# Wide Application of Percutaneous LAA Closure: Too Much Early?

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## *Disclosure Information*

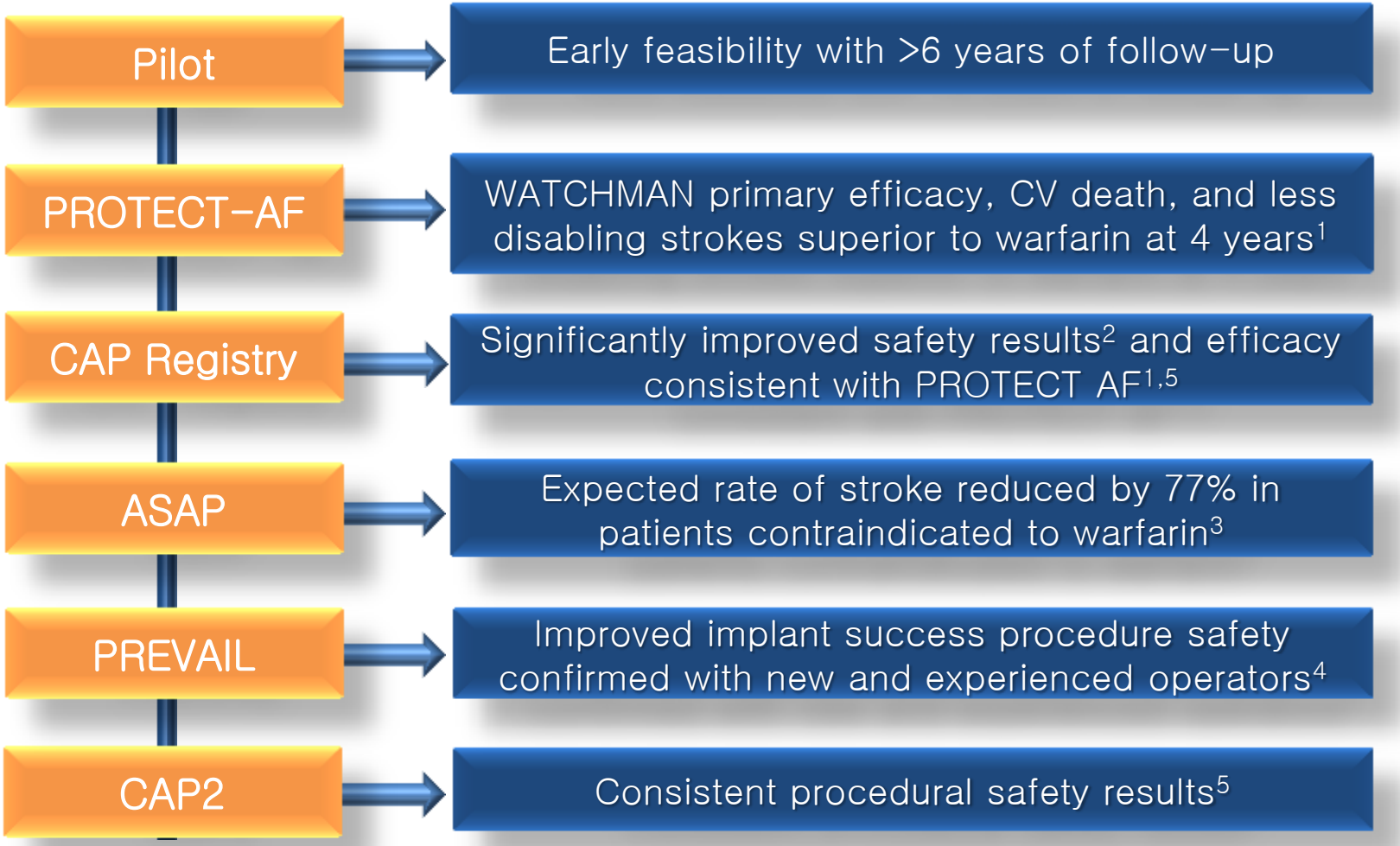
The following relationships exist:

*Grant support: Abbott, BSC, Edwards, WL Gore*
*Consultant: Abbott, BSC, Coherex, Edwards, JenaValve, Diiachi Sankyo-Lilly, WL Gore*

*Off label use of products and investigational devices will be discussed in this presentation*

# WATCHMAN™ Trials

>2,500 patients with >6,000 patient years follow-up

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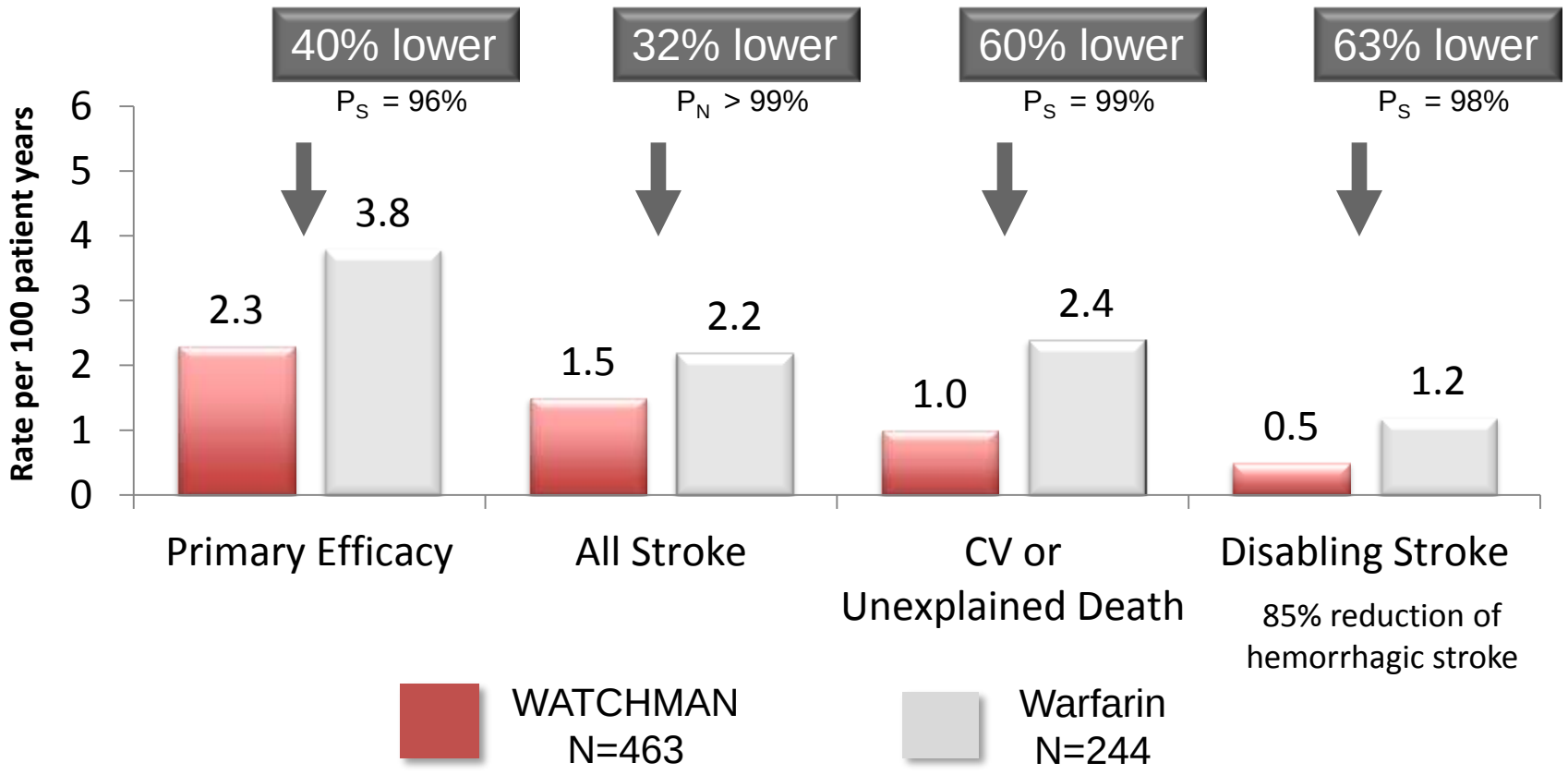
*1 Reddy, VY et al. JAMA. 2014; 312(19):1988-1998. 2 Reddy, VY et al. Circ. 2011;123:417-424; 3 Reddy, et al. JACC 2013; 61(25):2551-6. 4 Holmes, DR et al. JACC. 2014; 64(1):1-12. 5 FDA Panel October 2014.*

# PROTECT AF 4 Year: Results




$P_N$ = Posterior Probability for Non-Inferiority
Ps = Posterior Probability for Superiority
Disabling or fatal strokes were those with an MRS of 3-6 post stroke. Non-disabling were those with an MRS of 0-2 post stroke.
For Bayesian analysis, a posterior probability of 97.5% represents non-inferiority; ≥95% represents superiority.

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*Reddy, VY et al. JAMA. 2014; 312(19):1988-1998.*

# Patient Risk Factors

## Baseline Risk Factors

| | WATCHMAN N= 463 | | Control N= 244 | | P-value |
|---|---|---|---|---|---|
| $CHADS_2$ Score: | | | | | |
| 1 | 158/463 | 34.1% | 66/244 | 27.0% | |
| 2 | 157/463 | 33.9% | 88/244 | 36.1% | |
| 3 | 88/463 | 19.0% | 51/244 | 20.9% | 0.37 |
| 4 | 37/463 | 8.0% | 24/244 | 9.8% | |
| 5 | 19/463 | 4.1% | 10/244 | 4.1% | |
| 6 | 4/463 | 0.9% | 5/244 | 2.0% | |
| AF Pattern: | | | | | |
| Paroxysmal | 200/463 | 43.2% | 99/244 | 40.6% | |
| Persistent | 97/463 | 21.0% | 50/244 | 20.5% | |
| Permanent | 160/463 | 34.6% | 93/244 | 38.1% | |
| Unknown | 6/463 | 1.3% | 2/244 | 0.8% | |
| LVEF (%) | 57.3 ± 9.7 460 | 30.0, 82.0 | 56.7 ± | | |

**2/3 Low Risk**

| $CHADS_2$ Score | Stroke Risk n=2580 from AF trials |
|---|---|
| 0 | 0.8% |
| 1 | 2.2% |
| 2 | 4.5% |
| 3 | 8.6% |
| 4 | 10.9% |
| 5 | 12.3% |
| 6 | 13.7% |

*Gage BF, Circulation. 2004;110:2287-2292*

# CMS Coverage: FDA≠CMS

- criteria for FDA approval different from those used to determine if device is reasonable and necessary Medicare
- NGS has determined that there is not yet sufficient evidence to conclude that the Watchman is or would be “furnished in accordance with accepted standards”
  - no evidence based clinical practice guidelines which support the use of the WATCHMAN
- unclear as to when use of the WATCHMAN “meets, but does not exceed, patient’s medical need”
  - populations studied leading to approval or are at low risk of an event
- NOACs at least as effective as warfarin, safer, and studied for longer than WATCHMAN
- available data are for a relatively small population, less than 2000 subjects studied in the pivotal yet there are millions of individuals with NVAF
- Data brief time (several years at most), yet the device will remain in the body for decades
- FDA approval itself recognizes that additional data regarding safety and effectiveness are required
  - FDA approval itself recognizes that additional data regarding safety and effectiveness are required (post approval reporting and 2 studies required).
  - incomplete LAA occlusion with a gap between the WATCHMAN device surface and the LAA wall is relatively common, gaps are more likely to become bigger over time and persist, while new gaps also occur during follow-up
- the need for post-implantation anticoagulation
  - Protect-AF, some 7% of study participants remained on anticoagulation after the initial post-implantation period
- Since the proposed benefit of the device is to avoid the risks of anticoagulation, it will be important to see the how often and the reasons that anticoagulation is continued

# Left Atrial Appendage Closure or Occlusion

*None FDA approved for stroke prevention*

- Amplatzer Amulet
- Atricure Clip
- Lariat suture
- surgical occlusion of the LAA suboptimal
- LA occlusion during concomitant cardiac surgery lacks consensus
- LAA occlusion, ligation, closure or other manipulation is considered investigational for the prevention of stroke
- After thoroughly reviewing the evidence for left atrial appendage closure or occlusion by any technique for any indication, we have determined the evidence does not support a conclusion of improved health outcomes for our Medicare beneficiaries

- **PROTECT AF**
  - Randomized comparison of WATCHMAN & warfarin in low risk AF population
  - Panel No. 1 in 2009 voted 7-5 in favor of approval
  - Safety concerns
- **PREVAIL**
  - Safety trial
  - Randomized comparison of WATCHMAN & warfarin in higher risk AF population
  - Late follow-up incomplete
  - Panel No. 2 in Dec 2013 recommended by a vote of 13 to 1 to approve
- **Additional PREVAIL data**
  - Panel No. 3 in Oct 2014

# FDA Panel

April 23, 2009 (Gaithersburg, Maryland) — A US **Food and Drug Administration** advisory panel **voted 7 to 5 in favor of approving** a device for closure of the left atrial appendage (LAA) that they say is comparable to long-term warfarin therapy for the prevention of stroke in warfarin-eligible patients with nonvalvular atrial fibrillation (AF).

…advance of the panel, the FDA points to "confounding issues" it wants the panel to consider… patient selection… trial excluded patients at higher risk of poor outcomes, including those with advanced heart failure, recent stroke or MI, and carotid disease.

- **PROTECT AF**
  - Randomized comparison of WATCHMAN & warfarin in low risk AF population
  - Panel No. 1 in 2009 voted 7-5 in favor of approval
  - Safety concerns- 8.7% procedure related complications
- **PREVAIL**
  - Safety trial
  - Randomized comparison of WATCHMAN & warfarin in higher risk AF population
  - Late follow-up incomplete
  - Panel No. 2 in Dec 2013 recommended by a vote of 13 to 1 to approve
- **Additional PREVAIL data**
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# 2nd FDA Panel

- December 2013, the FDA held a second panel to evaluate early study results from an additional study Boston Scientific conducted to confirm the device's safety and effectiveness.
- The 2013 panel recommended by a vote of 13 to 1 to approve the device

# … late follow-up

- updated study data showing additional patient strokes in the Watchman group

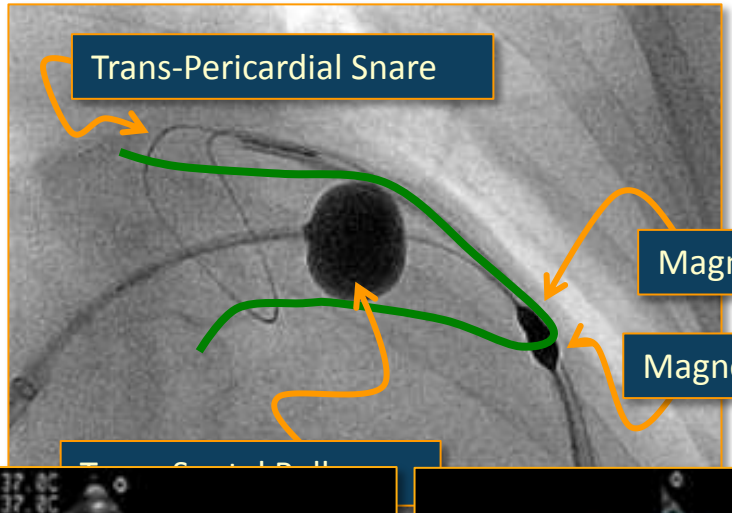
# 3rd FDA Panel

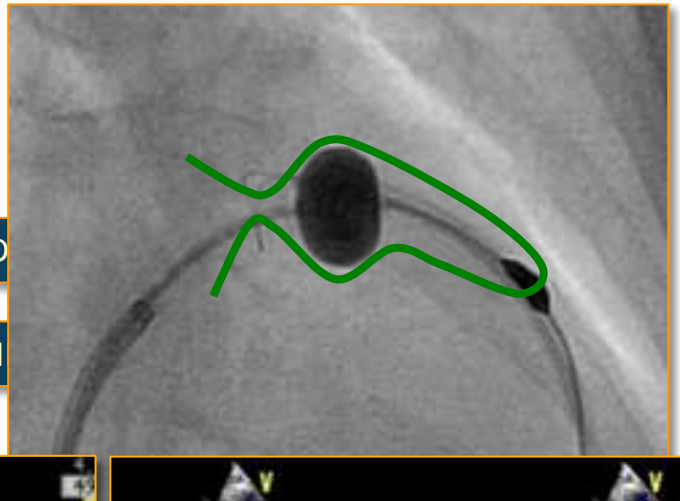
- October 8, 2014
- vote of 6 to 5 (with 1 abstention) benefits of the WATCHMAN Device outweigh the potential risks.
  - Voted of 12 to 0 reasonable assurance that the Device is safe
  - reasonable assurance of effectiveness, the Panel vote was unfavorable 6 Yes to 7 No

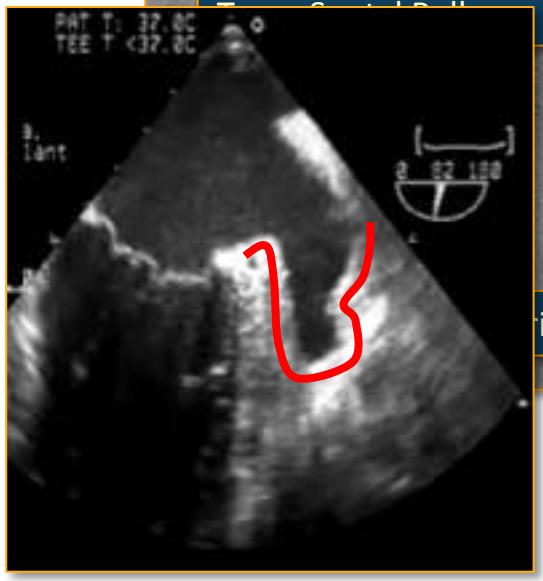
# 3rd FDA Circulatory System Devices Panel

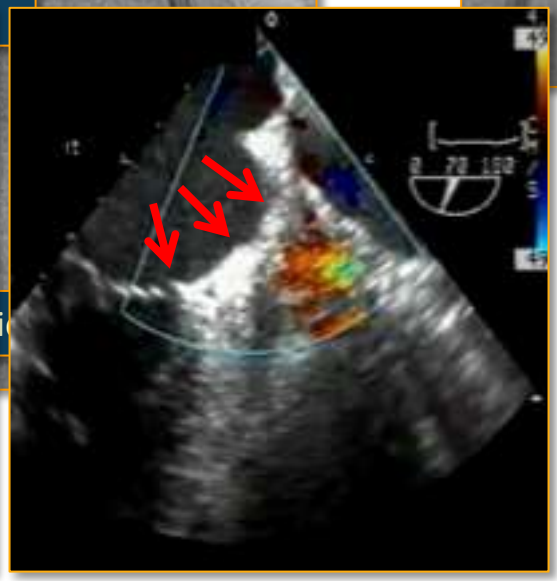
- agreement among the Panel members that the Device provides a much needed alternative to long-term anticoagulation for some patients.
- after much reflection and confusion over a Bayesian meta-analysis pooling two clinical trials, PREVAIL and the PROTECT-AF, the panel appeared to struggle with a **regulatory bind**:
  - **how to recommend the device as a second-line therapy** when the patient group indicated by the voting question, as well as the data, did not match the select subset of patients to whom panel members might hypothetically offer the device.
- Page, the committee chair, summed up the decision saying the majority of the committee felt the device should be considered as a 2nd-line therapy.
- "I think this device has a home, and we just need the FDA and the sponsor to work together to develop a description for an indication that's appropriate," he said.

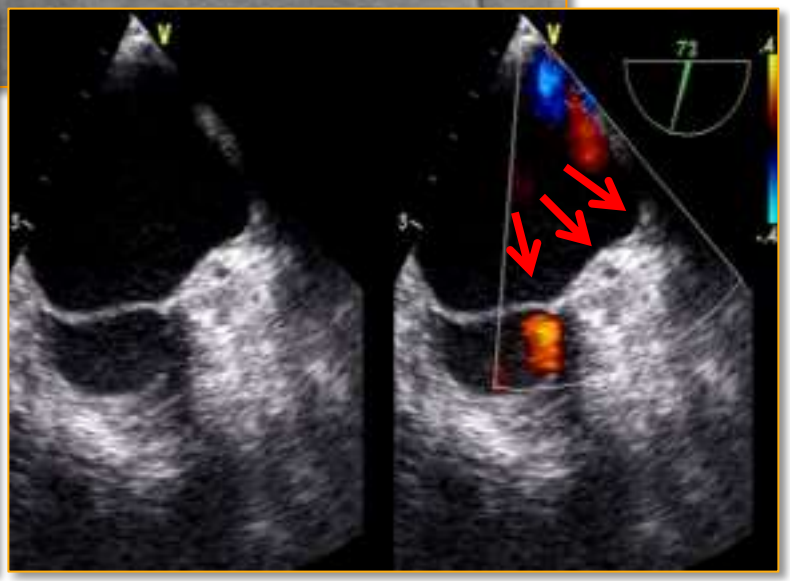
# LARIAT









PRE

Post

30 Days

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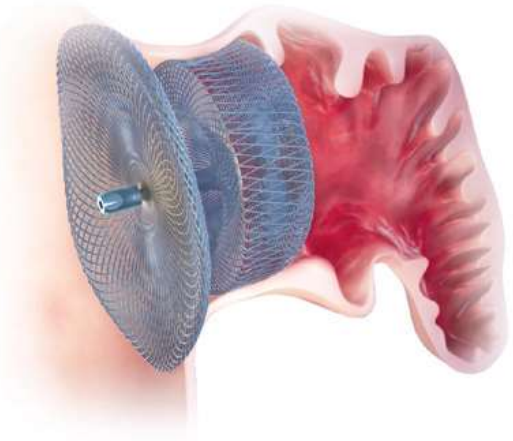
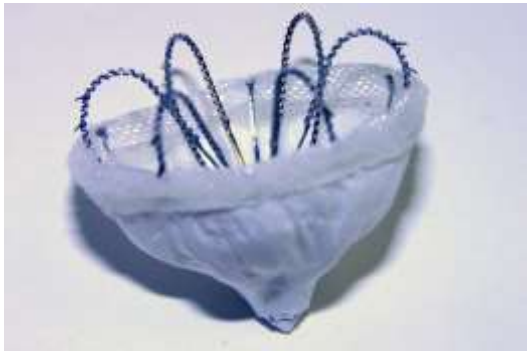


ACP

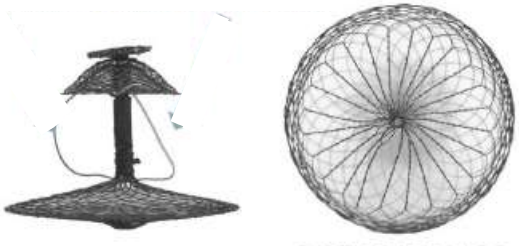


WaveCrest

Occulotech

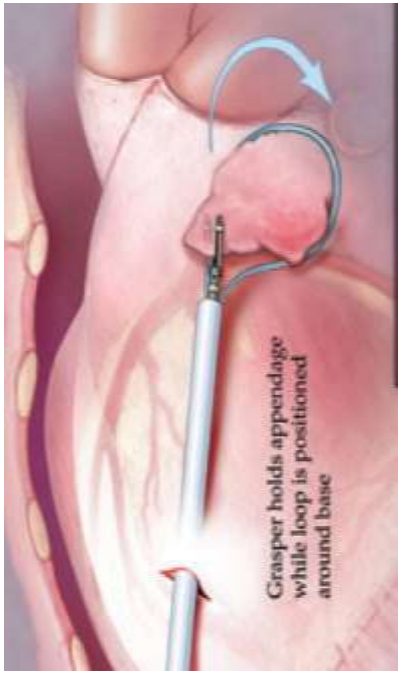
Sideris Patch

LifeTech



pfm

Cardia




AEGIS

# PROPOSED/DRAFT Local Coverage Determination (LCD): Draft LCD for Left Atrial Appendage Closure or Occlusion (DL35506)

In summary, the current data regarding LA occlusion at the time of concomitant cardiac surgery reveals a lack of clear consensus because of the inconsistency of techniques used for surgical excision, the highly variable rates of successful LAA occlusion, and the unknown impact LAA occlusion may or may not have upon future thromboembolic events.

**… the evidence does not support a conclusion of improved health outcomes for our Medicare beneficiaries.**

…vention of stroke associated with non-valvular atrial fibrillation. With the exception of the Watchman device, the majority of studies were case series which have inherent limitations in providing a level of reliable evidence of benefit for a procedure, especially a procedure where there are well recognized safety concerns and a need for long term follow-up for the safety of the implant and the durability of effectiveness when demonstrated. After thoroughly reviewing the evidence for left atrial appendage closure or occlusion by any technique for any indication, we have determined the evidence does not support a conclusion of improved health outcomes for our Medicare beneficiaries.