FIGURE 1** PROTECT AF/PREVAIL Combined: Kaplan-Meier Curves of the Major Efficacy Endpoints



# Primary Outcome Evaluation of a Next-Generation Left Atrial Appendage Closure Device

## Results From the PINNACLE FLX Trial

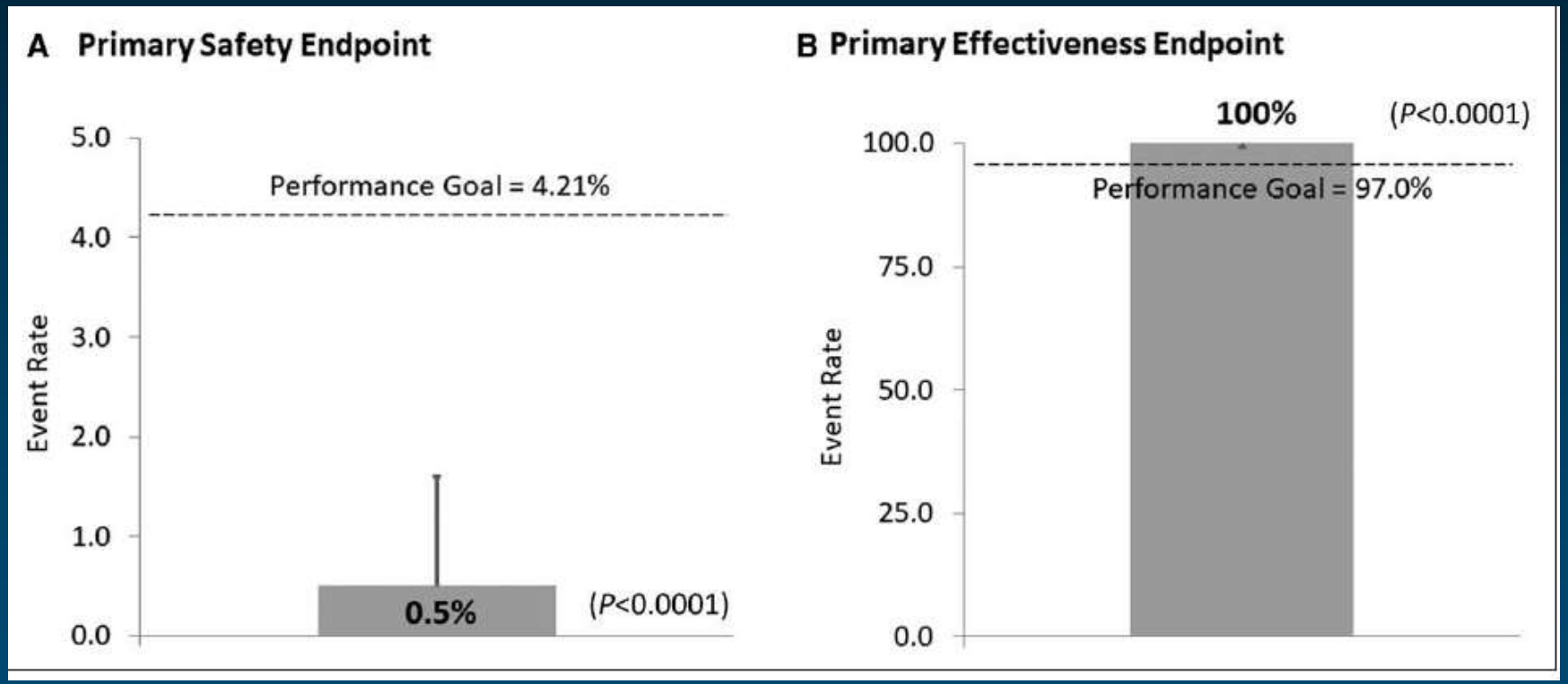



*Circulation*. 2021;143:1754–1762. DOI: 10.1161/CIRCULATIONAHA.120.050117

# Primary Outcome Evaluation of a Next-Generation Left Atrial Appendage Closure Device

## Results From the PINNACLE FLX Trial

Prospective randomized clinical trial of 400 pts (74yrs), CHADSVasc 4.2
Undergoing implantation of Watchman FLX.

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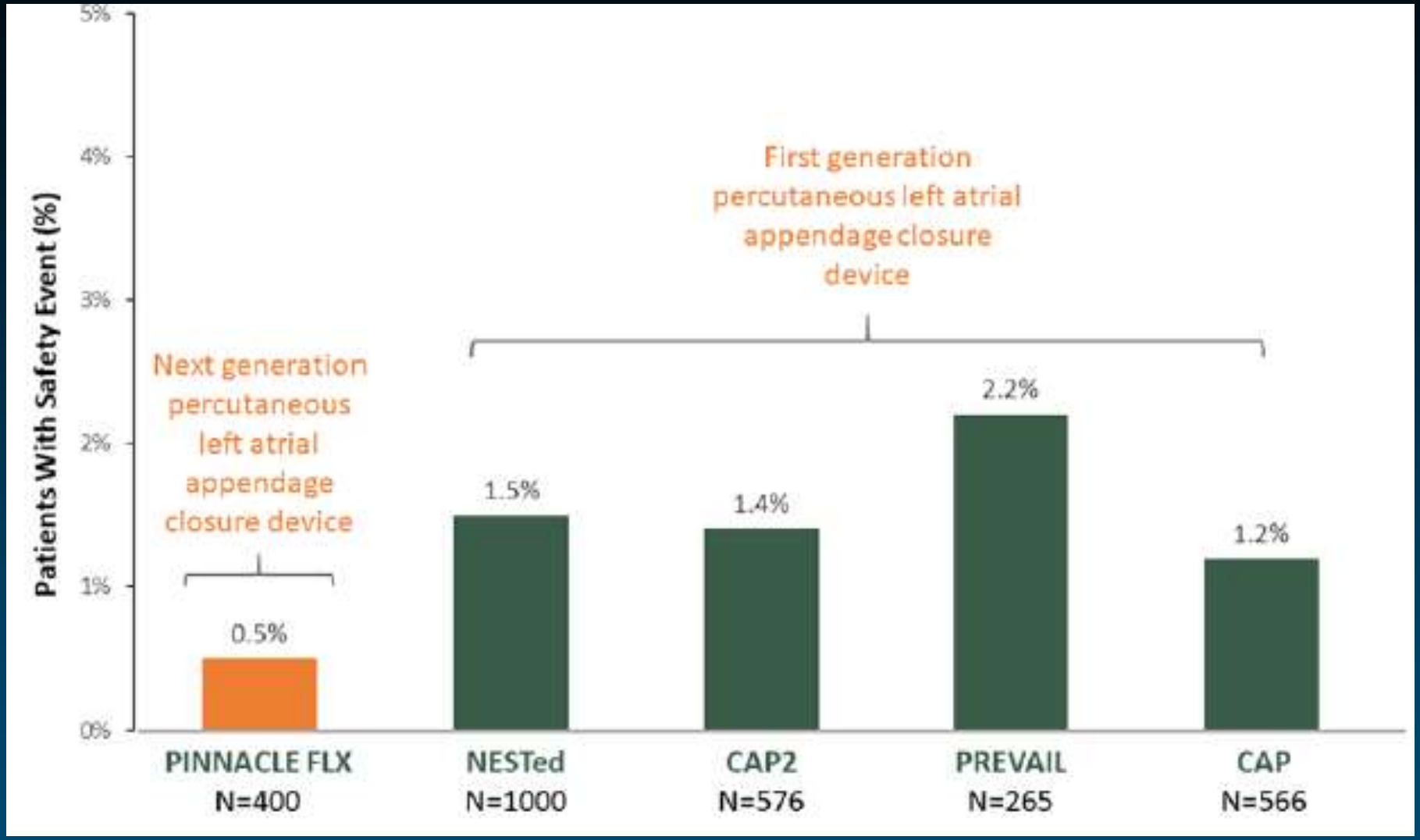



*Circulation*. 2021;143:1754–1762. DOI: 10.1161/CIRCULATIONAHA.120.050117

# Antithrombotic Therapy After Left Atrial Appendage Occlusion in Patients With Atrial Fibrillation

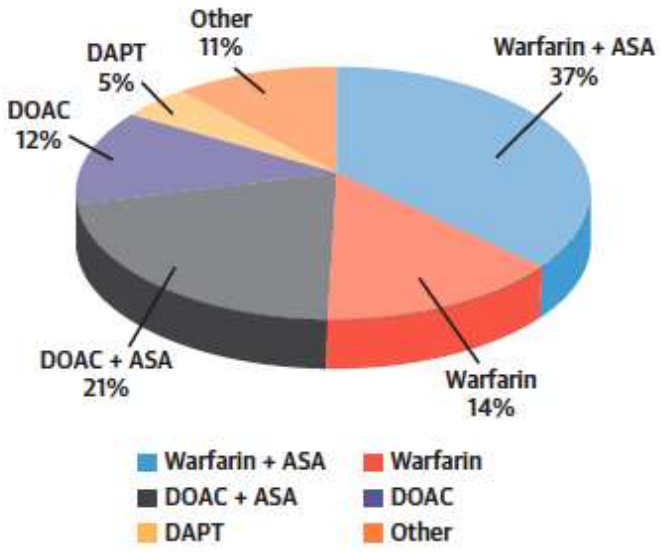
James V. Freeman, MD, MPH, MS,[a,b] Angela Y. Higgins, MD,[c] Yongfei Wang, MS,[a,b] Chengan Du, PhD,[b] Daniel J. Friedman, MD,[d] Usama A. Daimee, MD,[e] Karl E. Minges, PhD, MPH,[a,b] Lucy Pereira, BA,[b] Andrew M. Goldsweig, MD, MS,[f] Matthew J. Price, MD,[g] Vivek Y. Reddy, MD,[h] Douglas Gibson, MD,[g] Shephal K. Doshi, MD,[i] Paul D. Varosy, MD,[j,k] Frederick A. Masoudi, MD, MSPH,[l] Jeptha P. Curtis, MD[a,b]

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 79, NO. 18, 2022

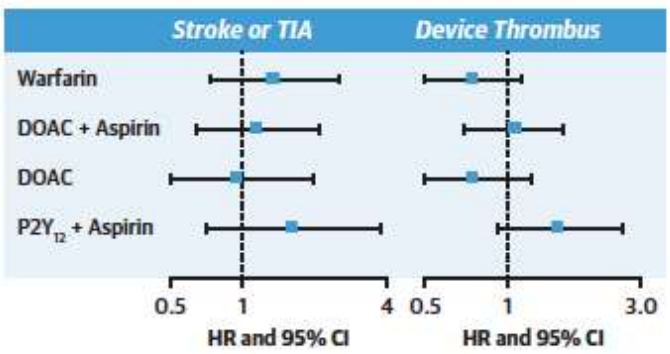
## *NCDR LAAO Registry*: 31,994 Patients With Watchman Implants

**Most Common Discharge Antithrombotic Strategies**

- ***Only 12.2% received FDA-approved postimplant regimen***




| *Any Adverse Event* | HR | 95% CI | *P* Value |
|---|---|---|---|
| Warfarin | **0.69** | **0.57 – 0.84** | **< 0.001** |
| DOAC + Aspirin | 1.00 | 0.83 – 1.21 | 0.96 |
| DOAC | **0.73** | **0.57 – 0.93** | **0.011** |
| $P2Y_{12}$ + Aspirin | 1.04 | 0.79 – 1.38 | 0.76 |




Freeman JV, et al. J Am Coll Cardiol. 2022;79(18):1785-1798.

# Our Preferred Anticoagulation at the Time of LAA Occlusion Implant

- Eliquis, at least 2.5 mg bid, both before implant and for at least 6 weeks after implant.
- At 6 weeks (after TEE), we give the option of switching from Eliquis to Plavix 75 mg + ASA 325 mg qd, but most patients choose to just stay on low dose Eliquis.
- At 6 months, we drop to just ASA 81 mg qd.
- Another alternative is Plavix + ASA from the start, rather than low dose Eliquis, but we think DAPT causes more bleeding than Eliquis, particularly compared to low dose Eliquis.

# FDA Device Labeling

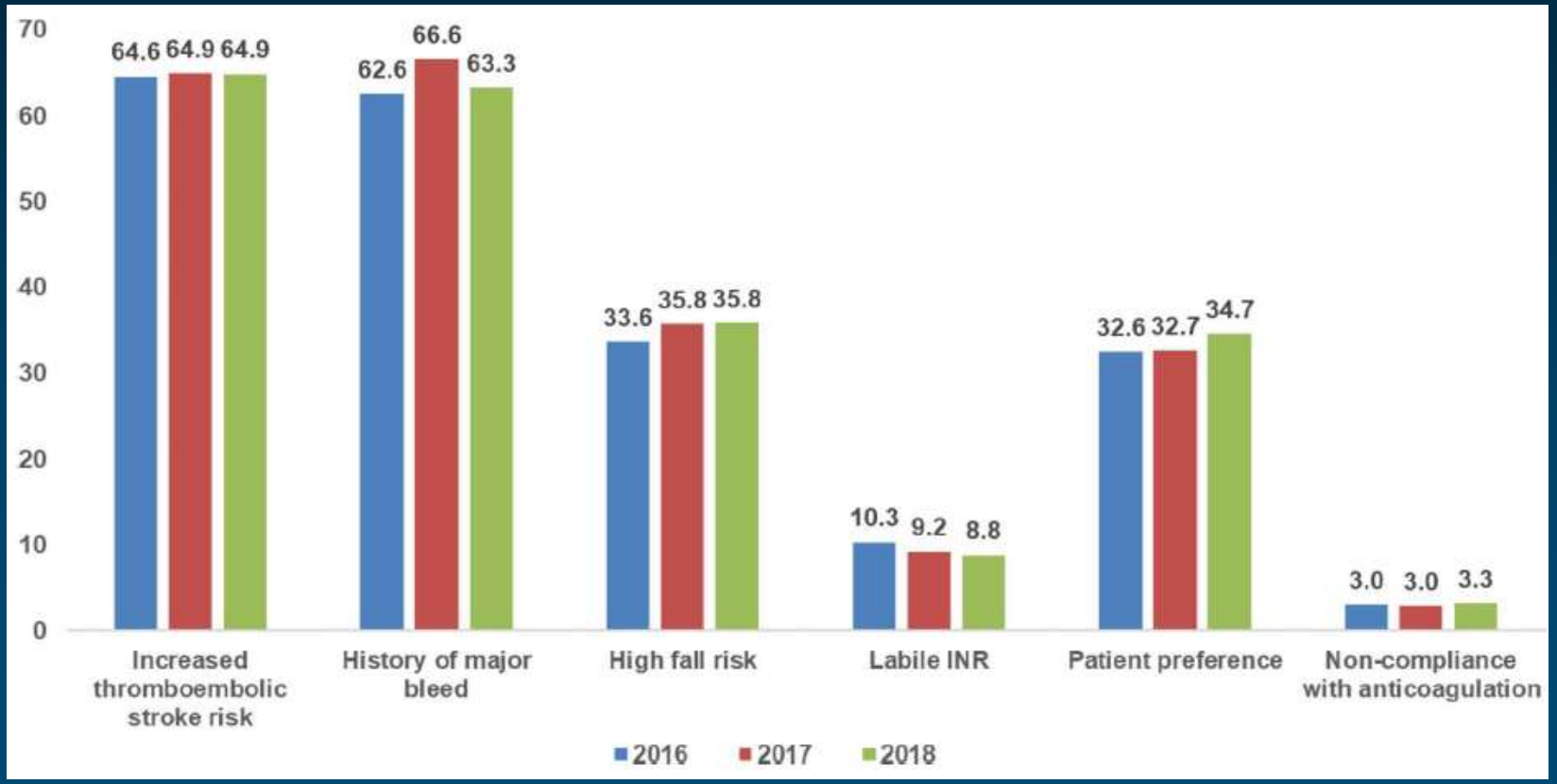
In considering the use of the Watchman Device, the rationale for seeking an alternative to long term anticoagulation therapy and the safety and effectiveness of the device compared to anticoagulation should be taken into account.

Specific factors to consider include:

- The presence of indications for anticoagulant therapy
- A history of major bleeds while taking anticoagulant therapy
- The patients prior experience with anticoagulation
- A medical condition, occupation, or lifestyle which place the patient at risk of major bleeding

# Indications for Left Atrial Appendage Occlusion in the United States and Associated In-Hospital Outcomes: Results From the NCDR LAAO Registry

Usama A. Daimee, MD; Yongfei Wang, MS; Frederick A. Masoudi, MD, MSPH; Paul D. Varosy, MD; Daniel J. Friedman, MD; Chengan Du, PhD; Cristina Koutras, RN; Vivek Y. Reddy, MD; Jacqueline Saw, MD; Matthew J. Price, MD; Fred M. Kusumoto, MD; Jeptha P. Curtis, MD; James V. Freeman, MD, MPH, MS



# Case Presentation

- 75 year old man
- Persistent AF
- Echocardiogram reveals 6 cm LA diameter
- Diabetes, Hypertension
- On Eliquis 5 mg bid
- Would like to stop anticoagulation

# Case Presentation
# What Would You Recommend?

- Continue Eliquis
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- Surgical LAA occlusion

# Case Presentation
# What Would You Recommend?

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# Conclusion

- Stroke prevention is the most important component of AF management.
- Stroke prevention can be addressed with warfarin, a NOAC, or appendage occlusion.
- The safety and efficacy of appendage occlusion devices continue to improve.
- I predict in the years ahead that appendage occlusion devices will play a bigger role in stroke prevention in AF patients

# Final Thoughts and Future Directions

I suspect that the indications for and role of LAA Appendage Occlusion Devices will continue to grow. One could imagine a world where all pts with AF and an increased stroke risk profile receive an LAA appendage occlusion device at first onset of AF thereby eliminating the lifelong need for anticoagulation.

But before this can occur we need:

1) To show in randomized trials that LAA occlusion is equivalent or better than anticoagution with NOACS.
2) The issue of device related thrombosis needs to be solved.
3) We need data in low stroke risk patients
4) The costs of the device and implantation need to fall.

# More Final Thoughts and Future Directions

- Another disruptive anticoagulation strategy is “pill in the pocket anticoagulation”.

- We now know that AF burden is related to stroke risk.

- Can we avoid anticoagulation in AF patients except at a time they are having an AF episode?

- The REACT-AF study will address this question.

- If this is true than the potential value of appendage occlusion will fall except in those with permanent AF.


THANK YOU!