Innovation & The Future of Heart Valve Disease Treatment

Heart Valve Voice US

Lisa M. Tate

Interim Executive Director, Heart Valve Voice US

• • •

Lisa M. Tate is a long-time health advocate, having held leadership positions for patient organizations, a hospital association, and a medical society. For the past ten years, she has focused on cardiovascular issues. As CEO of WomenHeart, the National Coalition for Heart Disease, she more than tripled the organization's revenue, enabling WomenHeart to reach millions more women. Currently Lisa has her own patient advocacy consulting firm, Health Futures Consulting: *Putting Patients at the Center*.

Heart Valve Voice US

Heart Valve Voice US is the only patient-led organization in the country that exclusively focuses on improving the diagnosis, treatment and management of heart valve disease.

Heart Valve Voice US

- Provides a voice for heart valve patients to improve access to the right treatment at the right time
- Raises awareness of symptoms and severity of heart valve disease, particularly in at-risk and underserved populations
- Educates patients so they can partner with their physicians in decision-making regarding their care
- Advocates for policy changes to ensure optimal treatment of heart valve, e.g., Medicare, research funding
- Partners with other organization to encourage them to focus on HVD

Heart Valve Voice US


Alliance
FOR AGING RESEARCH


NHMA
National Hispanic Medical Association


PARTNERSHIP TO ADVANCE
Cardiovascular
Health


Heart Valve
VOICE


MHN
Men's Health Network
www.menshealthnetwork.org


National Black Nurses Association, Inc.
NBNA


ABC
Association of Black Cardiologists, Inc.
Saving the Hearts and Minds of a Diverse America


AGING (ife CARE™
ASSOCIATION
The experts in aging well.


healthy
women


NMA
Since 1895
National
Medical
Association


Mended Hearts™


RetireSafe
Standing up for America's Seniors!


AfPA
Alliance for Patient Access


BLACK WOMEN'S
HEALTH IMPERATIVE


NATIONAL
Minority Quality Forum


CAREGIVER
ACTION
NETWORK
CAN


Heart Valve
Voice US

Susan Strong

Director of Communications and Patient Engagement, Heart Valve Voice US

Susan Strong is Director of Communications and Patient Engagement for Heart Valve Voice US. She was the founding President of the Board of Directors and is a passionate advocate for heart valve patients. In addition to her role at Heart Valve Voice US, Strong serves as an American Heart Association Heart Valve Ambassador and is actively involved as a patient stakeholder in clinical research.

Heart Valve Voice US

Joseph C. Cleveland Jr., MD

Cardiothoracic Surgery
Professor of Surgery

John C. Messenger, MD

Interventional Cardiology
Professor of Medicine

Heart Valve Voice US

Innovations and the Future of Valve Disease Treatment

Joseph C. Cleveland Jr, MD
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John C. Messenger, MD
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University of Colorado
Anschutz Medical Campus

Heart Valve Voice US

Disclosures

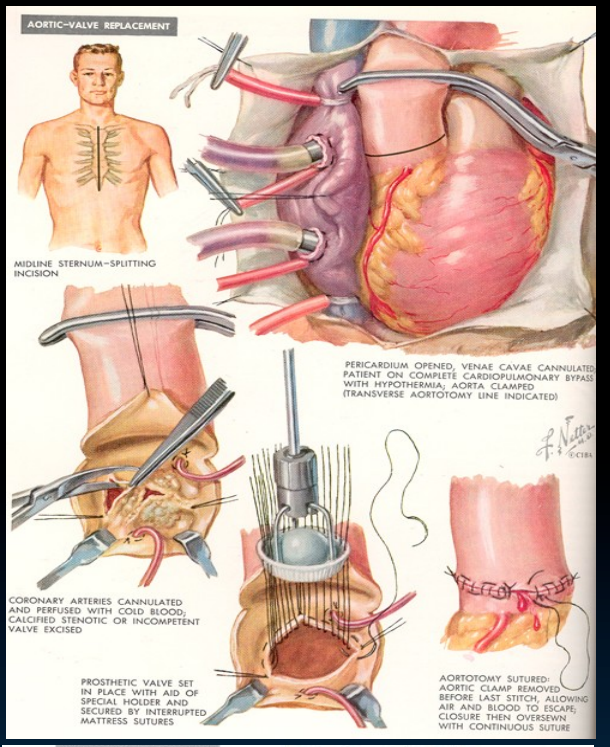
- Institutional Grant/Research Support
  - Philips Medical Systems
  - Edwards Lifesciences
  - Medtronic Corp
  - Abbott

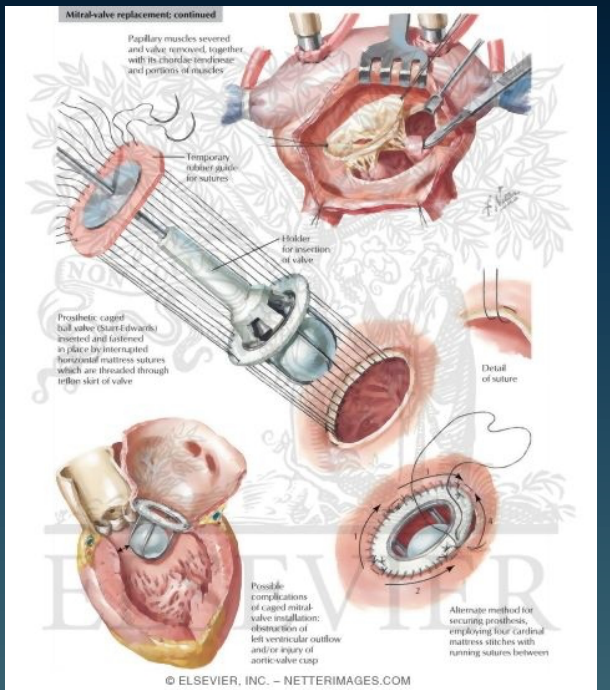
Outline

- Update on Transcatheter Aortic Valve Replacement
  - Emerging Indications for TAVR
- Update on Mitral Valve Technologies
  - MitraClip Indications
  - New Approaches
- Emerging Tricuspid Valve Therapies
- Q and A

Background

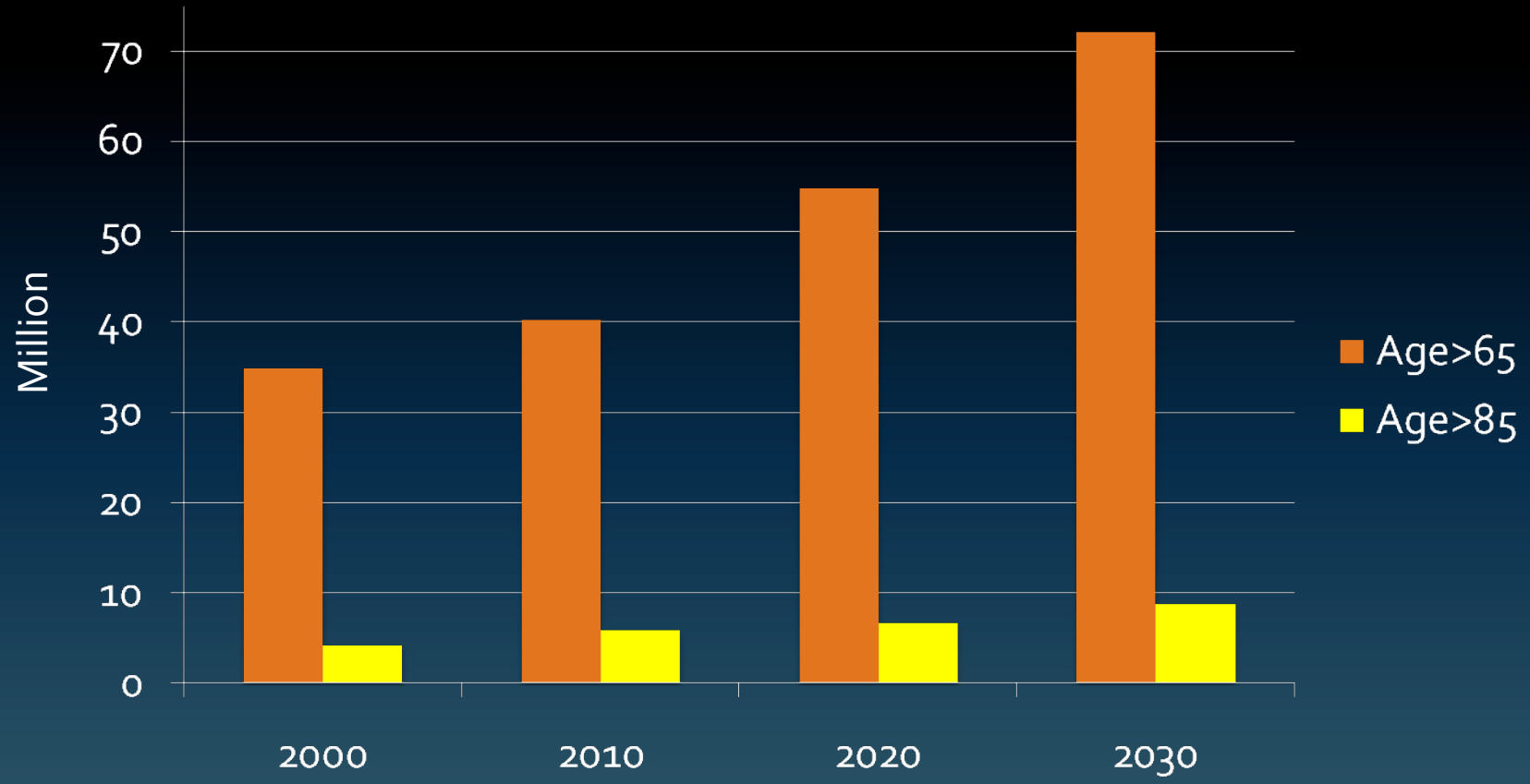
- Surgical Valve Replacement has been the gold standard for treatment of severe valve stenosis since the 1960's
- In 2011, the STS database reported over 48,000 patients underwent surgical mitral and aortic valve replacement in the US
- Median mortality rates for isolated surgical valve replacement in the TAVR era in the STS database in 2016:
  - 2.2 % for AVR
  - 4.4% for MVR
- Unfortunately, as our population ages, with more co-morbid conditions, the surgical risk is increasing!





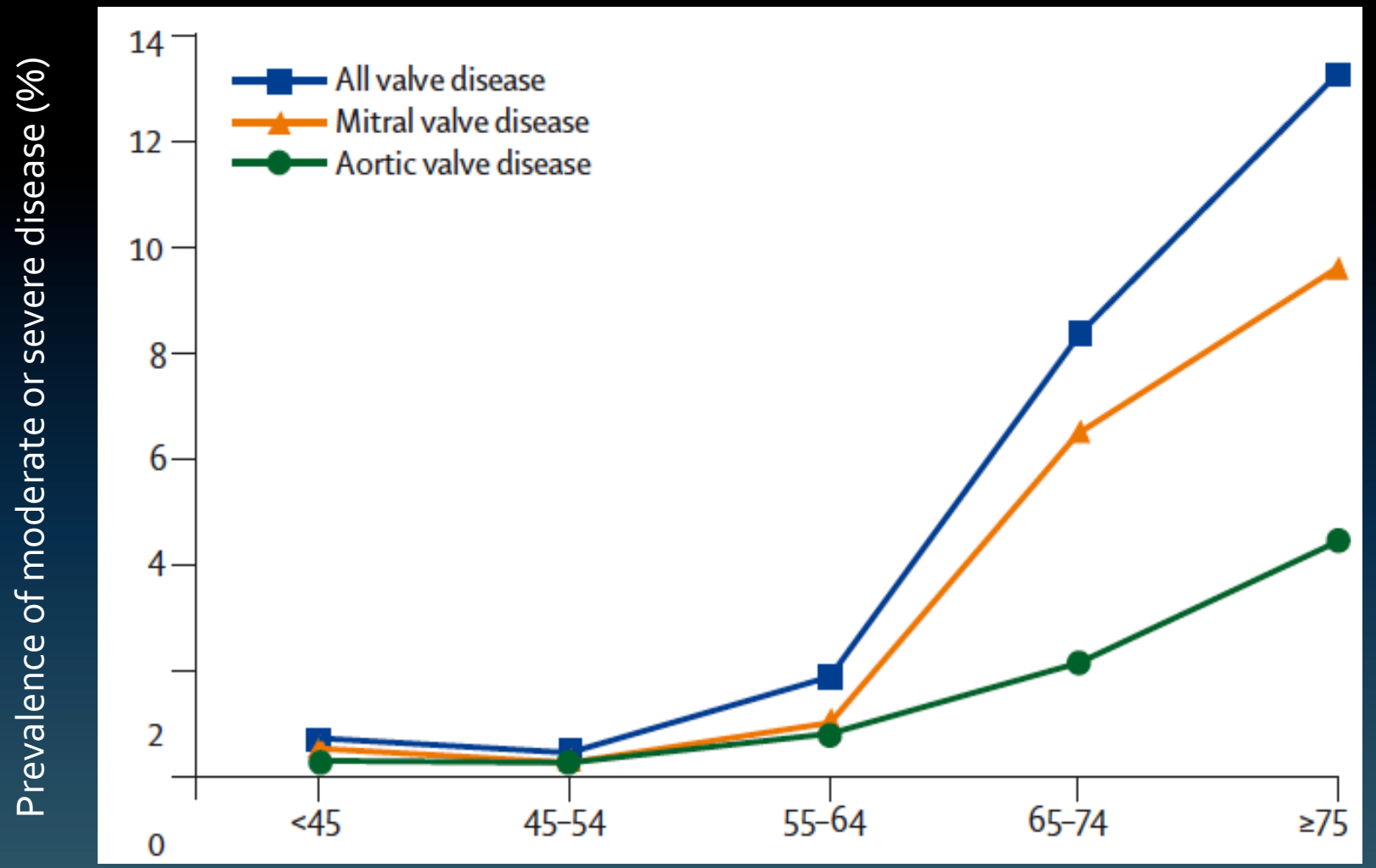
D'Agostino RA et al. Ann Thorac Surg 2018;105:15–23

US Population Projection by Age Group: US Census Bureau



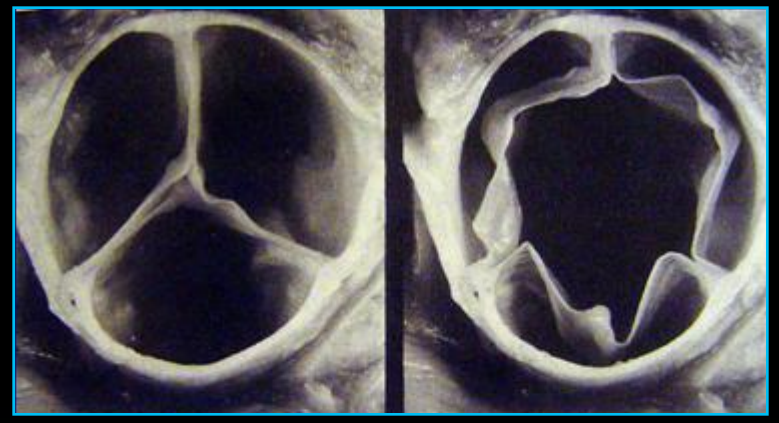
Figures for projections from 2010 through 2050 are from: Table 12. Projections of the Population by Age and Sex for the United States: 2010 to 2050 (NP2008-T12), Population Division, U.S. Census Bureau; Release Date: August 14, 2008

Valvular Heart Disease Increases with Age—
Pooled Echo Data from ARIC/CARDIA/CHS

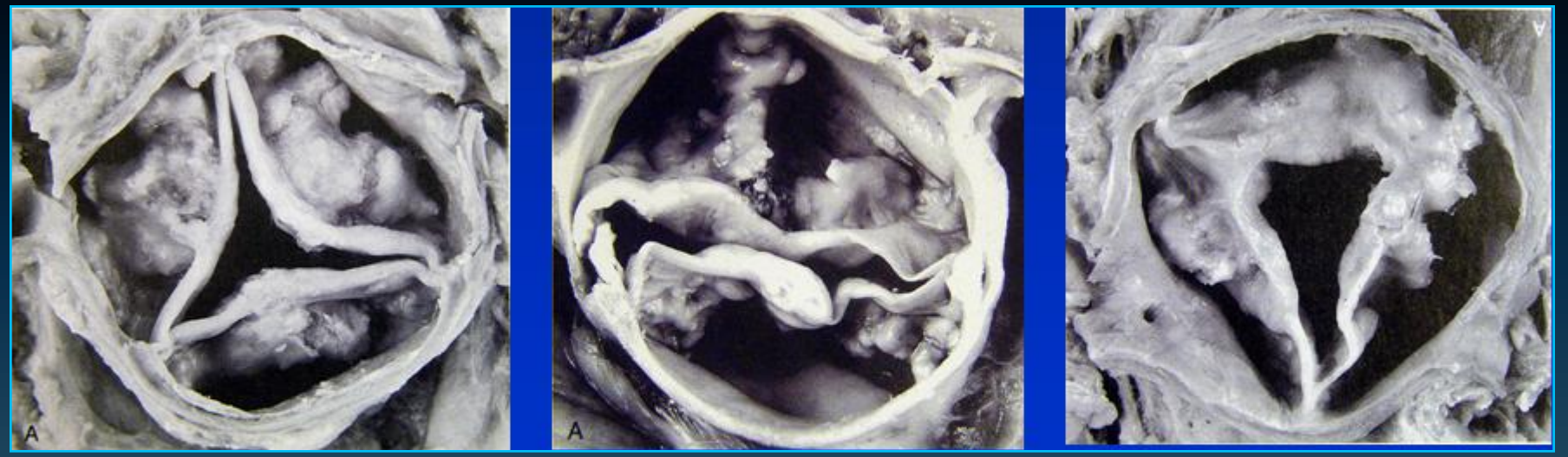


Nkomo VT et al. Lancet 2006, 368;1005-11

Aortic Stenosis



Normal



Degenerative Calcified

Bicuspid

Rheumatic

Factors Associated with Increased Risk for Surgical Aortic Valve Replacement

Clinical

- Prior Sternotomy
- Female gender
- Renal dysfunction
- Diabetes
- Moderate to severe COPD
- Low EF
- NYHA Class IV
- Cerebrovascular disease
- Immunosuppression

Anatomic

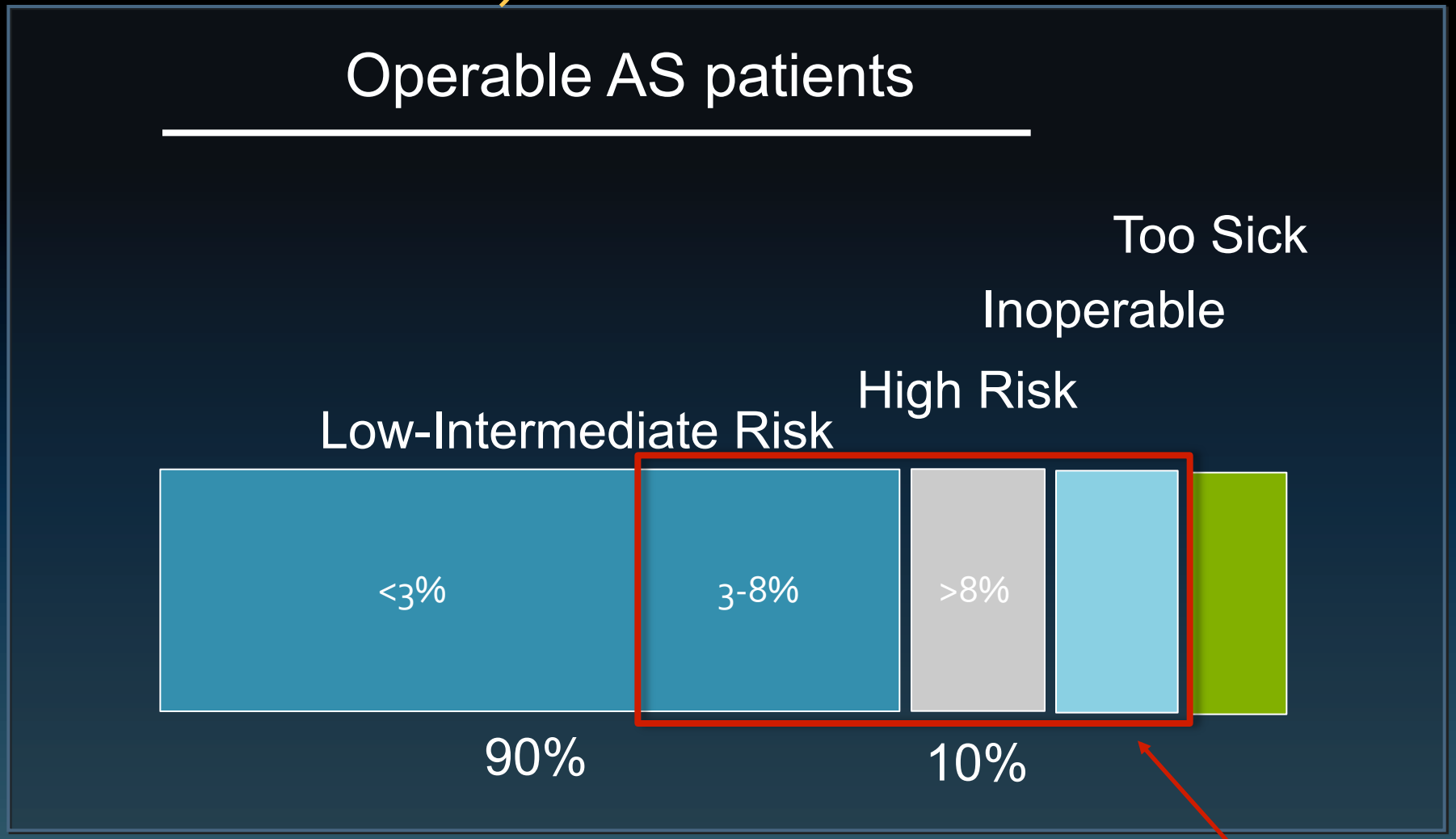
- Porcelain aorta
- Prior radiation
- Bypass graft course under sternum
- Prior sternectomy

Non-Traditional

- Frailty
- High operative risk
  - Cirrhosis
  - Pulmonary Hypertension

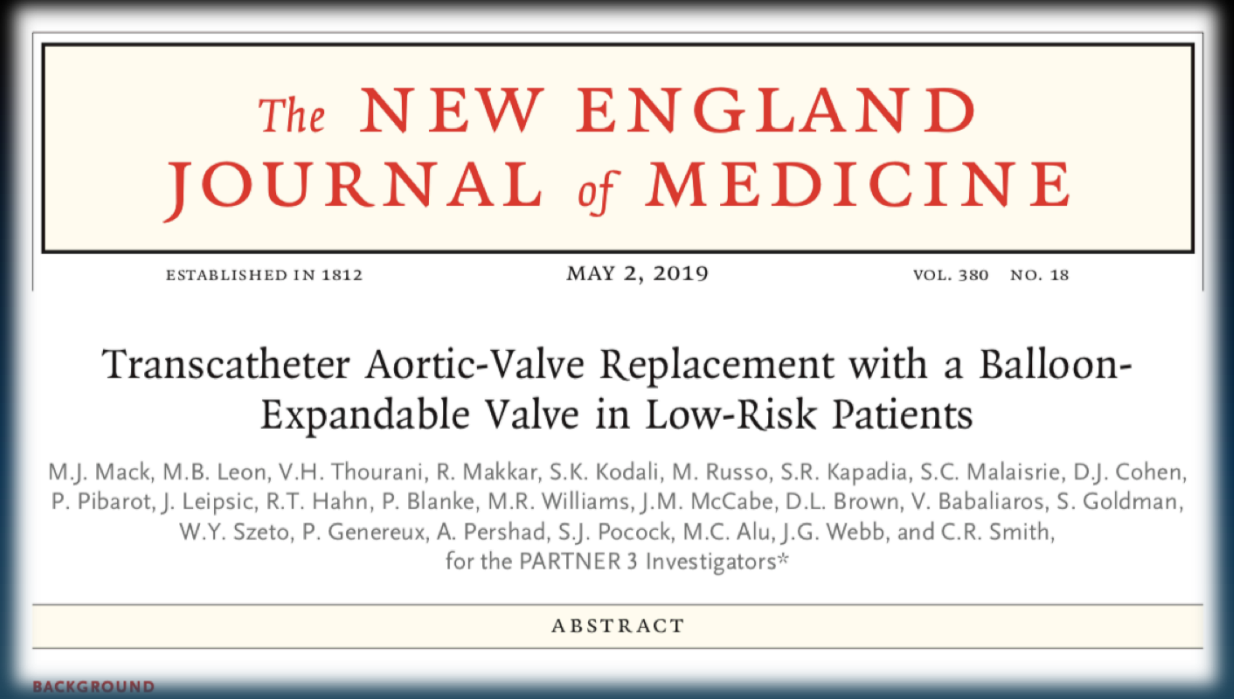
Surgical AVR Risk Categories

(risk is a continuum)



PARTNER 3 and Medtronic

Low Risk Trials



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 2, 2019 VOL. 380 NO. 18

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

ABSTRACT

BACKGROUND

The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

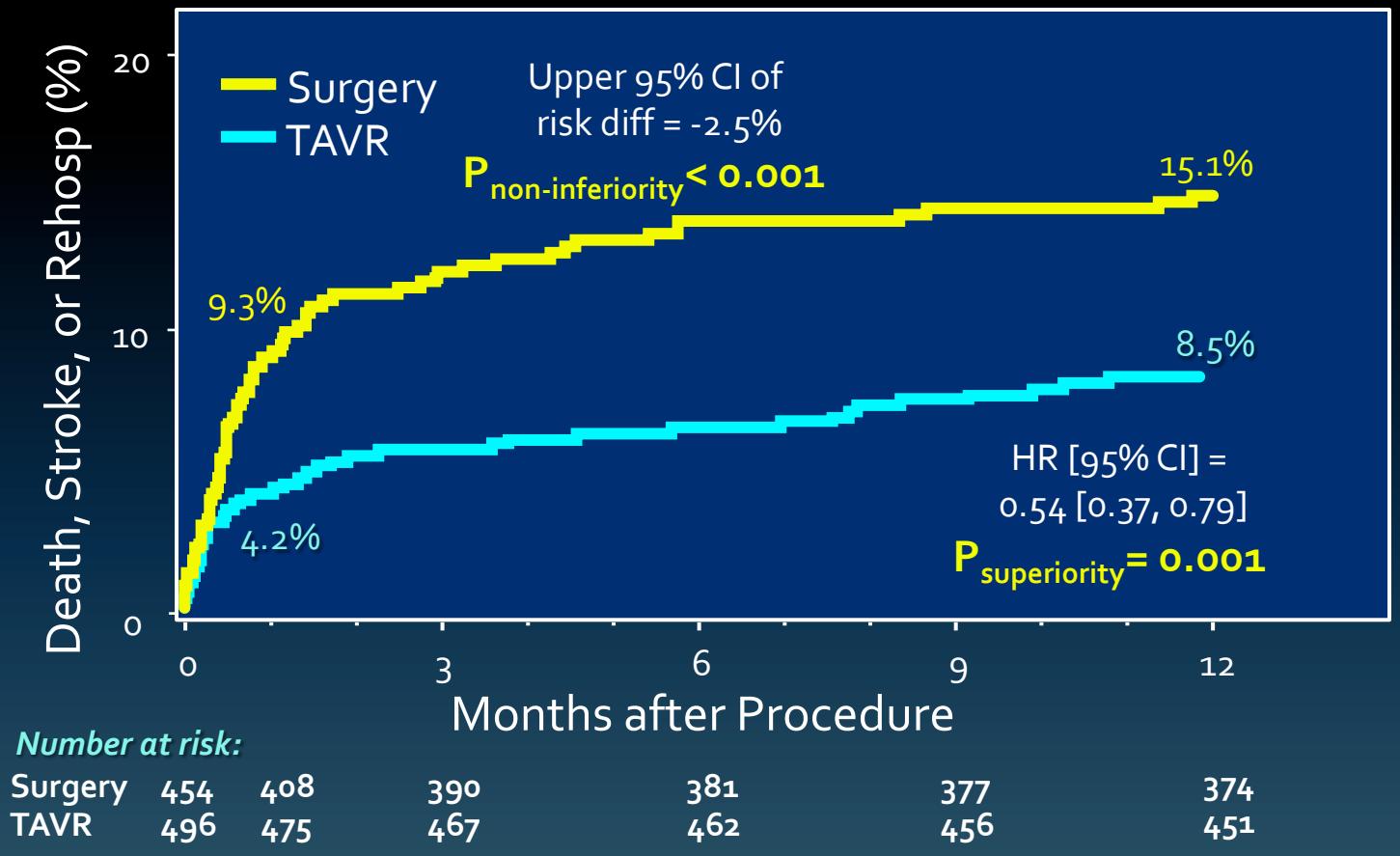
Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn, III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*

Mack MJ et al. *N Engl J Med* 2019; 380:1695-1705

Popma JJ et al. *N Engl J Med* 2019; 380:1706-1715

Primary Endpoint

Death, Stroke or Rehospitalization

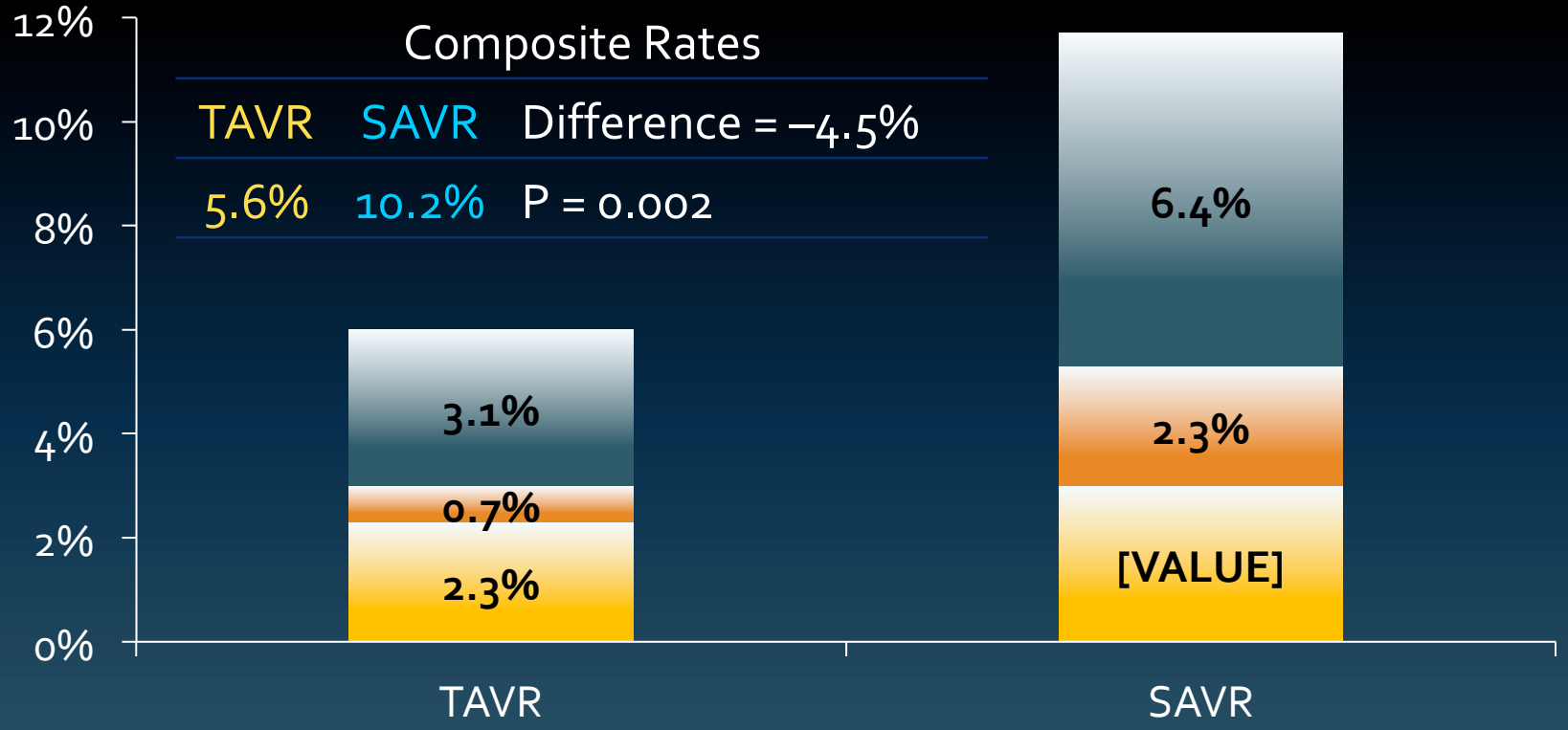


Mack MJ et al. *N Engl J Med* 2019; 380:1695-1705

Primary Endpoint

Death, Disabling Stroke and Heart Failure Hospitalizations to 1 Year

Evolut™ Low Risk Trial



Popma JJ et al. *N Engl J Med* 2019; 380:1706-1715

TAVR in Low Risk Patients—Will be approved in 2019!

EARLY TAVR Trial: *Study Flow*

Asymptomatic Severe AS and 2D-TTE (PV ≥4m/s or AVA ≤1 cm²)
Exclusion if patient is symptomatic, EF<50%, concomitant surgical indications, bicuspid valve, or STS >8

Treadmill Stress-Test

Stress-Test Normal

CTA and Angiography
TF- TAVR eligibility

Early-TAVR Randomized Trial

Randomization 1:1
Stratified by STS (<3 vs ≥3)

- TF- TAVR
- Clinical Surveillance

Stress-Test Abnormal

Early TAVR Registry

Primary Endpoint (superiority):
2-year composite of all-cause mortality, all strokes, and repeat hospitalizations (CV)

TAVR UNLOAD Trial: *Study Design*

(600 patients, 1:1 Randomized)

TAVR UNLOAD Trial

International Multicenter Randomized

Heart Failure
LVEF < 50%
NYHA ≥ 2
Optimal HF therapy (OHFT)
Moderate AS

R

TAVR + OHFT

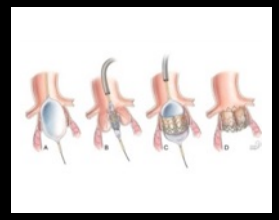
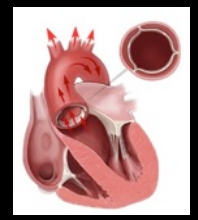
OHFT Alone

Follow-up:
1 month
6 months
1 year

Clinical endpoints
Symptoms
Echo
QoL

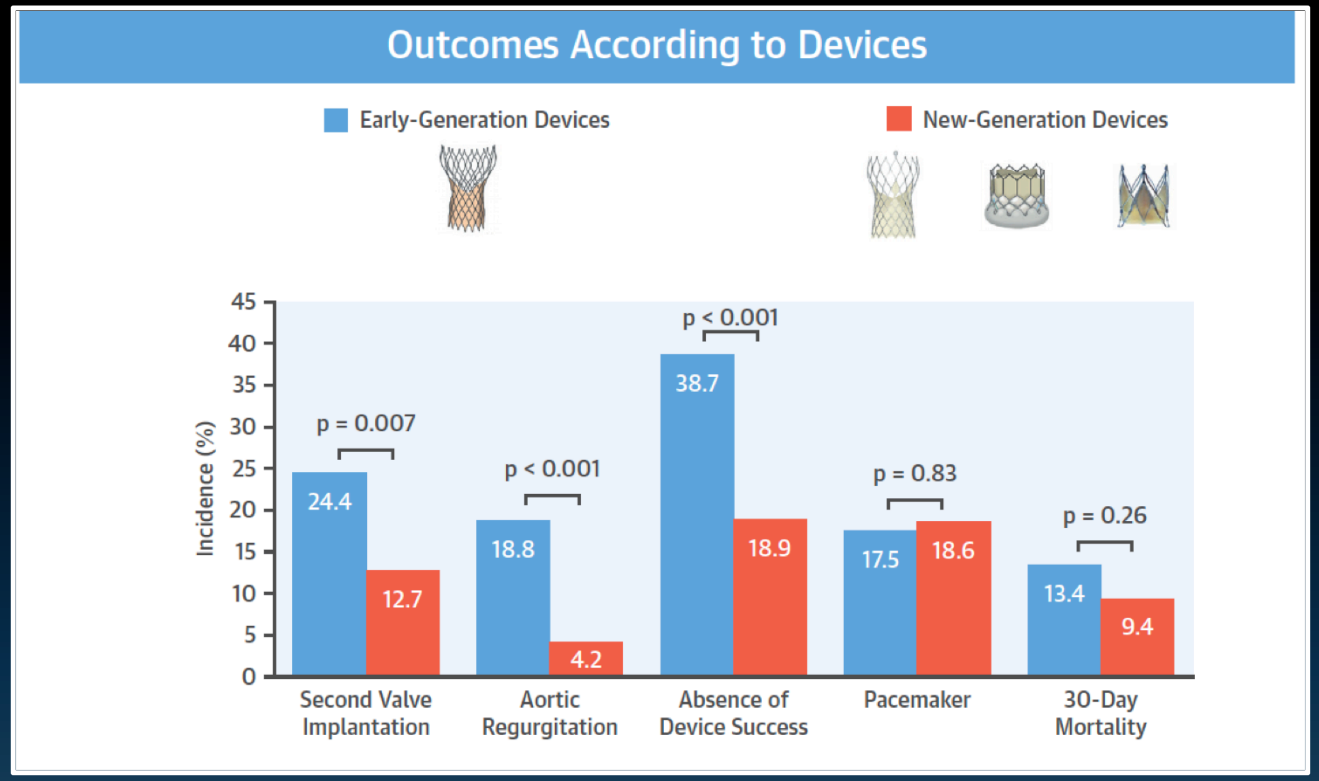
Primary Endpoint
Hierarchical occurrence of:
- **All-cause death**
- **Disabling stroke**
- **Hospitalizations for HF, aortic valve disease**
- **Change in KCCQ**

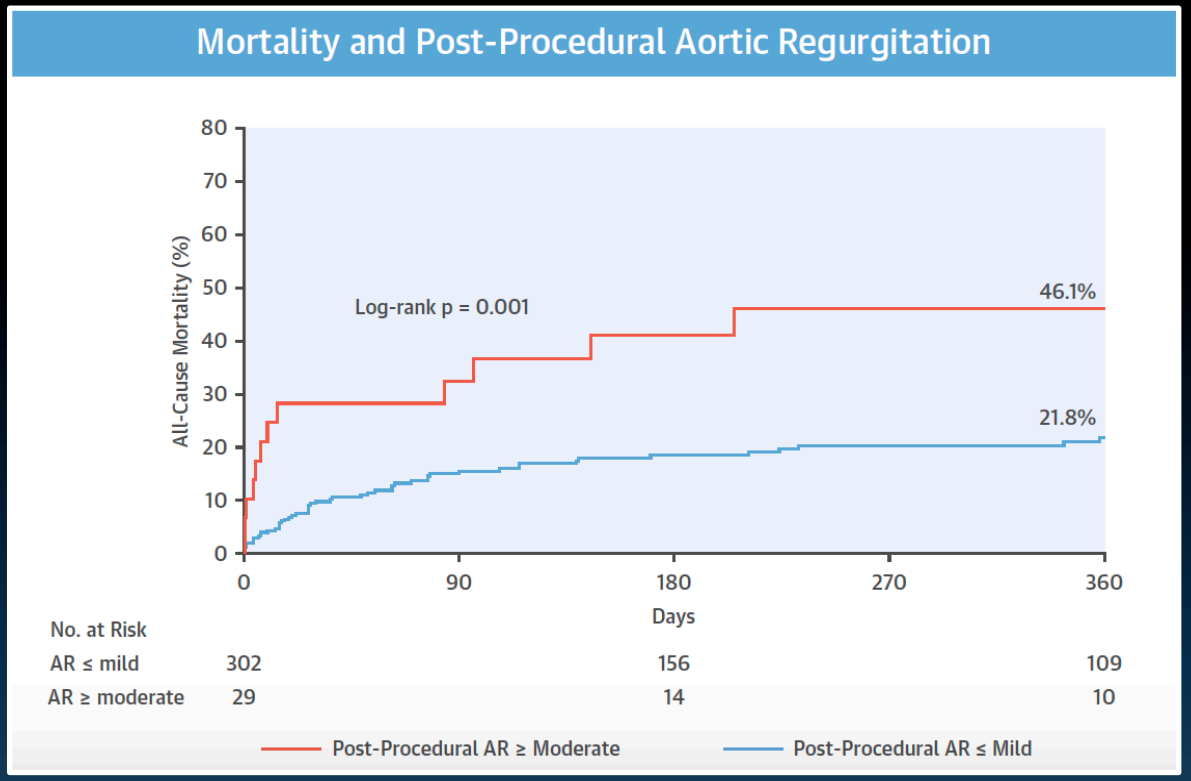


Reduced AFTERLOAD
Improved LV systolic and diastolic function

TAVR for Aortic Regurgitation

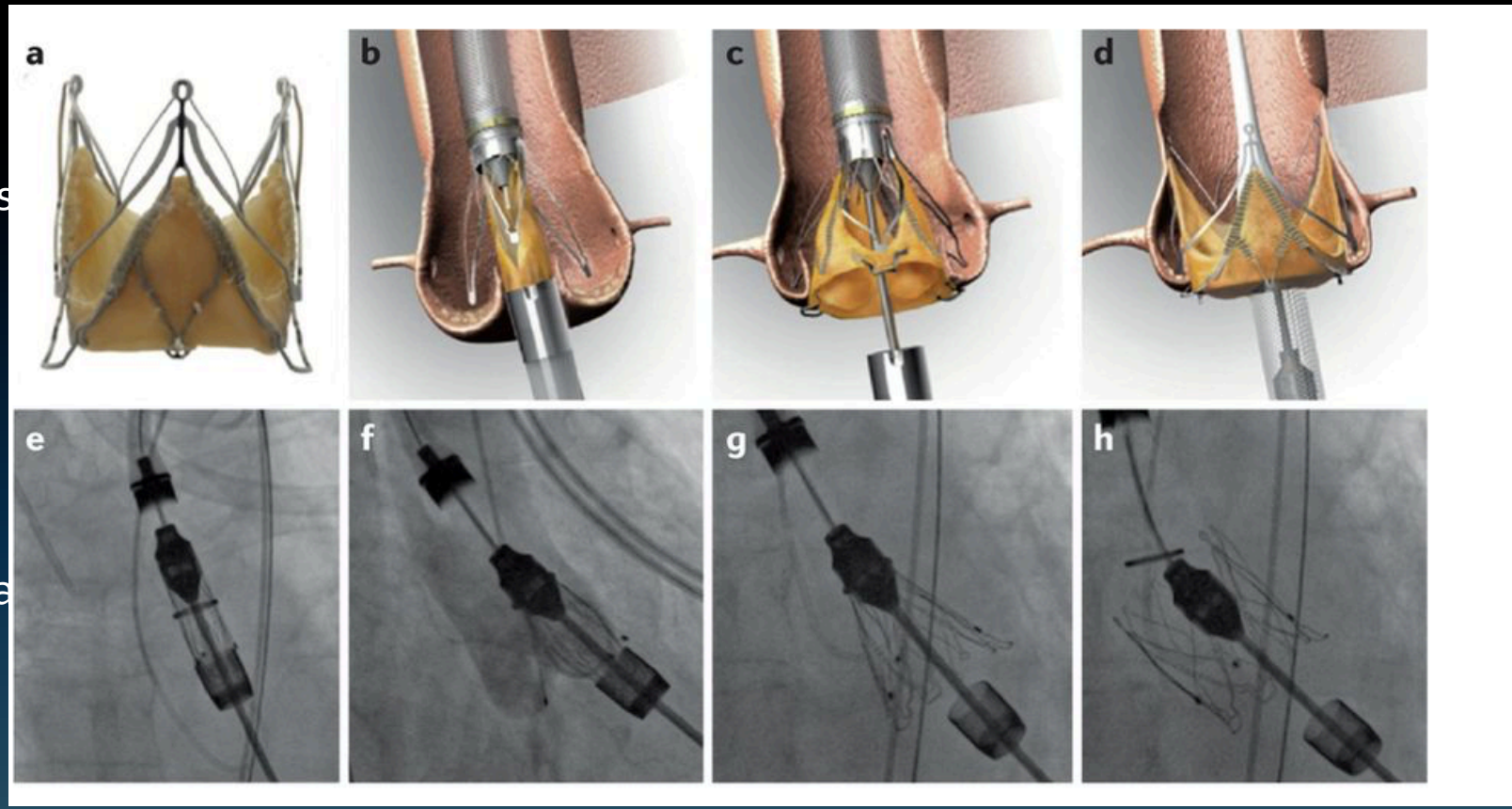




Yoon S.-H. et al. J Am Coll Cardiol. 2017;70(22):2752–63

Dedicated Valve for NVAR--JenaValve

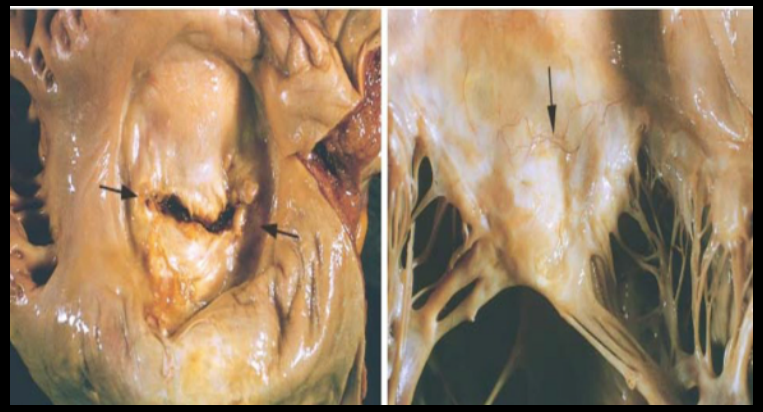
- Nitinol self expanding
- Three feelers for sinus stabilization, clips hold in place leaflets
- Recapturable, repositionable
- 23, 25 and 27 mm Valve
- CE Mark in 2013
- Gen 2 Device CE Mark Study underway a of 6/2018
- Only valve approved for NVAR



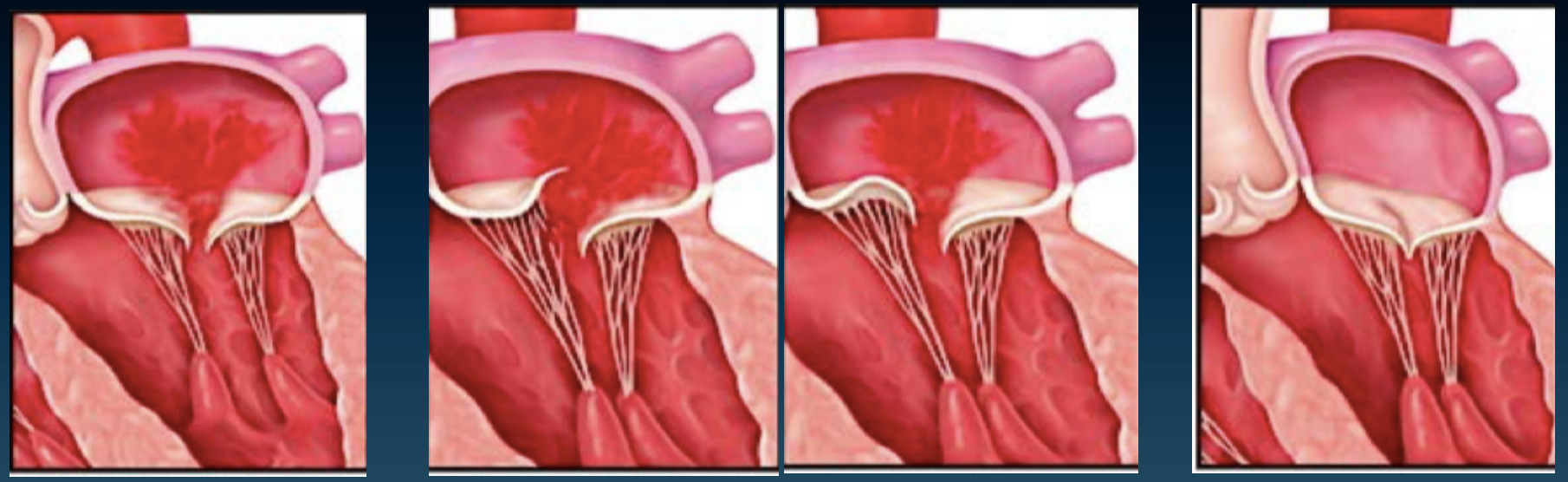
The Unique Challenges and Opportunities for Treating Mitral Valve Disease with Catheter Based Therapy

MITRAL VALVE: THE NEXT FRONTIER

Mitral Valve Disease



Rheumatic
MS and MR



Functional

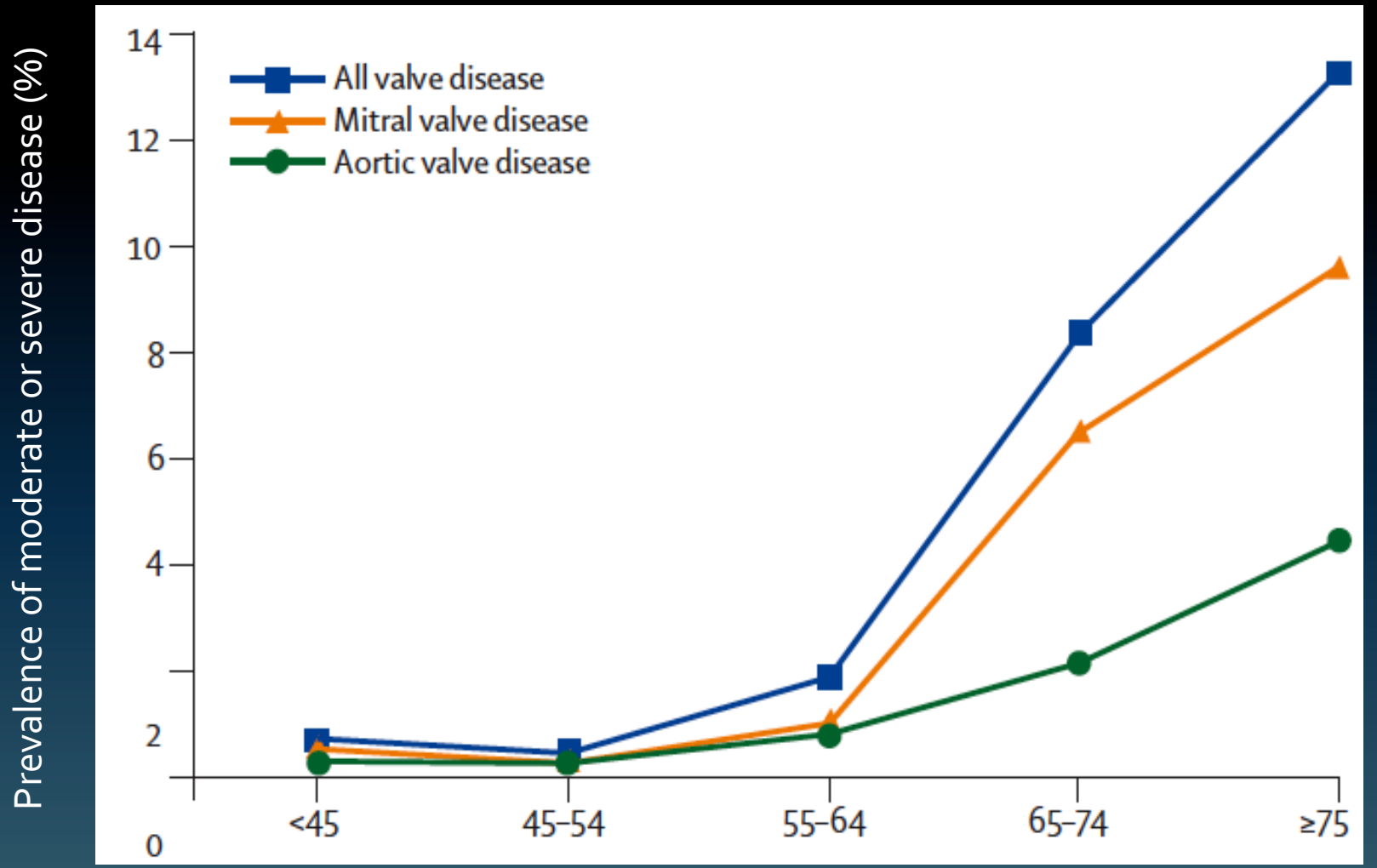
Degenerative

Normal

"Secondary"

"Primary"

Mitral Valve Disease Is Increasing Faster Than Aortic Valve Disease!



Nkomo VT et al. *Lancet* 2006, 368;1005-11

Key Issues

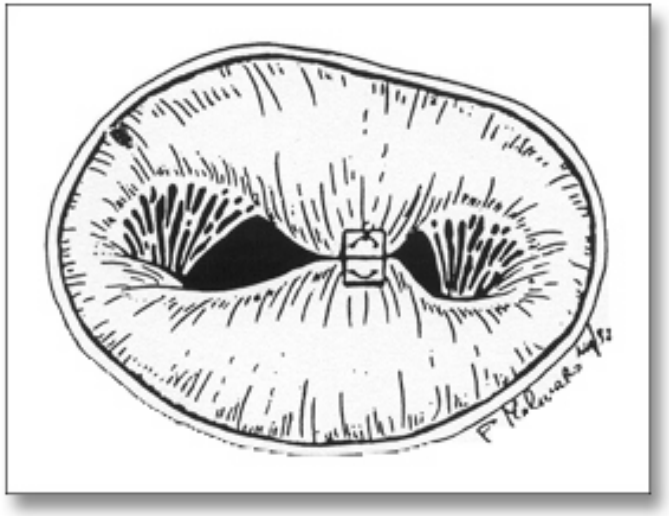
- Operative risk for MV replacement is about double that of AVR
- Patients with MR have more co-morbid conditions making them higher risk at baseline
- Patients with Functional MR don’t get surgical MVR

Alfieri Surgical Approach

A Simple Method:

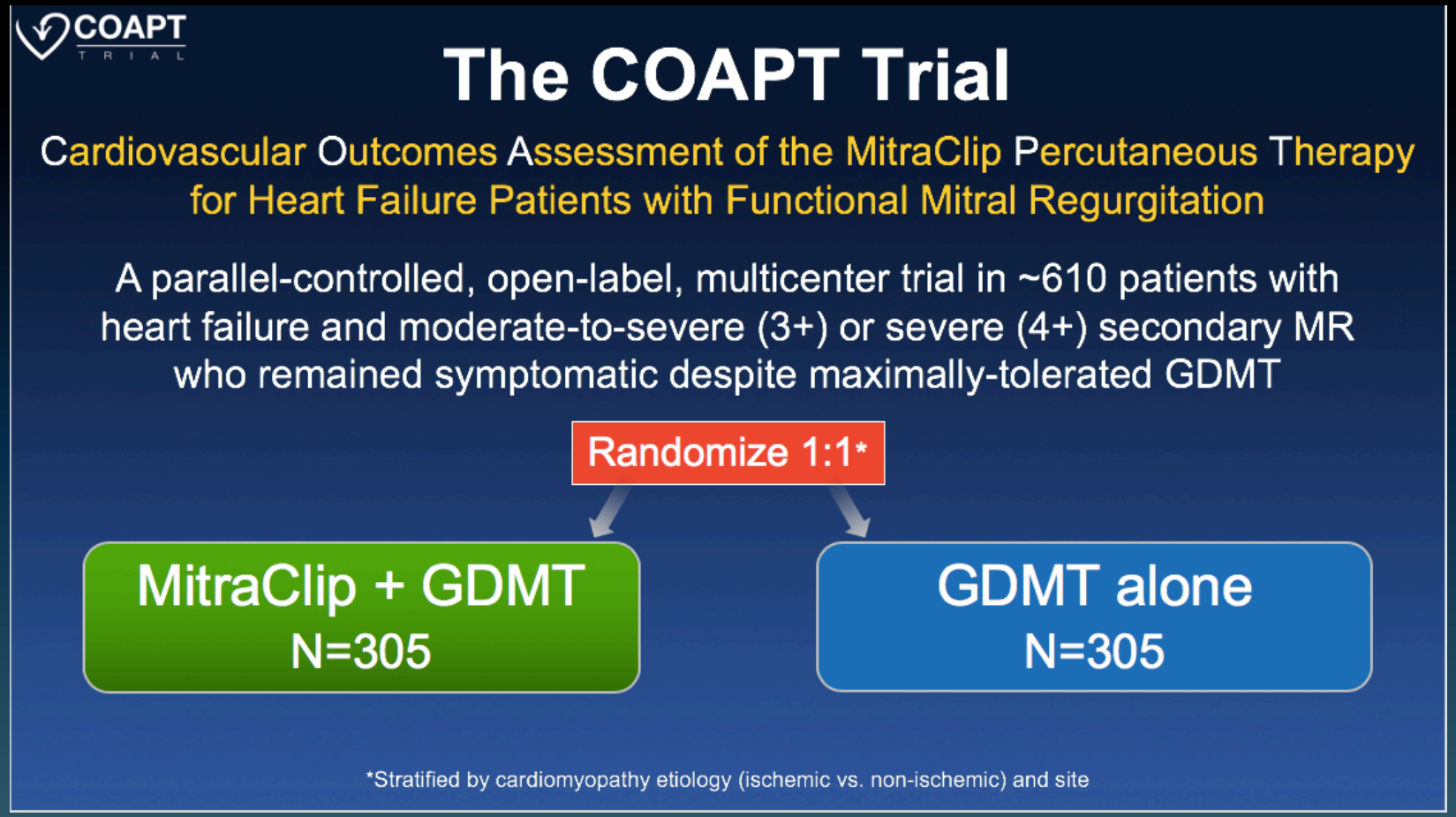
Surgical Edge-to-Edge Mitral Repair

- Approximate mid-sections of A2 and P2
- Suture in the center, creating a double orifice
- >600 procedures published in peer review journals



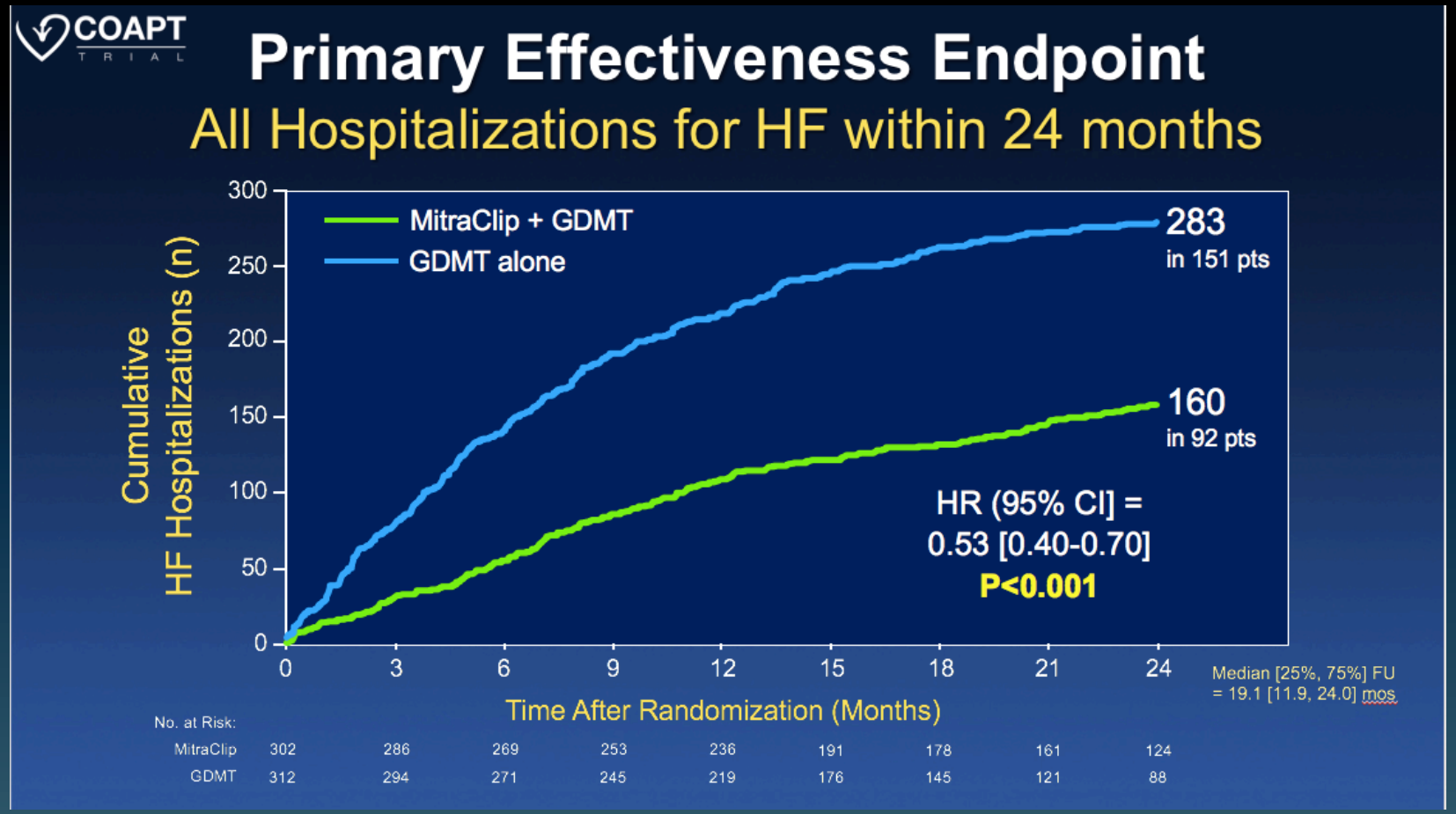
Alfieri O et al. *Eur J Cardiothorac Surg*. 1998 Mar;13(3):240-5

Treatment of Functional Mitral Regurgitation



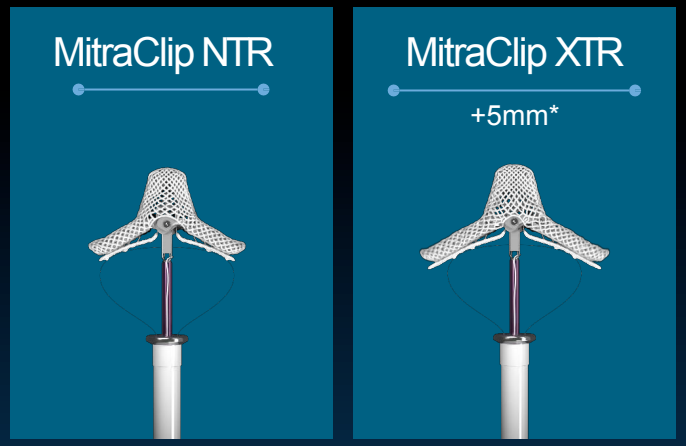
Slide From Stone, et al. COAPT Trial Presentation, TCT 2018

COAPT Trial Primary Endpoint



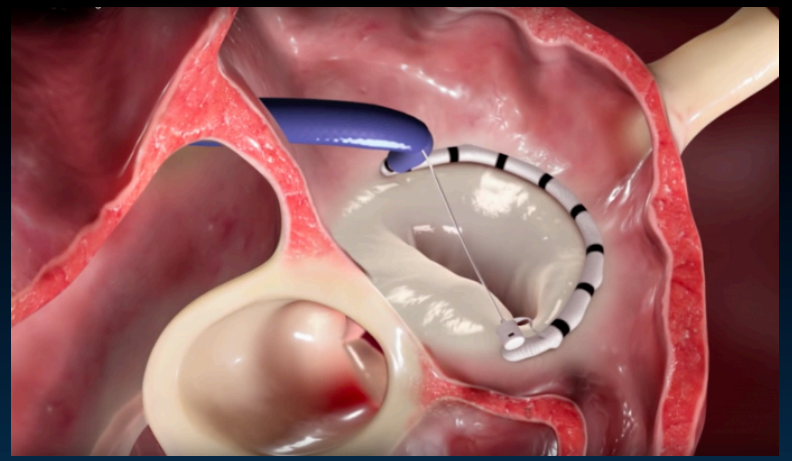
Slide From Stone, et al. COAPT Trial Presentation, TCT 2018

Transcatheter Mitral Valve Repair in Early Feasibility Studies in the US

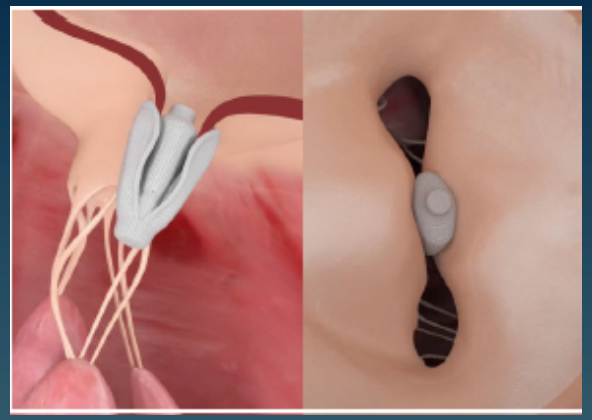


MitraClip XTR (Abbott)

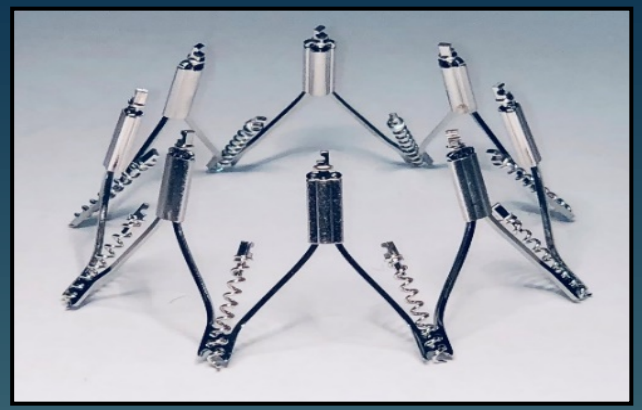
CARILLON Annuloplasty System (Cardiac Dimensions)



CardioBand Annuloplasty System (Edwards)

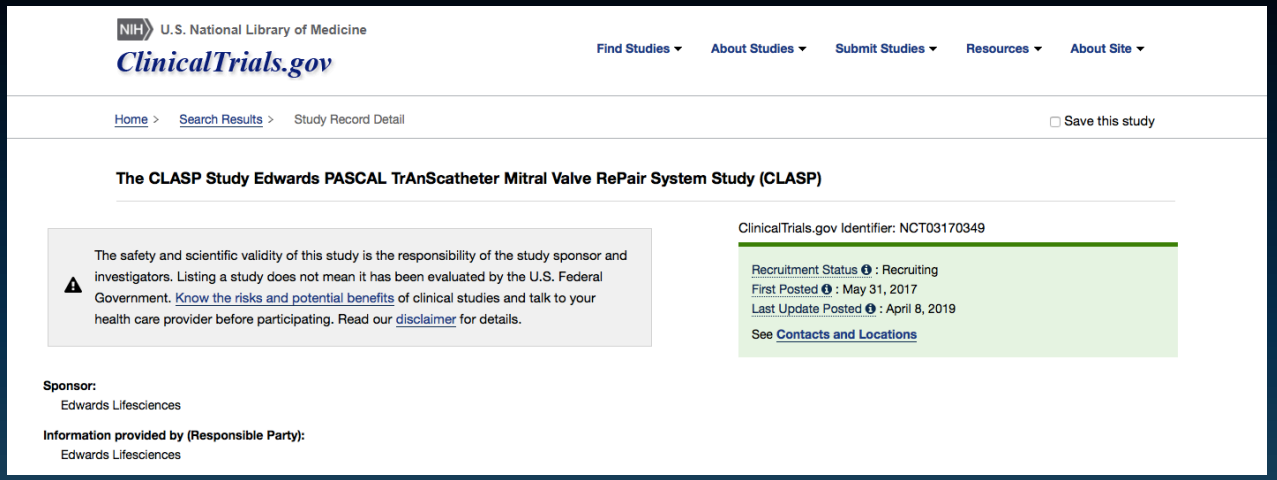


Pascal Spacer (Edwards)



Millipede Annuloplasty System

CLASP Clinical Trial



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The CLASP Study Edwards PASCAL TrAnScatheter Mitral Valve RePair System Study (CLASP)

⚠ The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

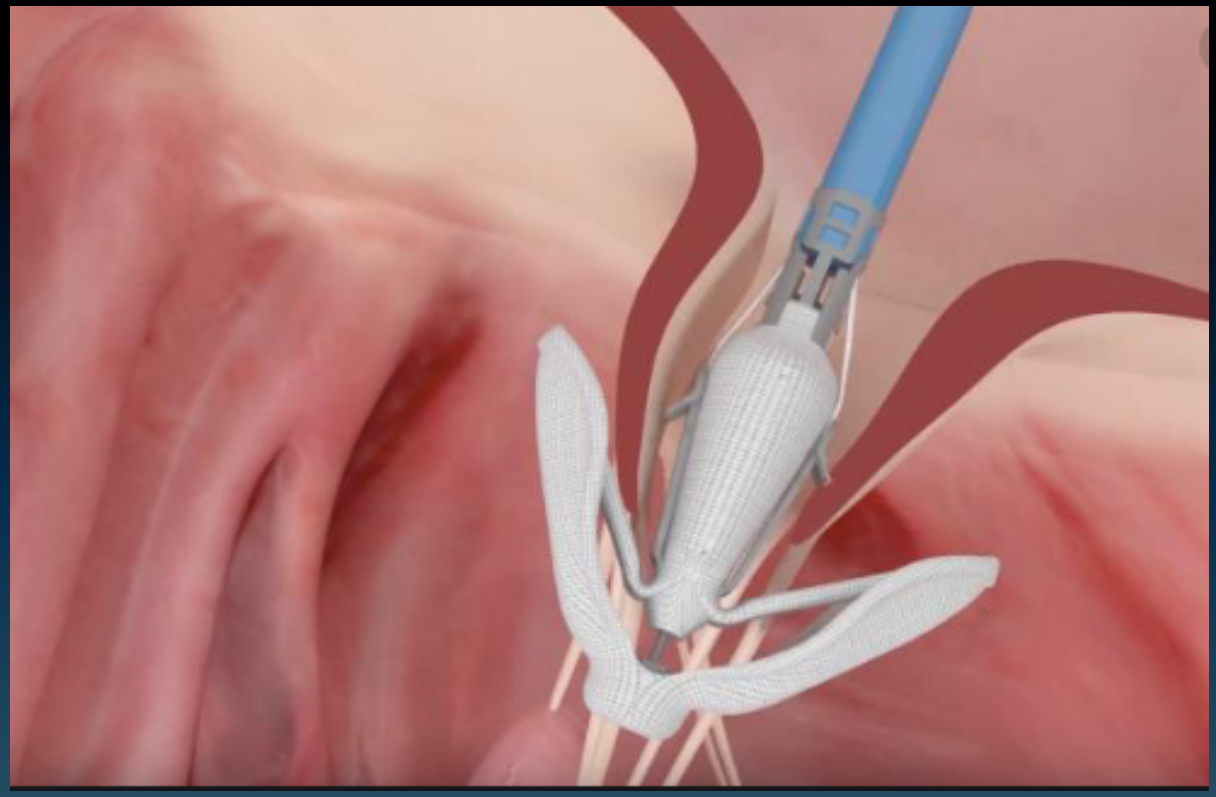
ClinicalTrials.gov Identifier: NCT03170349

Recruitment Status : Recruiting
First Posted : May 31, 2017
Last Update Posted : April 8, 2019

See Contacts and Locations

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences



Cardioband Trial

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Edwards Cardioband System ACTIVE Pivotal Clinical Trial (ACTIVE) (ACTIVE)

ClinicalTrials.gov Identifier: NCT03016975

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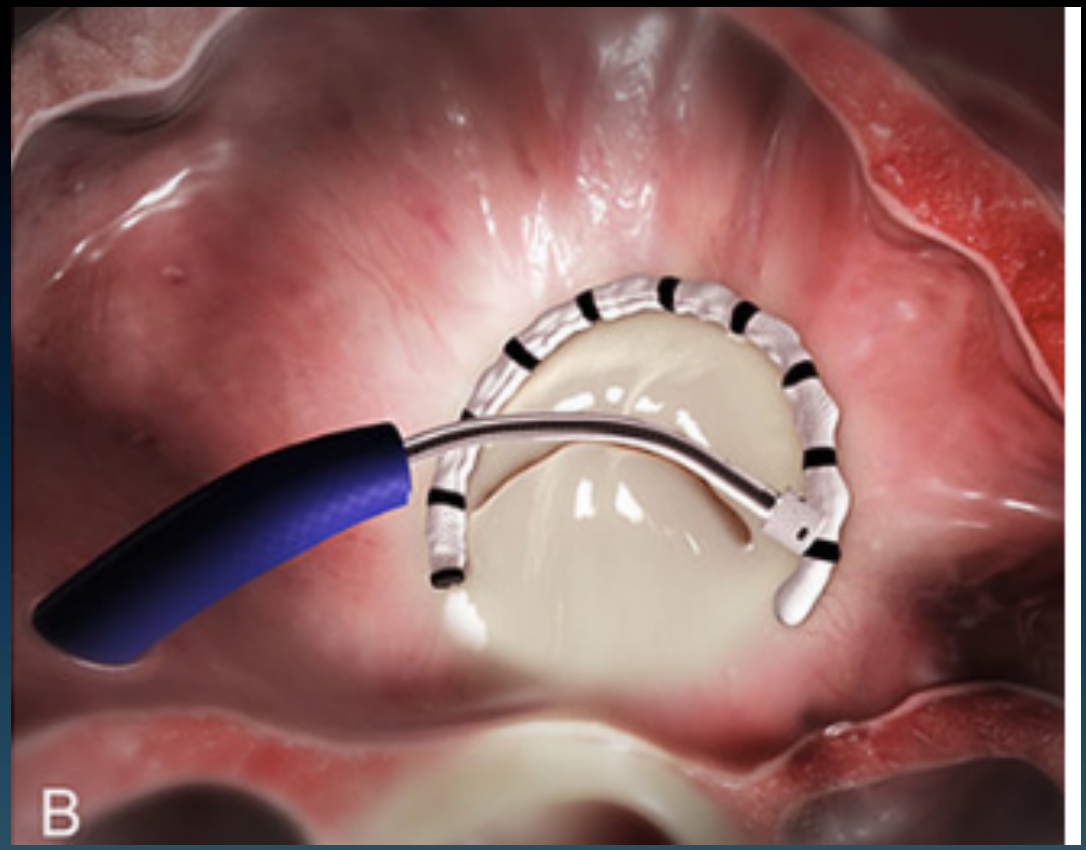
Recruitment Status : Active, not recruiting
First Posted : January 11, 2017
Last Update Posted : March 13, 2019

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences



Transcatheter Mitral Valve Therapies Approved for Early Feasibilty Study in US

Transapical

Tendyne
(Abbott)

Intrepid TMVI
(Medtronic)

Tiara
(Neovasc)

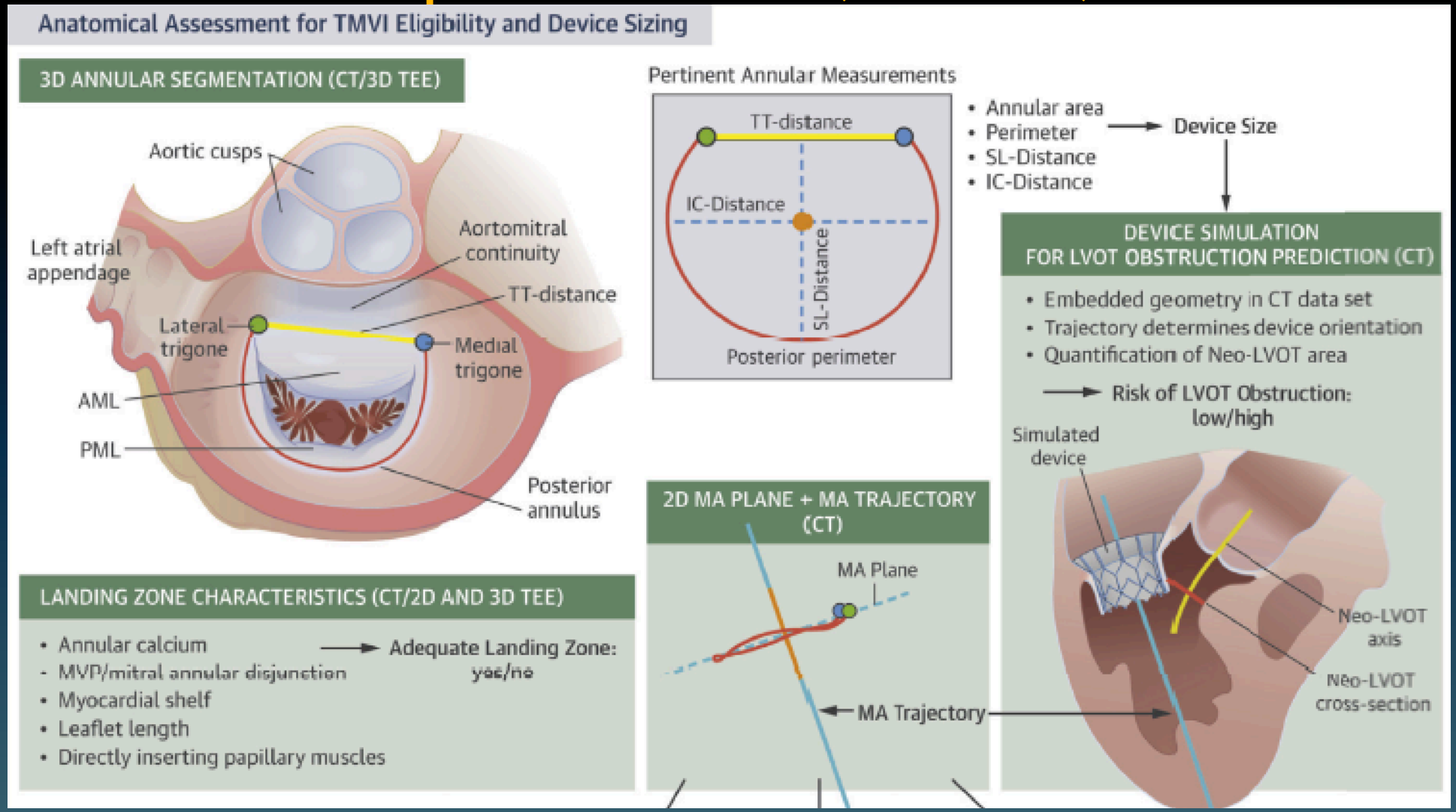
Transfemoral

CardiaQ
(Edwards)

Highlife M3
(Edwards)

Caisson
(LivaNova)

Anatomic Challenges Facing Transcatheter Mitral Valve Replacement (TMVR)



Technical Challenges With TMVR

- Current generation delivery systems are very large—Transapical route of delivery
- Different complications than TAVR
  - LVOT obstruction, conduction system abnormalities circumflex artery obstruction
- Impact on the LV function
- Prosthetic related events
  - thrombosis, endocarditis, embolization, paravalvular regurgitation
- Need for ongoing anticoagulation

Maisano et al. *EuroIntervention* 2015; 11:W37-W41

Tendyne Summit Trial

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☐ Save this study

Clinical Trial to Evaluate the Safety and Effectiveness of Using the Tendyne Mitral Valve System for the Treatment of Symptomatic Mitral Regurgitation (SUMMIT)

⚠ The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03433274

Recruitment Status : Recruiting
First Posted : February 14, 2018
Last Update Posted : May 23, 2019

See Contacts and Locations

Tricuspid Valve Disease—

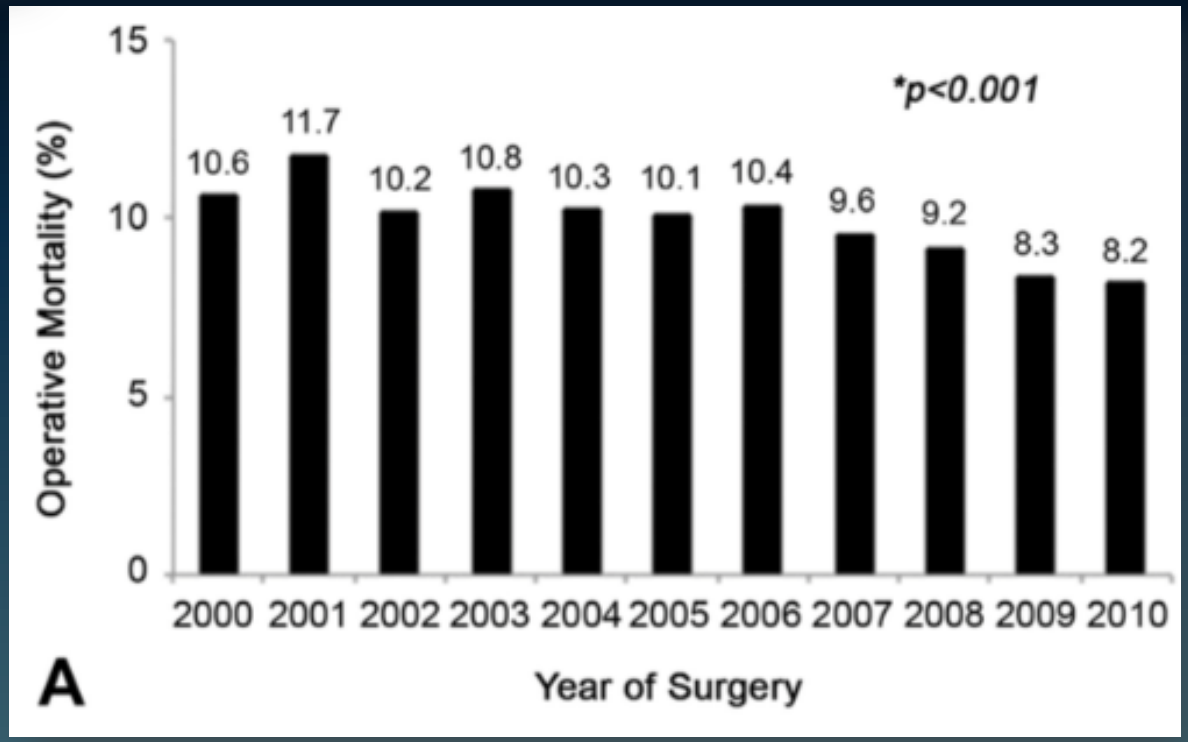
Trends and Outcomes of Tricuspid Valve Surgery in North America: An Analysis of More Than 50,000 Patients From The Society of Thoracic Surgeons Database

Arman Kilic, MD, Paramita Saha-Chaudhuri, PhD, J. Scott Rankin, MD, and John V. Conte, MD

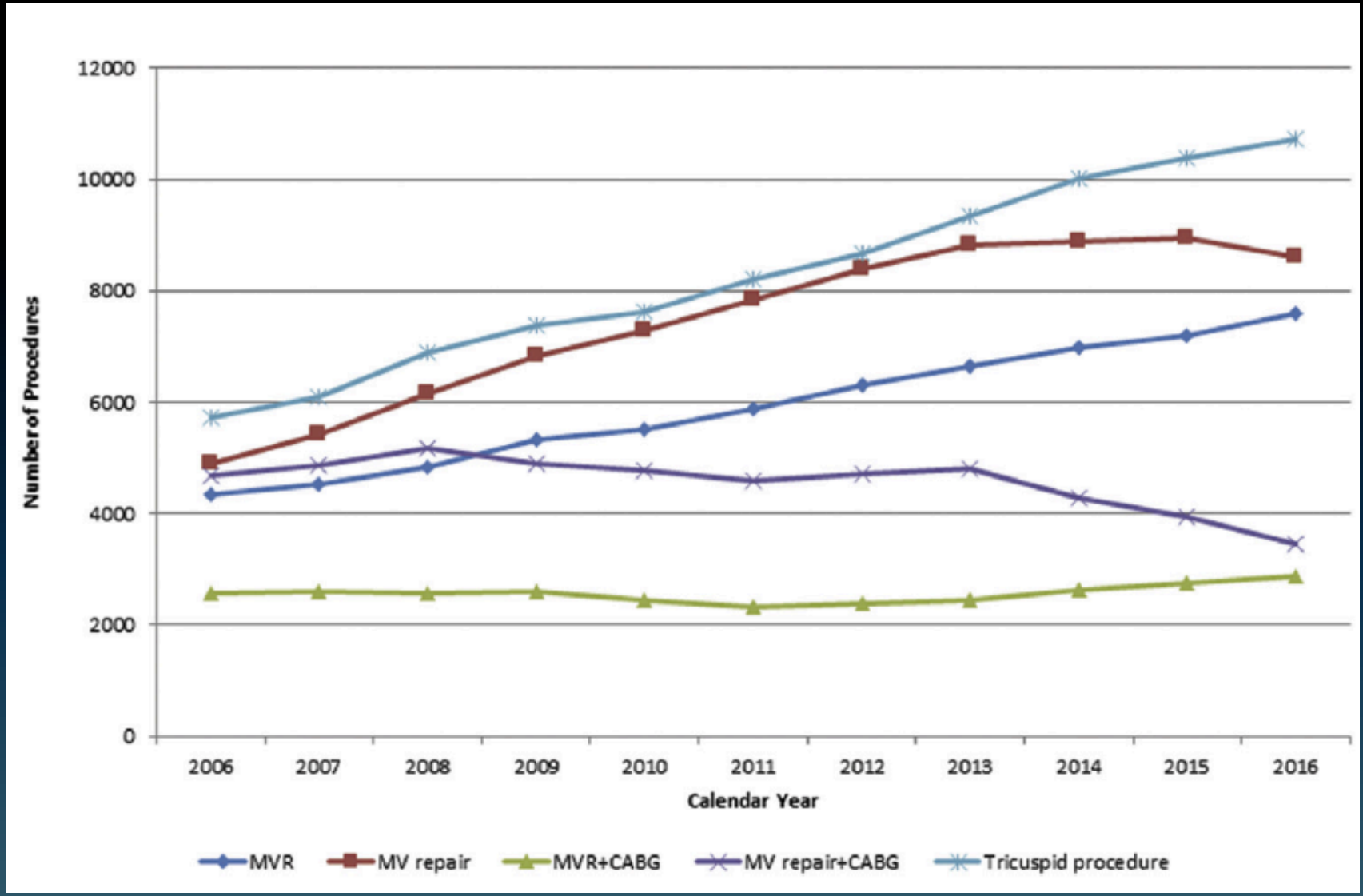
Division of Cardiac Surgery, Johns Hopkins Hospital, Baltimore, Maryland; Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, North Carolina; and Centennial Medical Center and Vanderbilt University, Nashville, Tennessee

Years-2000-2010
Procedures-54,375
- *4,943/year*
Concomitant-46,593 (85.7%)
Isolated- 7,782
707/year
88.9% Repair
30 day mortality-9.6%

- Currently high risk operation with open surgical intervention
- Percutaneous approaches challenging due to anatomy
- Imaging of the tricuspid valve for percutaneous interventions is difficult

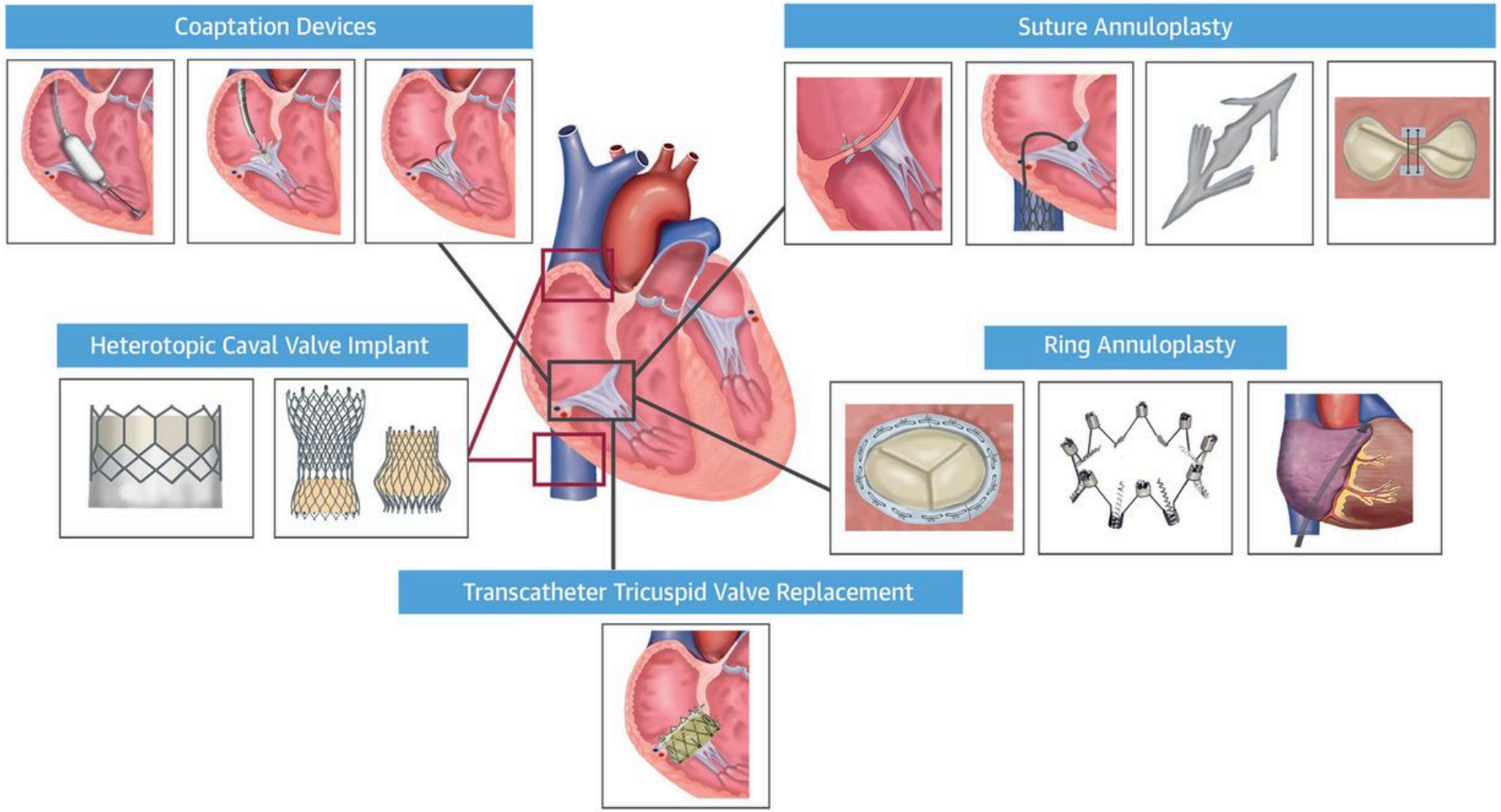


Tricuspid Valve Repair and Replacement



D'Agostino RA et al. *Ann Thorac Surg* 2018;105:15–23

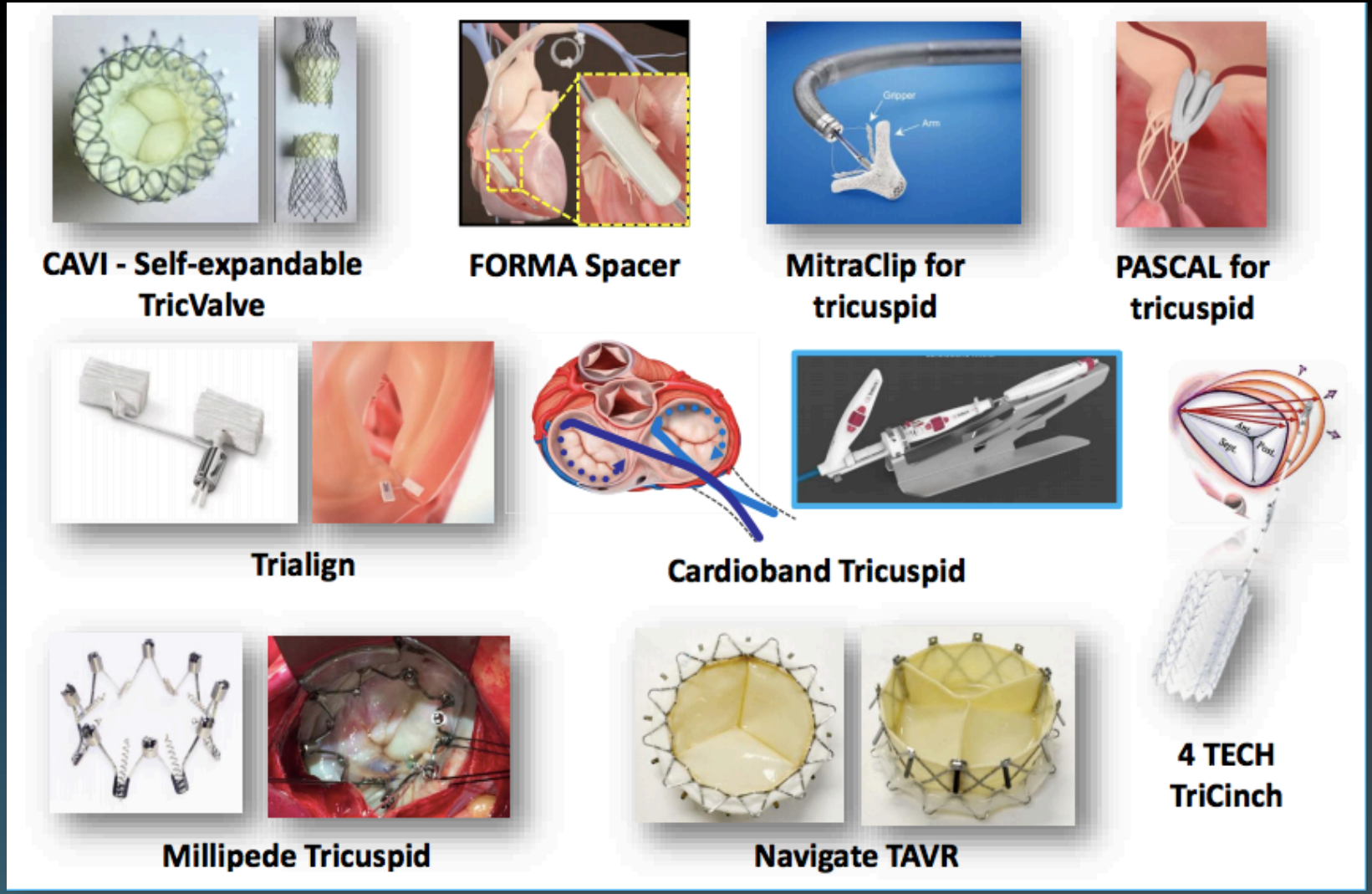
CENTRAL ILLUSTRATION: Transcatheter Tricuspid Landscape



Asmarats, L. et al. J Am Coll Cardiol. 2018;71(25):2935-56.

Tricuspid Valve Interventions—

All Investigational currently



Conclusions

- TAVR is currently FDA approved for treatment of inoperable, high risk and intermediate risk patients with symptomatic aortic stenosis
  - Including valve in valve and patients with bicuspid aortic valves
- TAVR has been demonstrated to be equivalent or superior to SAVR now in low surgical risk patients
  - Expect FDA approval soon!

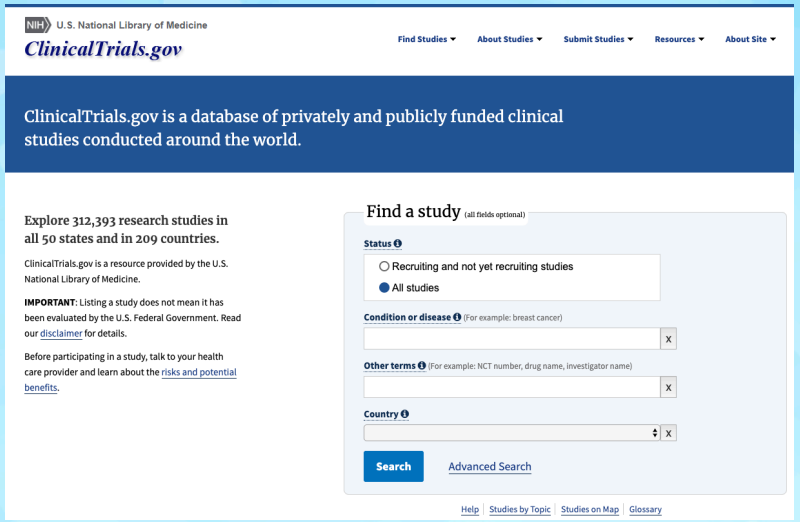
- TAVR being evaluated in:
  - Asymptomatic severe AS
  - Moderate AS with LV dysfunction
  - Aortic regurgitation
  - New and next generation valve technologies

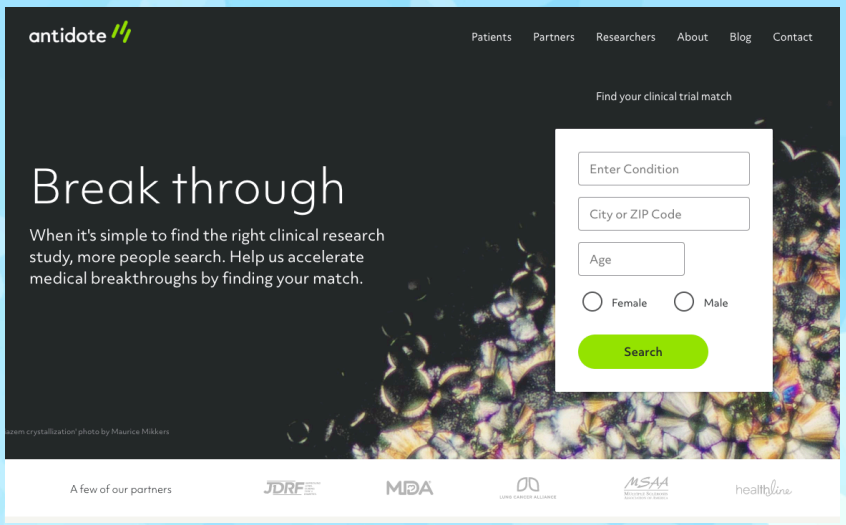
Conclusions (cont)

- Mitral valve repair/replacement timeline will be much longer than TAVR due to the complexity of the mitral valve
  - Transcatheter Mitral Valve Repair with MitraClip is only FDA approved for high surgical risk patients (STS>8%) with degenerative MR
- The COAPT Trial has established the superiority of MitraClip+GDMT to GDMT alone in patients with functional MR
  - Expect FDA approval soon!
- Transcatheter mitral valve replacement and repair has many promising technologies
  - Many first-in-human studies underway in the US.
- Tricuspid valve approaches are in their infancy but are moving forward quickly

Discussion/Questions

For Information about Clinical Trials for Your Condition, see:





https://www.clinicaltrials.gov/

https://www.antidote.me/

Heart Valve Voice US

Thank You!

Heart Valve Voice US