# The Odyssey of TAVR: From Concept to Clinical Reality


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COEX, Seoul, Korea
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tct 25

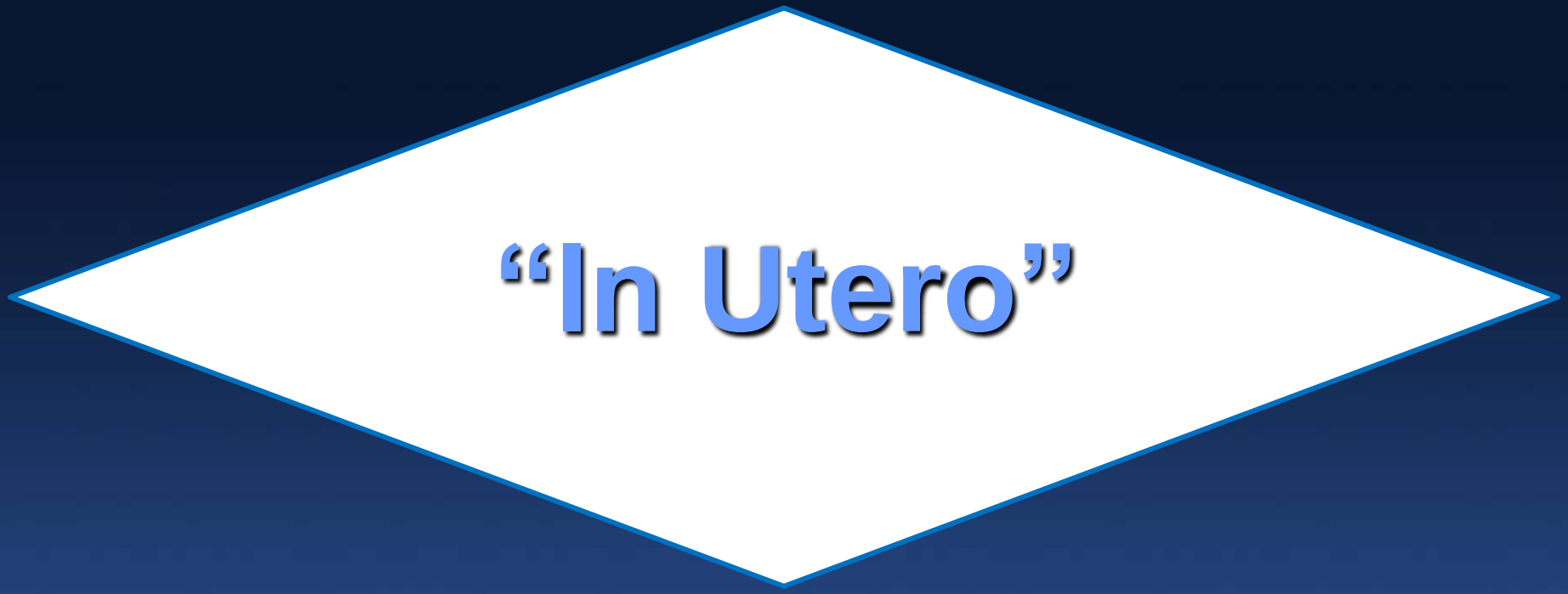
CARDIOVASCULAR RESEARCH FOUNDATION

# Disclosure Statement of Financial Interest
# TCTAP2014: Seoul, Korea; April 22-25, 2014
# Martin B. Leon, MD

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

| Affiliation / Financial Relationship | Company |
| --- | --- |
| • Grant / Research Support | • Abbott, Boston Scientific, Edwards Lifescience, Medtronic |
| • Consulting Fees / Honoraria | • Angioscore, Meril Lifescience, Micell, |
| • Shareholder / Equity | • Apica, Angiometrix, Backbeat, Caliber, Cappella, Claret, Coherex, Elixir, GDS, Medinol, Mitralign, Valve Medical |

# The TAVR Odyssey




HEART DISEASE

By

PAUL DUDLEY WHITE, M.D.

INSTRUCTOR IN MEDICINE, HARVARD MEDICAL SCHOOL; PHYSICIAN, MASSACHUSETTS

New York

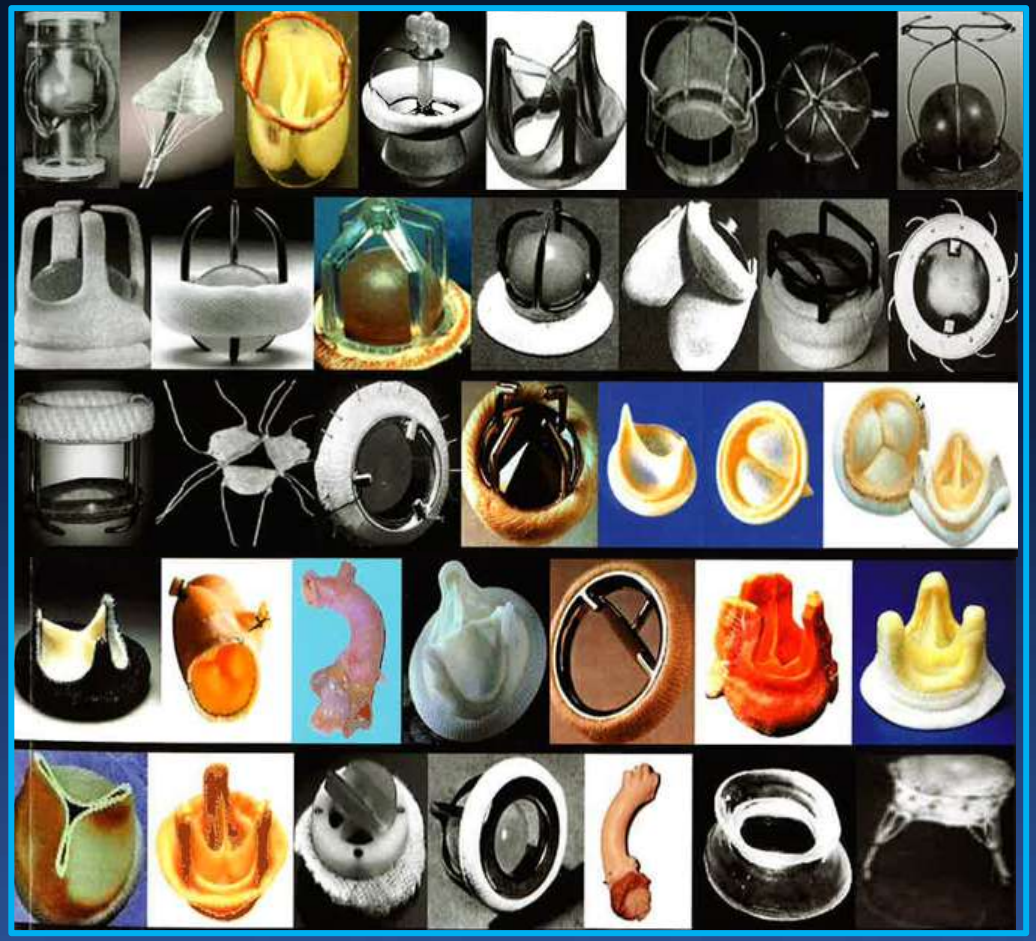
THE MACMILLAN COMPANY

1931

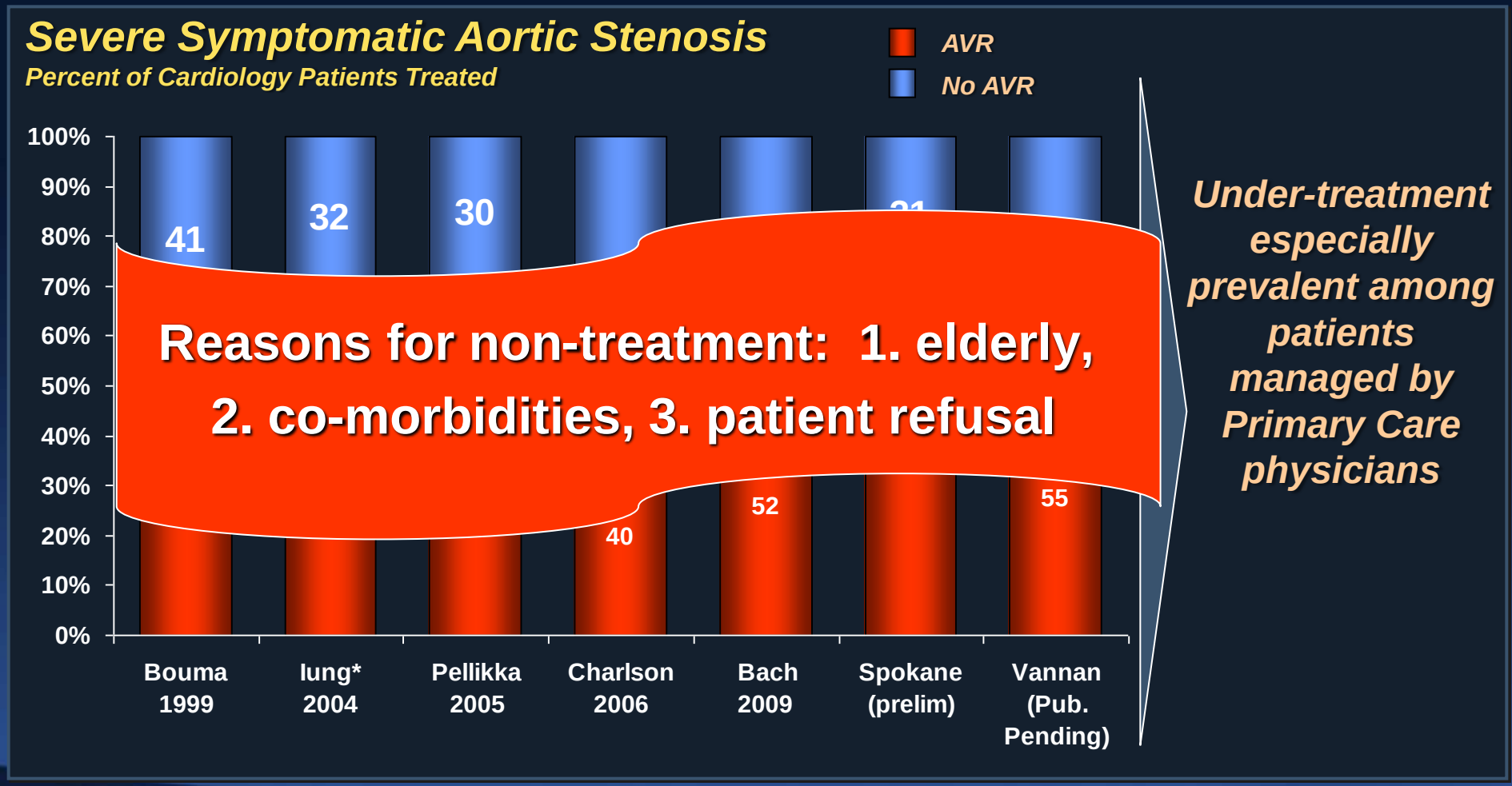
***"There is no treatment for aortic valve disease"***

# Aortic Valve Replacement

## *Dawn of a new era!*



# At Least 30% of Patients with Severe Symptomatic AS are "Untreated"!



# Aortic Valve Replacement

Transcatheter

Surgery

1960 ▬ ▬ ▬ ▬ ▬ ▬ ▶ 2000 2001 2002 2004 2007 2010-13

Mechanical heart valve – 1960

Homograft – 1962

Porcine valve – 1965

Pericardial tissue valve – 1969

First PVT animal implantation
A. Cribier

First Corevalve animal implantation
JC. Laborde

2010 PARTNER Cohort B

First Edwards/PVT Transapical Beating Heart AVR
Webb, Lichtenstein – Nov 29, 2005

First PVT Transcatheter AVR by Antegrade Approach
Alain Cribier - April 16, 2002

CE approval of CoreValve (May 16, 2007; 1,200 implants and Edwards Sapien (Sept 5, 2007; 500 implants)

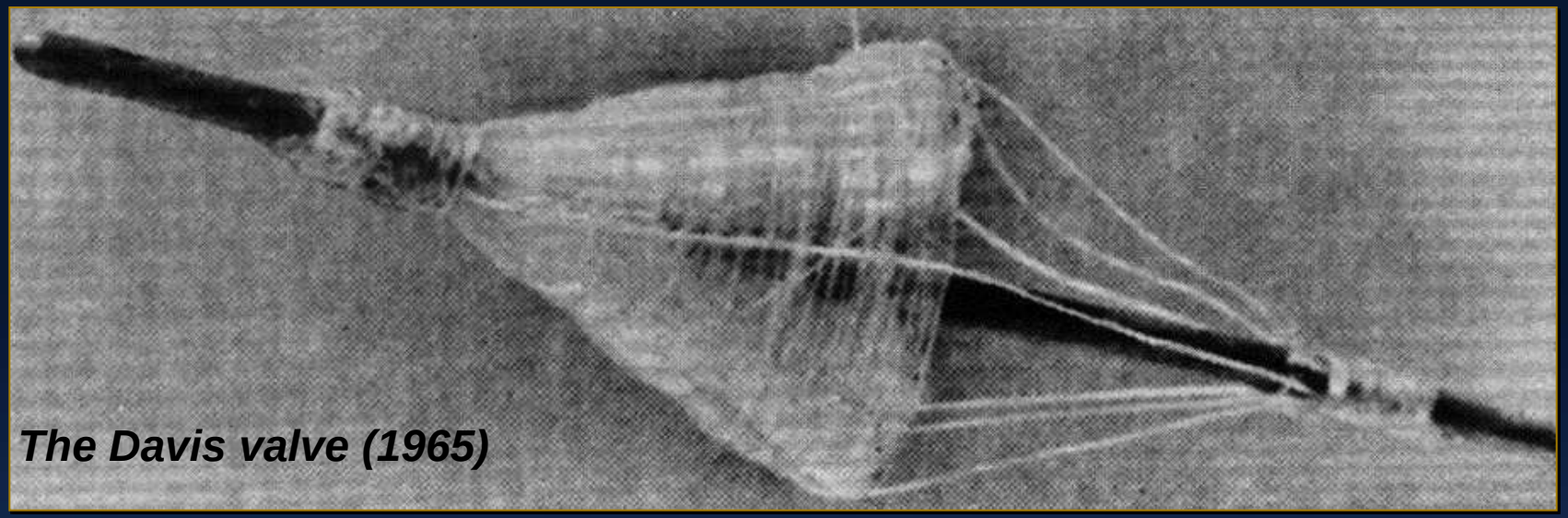
First CoreValve Transcatheter AVR by Retrograde Approach
Laborde, Lal, Grube – July 12, 2004

2011 PARTNER Cohort A

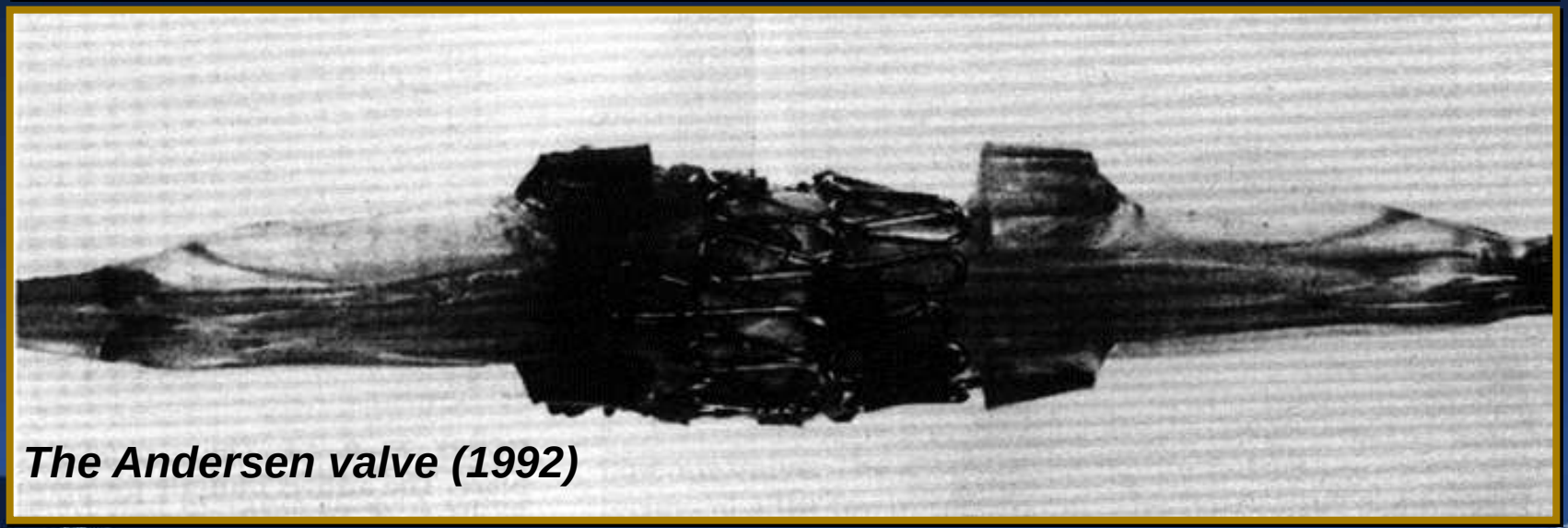
# The TAVR Odyssey

## The Early Childhood Years

# Early Catheter-Based AV Designs

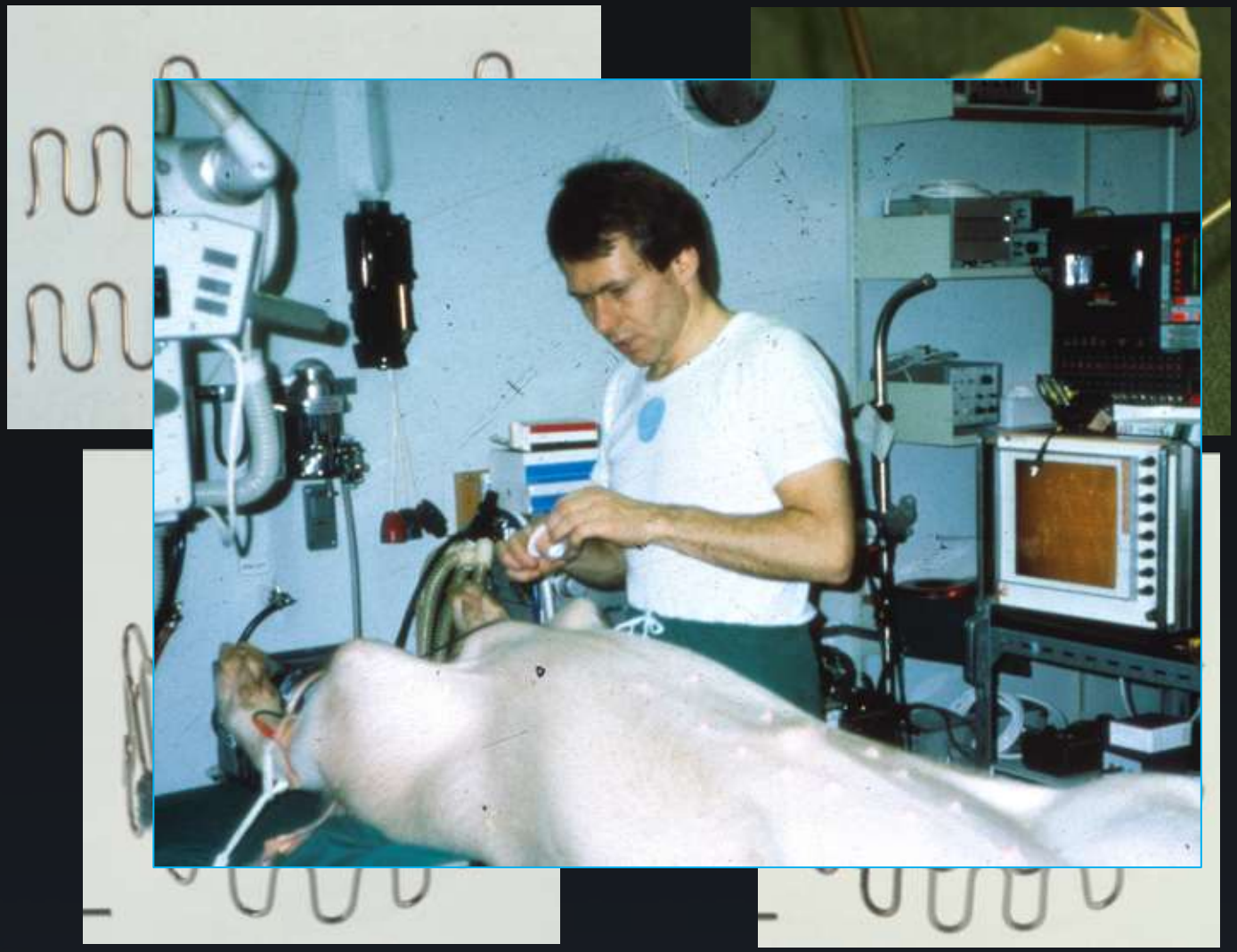


*The Davis valve (1965)*

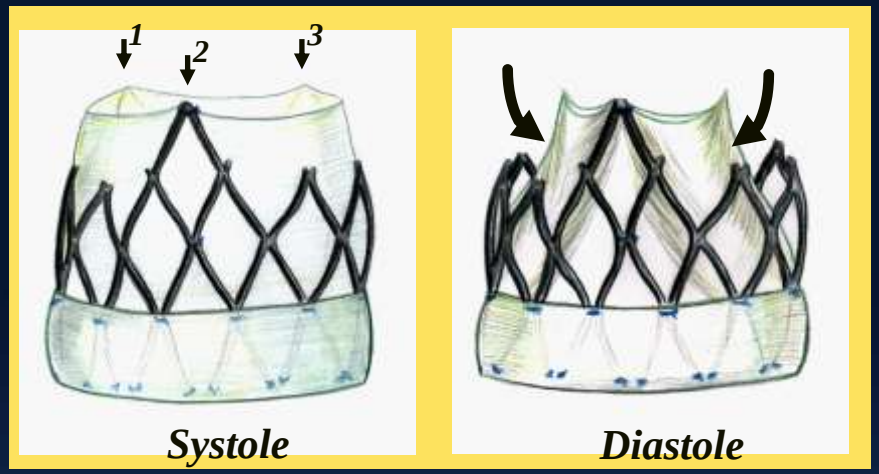


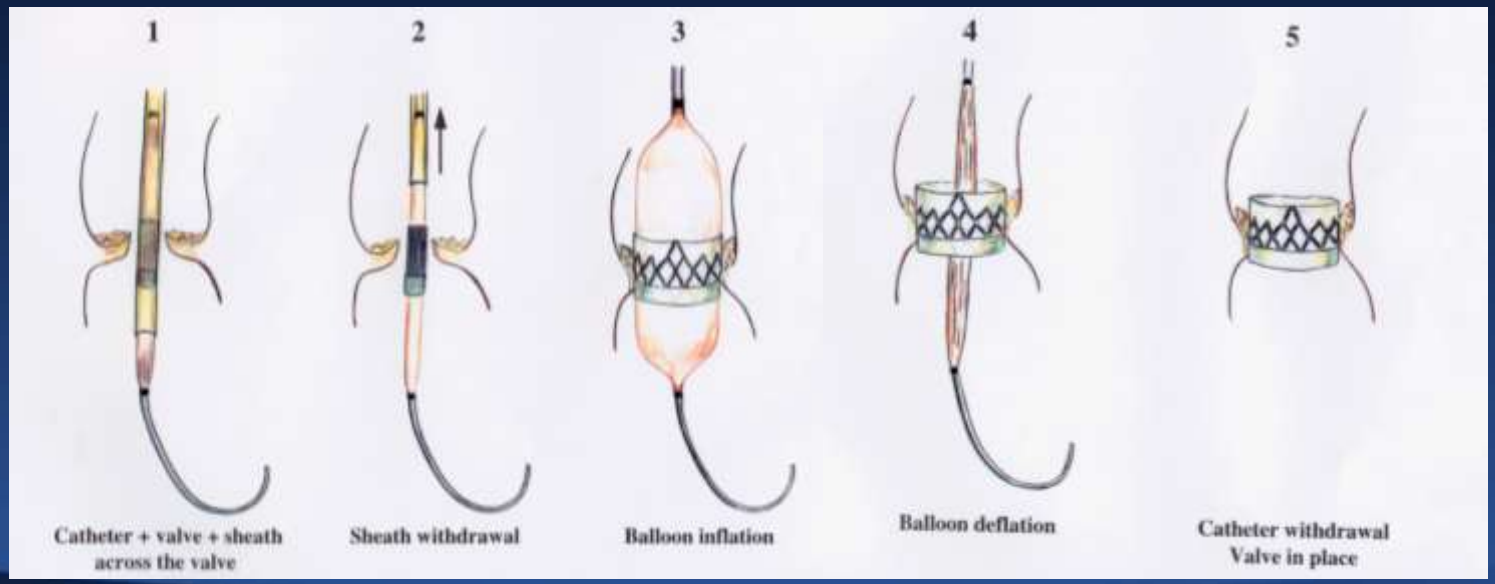
*The Andersen valve (1992)*

# The Andersen Stent-Valve (1989)



# Alain Cribier Sketches (1990)



# PVT - The Foundation…

***Percutaneous Valve Technologies***
***Aortic Heart Valve***

*Polyurethane*


*23mm max diameter*

*Bovine pericardium / Stainless steel stent*

# TAVR – The Early Skeptics

- Strokes
- Aortic rupture
- Coronary occlusion
- Mitral valve injury
- Valve instability – embolization
- Para-valvular regurgitation
- Vascular complications
- Valve durability
- Technical challenges insurmountable

***This is a crazy project that will fail!***

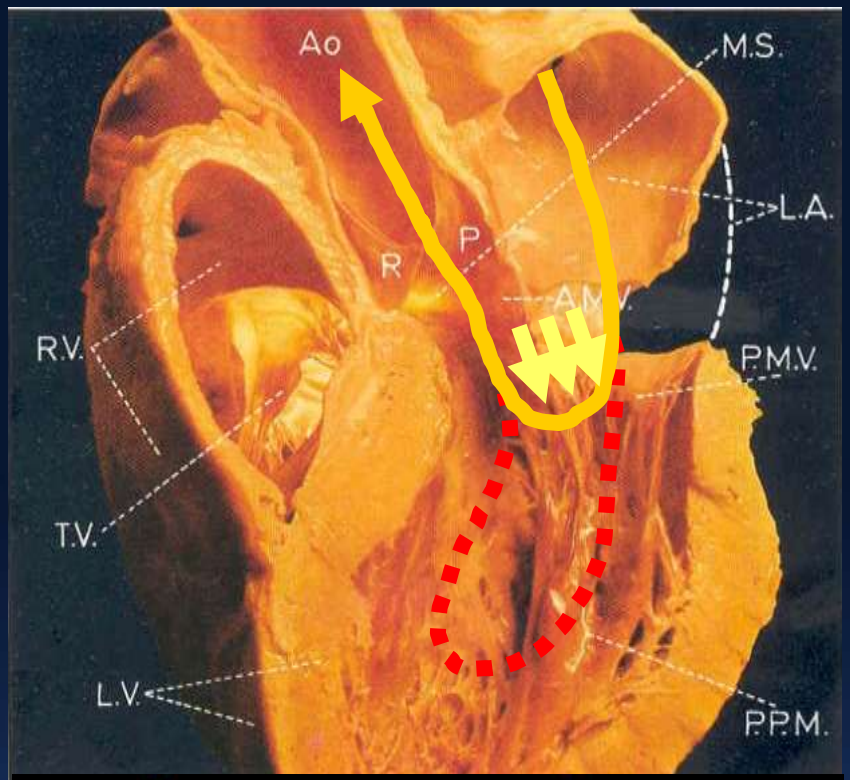
# Dr. Alain Cribier
## *First-in-Man PIONEER*

***It was impossible to predict the general application of this new procedure!***

***Conclusions—*** *Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.*

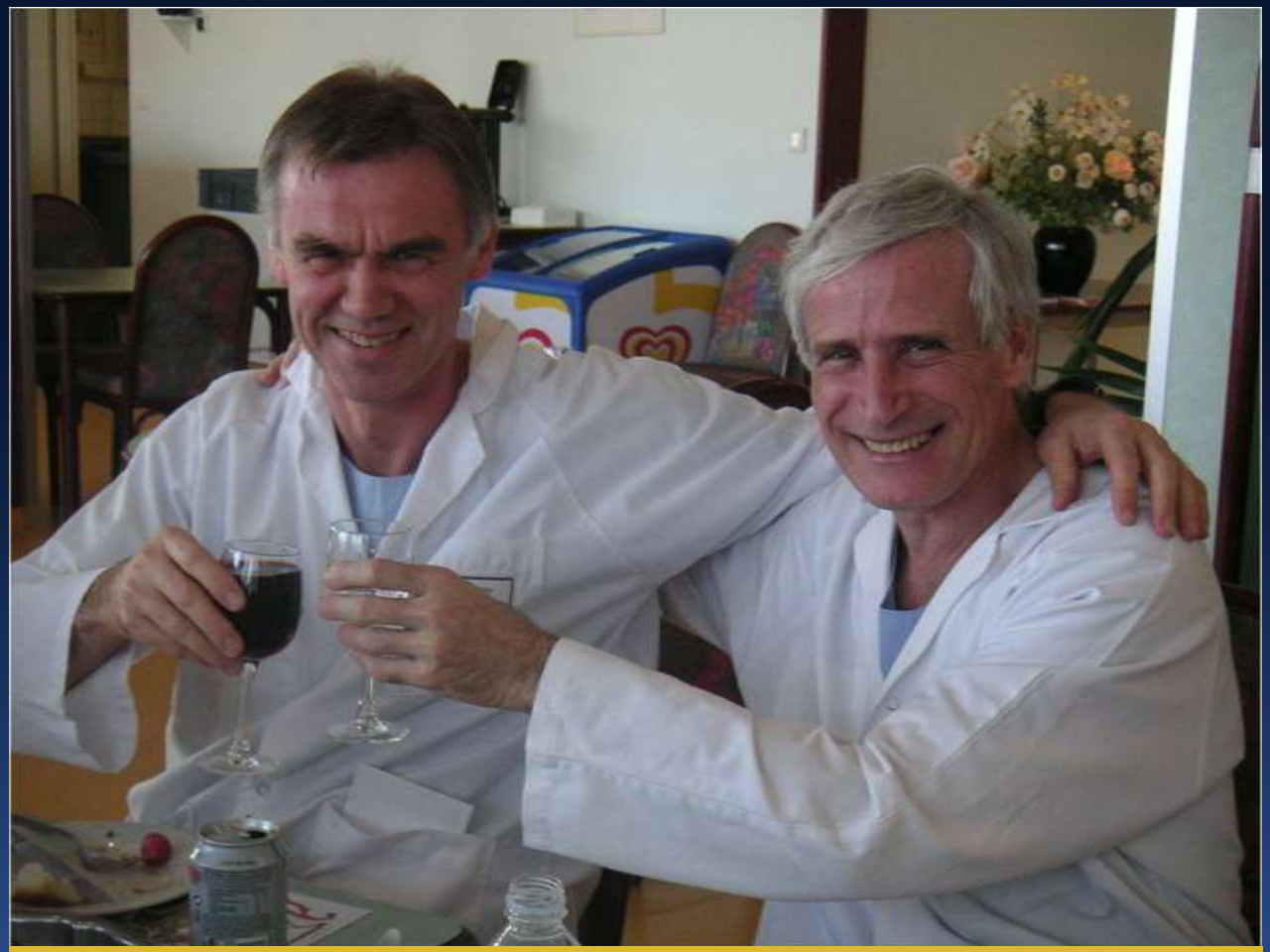
***April 16, 2002***

# Antegrade Approach: Guidewire Position in LV





# Collaboration across the seas….



***Drs. John Webb and Alain Cribier***

# The TAVR Odyssey

# The TAVR Odyssey
## *Adolescence*

- Characterization of high surgical risk patients
- Development of the Heart Team concept
- Technology development and maturation of procedural technique
- Refinement in clinical research processes (VARC) leading to PARTNER

# The severe AS-T

- Old…very old…
- Frail…very frail
- Lots of co-morbidi
  - Prior CABG (poor
  - CKD
  - Severe COPD
  - PVD
  - Chronic AF
  - Cancer in remissi


***But still enjoying life !***

# TAVR Categories
## *(risk is a continuum)*

***Operable AS patients***


**TAVR in 2014**

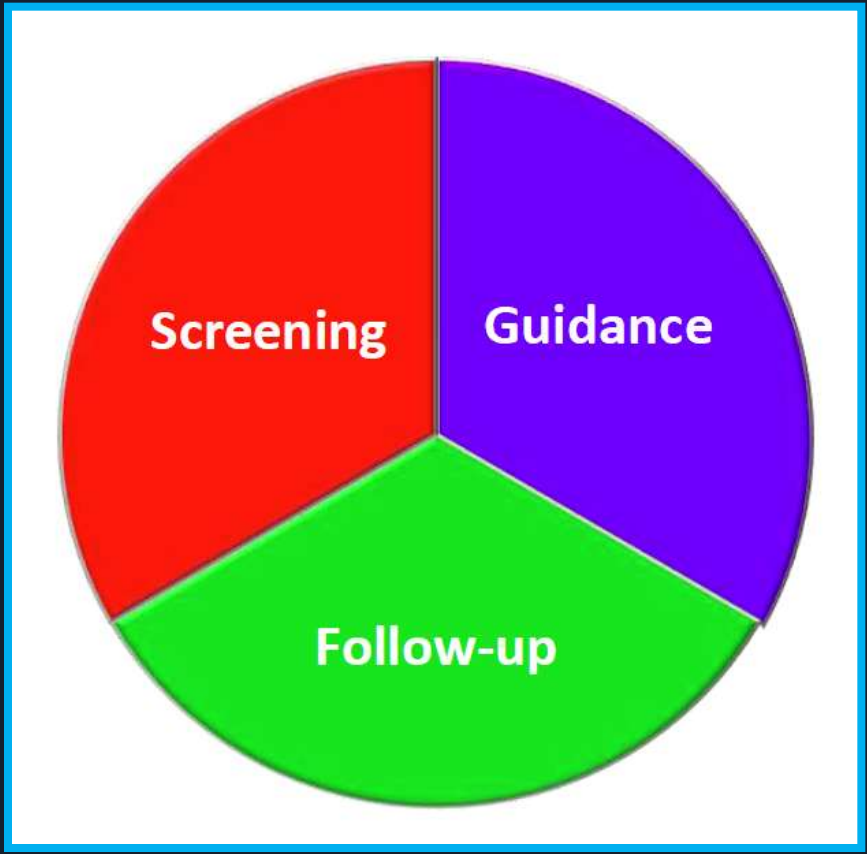
*irresponsible, reckless* — *"equipoise"* — *OK* — *preferred* — *No*



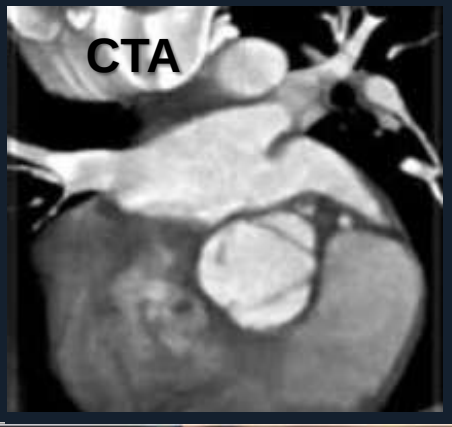
** Extreme risk = "inoperable"*

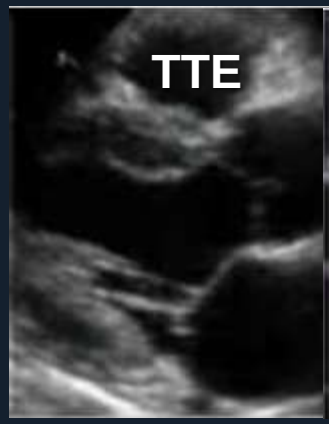
# Adjunctive Imaging for TAVR

## *Multi-modality Imaging is the RULE*





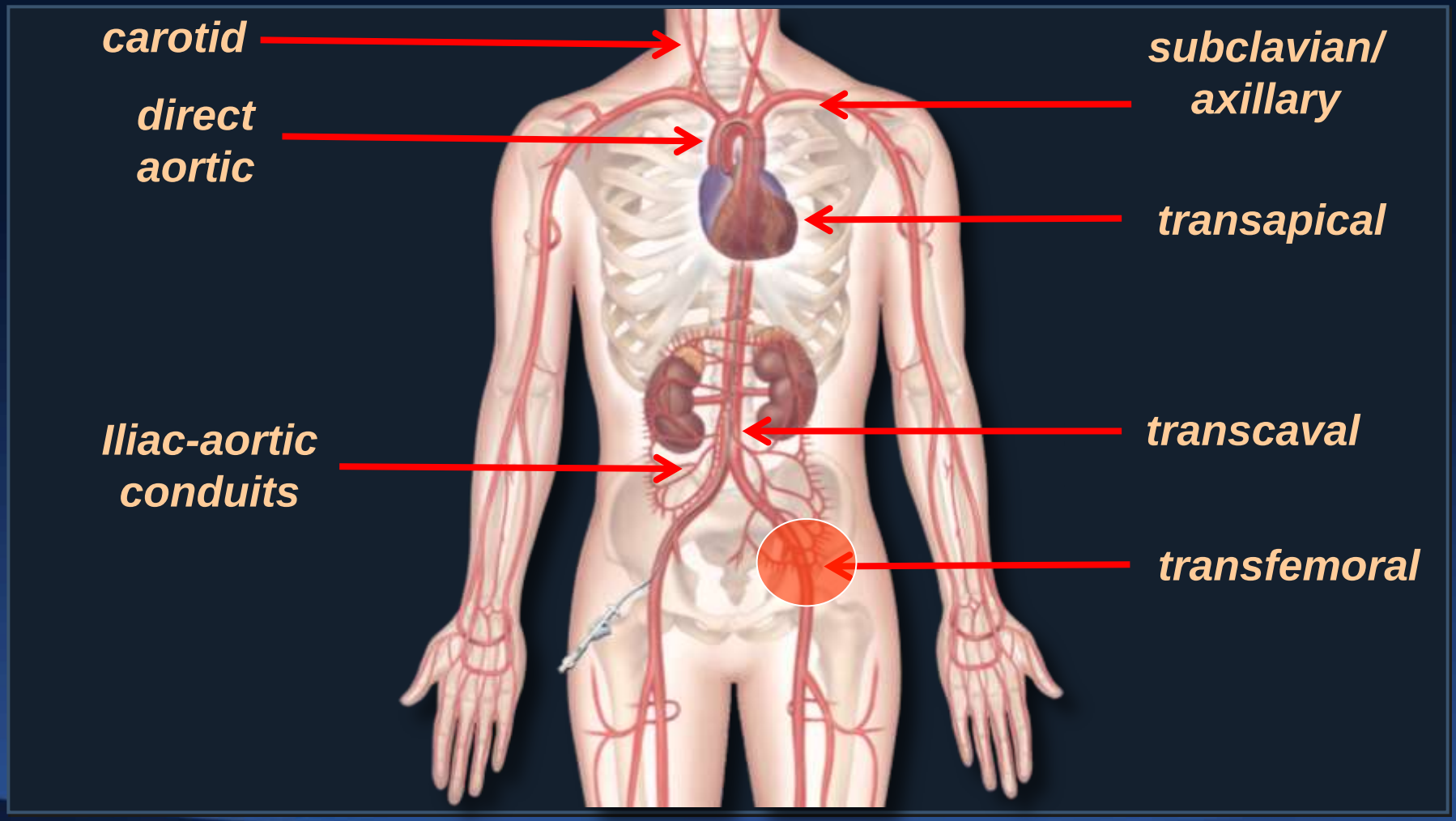




*Adapted from: Lutz Buellesfeld*

# TAVR – 2014
## *Access Alternatives*



# A Dedicated TAVR Milieu

# Edwards THV Evolution

- *Stainless Steel Frame*
- *Equine Pericardial Tissue*

***2004***

***Cribier-Edwards™ THV 23mm***

- *Stainless Steel Frame*
- *Bovine Pericardial Tissue*

***2007***

***Edwards SAPIEN™ THV 23 mm and 26 mm***

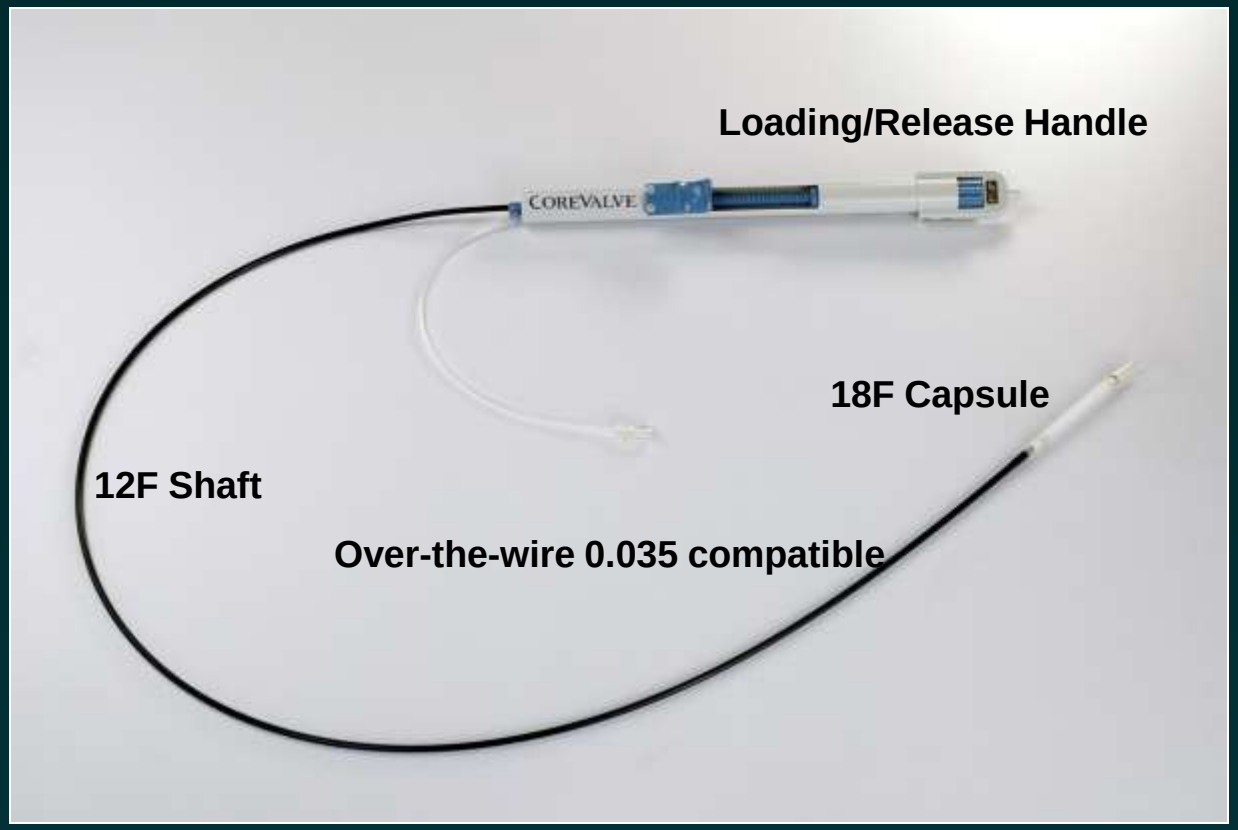
- *Cobalt-Chromium Frame*
- *Bovine Pericardial Tissue*
- *Semi-closed leaflets*
- *Reduced crimped profile*

***2010***

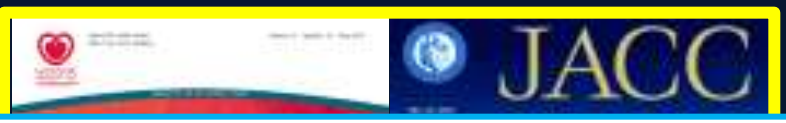
***Edwards SAPIEN XT ™ THV 23 mm, 26 mm, and 29mm***

# CoreValve ReValving System

## *18 Fr Delivery System*




# VARC MANUSCRIPT




European Heart Journal (2011) **32**, 205–217
doi:10.1093/eurheartj/ehq406

CLINICAL RESEARCH
*Valvular medicine*

## Standardized endpoint definitions for

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Mart
Dona
Roxa
Johar
John

Journal of the American College of Cardiology

Published by Elsevier Inc.

Vol. 57, No. 3, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.12.005

**CLINICAL RESEARCH** **Valvular Medicine**

# Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation Clinical Trials

## A Consensus Report From the Valve Academic Research Consortium

Martin B. Leon, Nicolo Piazza, Eugenia Nikolsky, Eugene H. Blackstone, Donald E. Cutlip, Arie Pieter Kappetein, Mitchell W. Krucoff, Michael Mack, Roxana Mehran, Craig Miller, Marie-angéle Morel, John Petersen, Jeffrey J. Popma, Johanna J. M. Takkenberg, Alec Vahanian, Gerrit-Anne van Es, Pascal Vranckx, John G. Webb, Stephan Windecker, Patrick W. Serruys

*New York, New York*

# VARC - 2

EXPEDITED REVIEW Heart Valve Disease

## Updated Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation

The Valve Academic Research Consortium-2 Consensus Document†

A. Pieter Kappetein,* Stuart J. Head, Philippe Généreux, Nicolo Piazza, Nicolas M. van Mieghem, Eugene H. Blackstone, Thomas G. Brott, David J. Cohen, Donald E. Cutlip, Gerrit-Anne van Es, Rebecca T. Hahn, Ajay J. Kirtane, Mitchell W. Krucoff, Susheel Kodali, Michael J. Mack, Roxana Mehran, Josep Rodés-Cabau, Pascal Vranckx, John G. Webb, Stephan Windecker, Patrick W. Serruys, Martin B. Leon

*Rotterdam, the Netherlands*

***VARC was an immediate success; VARC-2 is an important expansion and refinement of this dynamic clinical research process!***



*Kappetein AP, et al. J Am Coll Cardiol 2012;60:1438-54*

# The TAVR Odyssey

## College Years

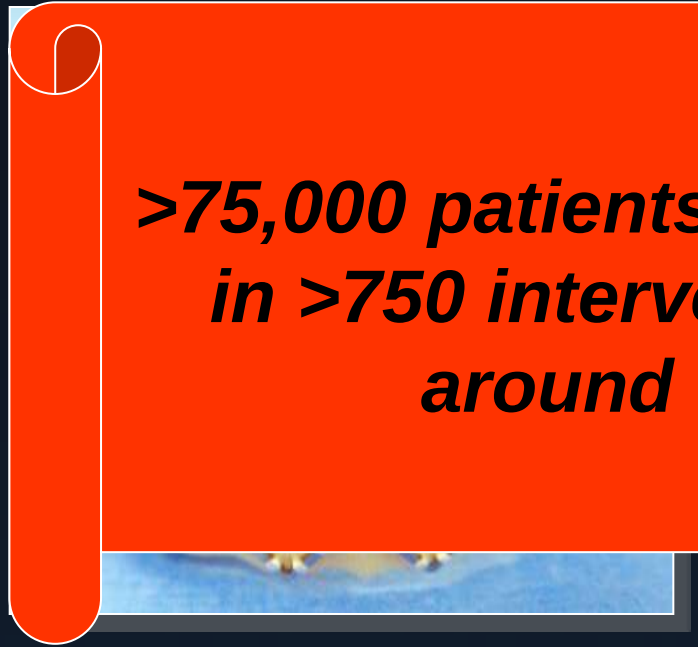
# The TAVR Odyssey
## *College Years*

- Dramatic proliferation of TAVR procedures and centers worldwide
- Evidence-based medicine validation of TAVR clinical benefit
  - Country registries
  - First RCT – The PARTNER Study
- Case selection refinement and recognition of TAVR complications

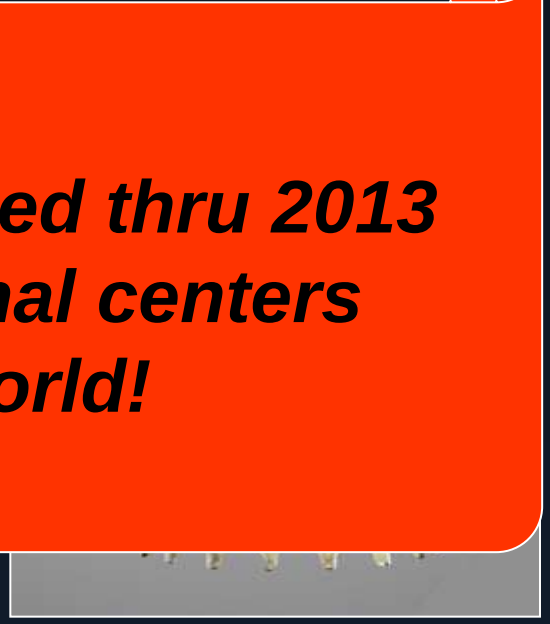
# TAVR Arrives

## *Current Generation Devices*

***>75,000 patients treated thru 2013 in >750 interventional centers around the world!***



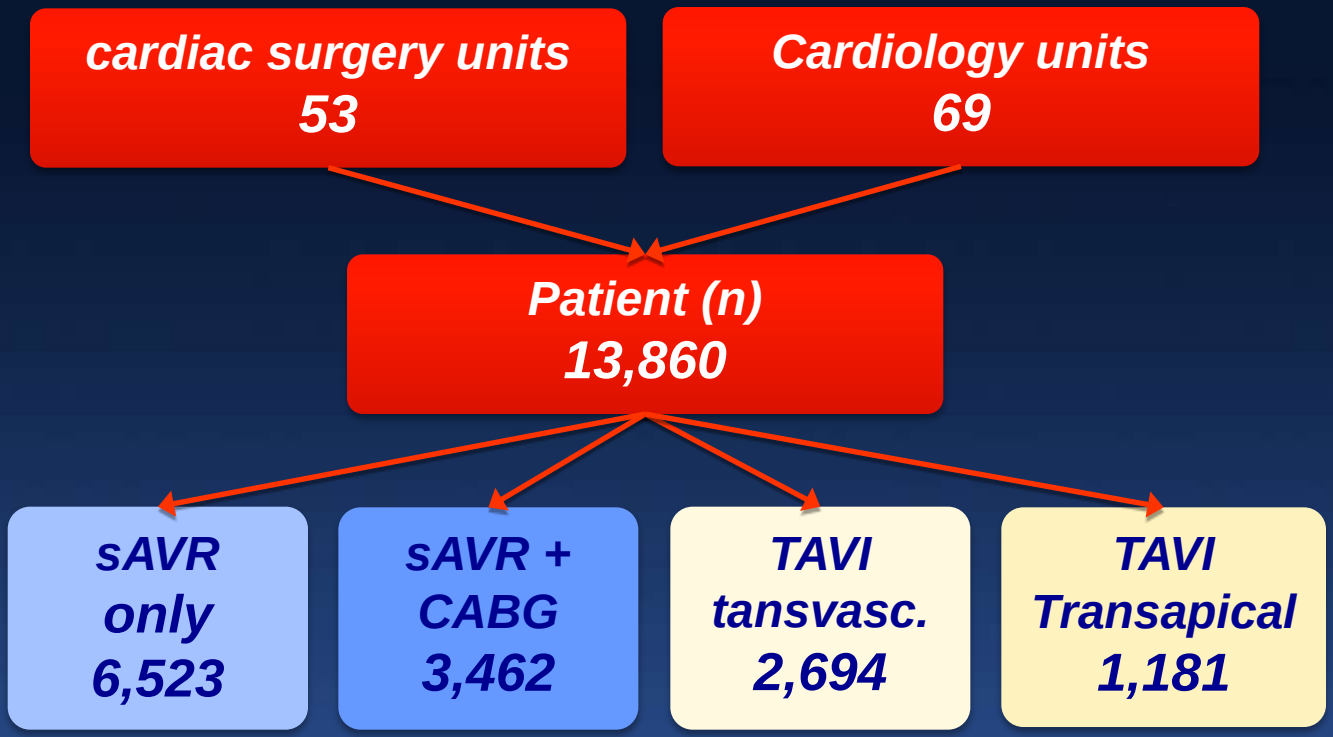
Edwards Lifesciences



Medtronic CoreValve

# The German Aortic Valve Registry (GARY) ESC 2012 Update

*Between Jan 1st 2011 and Dec 31st 2011*

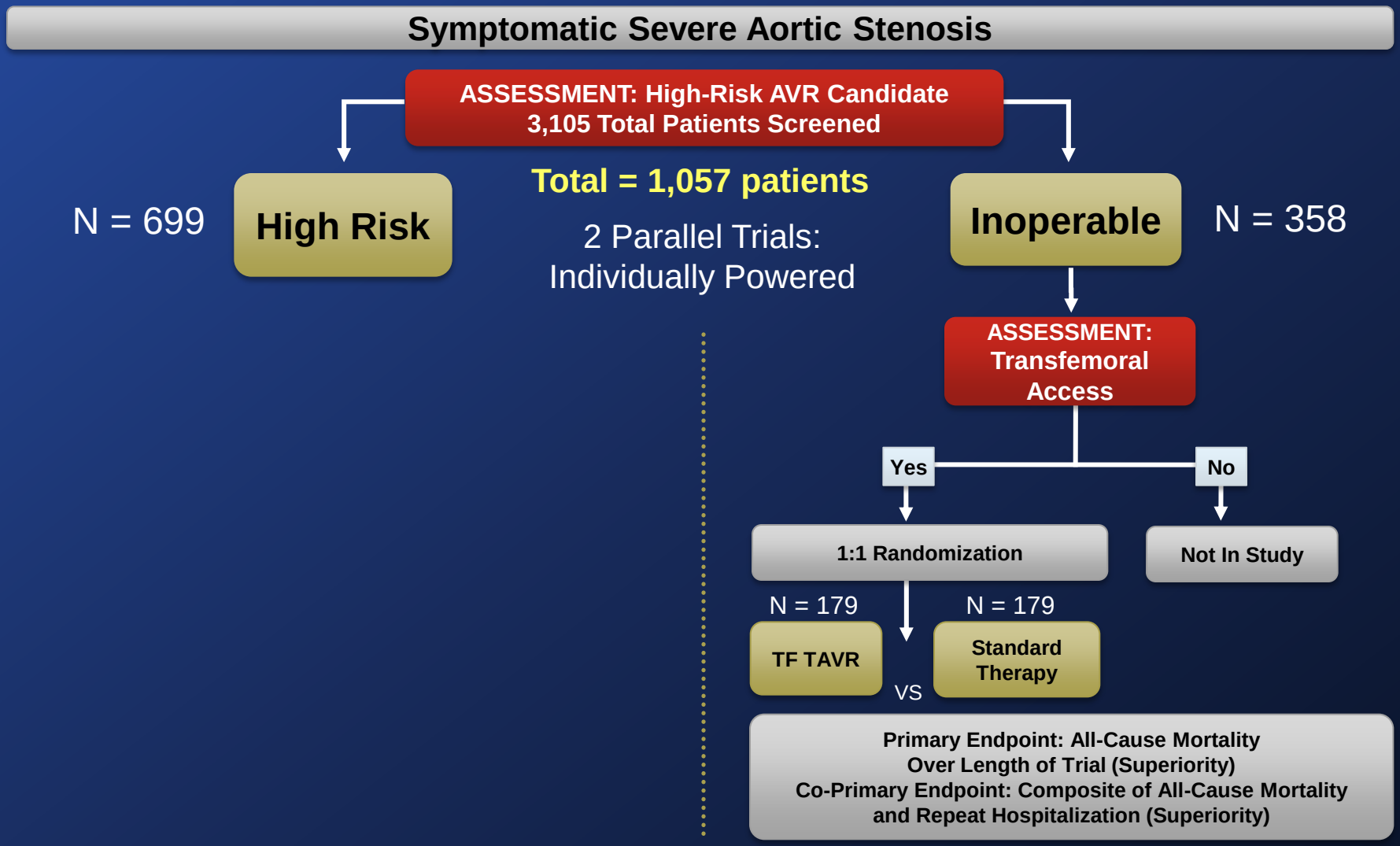



*NOTE: It represents 60-65% of total activity as reported in the AQUA 2011 report*

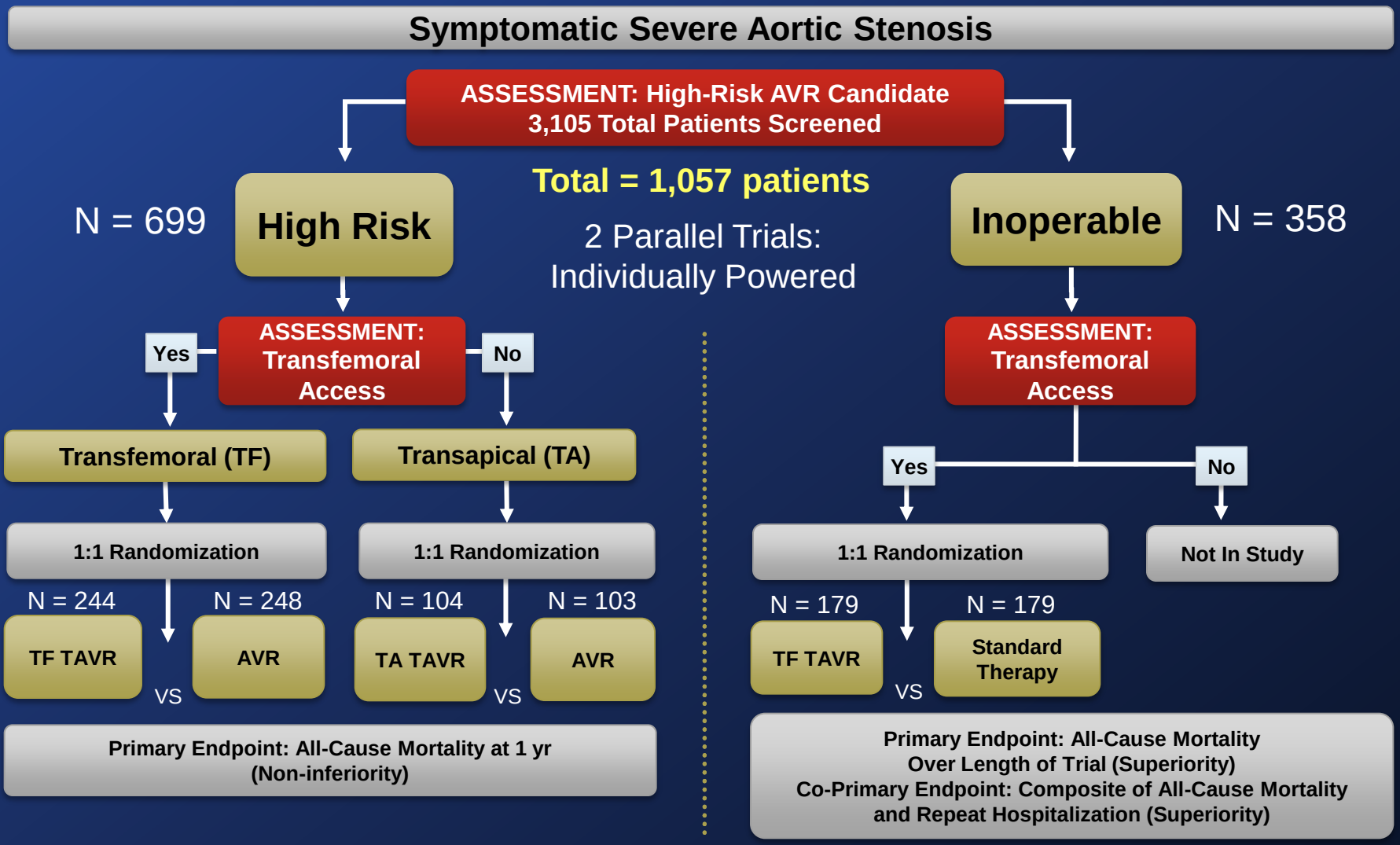


*SOURCE: GARY presentation by Pr. Hamm - ESC 2012*

# PARTNER Study Design



# PARTNER Study Design



# Heart Valve Team
## (Executive Committee)

# PARTNER Manuscripts in NEJM (October, 2010 – May, 2012)

THE PARTNER TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement for Inoperable Severe Aortic Stenosis

Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Hasan Jilaihawi, M.D., Samir Kapadia, M.D., Augusto D. Pichard, M.D., Pamela S. Douglas, M.D., Vinod H. Thourani, M.D., Vasilis C. Babaliaros, M.D., John G. Webb, M.D., Howard C. Herrmann, M.D., Joseph E. Bavaria, M.D., Susheel Kodali, M.D., David L. Brown, M.D., Bruce Bowers, M.D., Todd M. Dewey, M.D., Lars G. Svensson, M.D., Ph.D., Murat Tuzcu, M.D., Jeffrey W. Moses, M.D., Matthew R. Williams, M.D., Robert J. Siegel, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Stuart Pocock, Ph.D., Craig R. Smith, M.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

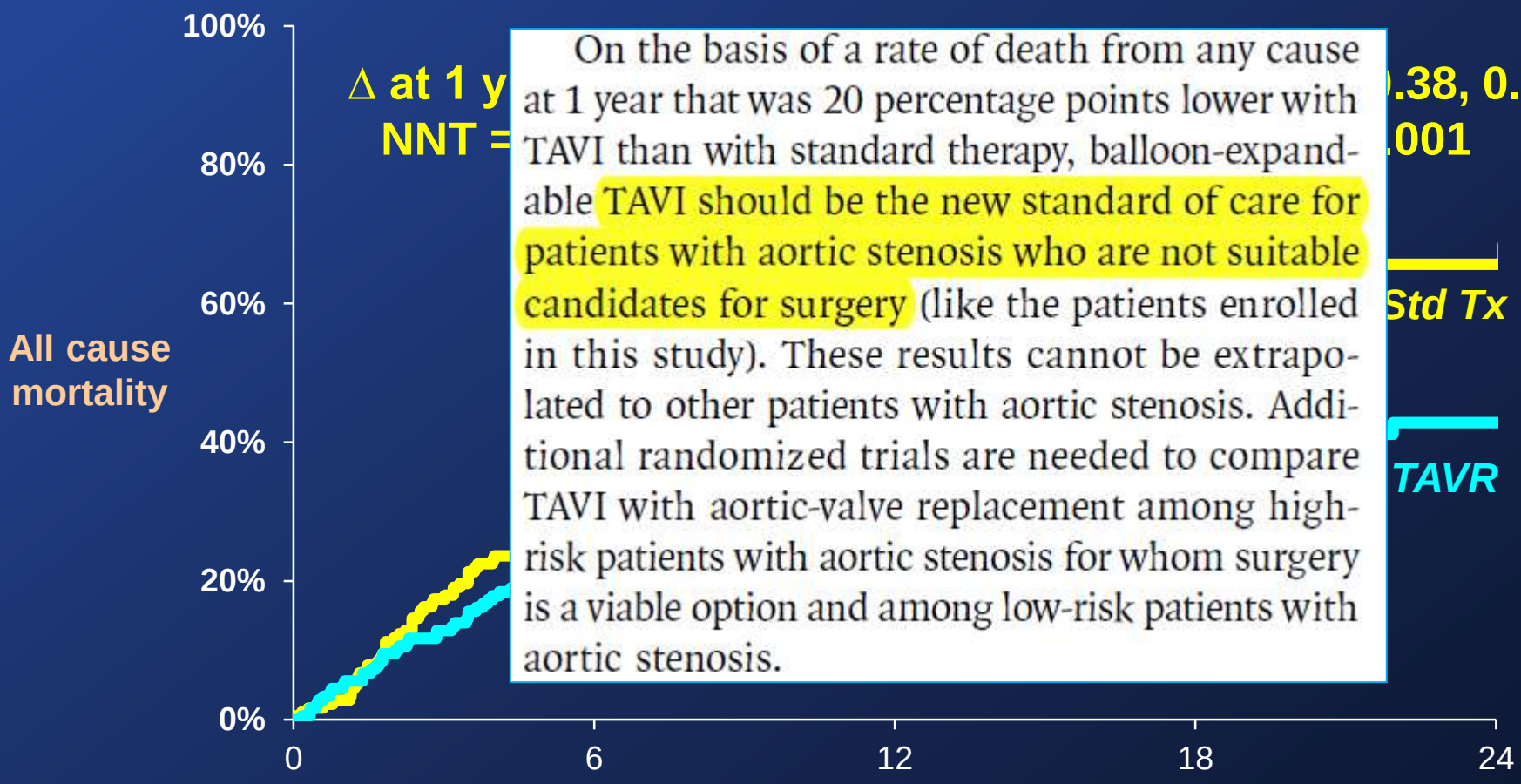
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

Susheel K. Kodali, M.D., Mathew R. Williams, M.D., Craig R. Smith, M.D., Lars G. Svensson, M.D., Ph.D., John G. Webb, M.D., Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Todd M. Dewey, M.D., Vinod H. Thourani, M.D., Augusto D. Pichard, M.D., Michael Fischbein, M.D., Wilson Y. Szeto, M.D., Scott Lim, M.D., Kevin L. Greason, M.D., Paul S. Teirstein, M.D., S. Chris Malaisrie, M.D., Pamela S. Douglas, M.D., Rebecca T. Hahn, M.D., Brian Whisenant, M.D., Alan Zajarias, M.D., Duolao Wang, Ph.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

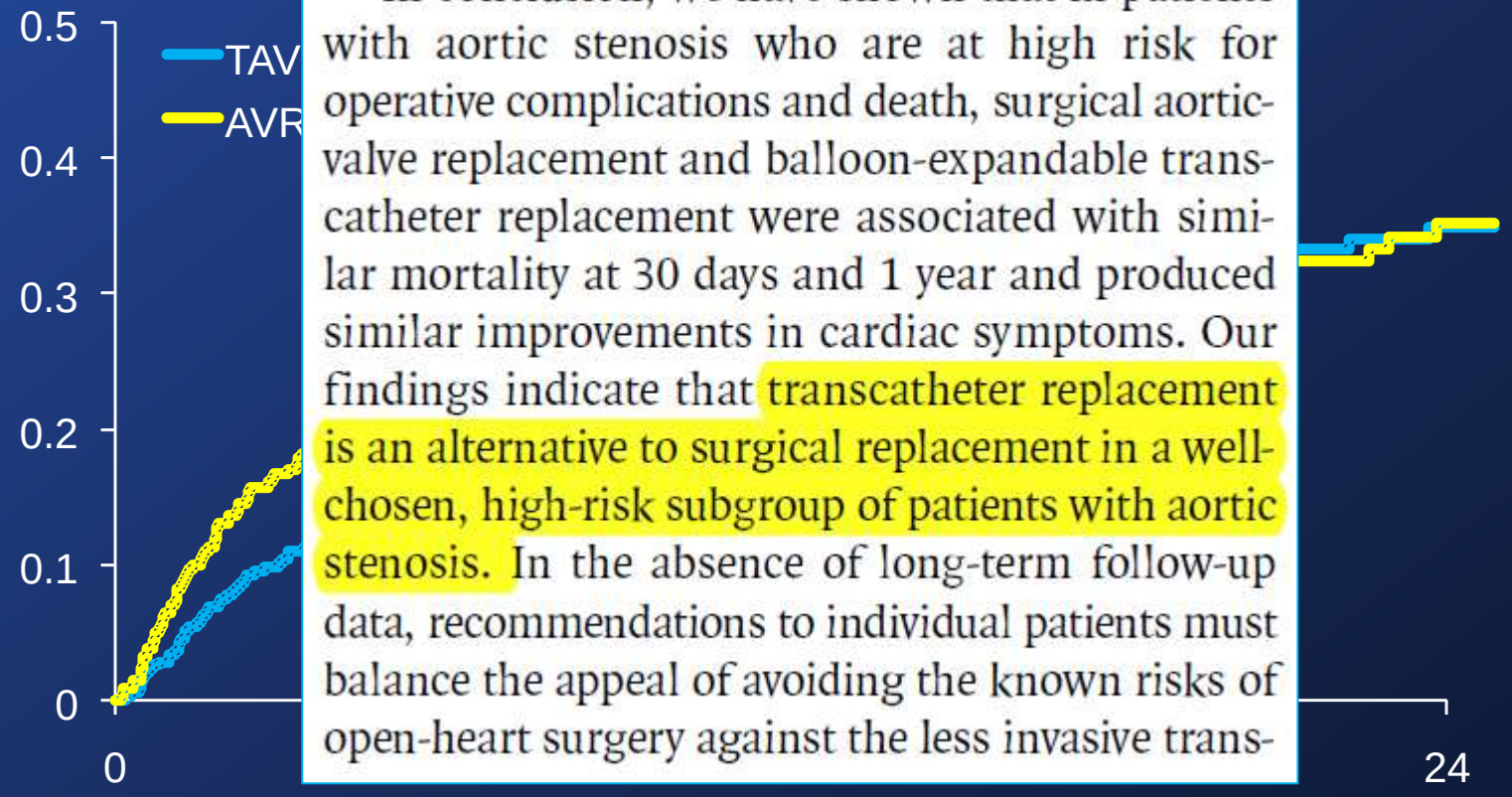
# Primary Endpoint: All Cause Mortality




On the basis of a rate of death from any cause at 1 year that was 20 percentage points lower with TAVI than with standard therapy, balloon-expandable TAVI should be the new standard of care for patients with aortic stenosis who are not suitable candidates for surgery (like the patients enrolled in this study). These results cannot be extrapolated to other patients with aortic stenosis. Additional randomized trials are needed to compare TAVI with aortic-valve replacement among high-risk patients with aortic stenosis for whom surgery is a viable option and among low-risk patients with aortic stenosis.

| Numbers at Risk | | | | | |
|---|---|---|---|---|---|
| Std Tx | 179 | 121 | 85 | 56 | 24 |
| TAVR | 179 | 138 | 124 | 103 | 60 |

# High-Risk Operable PARTNER Cohort
# Primary Endpoint: All-Cause Mortality




In conclusion, we have shown that in patients with aortic stenosis who are at high risk for operative complications and death, surgical aortic-valve replacement and balloon-expandable transcatheter replacement were associated with similar mortality at 30 days and 1 year and produced similar improvements in cardiac symptoms. Our findings indicate that transcatheter replacement is an alternative to surgical replacement in a well-chosen, high-risk subgroup of patients with aortic stenosis. In the absence of long-term follow-up data, recommendations to individual patients must balance the appeal of avoiding the known risks of open-heart surgery against the less invasive trans-

No. at Risk — Months

| | | | | | |
|---|---|---|---|---|---|
| **TAVR** | 348 | 298 | 260 | 147 | 67 |
| **AVR** | 351 | 252 | 236 | 139 | 65 |

# TAVR Patient Selection
## *Includes Careful Frailty Assessment*

***Patient A*** ***vs.*** ***Patient B***

***Same age and predicted risk***
***One passes the "eyeball test" – one does not***

*Frailty is being studied systematically as part of the PARTNER U.S. IDE study*

***Photos courtesy of Michael J. Mack, MD***
***Medical City Dallas***

# Cohort C – The Futile Patient

- Extreme co-morbidities – STS score > 15%
- Severe pulmonary disease
- Severe frailty (objective testing)
- Severe dementia
- Severe liver disease
- Severe CKD – on dialysis (?)
- Hemodynamic instability – e.g. pressor dependent
- Dependent social status – assisted-living, poor social support , wheelchair bound, etc.

# Published on-line June 5, 2011 @ NEJM.org and print June 9, 2011

## *Editorial Response*

EDITORIALS

### Transcatheter Aortic-Valve Implantation — At What Price?

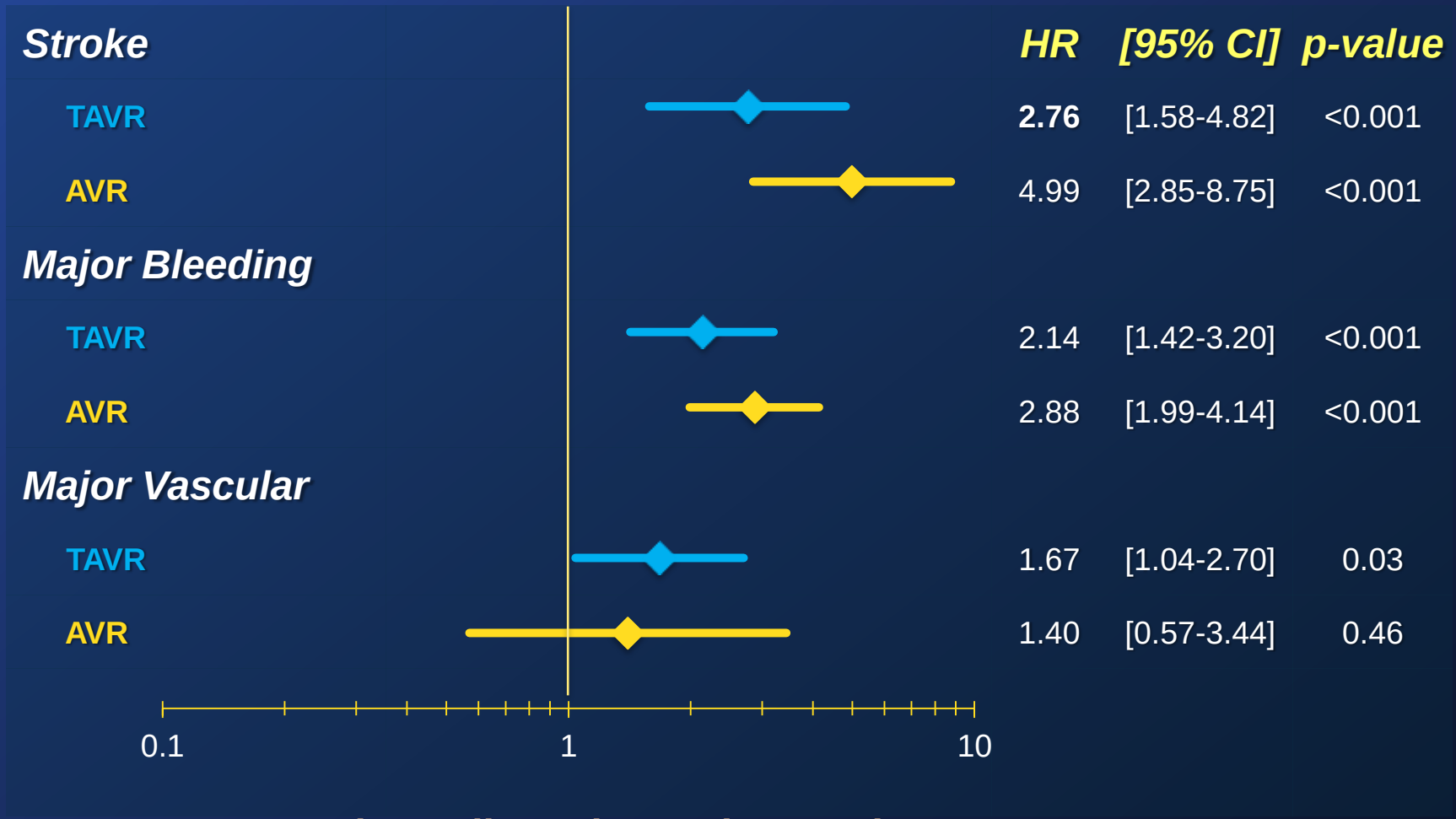
Hartzell V. Schaff, M.D.

In 2000, Bonhoeffer et al. described transvenous placement of a pulmonary-valve prosthesis and speculated that similar technology might be used in other cardiac valves, including the aortic position.[1] Two years later, the first transcatheter in-

patients who are eligible for transfemoral insertion and may decrease vascular injury.

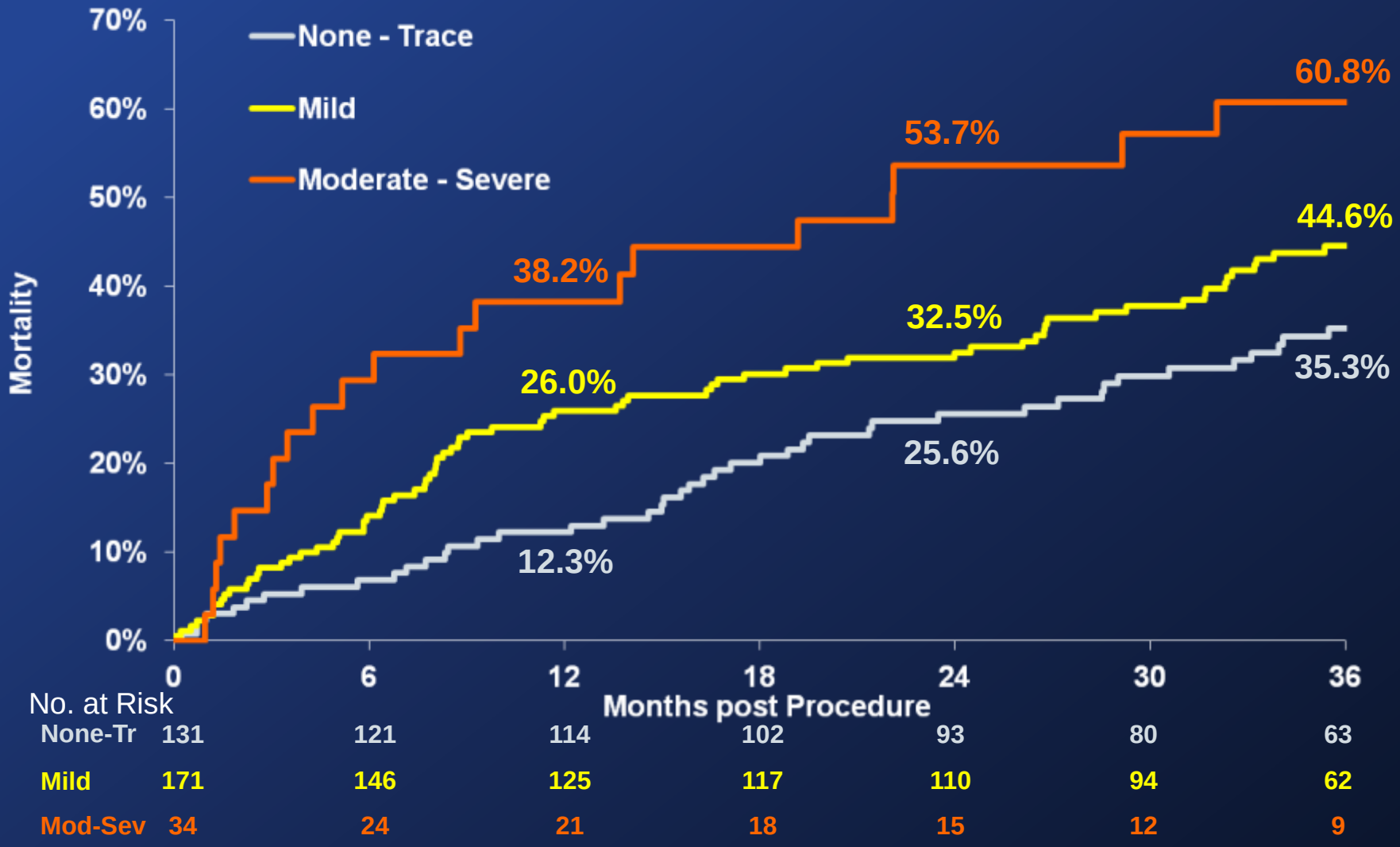
But the increased risk of stroke associated with transcatheter replacement, as compared with surgical replacement, is a special concern. Smith

# Procedural Predictors of Mortality
## High Risk Surgical




*Time adjusted covariate analyses*

# Impact of Total AR on Mortality (AT)
## TAVR Patients



# The TAVR Odyssey

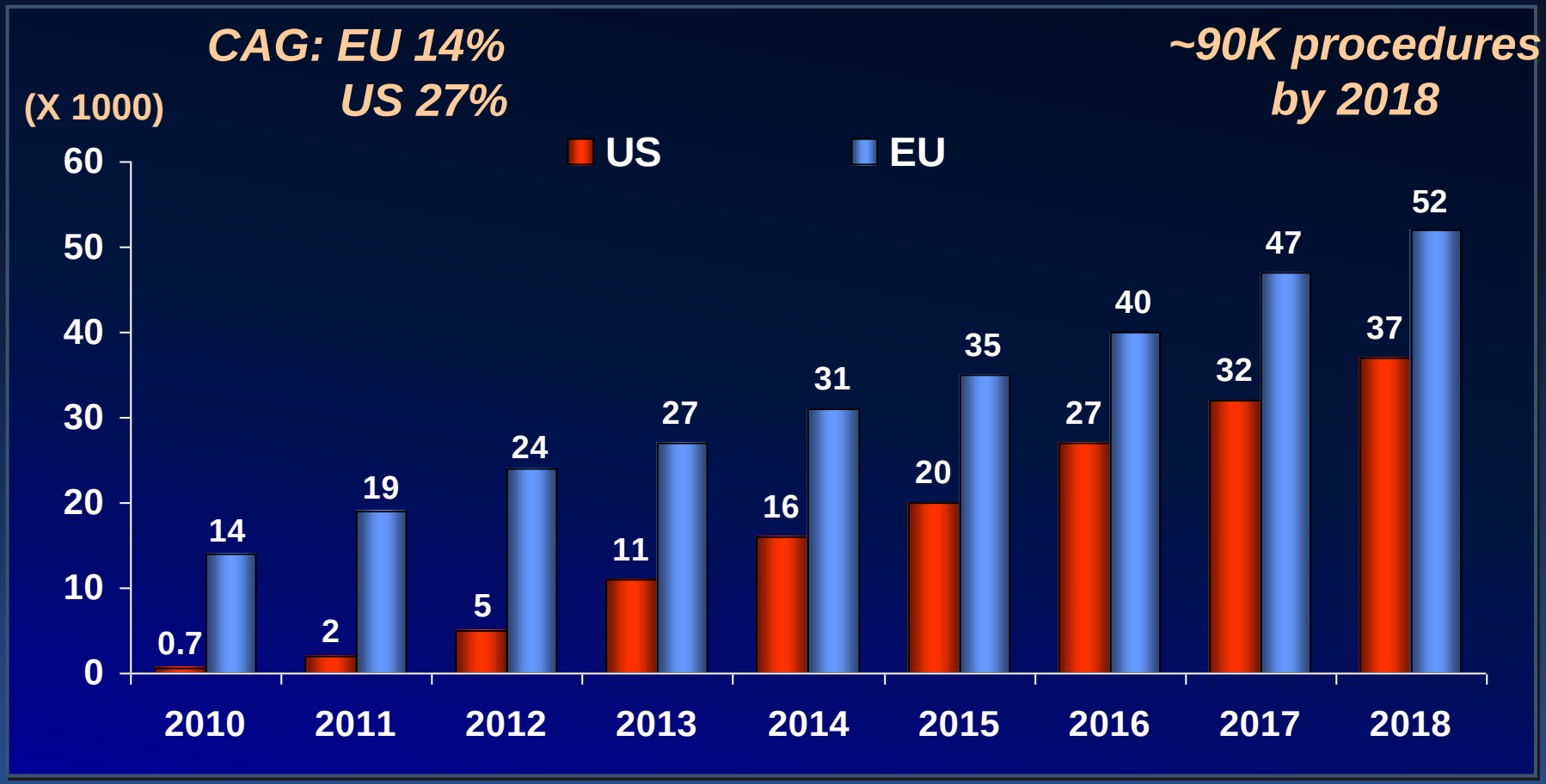
## Young Adulthood

# The TAVR Odyssey
## *Young Adulthood*

- Continued TAVR expansion
- Relentless pursuit of clinical data
  - TVT registry
  - Second RCT – The U.S. CoreValve Study
- Procedural enhancements and reduced TAVR complications
- New technology explosion
- New clinical indications

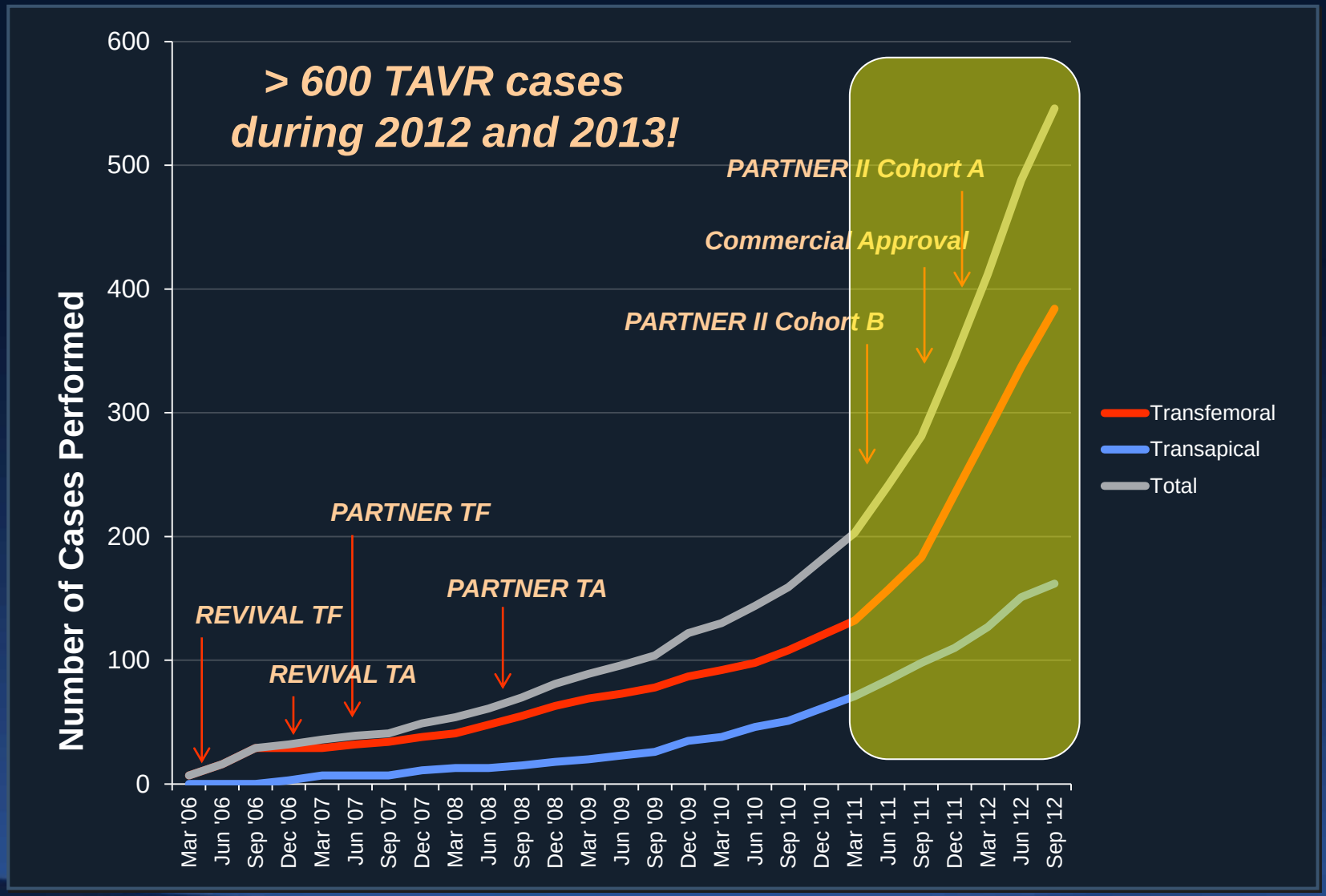
# TAVR Procedures

## *Growth from 2010 - 2018*




Multiple Industry Sources - 2013

# TAVR at Columbia - NYP



# Edwards Clinical Research Program

2002 | 2003 | 2004 | 2005 | 2006 | 207 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014

**Cribier-Edwards n=36**

FIM

iREVIVE Study

RECAST Study

***Since 2007, approved in >50 countries within Europe, Asia, Middle East, South America and Canada***

**Edwards SAPIEN n > 5,500**

REVIVE

REVIVAL

PARTNER EU

PARTNER I

CE Mark

SOURCE I and II

***>11,500 patients in clinical trials***

**Edwards SAPIEN XT n > 6,000**

FIM

CE Mark

SOURCE XT

PARTNER II

PREVAIL

# The STS-ACC Transcatheter Valve Therapy National Registry

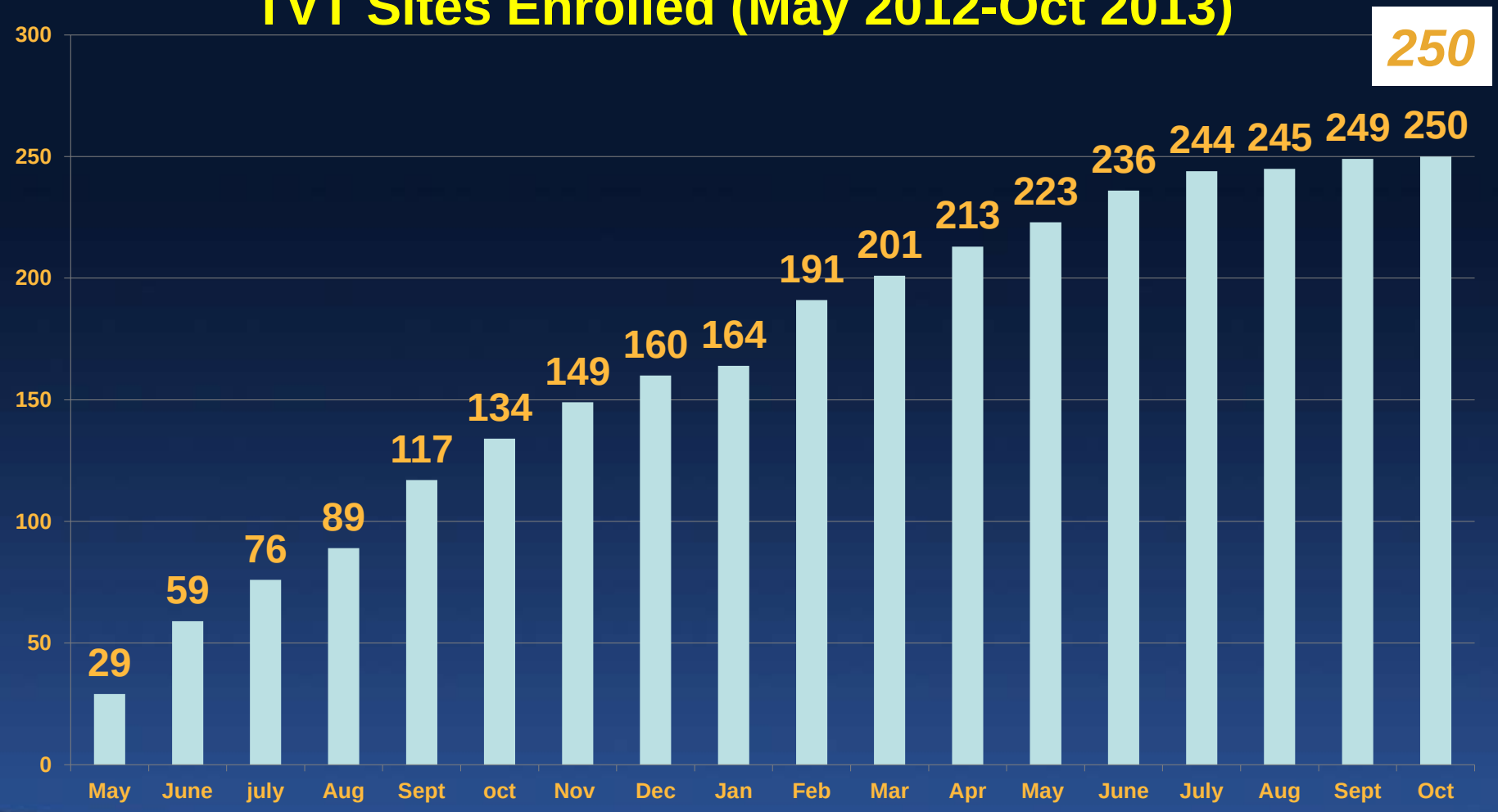
## A New Partnership and Infrastructure for the Introduction and Surveillance of Medical Devices and Therapies

John D. Carroll, MD,* Fred H. Edwards, MD,† Danica Marinac-Dabic, MD, PhD,‡ Ralph G. Brindis, MD, MPH,§ Frederick L. Grover, MD,* Eric D. Peterson, MD, MPH,‖ E. Murat Tuzcu, MD,¶ David M. Shahian, MD,# John S. Rumsfeld, MD, PhD,** Cynthia M. Shewan, PhD,†† Kathleen Hewitt, MSN, RN,‡‡ David R. Holmes, Jr, MD,§§ Michael J. Mack, MD‖‖

*Aurora and Denver, Colorado; Jacksonville, Florida; Washington, DC; San Francisco, California; Durham, North Carolina; Cleveland, Ohio; Boston, Massachusetts; Chicago, Illinois; Rochester, Minnesota; and Dallas, Texas*

JACC Vol. 62, No. 11, 2013
September 10, 2013:1026–34

# The U.S. TVT Registry




JAMA 2013; 310:2069-77

Original Investigation

## Outcomes Following Transcatheter Aortic Valve Replacement in the United States

Michael J. Mack, MD; J. Matthew Brennan, MD, MPH; Ralph Brindis, MD, MPH; John Carroll, MD; Fred Edwards, MD; Fred Grover, MD; David Shahian, MD; E. Murat Tuzcu, MD; Eric D. Peterson, MD, MPH; John S. Rumsfeld, MD, PhD; Kathleen Hewitt, MSN; Cynthia Shewan, PhD; Joan Michaels, RN; Barb Christensen, RN; Alexander Christian; Sean O'Brien, PhD; David Holmes, MD; for the STS/ACC TVT Registry

Editorial page 2045

Author Video Interview at jama.com

Supplemental content at jama.com

**IMPORTANCE** Transcatheter aortic valve replacement (TAVR) was approved by the US Food and Drug Administration for the treatment of severe, symptomatic aortic stenosis and inoperable status (in 2011) and high-risk but operable status (starting in 2012). A national registry (the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy [STS/ACC TVT] Registry) was initiated to meet a condition for Medicare coverage and also facilitates outcome assessment and comparison with other trials and international registries.

**OBJECTIVE** To report the initial US commercial experience with TAVR.

**DESIGN, SETTING, AND PARTICIPANTS** We obtained results from all eligible US TAVR cases (n=7710) from 224 participating registry hospitals following the Edwards Sapien XT device commercialization (November 2011–May 2013).

**MAIN OUTCOMES AND MEASURES** Primary outcomes included all-cause in-hospital mortality and stroke following TAVR. Secondary analyses included procedural complications and outcomes by clinical indication and access site. Device implantation success was defined as successful vascular access, deployment of a single device in the proper anatomic position, appropriate valve function without either moderate or severe AR, and successful retrieval of the delivery system. Thirty-day outcomes are presented for a representative 3133 cases (40.6%) at 114 centers with at least 80% complete follow-up reporting.

**RESULTS** The 7710 patients who underwent TAVR included 1599 (20%) cases that were inoperable and 6151 (80%) cases that were high-risk but operable. The median age was 84 years (interquartile range [IQR], 78-88 years); 3783 patients (49%) were women and the median STS predicted risk of mortality was 7% (IQR, 5%-11%). At baseline, 2176 patients (75%) were either not at all satisfied (1297 patients [45%]) or mostly dissatisfied (879 patients [30%]) with their symptom status; 2198 (72%) had a 5-m walk time longer than 6 seconds (slow gait speed). The most common vascular access approach was transfemoral (4972 patients [64%]), followed by transapical (2197 patients [29%]) and other alternative approaches (536 patients [7%]); successful device implantation occurred in 7060 patients (92%; 95% CI, 91%-92%). The observed incidence of in-hospital mortality was 5.5% (95% CI, 5.0%-6.1%). Other major complications included stroke (2.0%; 95% CI, 1.7%-2.4%), dialysis-dependent renal failure (1.9%; 95% CI, 1.6%-2.2%), and major vascular injury (6.4%; 95% CI, 5.8%-6.9%). Median hospital stay was 6 days (IQR, 4-10 days), with 4613 (63%) discharged home. Among patients with available follow-up at 30 days (n=3133), the incidence of mortality was 7.6% (95% CI, 6.7%-8.6%) (noncardiovascular cause, 52%); a stroke had occurred in 2.8% (95% CI, 2.3%-3.5%), new dialysis in 2.5% (95% CI, 2.0%-3.1%), and reintervention in 0.5% (95% CI, 0.3%-0.8%).

**CONCLUSIONS AND RELEVANCE** Among patients undergoing TAVR at US centers in the STS/ACC TVT Registry, device implantation success was achieved in 92% of cases, the overall in-hospital mortality rate was 5.5%, and the stroke rate was 2.0%. Although these postmarket US approval findings are comparable with prior published trial data and international experience, long-term follow-up is essential to assess continued efficacy and safety.

**TRIAL REGISTRATION** clinicaltrials.gov Identifier: NCT01731528

JAMA. 2013;310(19):2069-2077. doi:10.1001/jama.2013.281043

**Author Affiliations:** Heart Hospital Baylor Plano, Baylor Healthcare System, Plano, Texas (Mack); Duke Clinical Research Institute, Durham, North Carolina (Brennan, Peterson, Christian, O'Brien); University of California, San Francisco (Brindis); University of Colorado, Denver (Carroll, Grover, Rumsfeld); University of Florida, Jacksonville (Edwards); Massachusetts General Hospital, Boston (Shahian); Cleveland Clinic, Cleveland, Ohio (Tuzcu); American College of Cardiology, Washington, DC (Hewitt, Michaels, Christensen); Society of Thoracic Surgeons, Chicago, Illinois (Shewan); Mayo Clinic, Rochester, Minnesota (Holmes).

**Corresponding Author:** Michael J. Mack, MD, Baylor Health Care System, 1100 Allied Dr, Plano, TX 75093 (michael.mack@baylorhealth.edu).

***JAMA 2013 report from The TVT Registry on 7710 patients enrolled at 224 centers.***

***30-day outcomes reported on 3133 cases.***

***Median STS score for these inoperable and high-risk patients was 7% (IQR = 5-11%)***

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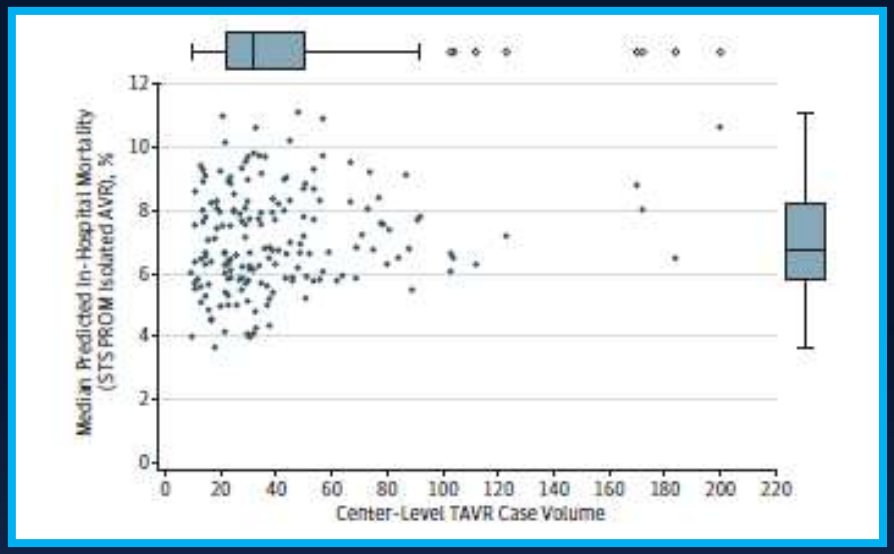


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## *In-hospital outcomes*

- **Mortality** **5.5%**
- **Strokes** **2.0%**
- **Major vasc events** **6.4%**

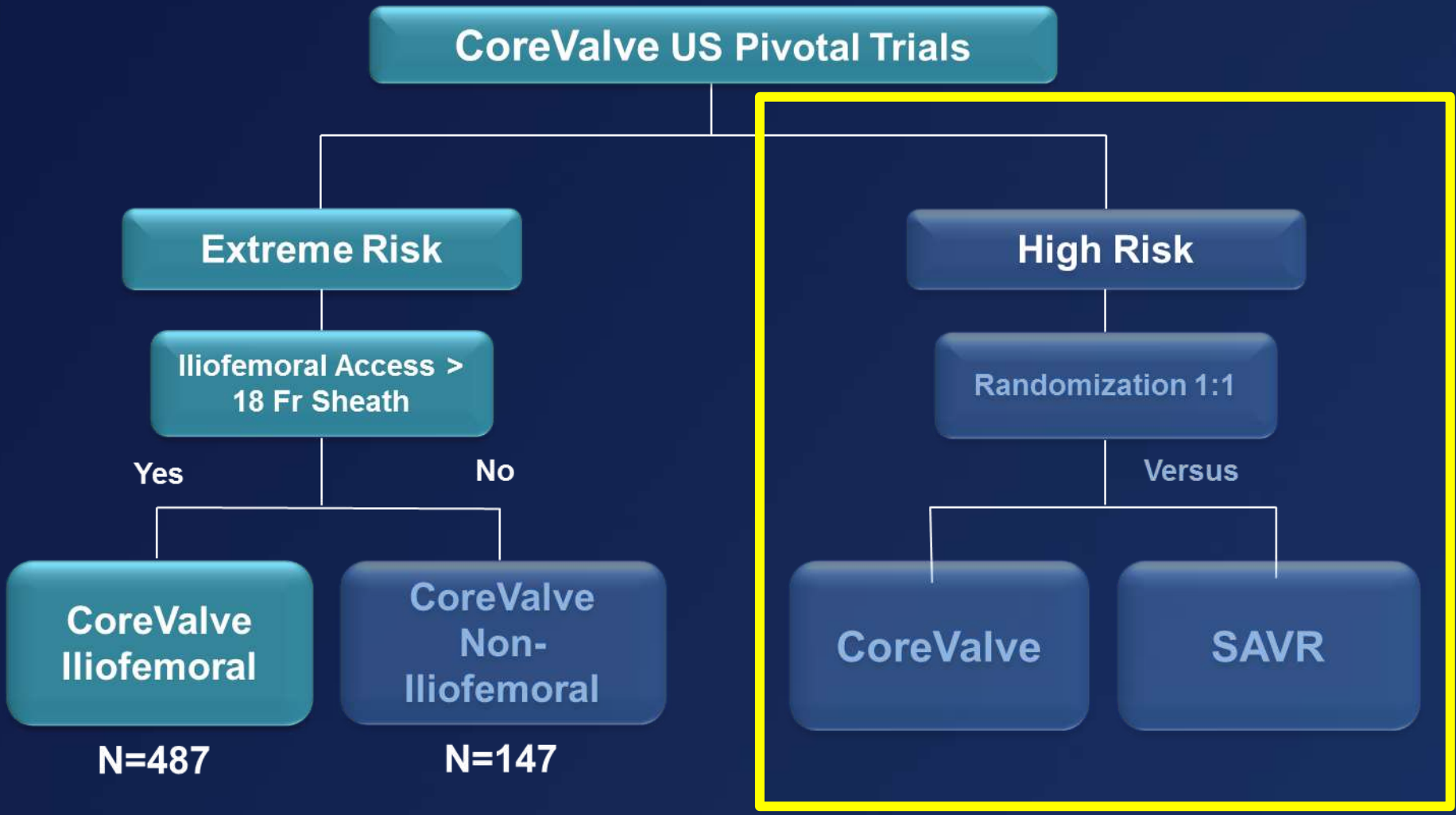
## *30-day outcomes*

- **Mortality** **7.6%**
- **Stroke** **2.8%**
- **Re-intervention** **0.5%**

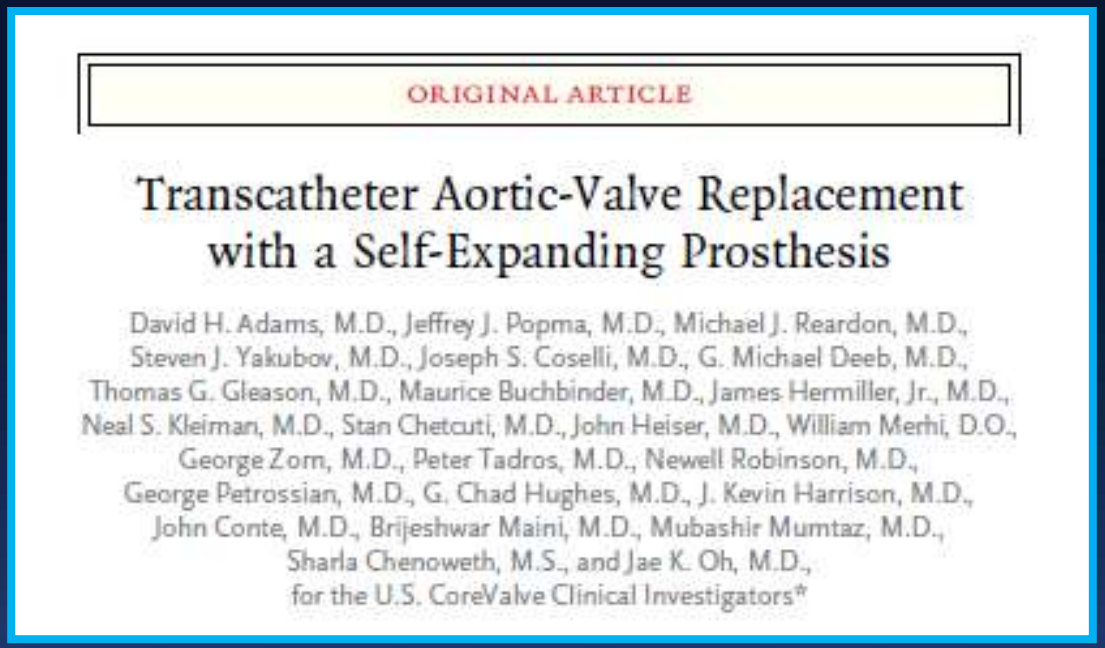


JAMA 2013; 310:2069-77

# Pivotal Trial Design



# CoreValve High-Risk U.S. Pivotal Trial (presented at ACC 2014)



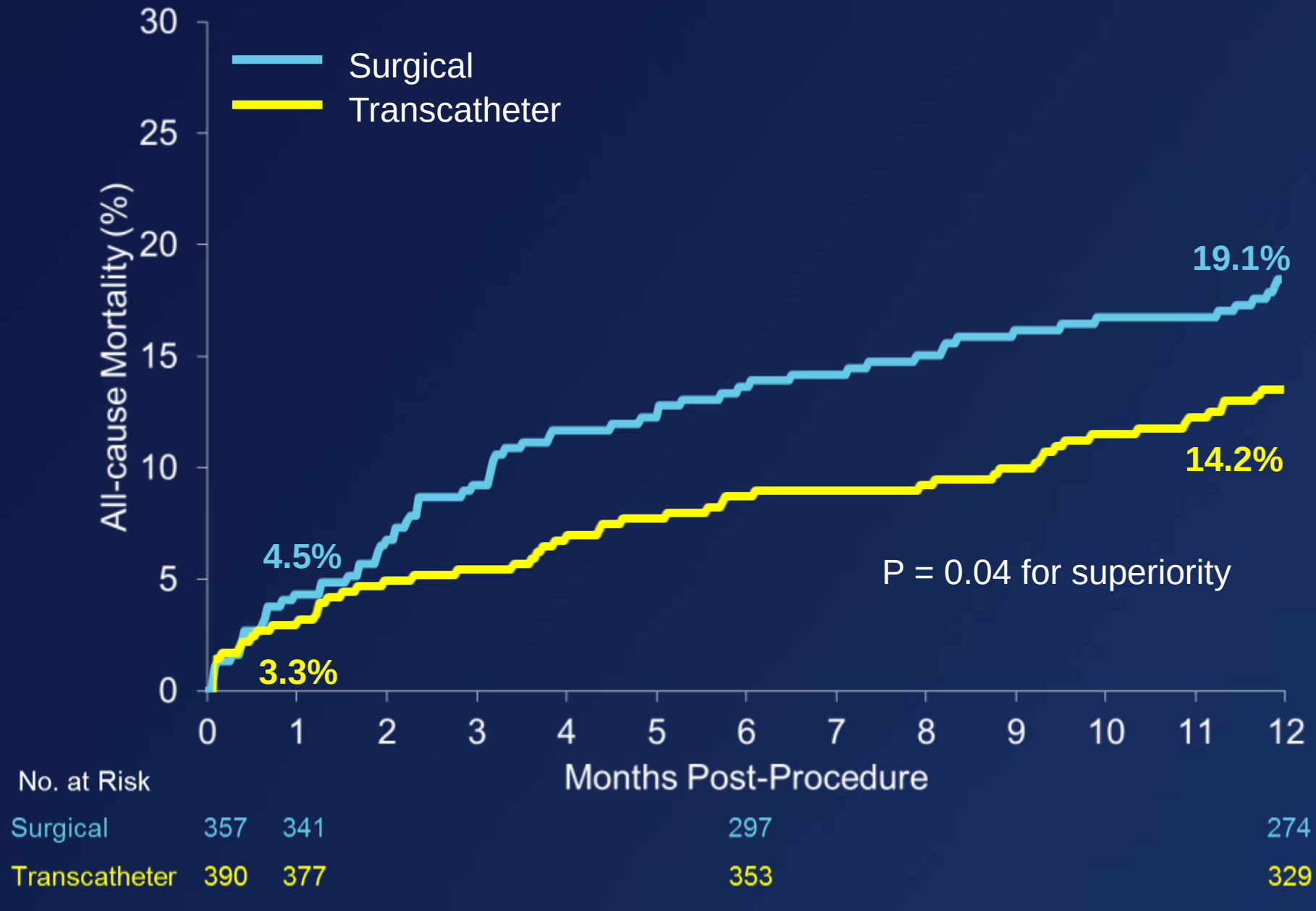
ORIGINAL ARTICLE

## Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

***Adams DH, Popma JJ, Reardon MJ, et al. Published in N Engl J Med on March 29, 2014 at NEJM.org***

# Primary Endpoint: 1 Year All-cause Mortality



European Heart Journal
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES

# Guidelines on the management of valvular heart disease (version 2012)

## The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)*, Ottavio Alfieri (Chairperson)* (Italy), Felicita Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Iung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

# ESC/EACTS Guidelines - 2012

| Recommendations | Class [a] | Level [b] |
|---|---|---|
| TAVI should only be undertaken with a multidisciplinary 'heart team' including cardiologists and cardiac surgeons and other specialists if necessary. | I | C |
| TAVI should only be performed in hospitals with cardiac surgery on-site. | I | C |
| TAVI is indicated in patients with severe symptomatic AS who are not suitable for AVR as assessed by a 'heart team' and who are likely to gain improvement in their quality of life and to have a life expectancy of more than 1 year after consideration of their comorbidities. | I | B |
| TAVI should be considered in high-risk patients with severe symptomatic AS who may still be suitable for surgery, but in whom TAVI is favoured by a 'heart team' based on the individual risk profile and anatomic suitability. | IIa | B |

***Class I:***

- **Heart Team required**
- **On-site cardiac surgery**
- **Pts not suitable for AVR**

***Class IIa:***

- **High-risk operable as an alternative to surgery; determined by heart team and case-based decisions**

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

# 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Rick A. Nishimura, Catherine M. Otto, Robert O. Bonow, Blase A. Carabello, John P. Erwin III, Robert A. Guyton, Patrick T. O'Gara, Carlos E. Ruiz, Nikolaos J. Skubas, Paul Sorajja, Thoralf M. Sundt III and James D. Thomas

*Circulation.* published online March 3, 2014;
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

| Recommendations | COR | LOE |
|---|---|---|
| Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.4) with low or intermediate surgical risk (Section 2.5 in the full-text guideline) | I | A |
| For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care | I | C |
| TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo | I | B |
| TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.4) and who have high surgical risk (Section 2.5 in the full-text guideline) | IIa | B |
| Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS | IIb | C |
| TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS | III: No Benefit | B |

# AHA/ACC TAVR Guidelines - 2014

## *Class I:*

- **Heart Valve Team should collaborate on decisions**
- **Pts not suitable for AVR and survival > 12 mos**

## *Class IIa:*

- **Reasonable alternative to surgical AVR in high surgical risk pts**

| Recommendations | COR | LOE |
|---|---|---|
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# New TAVR (and "Related") Technologies

- New TAVR Systems
- Access and Closure Strategies
- Cerebral Embolic Protection Devices
- Advanced Imaging Modalities

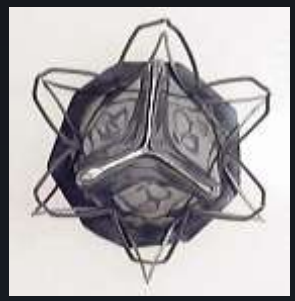
# New TAVR Systems - *Transfemoral*

- Direct Flow
- Sadra
- St. Jude
- AorTx
- HLT
- EndoTech
- ABPS PercValve





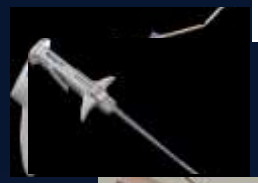
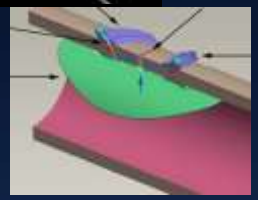
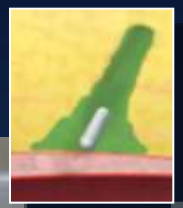


# New TAVR Systems - *Transapical*

- **Jena Valve**
  *(73 pts, + CE approval)*
- **MDT (Engager)**
  *(40 pts)*
- **Symetis**
  *(90 pts, + CE approval)*

# Large Vessel Closure Landscape

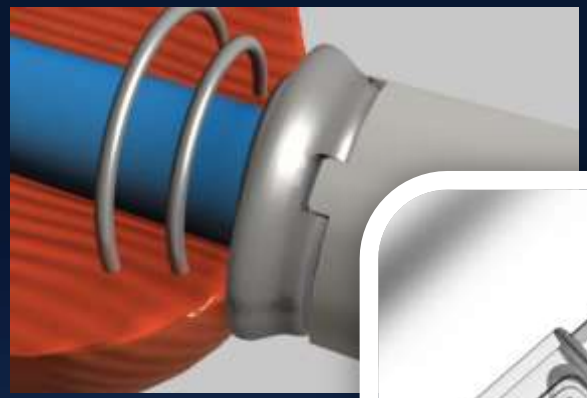
| Category | Company | Technology |
|---|---|---|
| Emerging Suture Based Technologies | Sutura Superstich |  |
| | MediGlobe |  |
| | SpiRx |  |
| | Vasostich |  |
| Emerging Patch or Plug Technologies | Vivasure |  |
| | Access Closure-GRIP |  |
| | InSeal |  |
| | Promed | |

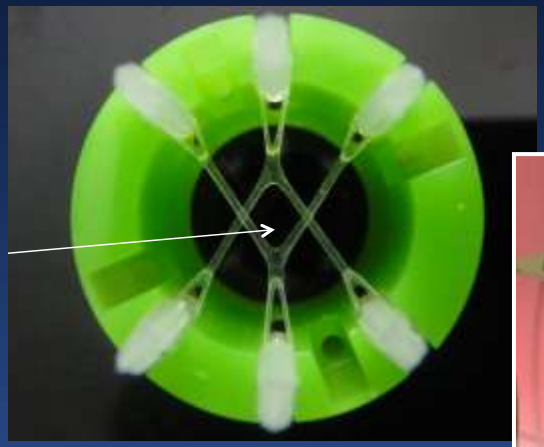
**Strategic Players**

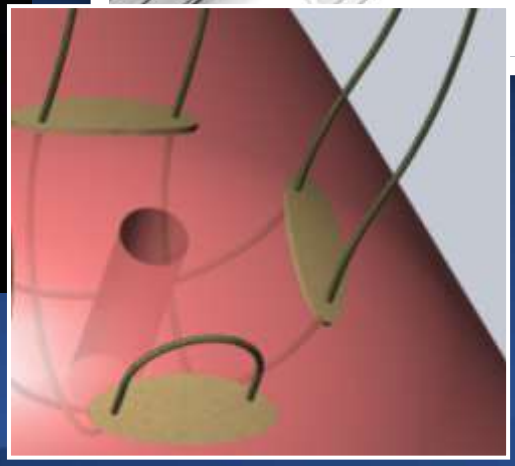
| *Medtronic, Inc.* | *Abbott Vascular* | *St. Jude Medical* | *Cook/Cardica* |
|---|---|---|---|
|  |  |  | COOK MEDICAL / cardica |

# Transcutaneous Ventricular Access and Closure (TVAC)

- *Apica*
- *Entourage CardioClose*
- *MID Permaseal*
- *Novogate*
- *SpiRx*
- *Cardiapex*

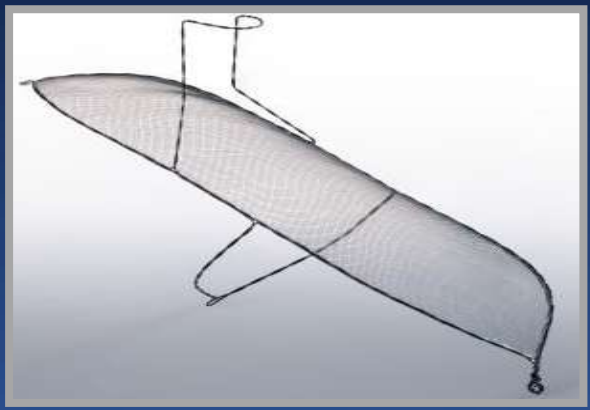




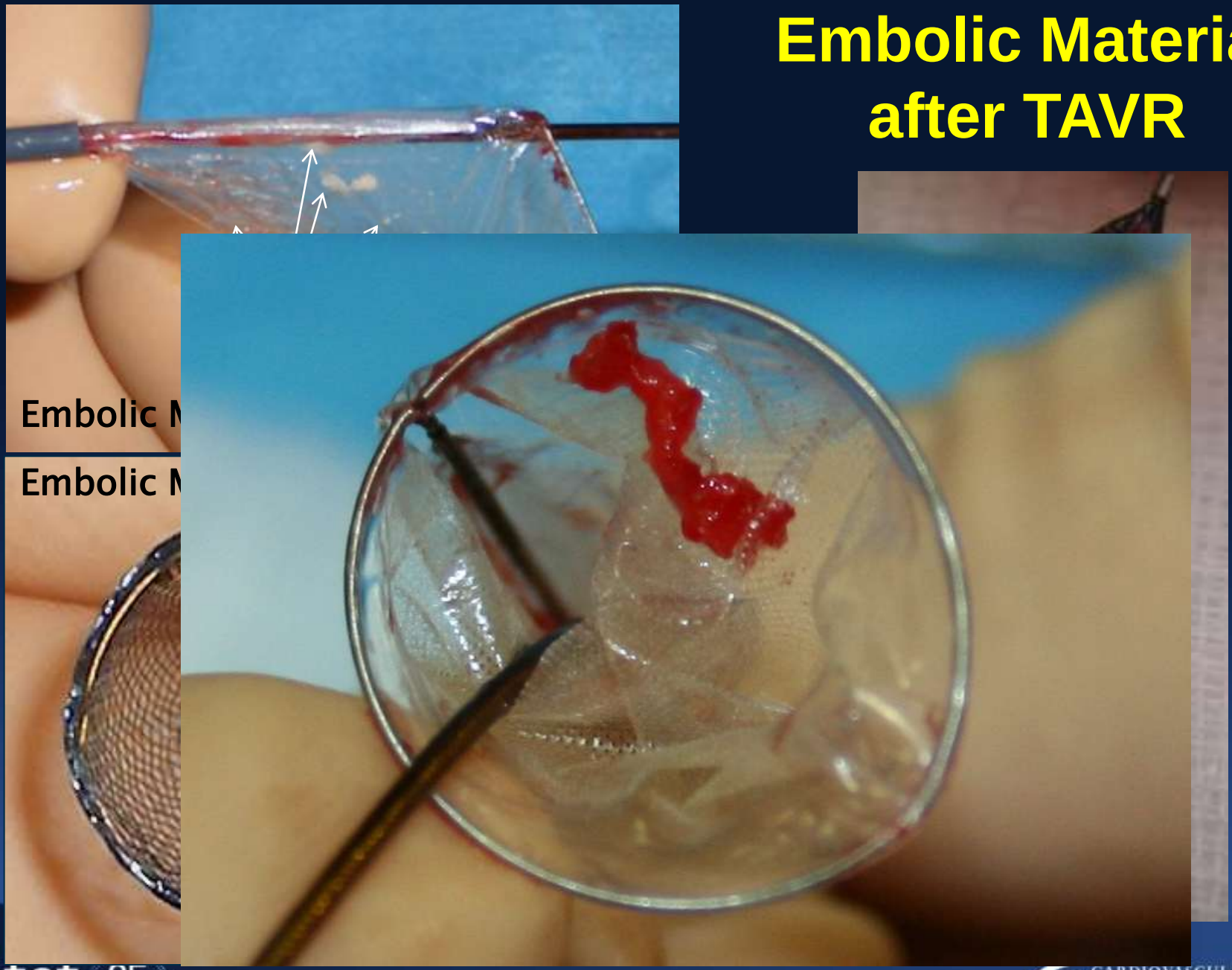


# Cerebral Embolic Protection Devices

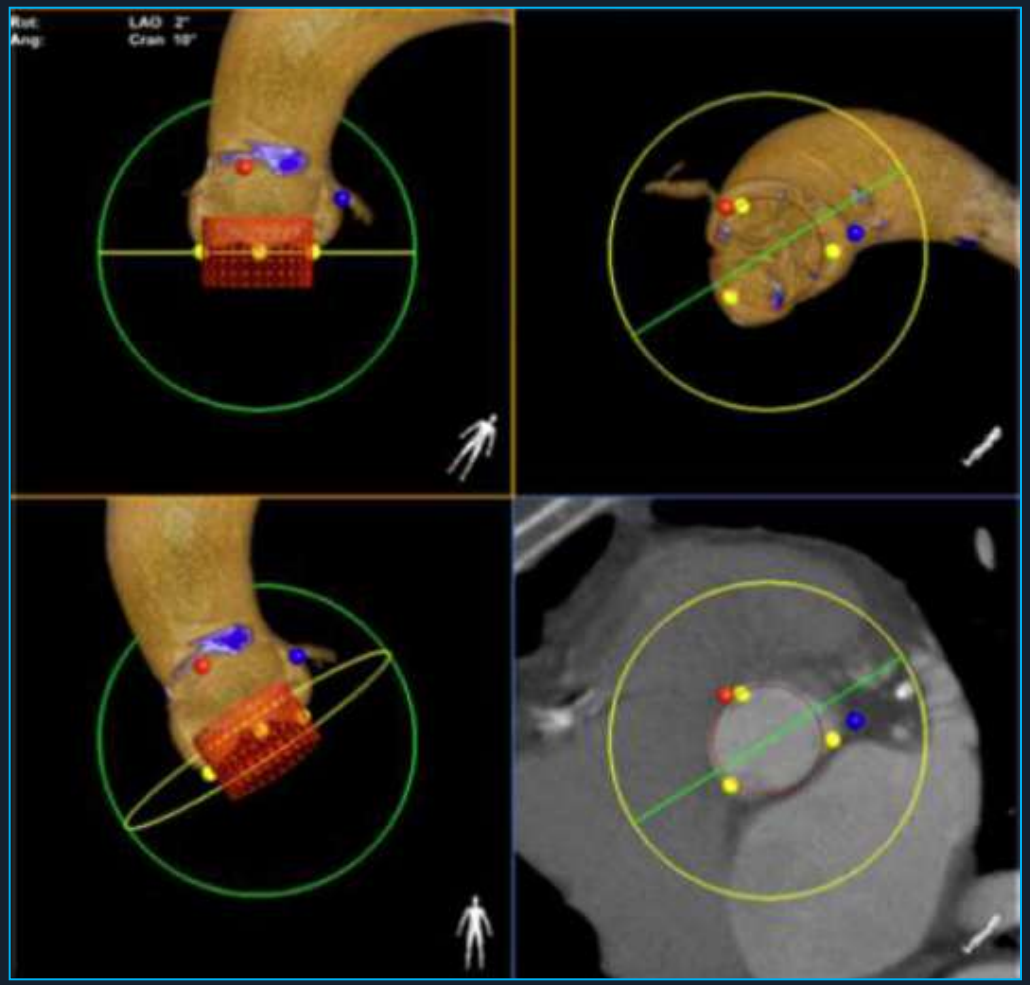
| TriGuard™ Cerebral | Embrella™ | Claret Sentinel™ |
|---|---|---|
| Deflector | Deflector | Dual Filter |
| Femoral Access | Radial Access | Radial Access |
| 9F Sheath (7F Delivery) | 6F Shuttle Sheath | 6F Radial Sheath |



# Embolic Material after TAVR



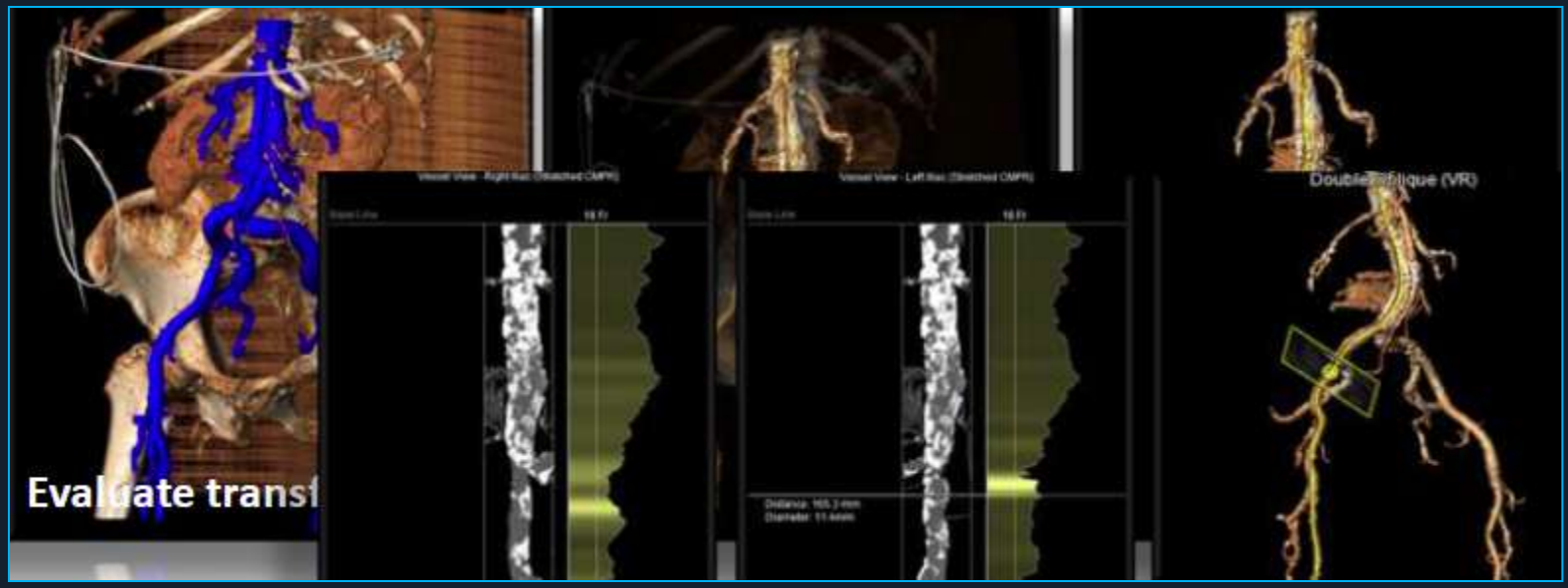
# Advanced Imaging Modalities




## *CTA*

- ***Philips***
  **3D Navigator**
- ***Siemens***
  **Dyna CT**
- ***GE***
  **Innova Vision**

# Advanced Imaging Modalities




*CTA*

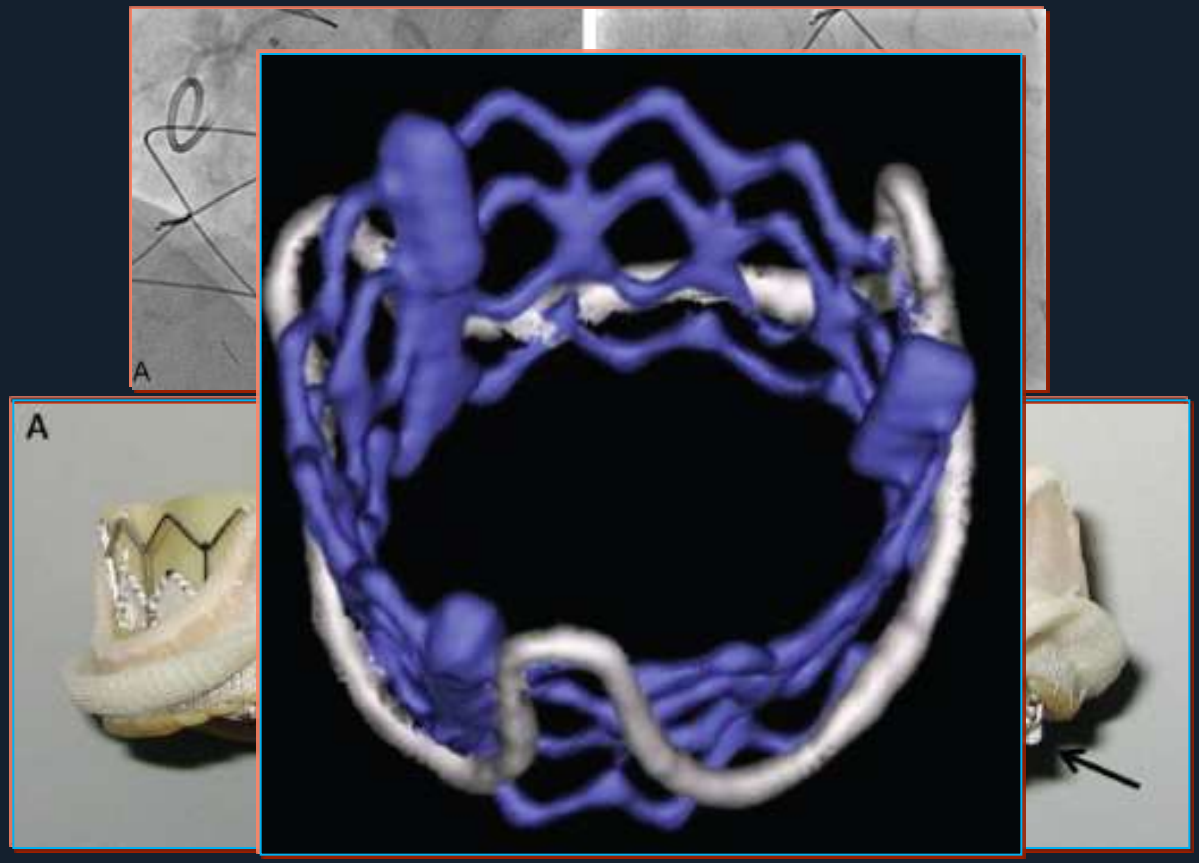
**3Mensio Valves**

# The TAVR Odyssey
## *Next Clinical Trials*

- Valve-in-valve for bio-prosthetic aortic and mitral valve failure
- Intermediate (moderate) risk AS patients
- Mixed AS and CAD patients
- Asymptomatic severe AS
- Low flow - low gradient AS – impedance mismatch
- Aortic regurgitation

# New TAVR Clinical Indications

## *Valve - in - Valve*



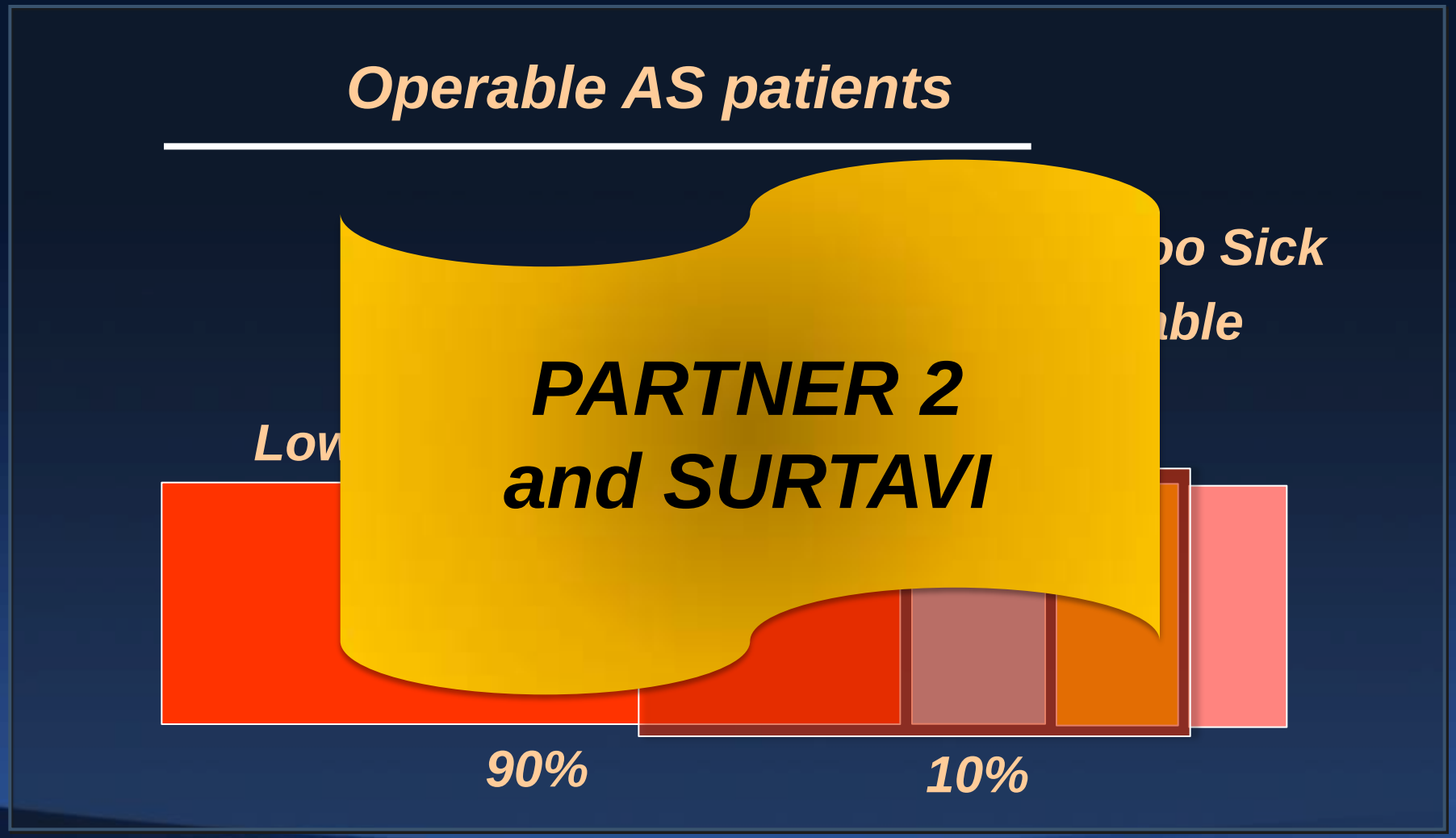

*Incorrect position* *Correct position*



Webb JG, Wood DA, Ye J, et al. Circulation 2010;121:1848-57

# The TAVR Odyssey

## *Moderate Risk Patients*



# The TAVR Odyssey

## Final Thoughts

# TAVR - The Early Years

## *Perspectives over time…*

- ***2000*** **"you're crazy, reckless idiots; won't get it funded; can't work and will kill patients"**
- ***2005*** **"you're merely irresponsible; procedure is too complicated; possibly in inoperable patients only"**

# TAVR – The Early Years

## *Rules of Engagement*

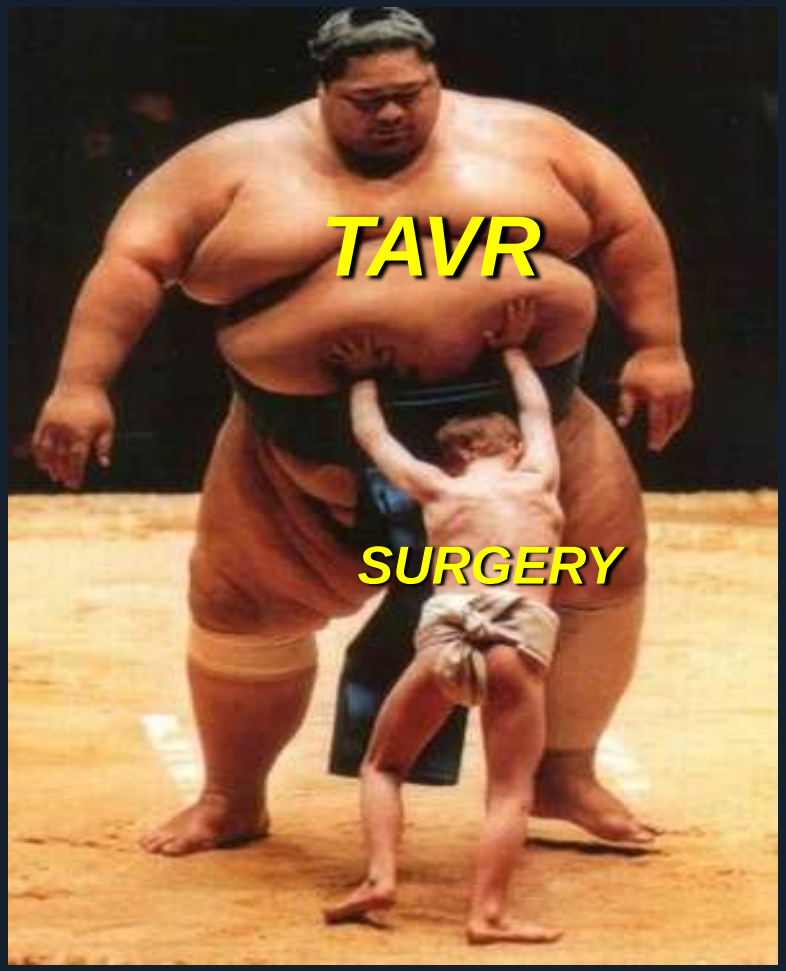
# TAVR - Now

## *Perspectives over time…*

- ***2000*** **"you're crazy, reckless idiots; won't get it funded; can't work and will kill patients"**
- ***2005*** **"you're merely irresponsible; procedure is too complicated; possibly in inoperable patients only"**
- ***2014*** **"you're a visionary; breakthrough procedure which is easily generalizable; will transform therapy for most AS patients!"**

# TAVR - Now

## *Rules of Engagement*



**Alain Cribier to Martin Leon, Stan Rowe, Stan Rabinovich, Assaf Bash**
**April 12, 2002**

*I have a fascinating case that I would like to discuss with you!*

**57 y/o**

**EF 10%**

*Transeptal BAV performed*

*BP 60 mmHg with vasopressors*

*Intra-LV thrombus*

*Imminent d*

*Valve impl… …sseptal approach !*

*… of the septum required*

*Externalization of wire*

*Highest risk !..*

**What do you think?**

**Martin Leon to Alain Cribier**
**April 12, 2002**

*You have my complete support to move ahead with the first PVT clinical placement in this desperately ill man.*

*IABP?*

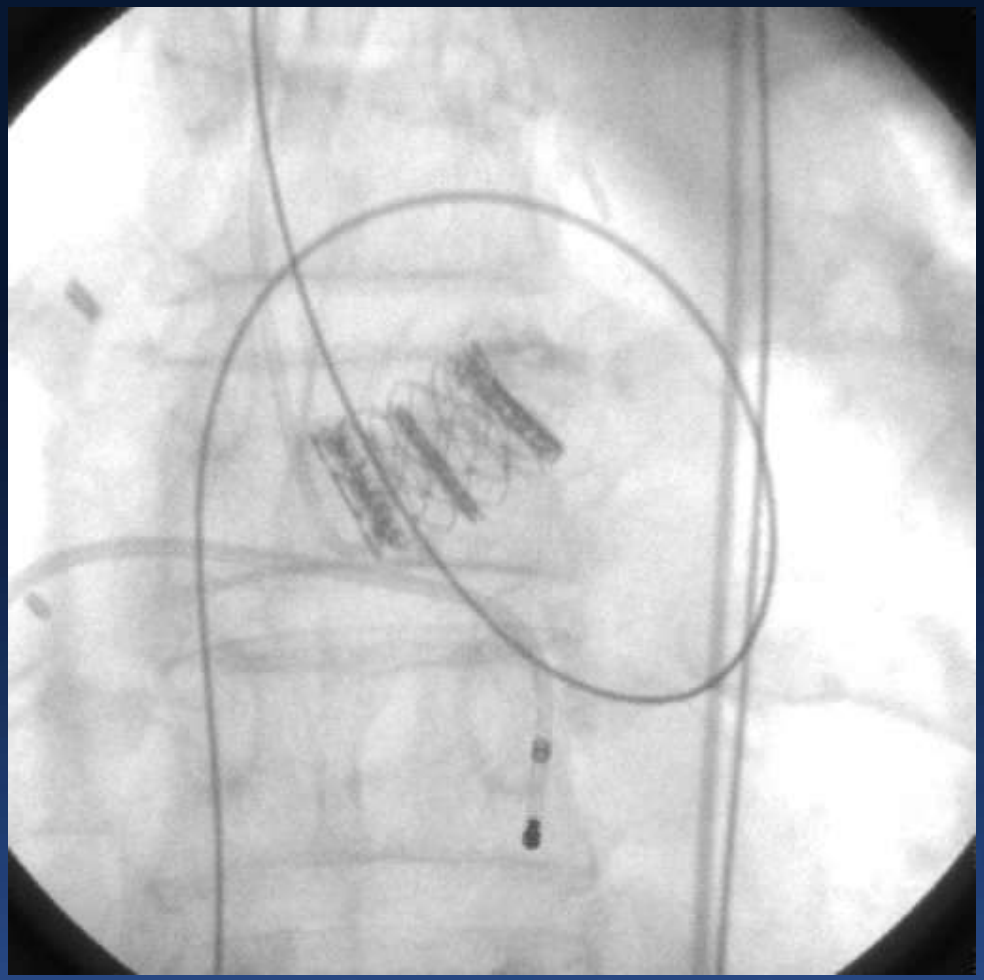
*Snaring the stiff wire is a good idea*

*Best operator in the world!*

*High likehood of failure but… it just might work and save his life!*

# *Valve Positioning*

# April 16, 2002, FIM-TAVI, Transseptal



***Valve deployment!***

# April 16, 2002, FIM-TAVI, Transseptal


15 min post-TAVI

**Nov 2011**
**Oct 2012**

**FDA Approval (non-surgical and high risk surgical)**

PARTNER US Pivotal

Since 2007

Post market registries

2007

CE mark commercialization

2005-07

2004

International TF and TA Feasibility Studies

2002-03

Edwards Lifesciences

2002

Feasibility Studies (antegrade)

2000

**F.I.M. THV implantation**

1999

Animal implantations (sheep)

1993-1994

« Percutaneous Valve Technology » (prototypes)

1985

Post-mortem studies of intra-valvular stenting

F.I.M. Balloon Aortic Valvuloplasty

# TAVR: A 10-Year Anniversary

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# What is a Breakthrough Technology?

## *60th Israel Heart Society*

***And Now,***

***"The Stamp"***

# The Patients are Simply AMAZING!

## Patient #1

***92 yo man with critical AS… TAVI at CUMC on 2/8/06… Playing golf in Palm Springs on 3/8/06!!!***