

# TAVR and Beyond – What is New in Structural Heart Interventions at Cox Health

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Interventional Cardiology  
Ferrell Duncan Clinic – Cox Health

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## Agenda

1. **Aortic Stenosis and Treatment**
2. Left Atrial Appendage Occlusion with Watchman for stroke prevention in atrial fibrillation with contraindication to long term anticoagulation
3. Transcatheter Mitral Valve Repair with Mitraclip

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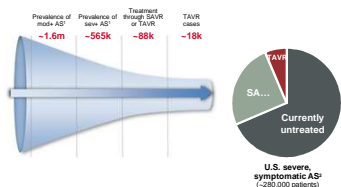
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### High number of US patients with severe aortic stenosis remain largely undertreated



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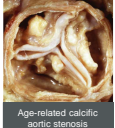
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### Symptoms of aortic stenosis

- Shortness of breath
- Syncope or presyncope
- Angina
- Fatigue
- Difficulty when exercising
- Swollen ankles and feet
- Rapid or irregular heartbeat
- Palpitations (an uncomfortable awareness of heart beating rapidly or irregularly)



Age-related calcific aortic stenosis

The symptoms of aortic disease are commonly misunderstood by patients as 'normal' signs of aging.<sup>1</sup> Many patients initially appear asymptomatic, but on closer examination up to 37% exhibit symptoms.<sup>2</sup>

1. Draz P. European Heart Journal. 2013;34(12):1029-1033.  
2. Levine SR et al. Circulation. 1988;78(2):108-115.

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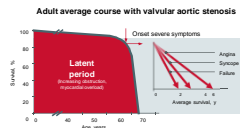
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### Severe aortic stenosis is life threatening and treatment is critical<sup>3</sup>



Adult average course with valvular aortic stenosis

After the onset of symptoms, patients with severe aortic stenosis have a survival rate as low as 50% at 2 years and 20% at 5 years without aortic valve replacement

3. Otto CM. Timing of aortic valve surgery. Heart. 2004;90:1271-1276.

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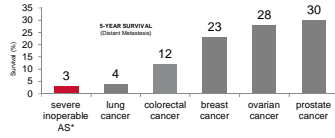
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### Severe aortic stenosis has a worse prognosis than many metastatic cancers



5-year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis

<sup>4</sup>Using SEER\*MedPAR data from the National Cancer Institute, LLC. Analysis courtesy of Robert Taylor, MD, Cleveland Clinic.

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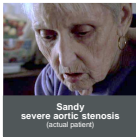
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**Timely intervention is critical for patients with symptoms\***

- In the absence of serious comorbid conditions indicated in the majority of symptomatic patients with severe aortic stenosis
- Consultation with or referral to a Heart Valve Center is reasonable when discussing treatment options for:
  - Asymptomatic patients with severe valvular heart disease
  - Patients with multiple comorbidities for whom valve intervention is considered
- Because of the risk of sudden death, replacing the aortic valve should be performed promptly after the onset of symptoms
- Age is not a contraindication to surgery



**Sandy**  
severe aortic stenosis  
(actual patient)

\* National Heart J. et al. JACC. 2014; 64: 1619-1630

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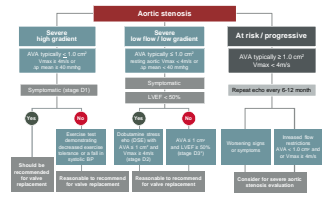
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**AHA/ACC guidelines for aortic valve replacement in patients with aortic stenosis**



The flowchart details the management of aortic stenosis based on severity and symptoms. It categorizes patients into 'Severe high gradient', 'Severe low flow/low gradient', and 'At risk/progressive'. For each category, it specifies criteria for aortic valve replacement (AVR) based on symptoms, left ventricular ejection fraction (LVEF), and the presence of aortic regurgitation (AR). Recommendations include 'Class I' (strongly recommended) and 'Class IIa' (reasonable) for AVR, and 'Class IIb' (reasonable) for transcatheter aortic valve replacement (TAVR).

\* ACC/AHA Guideline for the Management of Aortic Stenosis: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64:e57-103.

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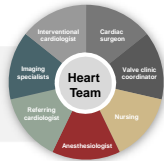
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**The specialized Heart Team**

**Cohesive, multi-disciplinary approach embodies**

- Optimal patient-centric care
- Dedication across medical specialties
- Collaborative treatment decision



**National coverage determination\***

The patient (preoperatively and postoperatively) is under the care of a Heart Team

\* National coverage determination (NCD) for transcatheter aortic valve replacement (TAVR), 2012

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**Devising the treatment plan is a collaborative process**

A Heart Team will conduct a comprehensive evaluation to determine whether the TAVR procedure is appropriate

- Obtain information required to make a recommendation for the best plan of care
- All treatment options, including hospice care, are discussed with the patient and caregivers
- Ultimate treatment choice is a collaborative decision between the physicians, patients and patient's family

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graph TD; A[Severe systemic native aortic valve stenosis] --> B[TAVR center]; B --> C[Surgery]; B --> D[TAVR]; B --> E[Medical therapy];
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**Alain Cribier:**  
First human transcatheter valve replacement (2002)

The collage includes a portrait of Alain Cribier, a close-up of a CoreValve prosthesis, a catheter, and a patient in a hospital bed during a procedure.

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**First CoreValve Implants**  
Laborde, Lal, Grube | 2004

The first image shows a group of surgeons in an operating room. The second image is a catheter with a valve, with text 'VALVE IMPLANTED FOR C.P. ORTH. 11/04' and 'HEATH 10000 01 P. LVA' visible.

**1<sup>st</sup> Clinical Implants Initiated in Summer 2004**  
**Patient N°19 in TAVI History**

\*Webb, presented at San Francisco 07/2004

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### Landmark Clinical Trials Extreme Risk

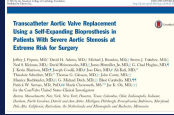
Foundational trials tested new TAVI therapy in patients without the option for a surgical aortic valve replacement



**US CoreValve Pivotal Trial**  
CoreValve, N=488, STS 10.3%



**PARTNER 1B**  
SAPIEN, N=479, STS 11.2%



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### Landmark Clinical Trials Extreme Risk | PARTNER 1B

The PARTNER Extreme Risk trial showed that by 5 years, patients randomized to TAVI had reduced mortality by over 20% compared to standard treatment



Vaccaro, et al., presented at ESC 2014

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### Landmark Clinical Trials Intermediate Risk

Randomized trial data comparing TAVI to SAVR in intermediate surgical risk patients recently became available



**SURTAVI and SURTAVI CAS**



**PARTNER 2A and PARTNER 2B**



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### Landmark Clinical Trials

#### Intermediate Risk | PARTNER 2A

The PARTNER 2A Trial showed that TAVI with SAPIEN XT was non-inferior to surgery for the primary endpoint of all-cause mortality or disabling stroke at 2 years.

Months from Procedure	Surgery (%)	TAVI (%)
0	0.0%	0.0%
3	1.0%	0.9%
6	2.3%	2.2%
9	3.8%	3.7%
12	5.2%	5.1%
15	6.5%	6.4%
18	7.9%	7.8%
21	9.3%	9.2%
24	16.4%	15.3%

**Primary Endpoint (ITT)**  
All-Cause Mortality or Disabling Stroke

HR (95% CI) = 0.89 (0.71, 1.08)  
p (non-inferiority) = 0.203

Months	Surgery	TAVI
0	465	465
3	458	458
6	451	451
9	444	444
12	437	437
15	430	430
18	423	423
21	416	416
24	409	409

\*Leon, et al., presented at ACC 2016

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### Landmark Clinical Trials

#### Low Risk

Recently, both Medtronic and Edwards presented and published results from randomized low risk trials.

#### Primary Results From the Evolut Low Risk Trial

Michael J. Reardon, MD, FACC  
Houston Methodist DeBakey Heart & Vascular Institute, Houston, TX  
For the Evolut Low Risk Trial Investigators

#### PARTNER 3

Transcatheter or Surgical Aortic Valve Replacement in Low Risk Patients with Aortic Stenosis

Martin B. Leon, MD & Michael J. Mack, MD  
on behalf of the PARTNER 3 Trial investigators

\*Reardon, et al., presented at ACC 2018; Leon, et al., presented at ACC 2018; Leon, et al., presented at EuroPCR 2018

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### Landmark Clinical Trials

#### Low Risk | Evolut Low Risk Trial

The PARTNER 3 low risk trial also demonstrated the success of TAVI in low risk patients. TAVI with Sapien 3 demonstrated significantly less death, stroke, or rehospitalization out to 1 year.

Months after Procedure	Surgery (%)	TAVI (%)
0	0.0%	0.0%
3	4.0%	2.5%
6	7.0%	4.0%
9	9.0%	5.5%
12	15.1%	8.2%

**Primary Endpoint**  
Death, Stroke, or Rehospitalization

HR (95% CI) = 0.54 (0.34, 0.83)  
P (superiority) = 0.001

Months	Surgery	TAVI
0	603	603
3	590	590
6	577	577
9	564	564
12	551	551

\*Leon, et al., presented at ACC 2018

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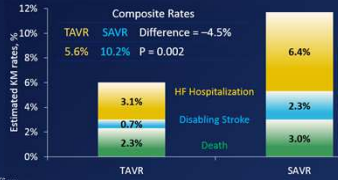
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**Landmark Clinical Trials**  
Low Risk | Evolut Low Risk Trial

The Evolut Low Risk Trial demonstrated success of the Evolut platform in low surgical risk patients with significantly less death, disabling stroke, or HF hospitalization out to 1 year compared to surgery. Additionally, the trial found significantly better hemodynamic results with the Evolut platform compared to surgery.



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**The PARTNER 3 Trial**  
*Clinical Implications*

- Based upon these findings, TAVR should be considered the preferred therapy in low surgical risk aortic stenosis patients.
- Over the past 12 years, the PARTNER trials clearly indicate that the benefit of TAVR is independent of surgical risk profiles.
- The choice of TAVR vs. surgery in aortic stenosis patients should be a shared-decision making process, respecting patient preferences; every patient should be informed of all treatment options.

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Is TAVR for Everyone?

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### Patient Selection Considerations

With TAVI now proven safe across the risk spectrum, several new factors will drive patient selection

- Valve Durability
- Hemodynamic Performance
- Coronary Access
- Conduction Disturbances and Pacemakers
- Stroke
- Paravalvular Leak
- Leaflet Thrombosis
- Challenging Anatomies (i.e. Bicuspid Aortic Stenosis)
- Treatment of Failed Bioprosthetics

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### Valve Durability???

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### AVR Durability Current Status

- Surgical aortic valve replacement (SAVR) has been the historical gold standard for treating severe symptomatic aortic stenosis.
- The durability of bioprosthetic valves has been reported, but variation in definitions of valve deterioration, methodology, and follow-up are major limitations in the literature.
- The first transcatheter aortic valve was commercialized in 2007. There are some data on early generation TAV recipients out to ~10 years, but these long-term data come from extreme- or high-risk populations where the competing risk for mortality is high.

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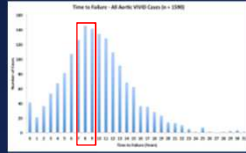


### SAVR Durability

#### Reporting by Freedom-from-Reintervention

While studies reporting freedom-from-reoperation may signal valve durability beyond 15 years, data from the VIVID Registry shows that most VIV procedures for failed surgical valves occurs around 8 or 9 years post-SAVR.

Historical surgical literature relying on freedom-from-reoperation to assess valve failure likely underestimates true rates of SVD for surgical valves. Standardized definitions and surveillance going forward will clarify valve deterioration rates in the AVR population.



\* Cappaloni & Williams. Presented at CRT 2016.

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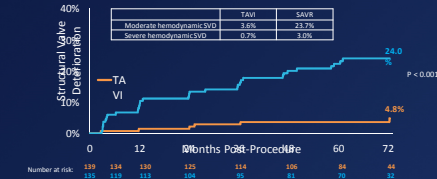
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### TAVI Durability

#### Clinical Trial | NOTION Low Risk 6-Year Results

ESC/EACTS/EAPCI Definition Structural Valve Deterioration

Randomized clinical trial data with the longest SVD follow-up comes from the NOTION Trial, which studied TAVI vs. SAVR in low-risk patients >70 years, implanted with a self-expanding TAV. Using the ESC/EACTS/EAPCI definition, SVD occurred in 4.8% of TAVI patients and 24.0% of SAVR.



\* Vandenberg, et al. JACC 2019;78(15):1454-61. \* Cappaloni et al. Eur J Cardiothorac Surg. 2017;52:488-97

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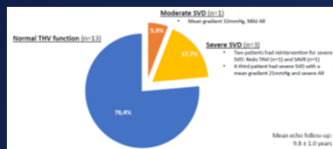
### TAVI Durability

#### Real World Experience | Vancouver Data at 8 Years

ESC/EACTS/EAPCI Definition Structural Valve Deterioration

The longest non-randomized data available on balloon-expanding valves are 8-year results from the prospective Vancouver study.

- This study did not use the ESC/EACTS/EAPCI definitions, since they were published after the analysis.
- Freedom from valve degeneration was approx. 80% at 6 years.



Sathananthan. Presented at EuroPCR 2013.

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## Agenda

1. Aortic Stenosis and Treatment
2. Left Atrial Appendage Occlusion with Watchman for stroke prevention in atrial fibrillation with contraindication to long term anticoagulation
3. Transcatheter mitral valve repair with Mitraclip
4. Patent Foramen Ovale (PFO) closure for stroke prevention

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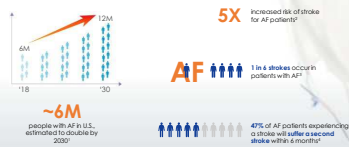
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### Atrial Fibrillation is a Prevalent and Growing Condition and a Leading Cause of Stroke



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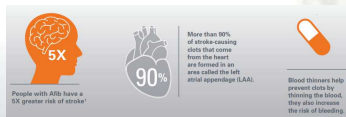
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### AF Creates Environment for Thrombus Formation in Left Atrium

The WATCHMAN Implant is an innovative one-time procedure designed to reduce the risk of strokes that originate in the left atrial appendage (LAA)

In non-valvular AF, >90% of stroke-causing clots that come from the left atrium are formed in the LAA<sup>1</sup>.



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### Long-Term Oral Anticoagulation is Not Ideal for All NVAF Patients

Warfarin and Direct Oral Anticoagulants come with risk factors for many NVAF patients.

**EXAMPLES OF RISK FACTORS**

WARFARIN	DIRECT ORAL ANTICOAGULANTS
Bleeding Risk	Bleeding Risk
Daily Regimen	Quality or Adherence Regimens
High Non-Adherence Rates	High Non-Adherence Rates
Regular INR Monitoring	Complexness Surgical Procedures
Food and Drug Interactions Issues	Linked Personal Agents
Complexness Surgical Procedures	High Cost

90% OF PATIENTS COME WITH RISK FACTORS FOR MANY NEW PATIENTS. SOME RISK FACTORS INCLUDE:

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### Patients Struggle with Compliance to Anticoagulation

68% of patients interested in learning more about WATCHMAN struggle with compliance while taking OACs!

**EXAMPLES OF REPORTED COMPLIANCE ISSUES FROM PATIENTS**

- Keeping regular doctors appointments
- Following dietary restrictions
- Remembering to take medications
- Struggling to stay in range

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### Adherence to Anticoagulation Remains a Challenge

About half of patient with AF are not treated with OAC

Despite increasing risk of stroke, the use of OAC in AF patients peaks at ~50%

Of those taking OACs a significant number won't continue long-term

~30% of patients taking a DOAC and ~50% of patients taking a VKA discontinue treatment at 2 years

CHA<sub>2</sub>DS<sub>2</sub>-VASc Score

Legend: NOAC (N=10267), VKA (N=2088)

Legend: NOAC (N=451), VKA (N=342)

Legend: NOAC (N=139), VKA (N=41)

NCDR Pinnacle Registry

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### Many Patient Struggle to Maintain Therapeutic Range on Warfarin

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>.

44% of bleeding events occur in patients above therapeutic range

48% of thromboembolic events occur in patients below therapeutic range

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### Bleeding Risks on Anticoagulants Compound Over Time

The risk of bleeding associated with OACs compounds year over year, while WATCHMAN is a one-time procedure with a low complication rate

HAS-BLED* Score	Annual % Bleed Risk	Estimated 10-Year Bleeding Risk (%)
0	0	0
1	1.3	1.4
2	2.2	4.1
3	3.2	1.8
4	4.0	6.9
5	4.7	9.1

\*HAS-BLED\* score is a validated bleeding risk score for patients on oral anticoagulation. It is based on the following criteria: 1 point for each of the following: 1. Hemoglobin or hematocrit > 3 g/dL or > 30% (men) or > 25% (women); 2. Abnormal renal or liver function; 3. Labile INR; 4. Concomitant use of antiplatelet drugs; 5. Concomitant use of drugs that increase the risk of bleeding; 6. History of bleeding; 7. Age > 65 years; 8. Falls; 9. Alcohol consumption > 3 drinks per day; 10. Drug-drug interactions. HAS-BLED\* score is a validated bleeding risk score for patients on oral anticoagulation. It is based on the following criteria: 1 point for each of the following: 1. Hemoglobin or hematocrit > 3 g/dL or > 30% (men) or > 25% (women); 2. Abnormal renal or liver function; 3. Labile INR; 4. Concomitant use of antiplatelet drugs; 5. Concomitant use of drugs that increase the risk of bleeding; 6. History of bleeding; 7. Age > 65 years; 8. Falls; 9. Alcohol consumption > 3 drinks per day; 10. Drug-drug interactions.

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### Patients are Looking for an Alternative to Oral Anticoagulants

**83%** More than 4 in 5 people with Afib taking an oral anticoagulant (83%) say they would be willing to try a different treatment to help reduce their risk of stroke<sup>1</sup>

Over a third of people with Afib (38%) feel trapped between the fear of having a stroke and fear of the risks associated with oral anticoagulants.

National Online Survey conducted of more than 400 people (aged 45 and older) living with AF.

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**WATCHMAN is a One-Time Procedure that Provides a Lifetime of Stroke Risk Reduction**

- 1** Using a minimally invasive procedure, a catheter is inserted into the heart to deliver the WATCHMAN device.
- 2** The high-strength permanent implant is positioned in the heart to prevent blood clots from traveling to the brain.
- 3** The device is left in place for 24 hours to ensure it is fully implanted and secure.
- 4** WATCHMAN is a one-time procedure that provides a lifetime of stroke risk reduction.
- 5** Stroke risk is reduced by up to 64% with WATCHMAN. Patients can return to their normal lives.

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**WATCHMAN has Clinically Proven Long-Term Outcomes**

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**Long-Term Results Demonstrated WATCHMAN Reduced Risk of Stroke, Bleeding and Mortality vs. warfarin**

Five-year data from a patient-level meta-analysis of the PROTECT AF and PREVAIL trials demonstrated that WATCHMAN offered:

- Comparable primary efficacy and all-cause stroke reduction

Outcome	HR (95% CI)	p-value
Efficacy	0.82 (0.62, 1.08)	0.2
All stroke or SE	0.56 (0.41, 0.76)	0.0001
CV/unexplained death	0.59 (0.41, 0.84)	0.003
All-cause death	0.73 (0.54, 0.98)	0.04

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**WATCHMAN studies have shown that WATCHMAN is safe, effective, and enables patients to discontinue OAC medications.**

A robust body of evidence, including long-term data from numerous clinical studies (PROTECT AF, CAP Registry, PREVAIL, CAP 2 Registry) supports the WATCHMAN implant U.S. Food and Drug Administration (FDA) approval and the subsequent Centers for Medicare and Medicaid Services (CMS) national coverage decision for first implant in the U.S., as well as approval and licensure of the WATCHMAN implant in 75 countries.

In a real-world, post-approval analysis, the WATCHMAN implant has demonstrated high rates of procedural success and low rates of complications for patients with non-valvular atrial fibrillation who are seeking an alternative to long-term warfarin therapy.

**WATCHMAN studies have shown**

<b>SAFETY</b>	Procedure is safe	1.5% complication rate
<b>PRIMARY EFFICACY</b>	Comparable to warfarin	18% reduction in stroke (p<0.001)
<b>RELAYING DECISION</b>	92% of patients discontinued after 45 days	99% of patients discontinued after 1 year
<b>STROKE</b>	Reduction in ischemic stroke	55% reduction in stroke (p<0.001) vs warfarin
<b>MORTALITY</b>	Reduction in stroke mortality	27% reduction in stroke mortality (p<0.001)
<b>QUALITY OF LIFE</b>	Improved quality of life	72% reduction in warfarin-related quality of life (p<0.001)

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**WATCHMAN Comparable to Warfarin for Ischemic Stroke Risk Reduction**

WATCHMAN offers NVAF patients a lifetime of stroke risk reduction vs. no therapy

Ischemic Stroke Risk (Events per 100 pt-yr)

Legend:   
○ Untreated AF   
△ Treated with Warfarin

Baseline CHA<sub>2</sub>DS<sub>2</sub>-VASc Score: 1, 2, 3, 4, 5

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**WATCHMAN Enables Patients to Discontinue Long-term OAC Medication**

Five-year results have confirmed that WATCHMAN is safe, effective, and enables patients to discontinue OAC medications

92% Of patients were able to discontinue warfarin after 45 days<sup>1</sup>

99% Of patients were able to discontinue warfarin after 1 Year<sup>1</sup>

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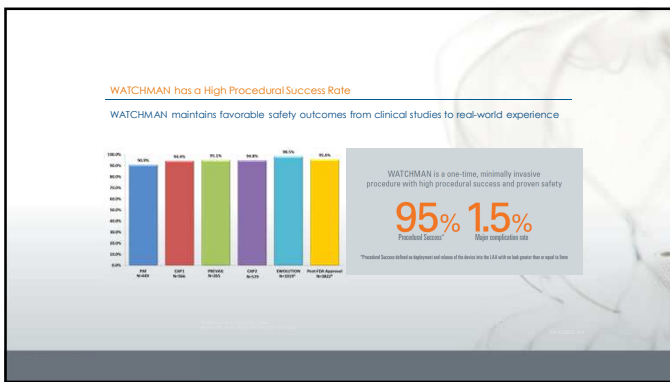
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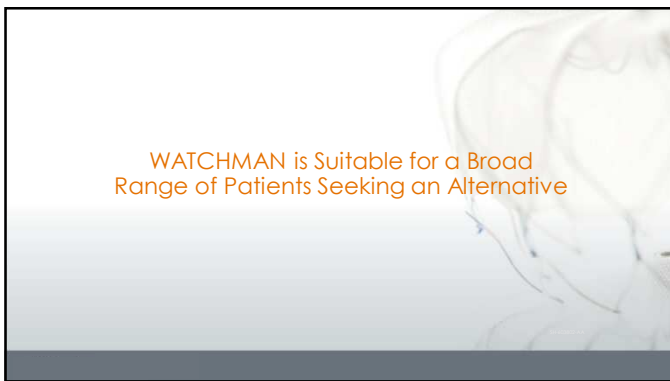
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Consider WATCHMAN for your Patients that Need an Alternative

There are a broad range of patients that may have a reason to seek an alternative to blood thinners. Some examples include:

- Stroke**  
Major stroke and recurrent strokes
- Stroke prevention**  
Stroke prevention in patients with atrial fibrillation
- Stroke prevention**  
Stroke prevention in patients with atrial fibrillation and contraindications to long-term anticoagulation
- Stroke prevention**  
Stroke prevention in patients with atrial fibrillation and contraindications to long-term anticoagulation
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Stroke prevention in patients with atrial fibrillation and contraindications to long-term anticoagulation

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**MitraClip®**  
Transcatheter Mitral Valve Repair

Transcatheter Mitral Valve Repair



Indicated for the transcatheter mitral valve repair in patients with mitral regurgitation due to degenerative mitral regurgitation. The MitraClip device is a transcatheter mitral valve repair device. It is not a replacement for surgical mitral valve repair. The MitraClip device is not intended for use in patients with mitral regurgitation due to other causes. See MitraClip safety information for more details.

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Mitral Valve Disease is Common and Increases with Age

Mitral regurgitation (MR) is the most common type of heart valve insufficiency in the US<sup>1,2</sup> Represents 60% of all Valve Disease

**Prevalence of Valvular Heart Disease by Age**

Age (years)	All valve disease (%)	Mitral valve disease (%)	Aortic valve disease (%)
<40	~0.5	~0.2	~0.3
40-54	~1.0	~0.5	~0.5
55-64	~2.0	~1.0	~1.0
65-74	~5.0	~3.0	~2.0
>75	~10.0	~6.0	~4.0

MR Represents largest unmet clinical need

1. Heart Disease and Stroke Statistics 2012 Update: A Report From the American Heart Association. Circulation. 2012;125:e67-129.  
2. National Heart, Lung, and Blood Institute. Atherosclerosis Risk in Communities Study. National Heart, Lung, and Blood Institute.

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Mitral regurgitation is a heart valve disorder with serious clinical consequences

MR occurs when the mitral valve fails to close completely, causing blood flow to move backward.

- Untreated MR results in heart failure<sup>1</sup>
- 1-year mortality up to 57%<sup>2</sup>
- 30-day rehospitalization rate 25%-50%<sup>3</sup>

Abbreviation: MR, mitral regurgitation.

1. Cohn JN, Griffin B, Casey WC. Cleveland Clinic Current Clinical Medicine. 2014; 10(1):10-15.  
2. Cohn JN. Am J Geriatr Pharm. 2005;7(1):110-112.  
3. O'Connor M, et al. J Am Coll Cardiol. 2010;55(2):206-211.

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Mitral Regurgitation 2012 U.S. Prevalence  
A Largely Untreated Patient Population

**Total MR Patients<sup>1,2</sup>** 4,100,000

**Eligible for Treatment<sup>3,4</sup>** (MR Grade 3+) 1,670,000

**Annual Incidence<sup>3</sup>** (MR Grade 3+) 50,000

**Annual MV Surgery<sup>5</sup>** 50,000 (Only 3% Treated Surgically)

Large and Growing Clinical Unmet Need Left Untreated

4% Newly Diagnosed Each Year

1. CDC Chronic Diseases and Disability Prevention Division. 2010. Table 10.  
2. National Heart, Lung, and Blood Institute. Atherosclerosis Risk in Communities Study. National Heart, Lung, and Blood Institute.  
3. National Heart, Lung, and Blood Institute. Atherosclerosis Risk in Communities Study. National Heart, Lung, and Blood Institute.  
4. National Heart, Lung, and Blood Institute. Atherosclerosis Risk in Communities Study. National Heart, Lung, and Blood Institute.  
5. National Heart, Lung, and Blood Institute. Atherosclerosis Risk in Communities Study. National Heart, Lung, and Blood Institute.

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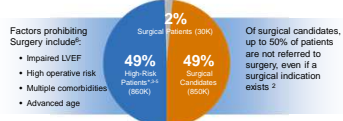
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Many patients are not considered appropriate candidates for mitral valve surgery

Large portion of mitral regurgitation patients are left untreated—  
ineligible for surgical treatment or denied surgical intervention<sup>1-2</sup>



<sup>1</sup>Topol, High-Risk Patients, one defined as any patient with an EF < 40% or an age of > 70.  
<sup>2</sup>Liaw et al. J Am Coll Cardiol. 2015;65(19):2071-2076.  
<sup>3</sup>Liaw et al. J Am Coll Cardiol. 2015;65(19):2071-2076.  
<sup>4</sup>ACC/AHA Guideline for the Management of Aortic Regurgitation. Circulation. 2014;129(25):e359-368.  
<sup>5</sup>ACC/AHA Guideline for the Management of Aortic Regurgitation. Circulation. 2014;129(25):e359-368.  
<sup>6</sup>ACC/AHA Guideline for the Management of Aortic Regurgitation. Circulation. 2014;129(25):e359-368.

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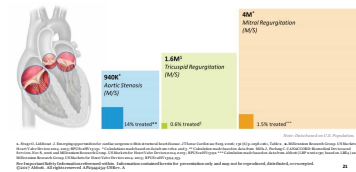
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# MitraClip®

## A patient-centric approach UNDERTREATED POPULATIONS ACROSS AORTIC, TRICUSPID, AND MITRAL



<sup>1</sup>Report published in JAMA Cardiology. Aortic regurgitation (AR) is the most common valvular heart disease. It is caused by the backflow of blood from the aorta into the left ventricle. It is most commonly caused by aortic root dilation, aortic valve leaflet degeneration, and aortic valve prolapse.  
<sup>2</sup>Report published in JAMA Cardiology. Aortic regurgitation (AR) is the most common valvular heart disease. It is caused by the backflow of blood from the aorta into the left ventricle. It is most commonly caused by aortic root dilation, aortic valve leaflet degeneration, and aortic valve prolapse.  
<sup>3</sup>Report published in JAMA Cardiology. Tricuspid regurgitation (TR) is the most common valvular heart disease. It is caused by the backflow of blood from the right ventricle into the right atrium. It is most commonly caused by right ventricular dilation, tricuspid valve leaflet degeneration, and tricuspid valve prolapse.  
<sup>4</sup>Report published in JAMA Cardiology. Tricuspid regurgitation (TR) is the most common valvular heart disease. It is caused by the backflow of blood from the right ventricle into the right atrium. It is most commonly caused by right ventricular dilation, tricuspid valve leaflet degeneration, and tricuspid valve prolapse.  
<sup>5</sup>Report published in JAMA Cardiology. Mitral regurgitation (MR) is the most common valvular heart disease. It is caused by the backflow of blood from the left ventricle into the left atrium. It is most commonly caused by mitral valve leaflet degeneration, mitral valve prolapse, and mitral valve annular calcification.  
<sup>6</sup>Report published in JAMA Cardiology. Mitral regurgitation (MR) is the most common valvular heart disease. It is caused by the backflow of blood from the left ventricle into the left atrium. It is most commonly caused by mitral valve leaflet degeneration, mitral valve prolapse, and mitral valve annular calcification.

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Overview of Patient Selection.

Functional MR	Degenerative MR
<ul style="list-style-type: none"> <li>• Abnormal function of anatomically normal leaflets</li> <li>• Annular enlargement secondary due to left ventricular dilatation</li> <li>• Papillary muscle displacement due to left ventricular remodeling may result in excessive tenting of the leaflet</li> </ul>	<ul style="list-style-type: none"> <li>• Elongation or rupture of the chordae</li> <li>• Leaflet tissue expansion and thickening (Barlow's Disease)</li> <li>• Fibroelastic deficiency resulting in a thinning of leaflet tissue or rupture of chordae</li> <li>• Generally occurs in the older population (60+ years)</li> </ul>
Now FDA Approved	Commercial Therapy

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### Mitral Regurgitation: An Undertreated Disease



**Conclusions**

Among patients with severe organic MR, surgical intervention occurred in approximately one-half eligible patients. However, accepted guideline indications for intervention were present in the majority patients not operated on. Objectively assessed operative risk was not prohibitive in many patients not operated on.

Small and Failure of Guideline Adherence for Intervention in Patients With Severe Mitral Regurgitation. J Am Coll Cardiol 2013;61:2283-91.

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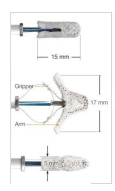
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### A Closer Look at the MitraClip Device



- Design Features**
  - Ability to accurately position and reposition
  - Mitral repair without creating the heart (no need for cardiopulmonary bypass)
  - Real time assessment of MR reduction under normal loading conditions.
- MitraClip Device (Implant)**
  - Cobalt chromium construction
  - MRI conditional to 3 Tesla\*
  - Polyester cover designed to promote tissue growth†

Small and MitraClip Device. J Am Coll Cardiol 2013;61:2283-91.

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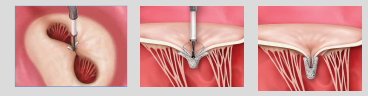
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### Design Principles & Results

- Establishes vertical coaptation capturing leaflets and drawing them together
- Mitral repair on a beating Heart (no need for cardiopulmonary bypass)
- Repositionable with unique steering for precise placement
- Mitral regurgitation assessed in real time under normal loading conditions allowing repositioning for optimal desired outcome.
- Surgical intervention remains preserved†




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### MitraClip Therapy Filling a Treatment Gap

- Medical therapy is limited to symptom management
- MV surgery has been the only option that reliably reduces MR
- A significant gap exists between medical and surgical options
- MitraClip therapy is a percutaneous option to reduce MR in select patients\*

Source: MitraClip Clip Delivery System, System Instructions for Use

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### Minimally invasive procedures are driving growth in cardiovascular services

#### Valve Disease Treatment Options

At the end of 2014, percutaneous heart valve procedures represent 23% of all heart valve procedures compared to 10% percent in 2009.

\* American Heart Association. 2014. AHA/ACC Guideline for the Management of Aortic Valve Disease. Copyright 2014.

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### Structural Heart Team

CoxHEALTH

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