Global update TAVR

Vinayak Bapat

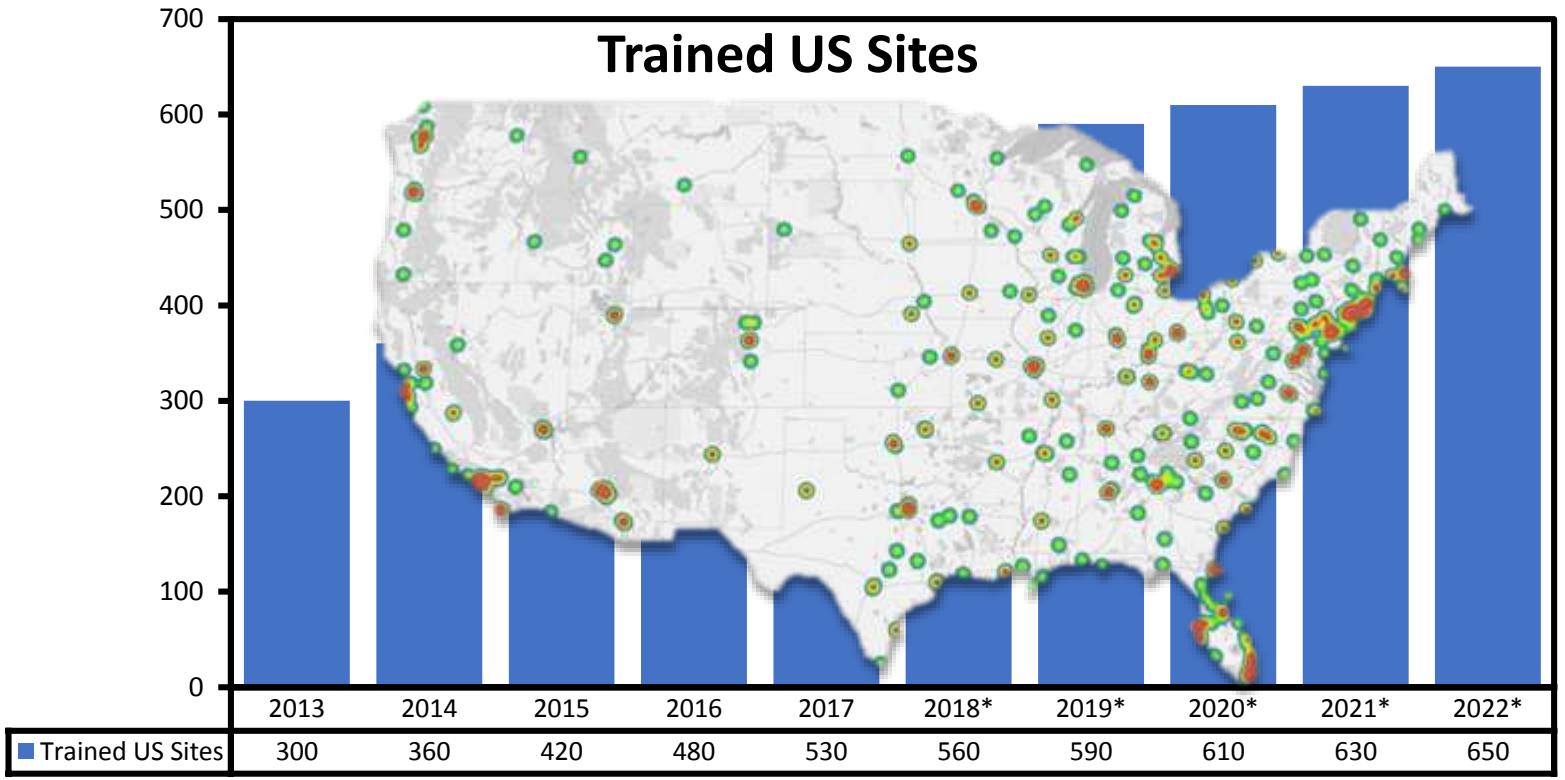
Columbia University Medical Center

Speaker's name : Vinayak, Bapat, New york

☑ I have the following potential conflicts of interest to report:

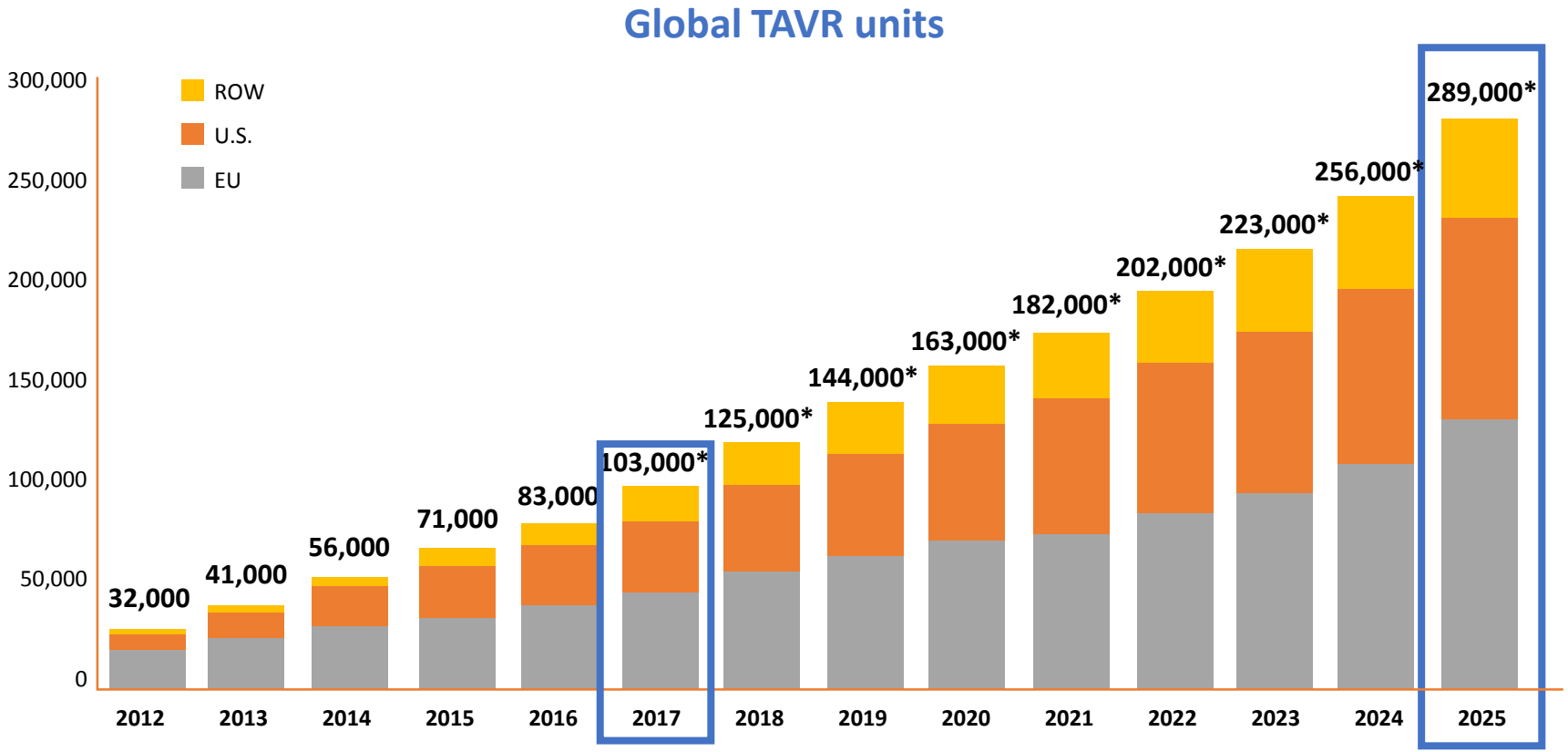
: Consultant: Edwards Lifesciences
Medtronic Inc
Abbott
4Tech
4C
Cephea

Estimated Evolution of US TAVR Sites



*Estimates

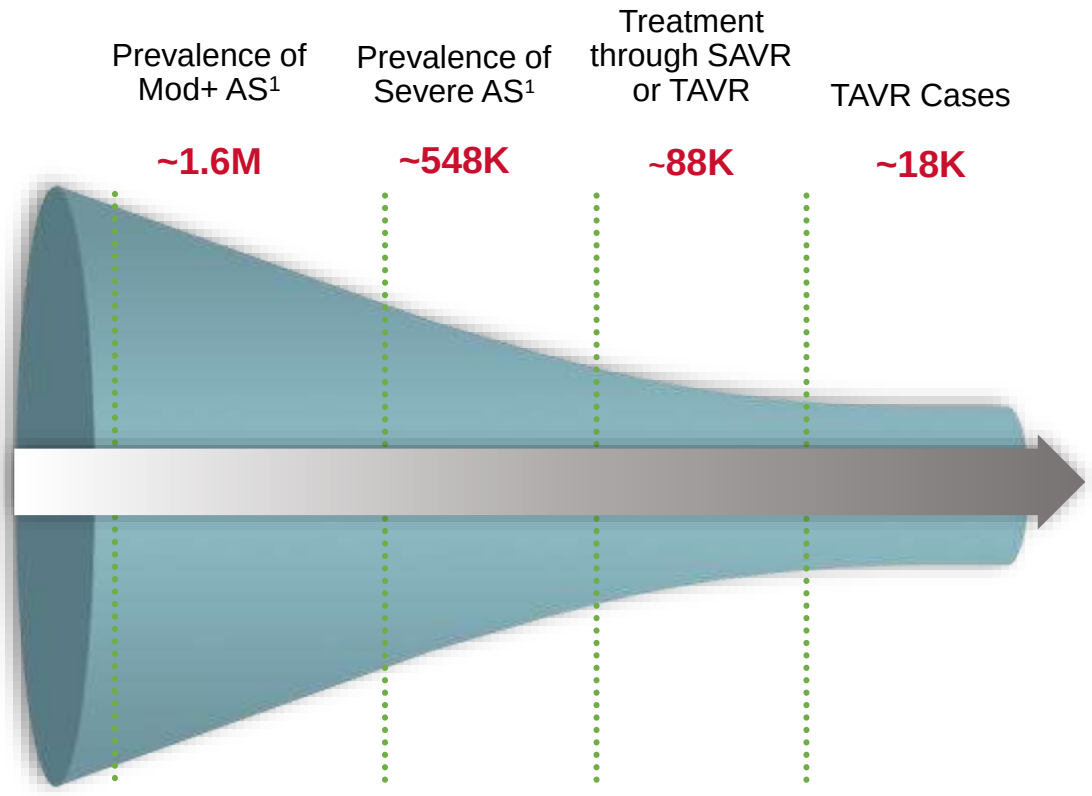
Estimated Global TAVR Cases

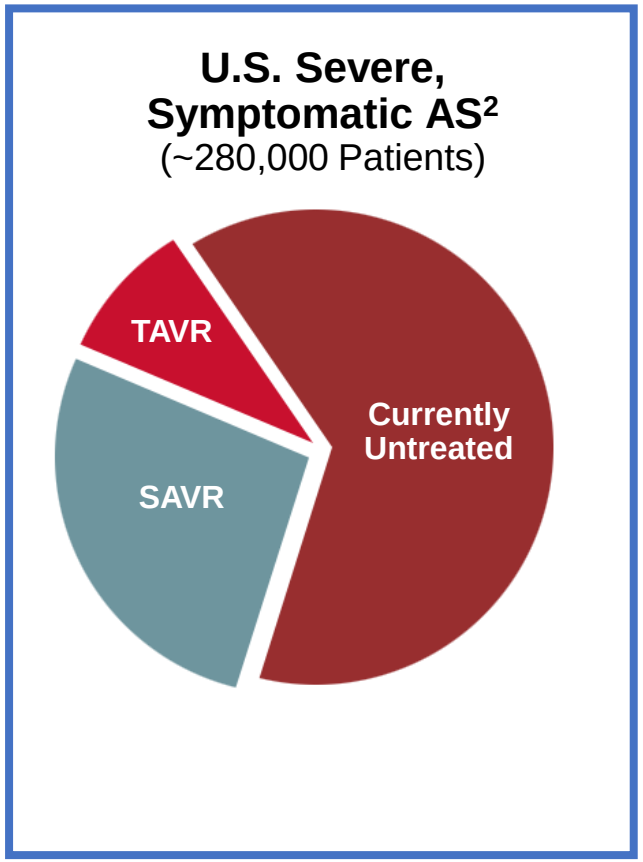


By 2025, TAVR is predicted to increase 3X globally

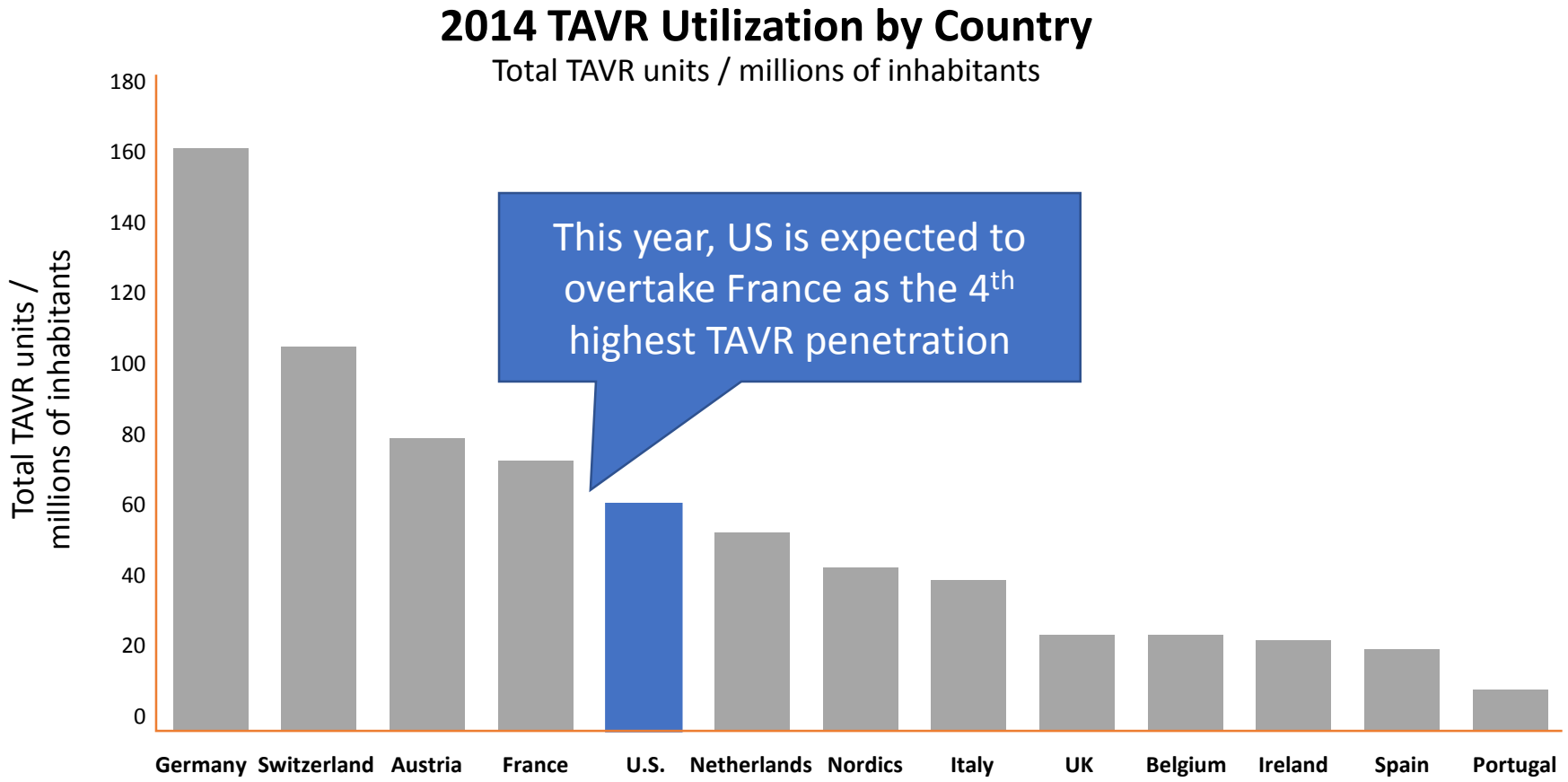
*Estimates

High Number of US Patients with Severe Aortic Stenosis Remain Largely Undertreated



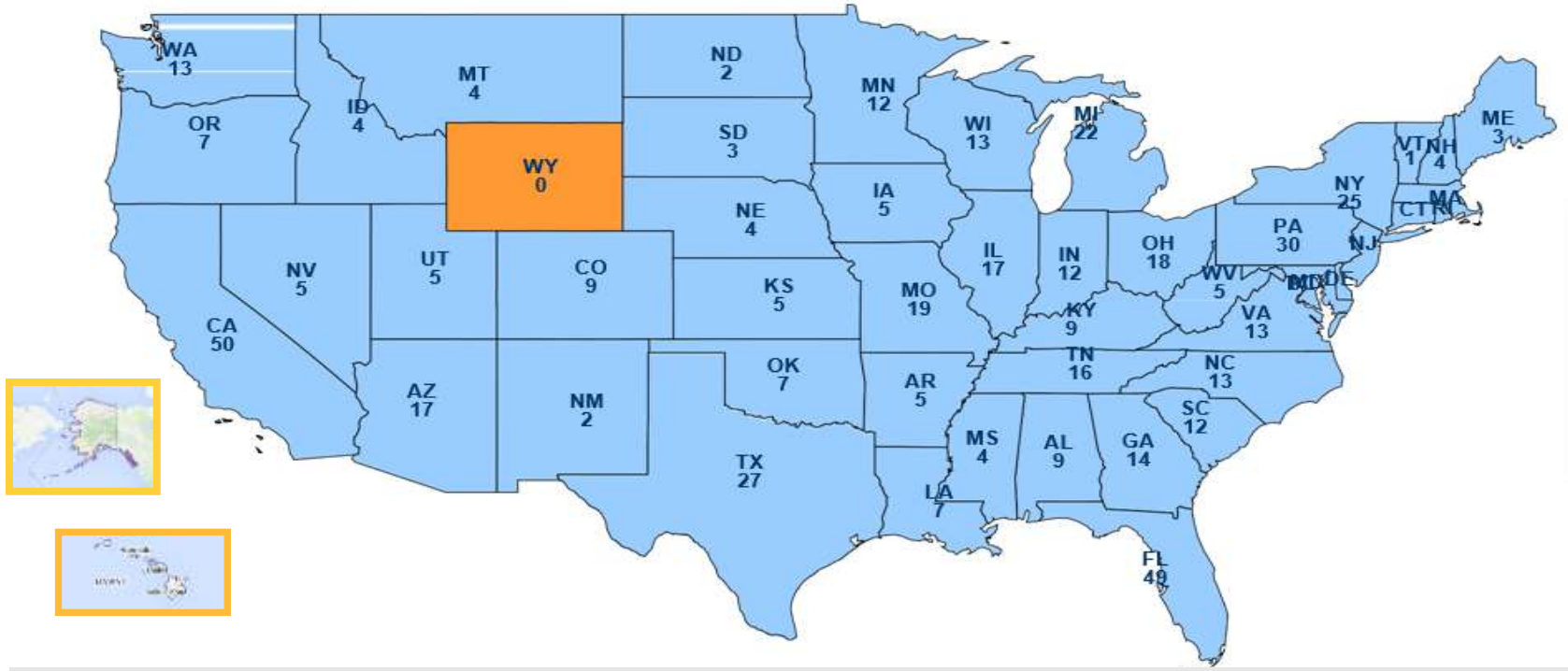


Improvements in Health Policy and Reimbursement are Addressing TAVR Penetration



Insights from the TVT Registry

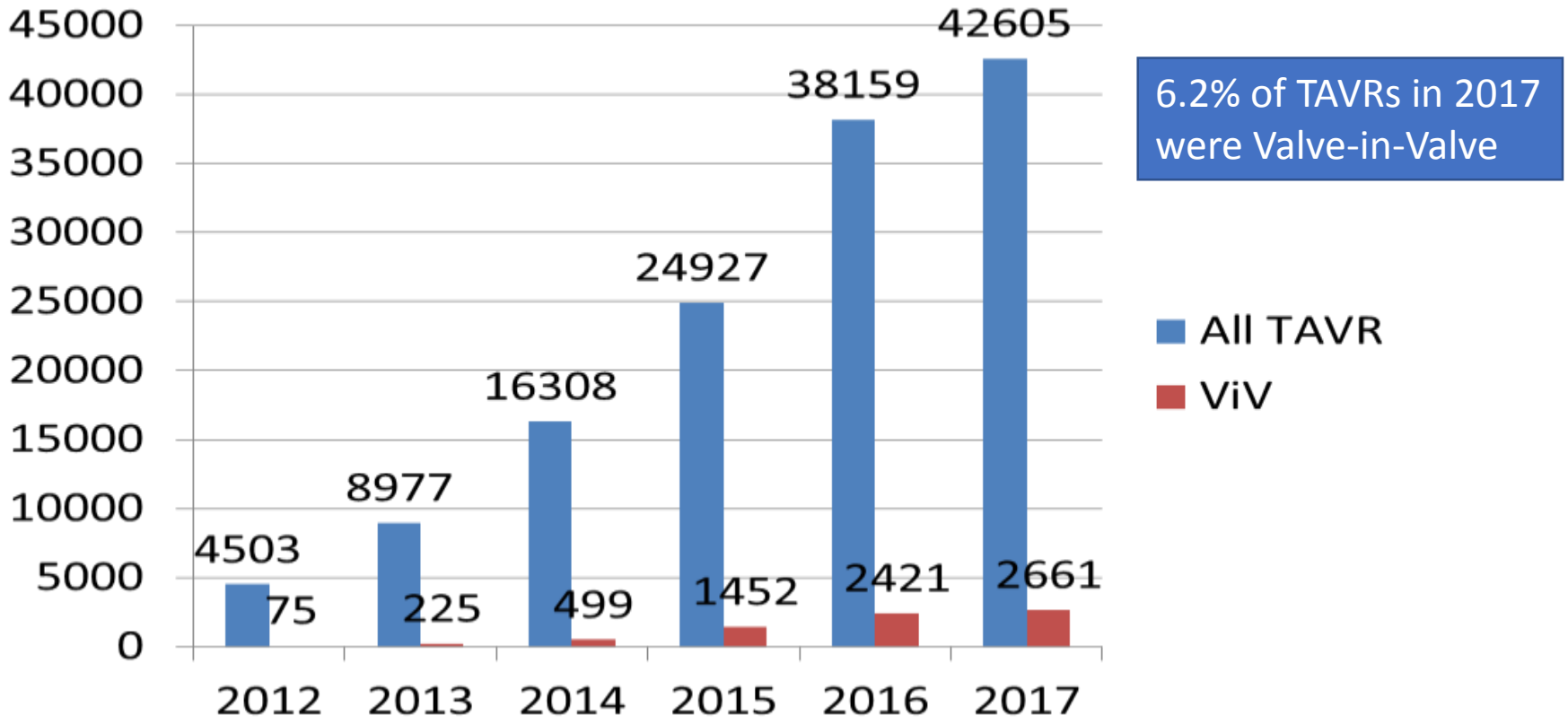
Sites Participating in the STS/ACC TVT Registry



CT	7
DC	2
DE	2
MA	13
MD	7
NJ	13
RI	1

577 TAVR Sites enrolled.
298 Sites performing Leaflet Procedures
178 TMVR Sites

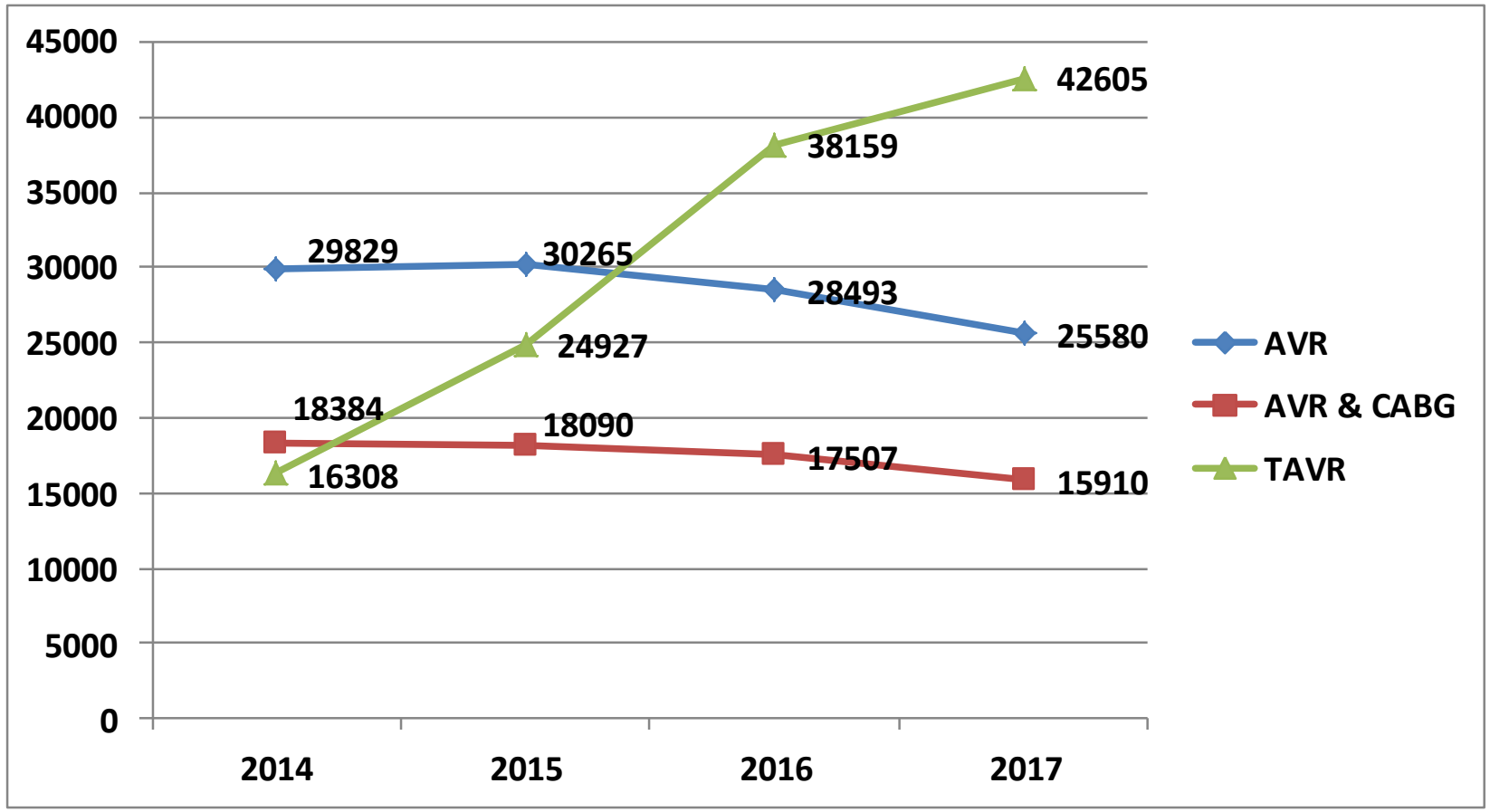
Commercial TAVR Submitted to the TVT Registry TAVR and TAVR ViV Procedures



6.2% of TAVRs in 2017 were Valve-in-Valve

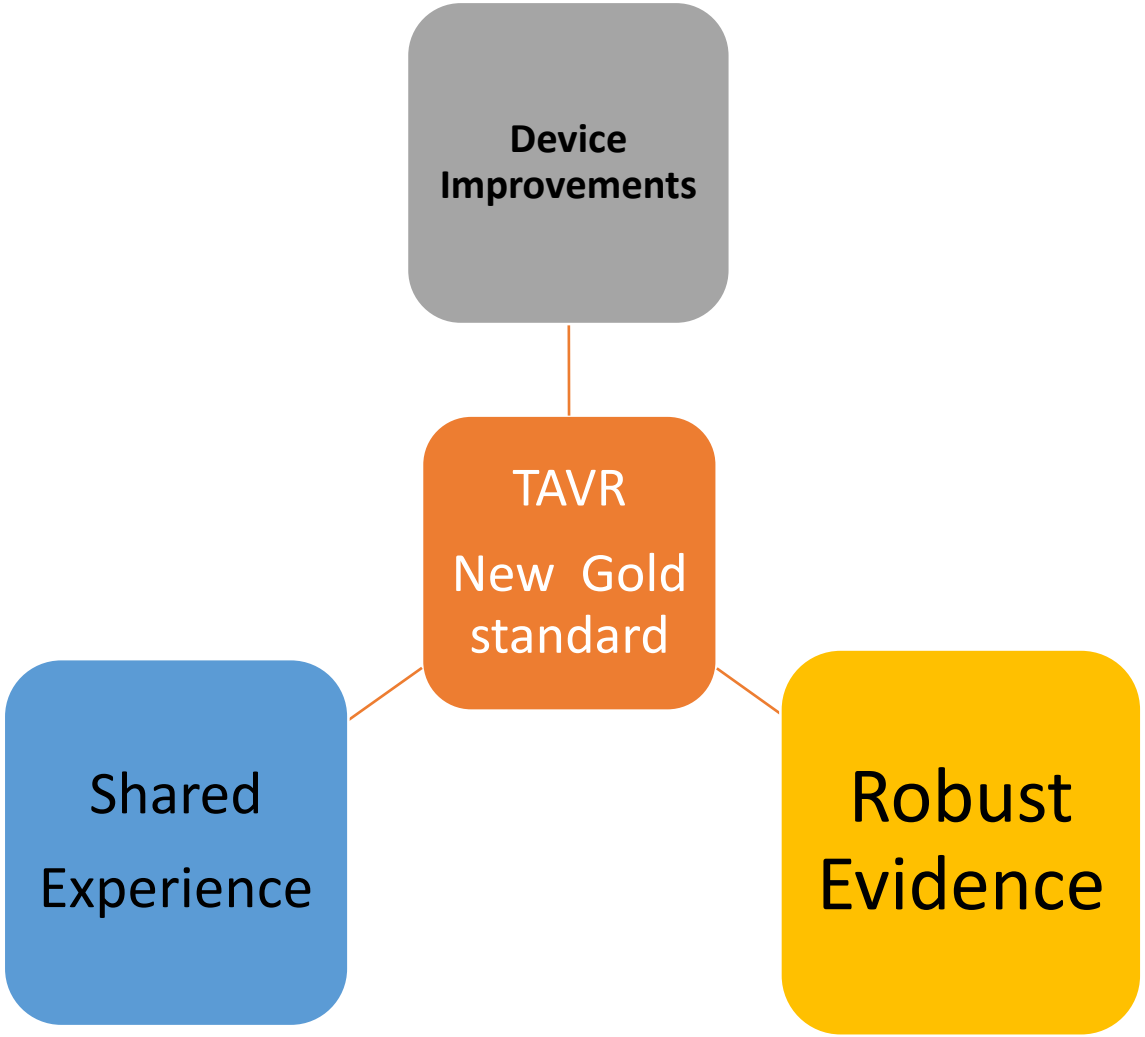
STS/ACC TVT Registry Database as of 3-1-18

SAVR & TAVR Volumes



STS/ACC TVT Registry Database as of 3-1-18

Why this has happened and where is it going!



Device Improvements

- Simple
- Predictable
- Reliable
- Versatile

Evolution of the Edwards Balloon-Expandable Transcatheter Valves

Cribier-Edwards

2002

SA PIEN

2006

SAPIEN XT

2009

SAPIEN 3

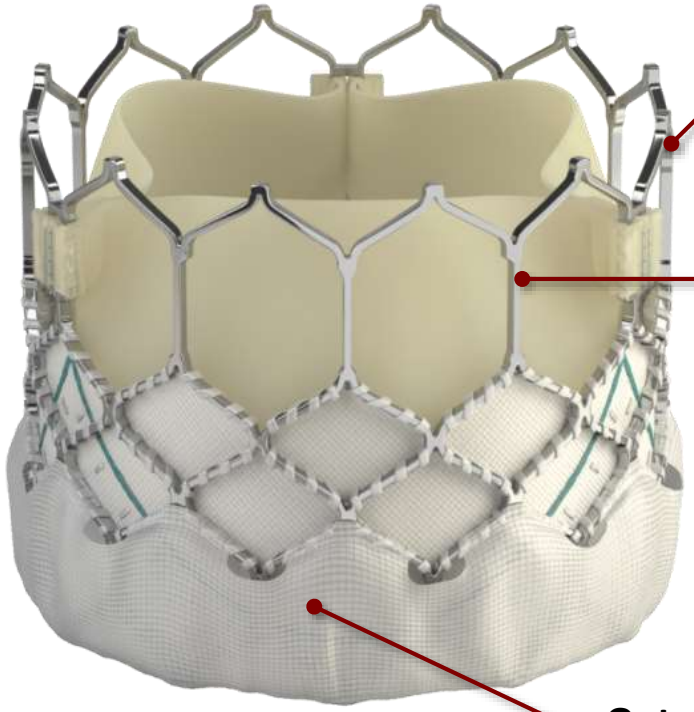
2013

Early issues with TAVR

1. Stroke
2. Pacemaker
3. PV leak
4. Coronary access
5. Durability

- Embolic protection devices
- High placements
- PV leak solution
- Shorter frame
- Time factor

SAPIEN 3 Transcatheter Heart Valve



Enhanced frame geometry for ultra-low delivery profile

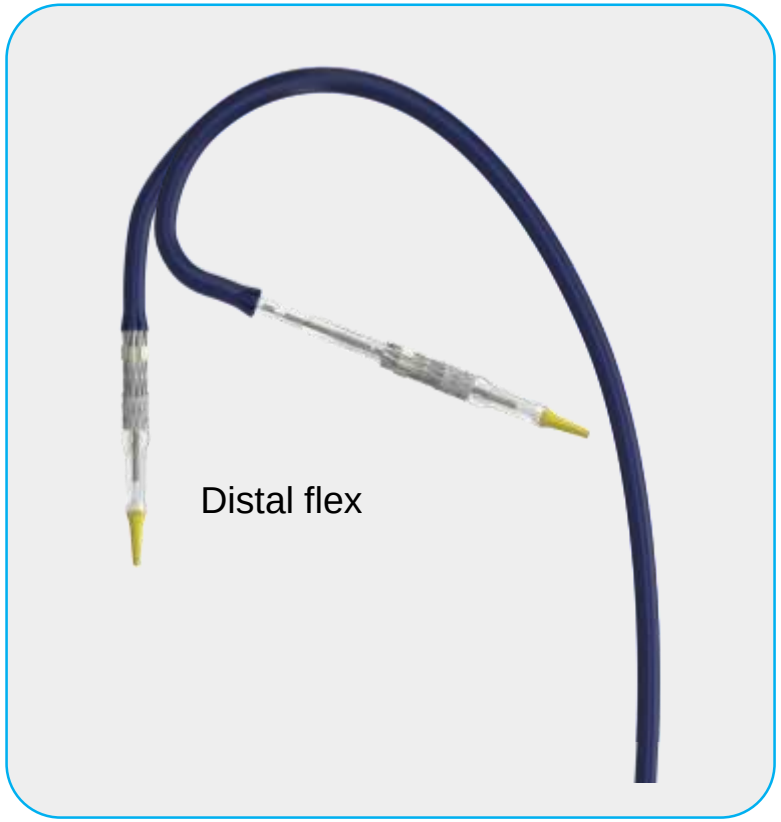
Bovine pericardial tissue

Low frame height

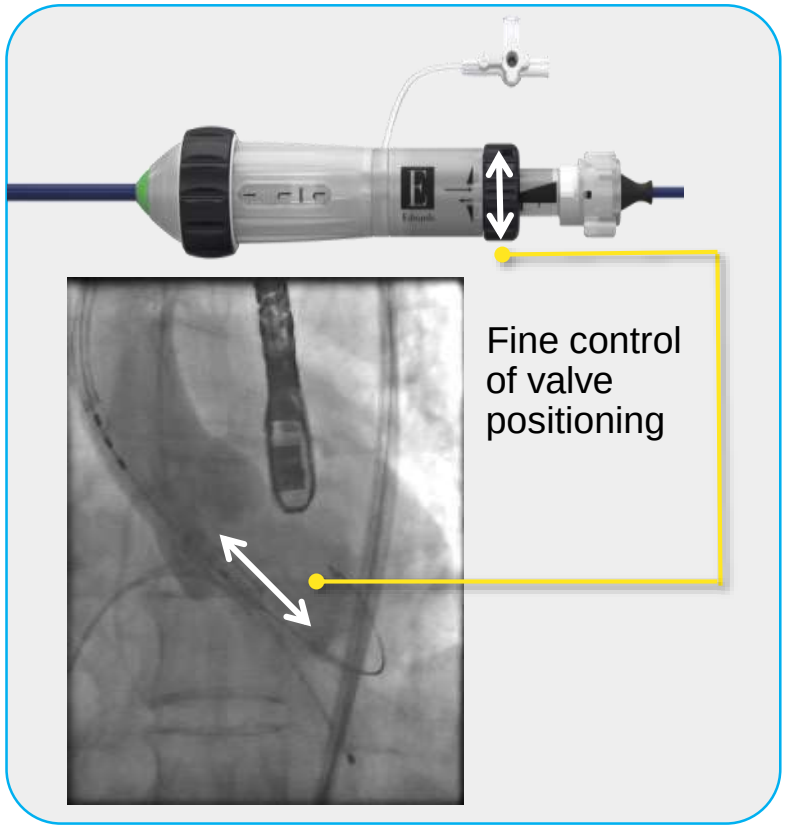
Outer skirt to reduce PVL

SAPIEN 3 Commander Delivery System

- Improved coaxial alignment



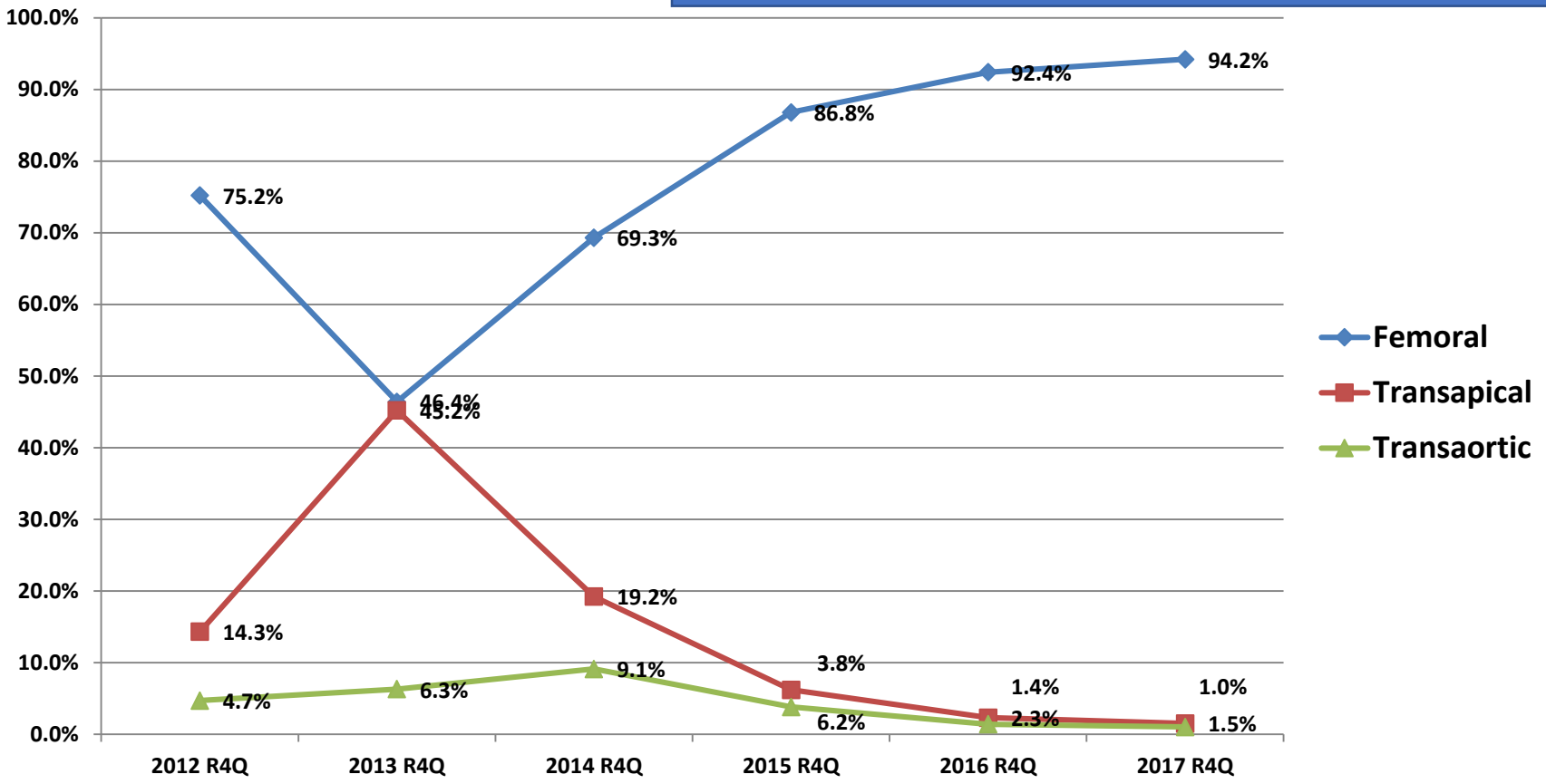
- Accurate positioning



SAPIEN 3 Valve Size	20 mm	23 mm	26 mm	29 mm
Expandable Sheath	14F	14F	14F	16F
Minimum Access Vessel Diameter	5.5 mm	5.5 mm	5.5 mm	6.0 mm

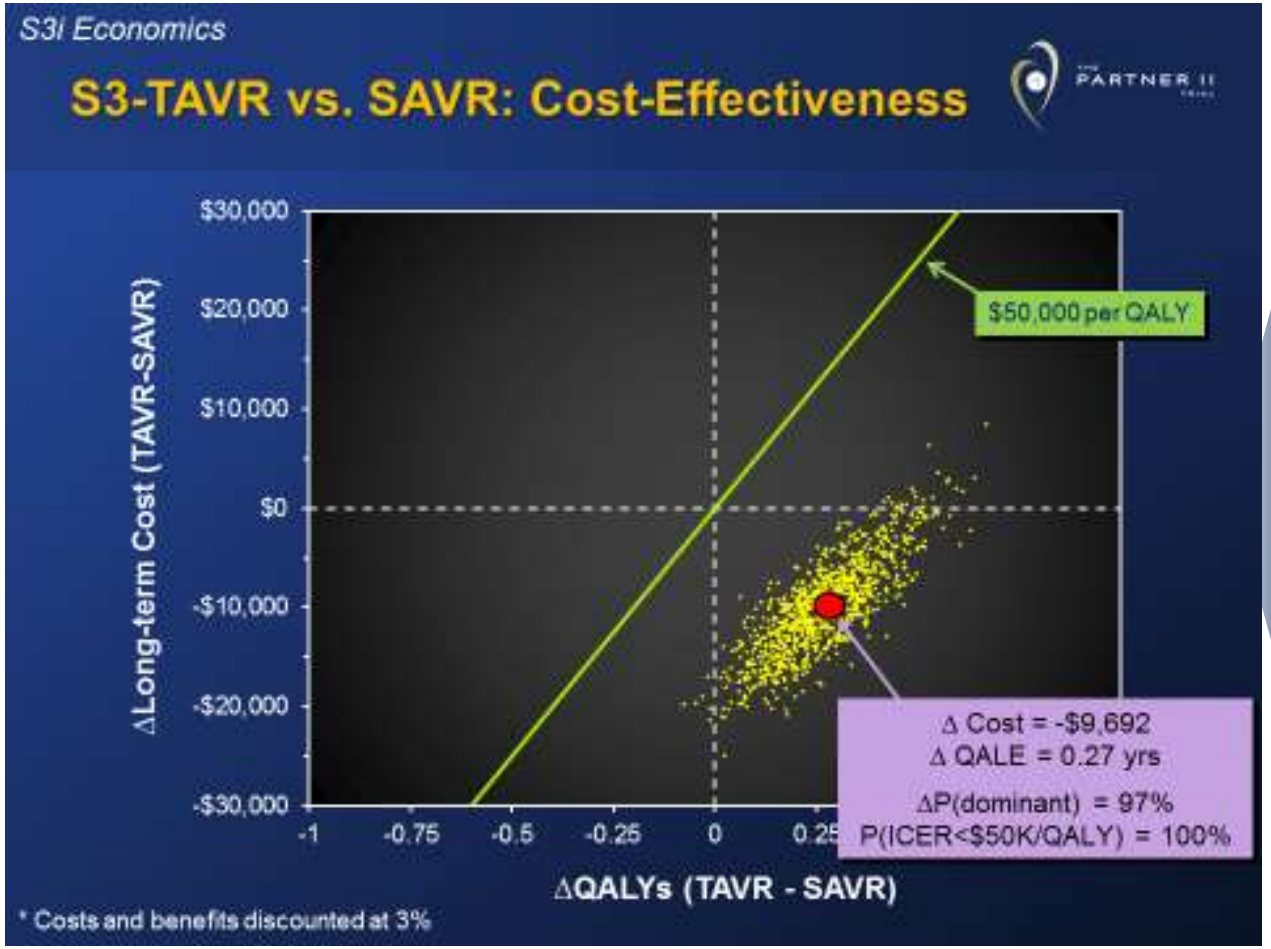
TAVR Access Site

Transfemoral access continues to increase but is plateauing.
Subclavian/axillary access is now 3.0% of all TAVRs



Source: STS/ACC TVT Registry Outcomes Report as of Oct 17, 2017

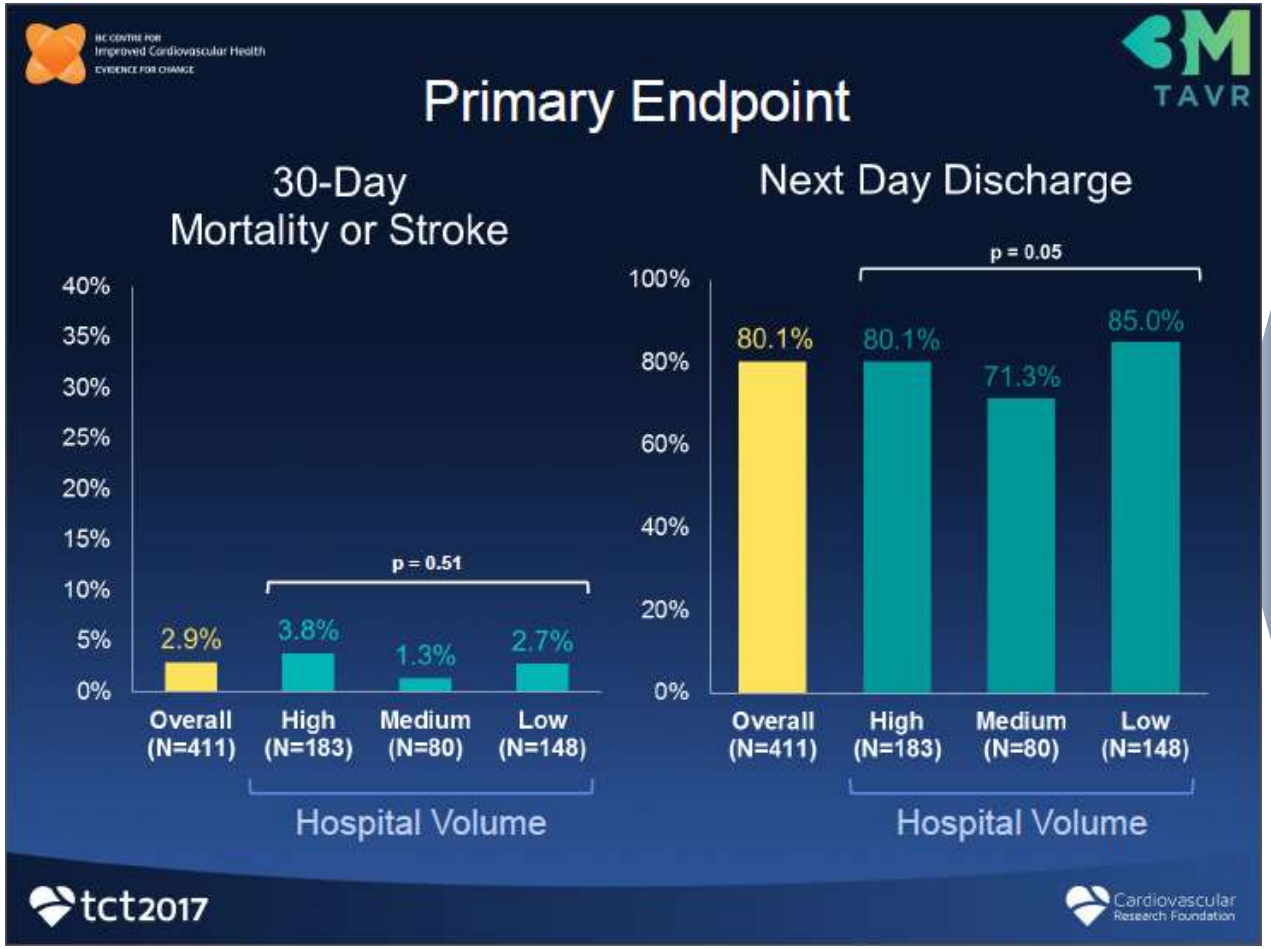
TAVR with SAPIEN 3 Shown To Be Highly Cost-Effective



SAPIEN 3 TAVR is Economically Dominant compared to surgery

Better Outcomes + Lower Cost

With The Right Clinical Pathway, Patients Can Safely Go Back Home The Next Day



1.5% mortality
1.5% Stroke

80% discharged home the next day.

Robust Evidence

- Partner Trials
- SOURCE Registries
- Regional Registries

- Inoperable
- High Risk
- Intermediate Risk
- Low Risk

THE PARTNER 3 TRIAL

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

THE PARTNER 3 TRIAL

Background (1)

- Previous PARTNER studies have shown that TAVR was superior to standard therapy in extreme-risk patients and non-inferior to surgery in high- and intermediate-risk patients.
- Over the past decade, technology enhancements and procedural refinements have reduced complications and improved clinical outcomes after TAVR.
- The majority of AS patients treated with surgery have low surgical risk profiles and TAVR vs. surgery in such patients has not been investigated in rigorous clinical trials.

Background (2)

THE PARTNER 3 TRIAL

?

PARTNER 3

- RCT 1:1
- vs. Surgery
- N = 1000 pts

Low Risk

The NEW ENGLAND JOURNAL of MEDICINE

OCTOBER 21, 2010

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

APRIL 28, 2016

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

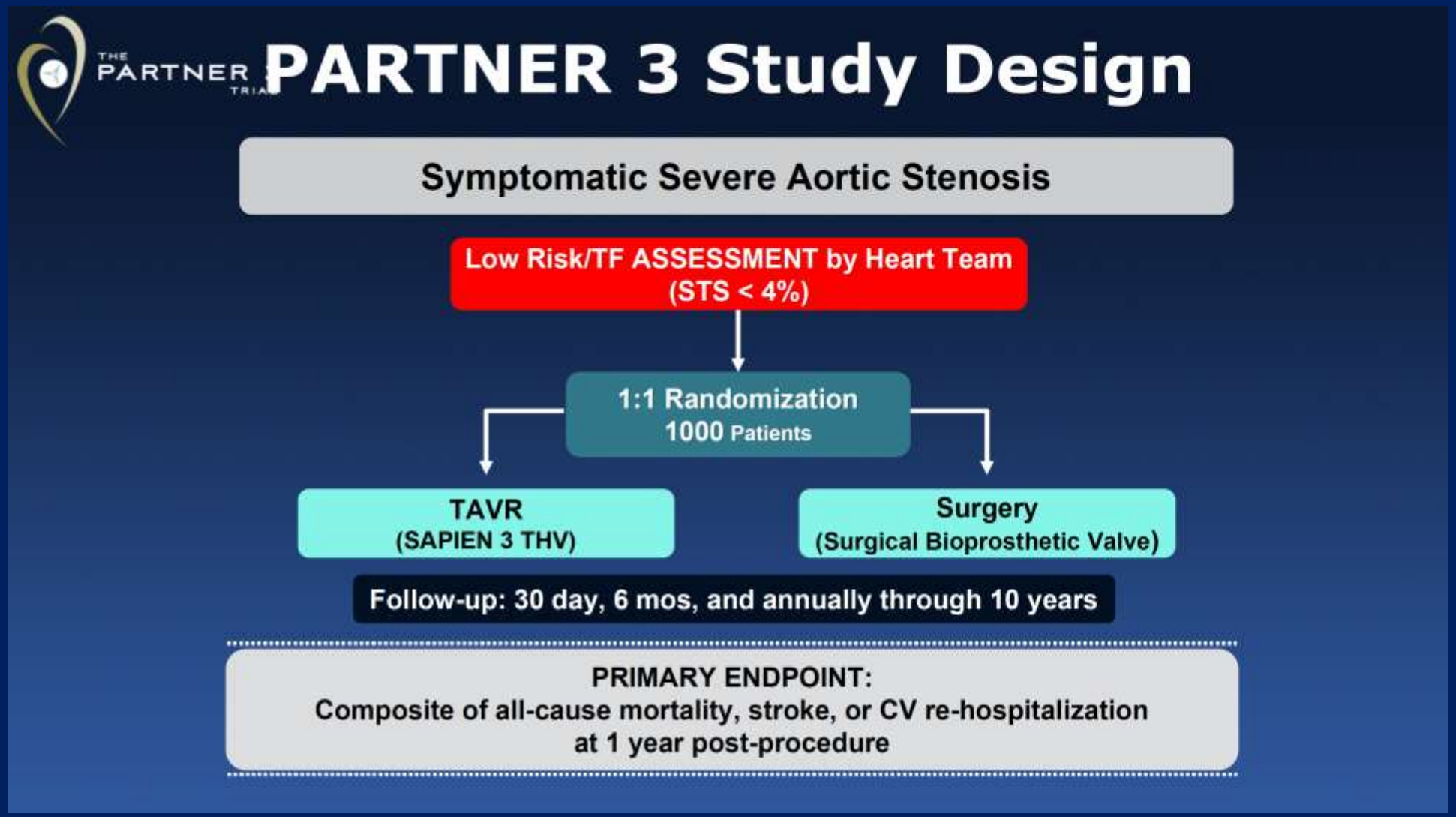
JUNE 9, 2011

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*

Purpose

To compare the safety and effectiveness of the SAPIEN 3 TAVR system versus conventional surgery in patients with severe symptomatic aortic stenosis who are at *low surgical risk*.


THE PARTNER TRIAL
PARTNER 3 Study Design
Symptomatic Severe Aortic Stenosis
Low Risk/TF ASSESSMENT by Heart Team
(STS < 4%)
1:1 Randomization
1000 Patients
TAVR
(SAPIEN 3 THV)
Surgery
(Surgical Bioprosthetic Valve)
Follow-up: 30 day, 6 mos, and annually through 10 years
PRIMARY ENDPOINT:
Composite of all-cause mortality, stroke, or CV re-hospitalization
at 1 year post-procedure


THE PARTNER 3 TRIAL
PARTNER 3 Clinical Sites
1 site
CANADA
St. Paul's Hospital
Vancouver, BC
University of Washington Seattle
Seattle, WA
Providence Heart & Vascular Institute Portland
Portland, OR
NorthShore University Health System Research Institute Evanston
Evanston, IL
Northwestern University
Chicago, IL
University of Buffalo - Kaleida Health
Buffalo, NY
Dartmouth-Hitchcock Medical Center
Lebanon, NH
Central Maine Medical Center
Lewistown, ME
William Beaumont Royal Oak
Royal Oak, MI
The Cleveland Clinic Foundation
Cleveland, OH
Newark Beth Israel Medical Center
Newark, NJ
University of Minnesota Medical Center
Minneapolis, MN
University of Wisconsin
Madison, WI
Mayo Clinic
Rochester, MN
University at Buffalo
Buffalo, NY
Albany Medical College
Albany, NY
Brigham and Women's Hospital
Boston, MA
Hartford Hospital
Hartford, CT
Winthrop-University Hospital Mineola
Mineola, NY
Columbia University Medical Center
New York, NY
Cornell (New York Hospital)
New York, NY
New York Presbyterian Hospital
New York, NY
NYU Langone Medical Center
New York, NY
Morristown
Morristown, NJ
Lankenau Medical Center
Wynnewood, PA
University of Pennsylvania Philadelphia
Philadelphia, PA
Inova Heart and Vascular Institute
Falls Church, VA
Sentara Cardiovascular Research Institute, Norfolk
Norfolk, VA
NC Heart and Vascular
Raleigh, NC
Carolina's Health System
Charlotte, NC
Henry Ford Hospital Detroit
Detroit, MI
York Hospital
York, PA
Allegheny-Singer Research Institute
Pittsburgh, PA
Kaiser San Francisco Medical Center
San Francisco, CA
Intermountain Medical Center
Murray, UT
Medical Center of the Rockies
Loveland, CO
University of Iowa Hospitals and Clinics
Iowa City, IA
Sutter Medical Center, Sacramento
Walnut Creek, CA
Nebraska Heart Institute
Lincoln, NE
Rush University Medical Center
Chicago, IL
Mount Carmel Health System
Columbus, OH
Mills-Peninsula Health Services
Burlingame, CA
Stanford University Medical Center
Stanford, CA
St. Luke's Hospital
Kansas City, MO
Prairie Education and Research Cooperative
Springfield, IL
The Christ Hospital
Cincinnati, OH
University of Virginia Charlottesville
Charlottesville, VA
Cedars-Sinai Medical Center
Los Angeles, CA
UCLA
Los Angeles, CA
Cardiovascular Research Institute of Kansas
Wichita, KS
Washington University/ Barnes-Jewish Hospital Saint Louis
Saint Louis, MO
Saint Thomas Health
Nashville, TN
Oklahoma Cardiovascular Research Group
Oklahoma City, OK
Baptist Memorial Hospital
Memphis, TN
Hoag Memorial Hospital
Newport Beach, CA
Banner University Medical Center
Phoenix, AZ
Emory University Atlanta
Atlanta, GA
University of Alabama
Birmingham, AL
Medical City Dallas
Dallas, TX
The Heart Hospital Baylor Plano
Plano, TX
Ochsner Clinic Foundation
New Orleans, LA
University of Florida
Gainesville, FL
Florida Hospital
Orlando, FL
JFK Medical Center
Atlantis, FL
Mount Sinai Medical Center
Miami Beach, FL
The Queen's Medical Center
Honolulu, HI
HAWAII
Austin Heart
Austin, TX
The University of Texas Health Science Center at Houston
Houston, TX
65 sites
3 sites
JAPAN
Osaka University Hospital
Keio University Hospital
Tokyo
Teikyo University Hospital
Tokyo
1 site
AUSTRALIA
NEW ZEALAND
1 site

Key Inclusion Criteria

Severe Calcific Aortic Stenosis

- AVA ≤ 1.0 cm^2 or AVA index ≤ 0.6 cm^2/m^2
- Jet velocity ≥ 4.0 m/s or mean gradient ≥ 40 mmHg, AND
  - § NYHA Functional Class ≥ 2, OR
  - § Abnormal exercise test with severe SOB, abnormal BP response, or arrhythmia, OR
  - § Asymptomatic with LVEF < 50%

Low Surgical Risk

- Determined by multi-disciplinary heart team
- STS < 4%
- Adjudicated by case review board

Key Exclusion Criteria

Anatomic

- Aortic annulus diameter < 16 mm or > 28 mm (3D imaging)
- Bicuspid valve (CT imaging)
- Severe AR (> 3+) or MR (> 3+)
- Severe LV dysfunction (LVEF < 30%)
- Severe calcification of aortic valvar complex (esp. LVOT)
- Vascular anatomy not suitable for safe femoral access
- Complex CAD: ULM, Syntax score > 32, or not amenable for PCI
- Low coronary takeoff (high risk for obstruction)

Clinical

- Acute MI within 1 month
- Stroke or TIA within 90 days
- Renal insufficiency (eGFR < 30 ml/min) and/or renal replacement Rx
- Hemodynamic or respiratory instability
- Frailty (objective assessment; > 2/4+ metrics)

THE PARTNER 3 TRIAL SAPIEN Valve Evolution

	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility			
Available Valve Sizes	 23 mm, 26 mm	 23 mm, 26 mm, 29 mm	 20 mm, 23 mm, 26 mm, 29 mm
FDA Approval of Valve:	PARTNER 1 2011	PARTNER 2 2014	PARTNER 3 2015

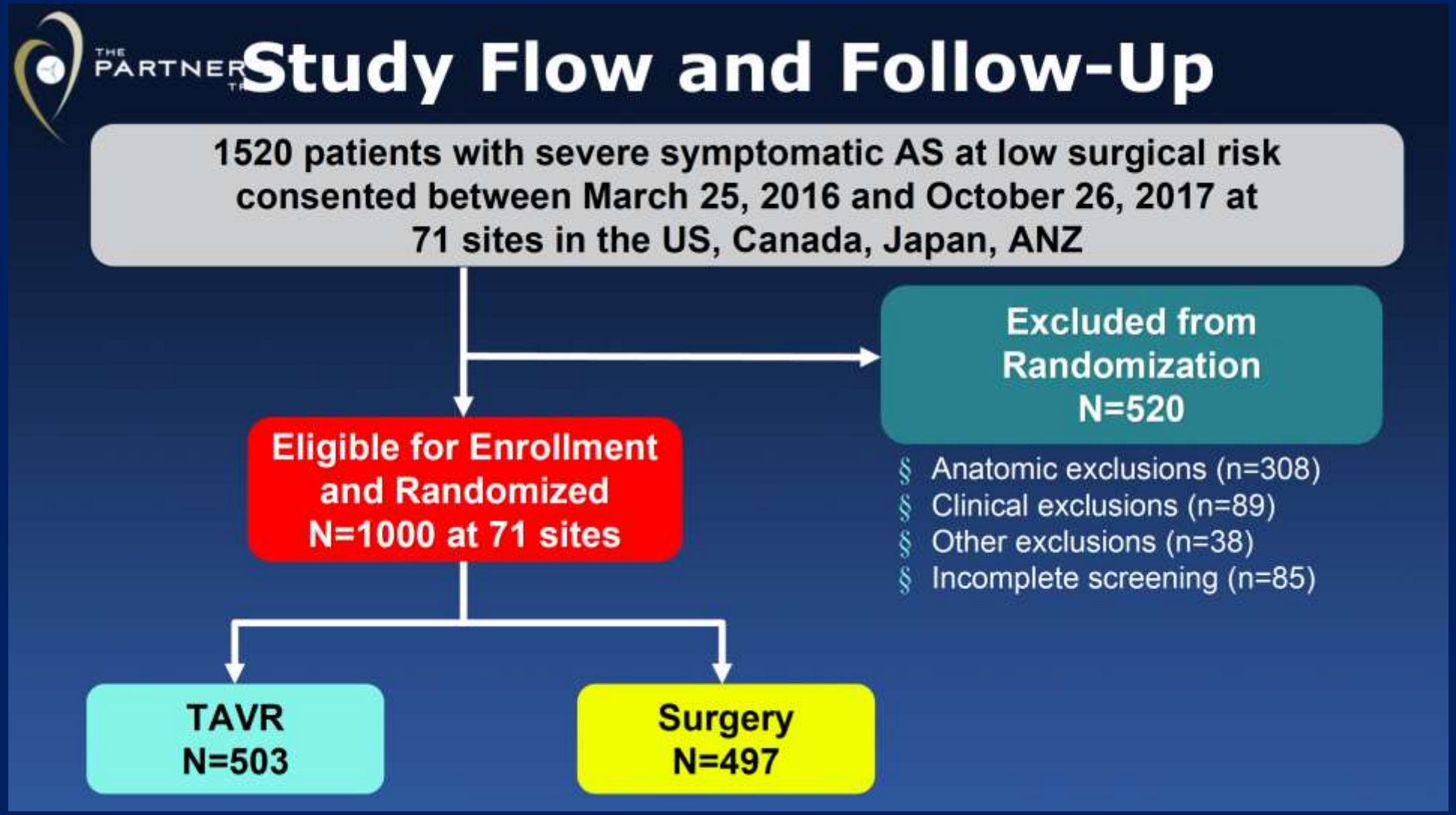
THE PARTNER 3 TRIAL

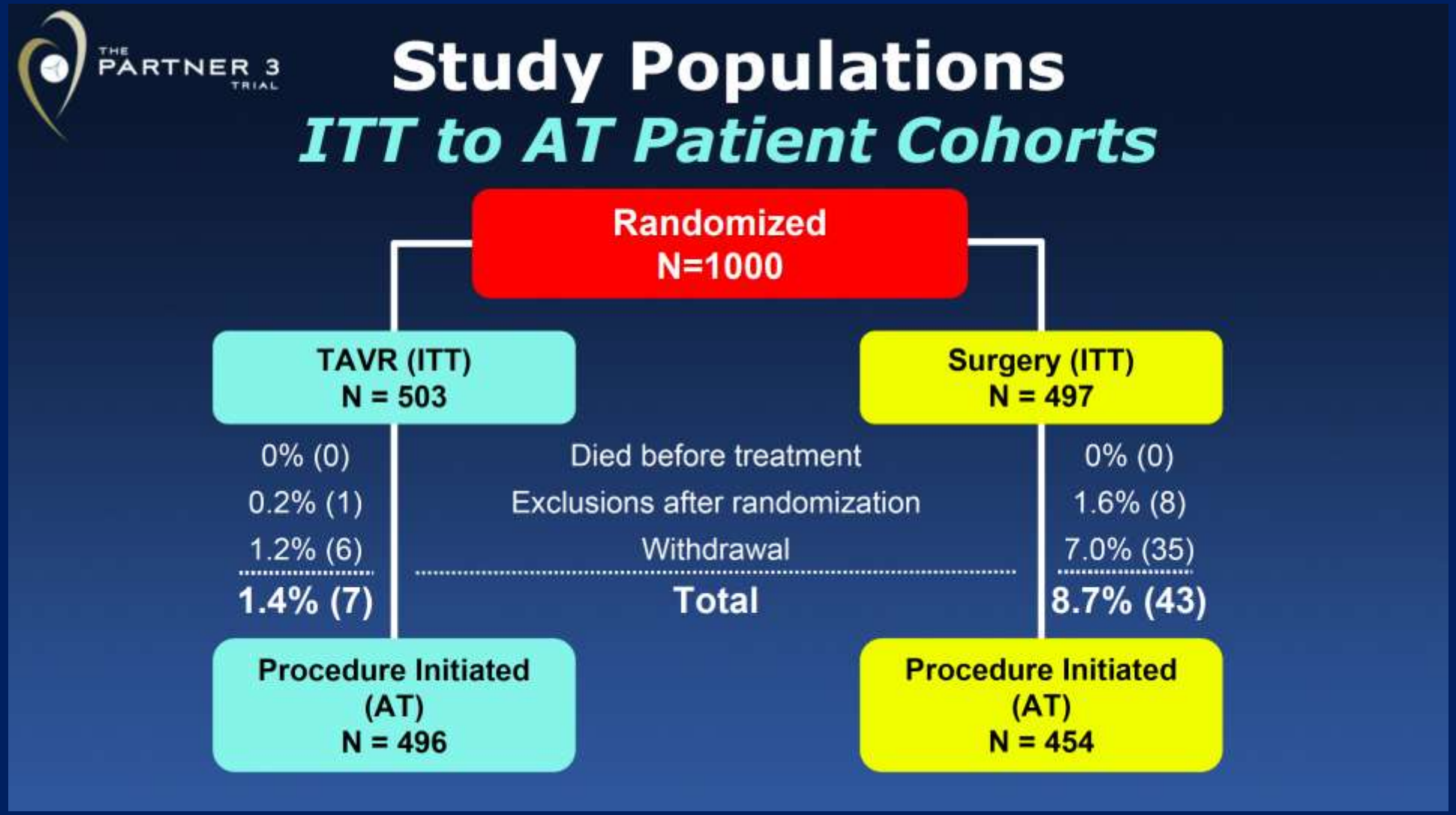
Study Methodology

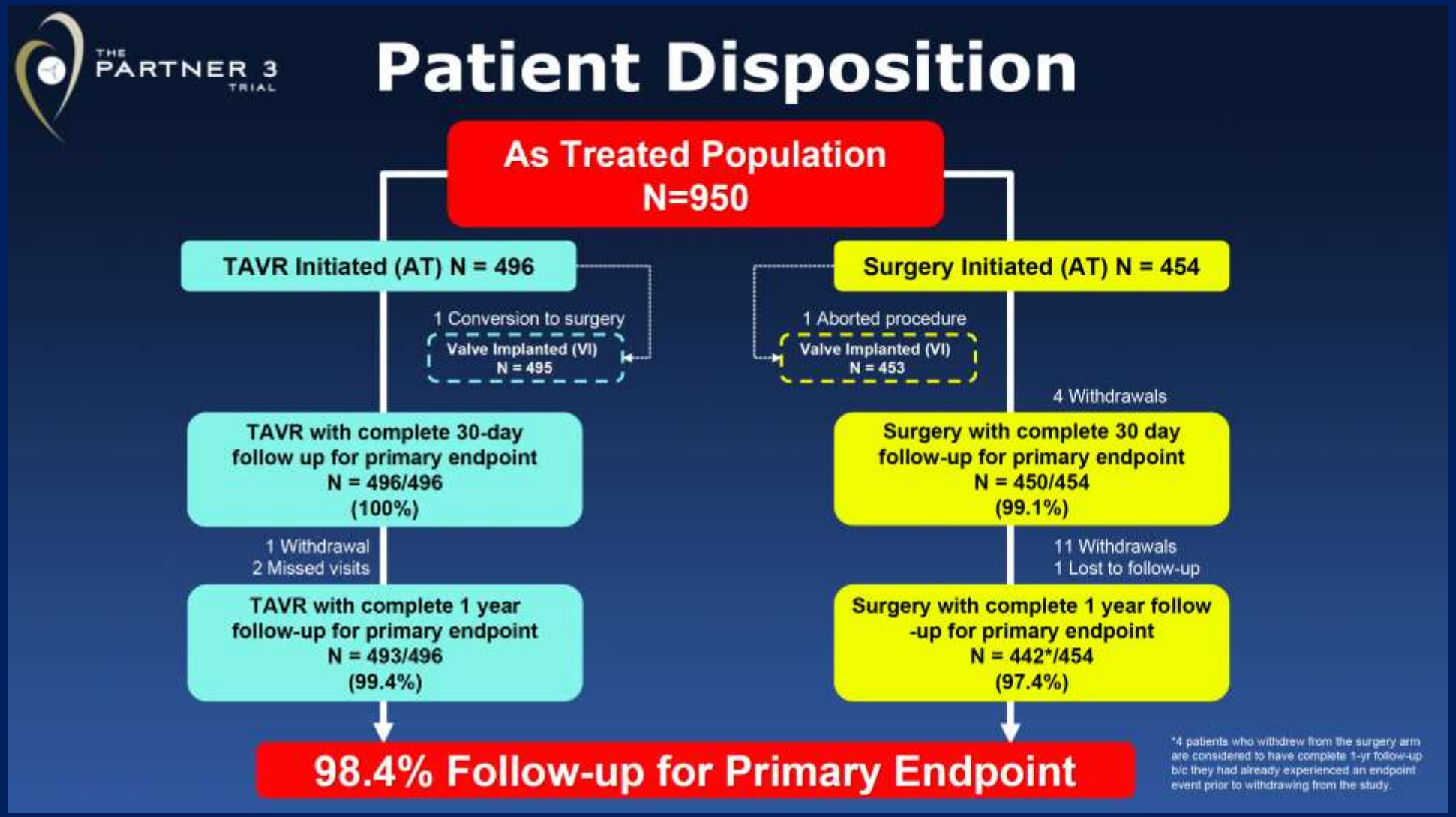
- Every patient reviewed (including imaging studies) by multi-disciplinary heart team AND case review board
- Baseline and 30-day neuro assessment in all patients; serial neurologist examinations and neuro-imaging for suspected neuro events
- 3D cardiac imaging (CT or TEE) prior to randomization
- Same day or staged concomitant PCI procedures (or surgery + CABG) were allowed if approved during case review
- 100% CEC adjudication of all major endpoint events (VARC-2 definitions when applicable)
- 10-year clinical and echocardiography follow-up in all patients

Primary Endpoint

- **Non-hierarchical composite of all-cause mortality, all strokes, or CV re-hospitalization at 1 year**
  - § Primary analysis was non-inferiority, followed by superiority
  - § Analysis cohort was the 'as-treated' (AT) population, defined as all randomized patients in whom the procedure was initiated.
  - § Multiple sensitivity analyses performed


THE PARTNER TRIAL
Study Flow and Follow-Up
1520 patients with severe symptomatic AS at low surgical risk consented between March 25, 2016 and October 26, 2017 at 71 sites in the US, Canada, Japan, ANZ
Excluded from Randomization N=520
§ Anatomic exclusions (n=308)
§ Clinical exclusions (n=89)
§ Other exclusions (n=38)
§ Incomplete screening (n=85)
Eligible for Enrollment and Randomized N=1000 at 71 sites
TAVR N=503
Surgery N=497


THE PARTNER 3 TRIAL
Study Populations
ITT to AT Patient Cohorts
Randomized
N=1000
TAVR (ITT)
N = 503
Surgery (ITT)
N = 497
0% (0)
0.2% (1)
1.2% (6)
1.4% (7)
Died before treatment
Exclusions after randomization
Withdrawal
Total
0% (0)
1.6% (8)
7.0% (35)
8.7% (43)
Procedure Initiated
(AT)
N = 496
Procedure Initiated
(AT)
N = 454


THE PARTNER 3 TRIAL
Patient Disposition
As Treated Population
N=950
TAVR Initiated (AT) N = 496
Surgery Initiated (AT) N = 454
1 Conversion to surgery
Valve Implanted (VI)
N = 495
1 Aborted procedure
Valve Implanted (VI)
N = 453
4 Withdrawals
TAVR with complete 30-day follow up for primary endpoint
N = 496/496
(100%)
Surgery with complete 30 day follow-up for primary endpoint
N = 450/454
(99.1%)
1 Withdrawal
2 Missed visits
11 Withdrawals
1 Lost to follow-up
TAVR with complete 1 year follow-up for primary endpoint
N = 493/496
(99.4%)
Surgery with complete 1 year follow -up for primary endpoint
N = 442*/454
(97.4%)
98.4% Follow-up for Primary Endpoint
*4 patients who withdrew from the surgery arm are considered to have complete 1-yr follow-up b/c they had already experienced an endpoint event prior to withdrawing from the study.

Baseline Patient Characteristics

% or mean ± SD

Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)	Other Co-Morbidities	TAVR (N=496)	Surgery (N=454)
Age (years)	73.3 ± 5.8	73.6 ± 6.1	Diabetes	31.3%	30.2%
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI – kg/m^2	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	1.9 ± 0.7	1.9 ± 0.6	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	27.7%	28.0%	Atrial Fibrillation (h/o)	15.7%	18.8%
Prior CABG	3.0%	1.8%	Permanent Pacemaker	2.4%	2.9%
Prior CVA	3.4%	5.1%	Left Bundle Branch Block	3.0%	3.3%
Peripheral Vascular Disease	6.9%	7.3%	Right Bundle Branch Block	10.3%	13.7%

*p = 0.01

Baseline Echo and CT Characteristics

% or mean ± SD

Characteristic	TAVR (N=496)	Surgery (N=454)
Aortic Valve Area (cm^2)	0.8 ± 0.2	0.8 ± 0.2
Mean Gradient (mmHg)	49.4 ± 12.8	48.3 ± 11.8
LVEF (%)	65.7 ± 9.0	66.2 ± 8.6
LV Mass Index (g/m^2)	104.5 ± 25.7	101.5 ± 25.4
≥ Moderate MR	1.3%	3.2%
≥ Moderate AR	3.9%	2.5%
≥ Moderate TR	1.7%	2.3%
CT – Annulus Perimeter (mm)	78.1 ± 6.9	78.6 ± 7.2
CT – Annulus Area (mm^2)	473.5 ± 83.3	479.6 ± 87.6

Procedural & Hospital Findings

% or mean ± SD

Variable	TAVR (N=496)	Surgery (N=454)	P-value
Conscious Sedation	65.1%	NA	NA
Procedure Time (min)	58.6 ± 36.5	208.3 ± 62.2	<0.001
Fluoroscopy Time (min)	13.9 ± 7.1	NA	NA
Aortic Cross-Clamp Time (min)	NA	74.3 ± 27.8	NA
Total CPB Time (min)	NA	97.7 ± 33.8	NA
Median ICU Stay (days)	2.0	3.0	<0.001
Median Total LOS (days)	3.0	7.0	<0.001
Discharge to Home/Self-care	96.0%	73.1%	<0.001
Concomitant Procedures	7.9%	26.4%	<0.001

THE PARTNER TRIAL Procedural Complications

In-Hospital

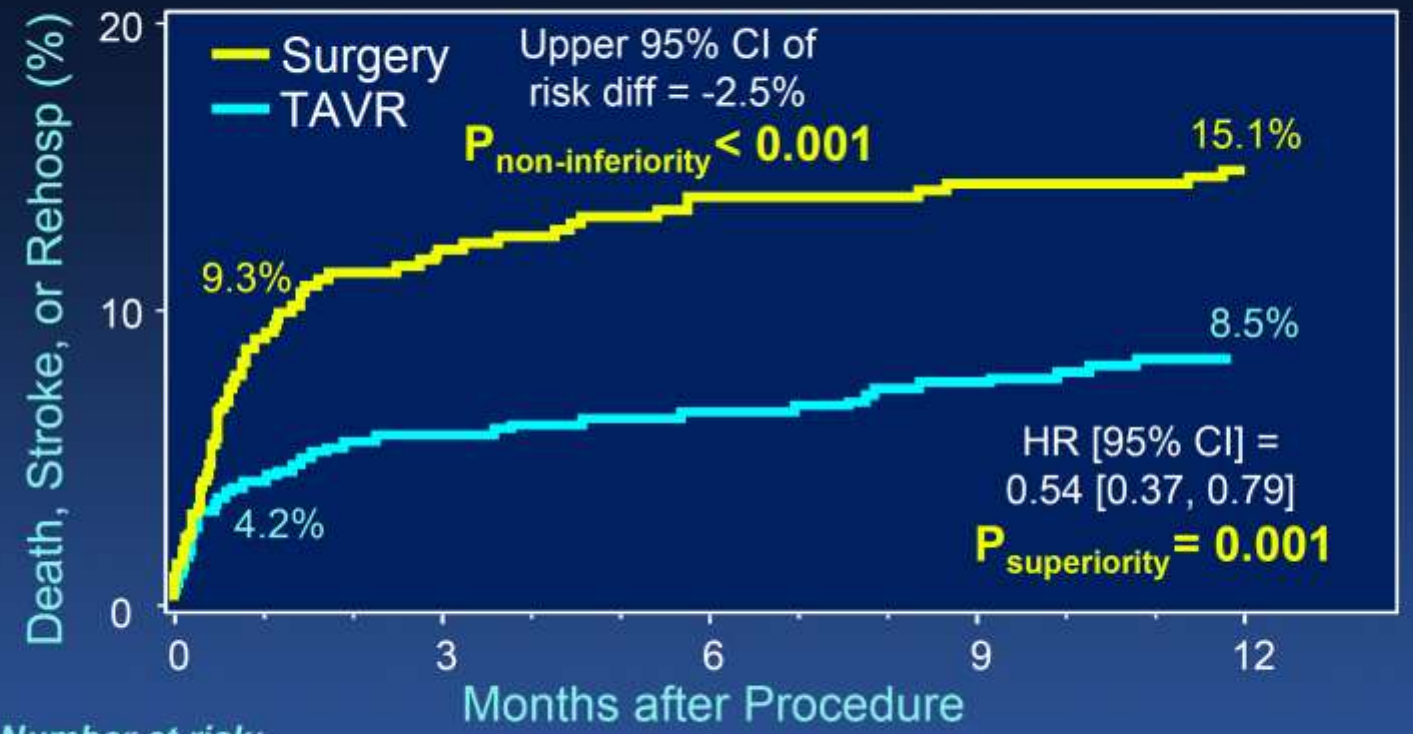
% or mean ± SD

Complication	TAVR (N=496)	Surgery (N=454)	P-value
In-hospital Death	0.4% (2)	0.9% (4)	0.43
≥ 2 Transcatheter Valves Implanted*	0.2% (1)	NA	NA
Valve Embolization	0	NA	NA
Aortic Dissection	0	NA	NA
Annular Rupture	0.2% (1)	NA	NA
Ventricular Perforation	0.2% (1)	0.4% (2)	0.61
Coronary Obstruction	0.2% (1)	0.4% (2)	0.61
Access Site Infections	0.4% (2)	1.3% (6)	0.16

*Valve-in-valve

THE PARTNER 3 TRIAL

Primary Endpoint

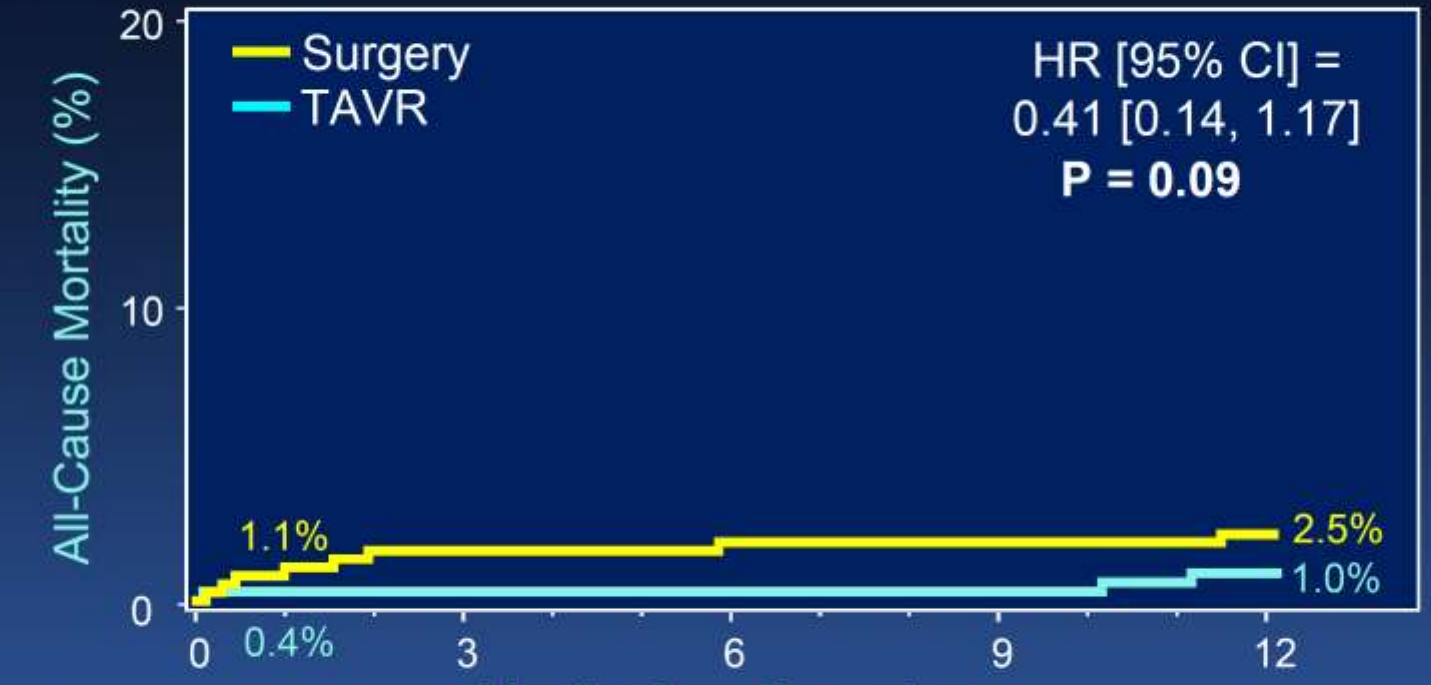


Number at risk:

Surgery	454	408	390	381	377	374
TAVR	496	475	467	462	456	451

THE PARTNER 3 TRIAL

All-Cause Mortality

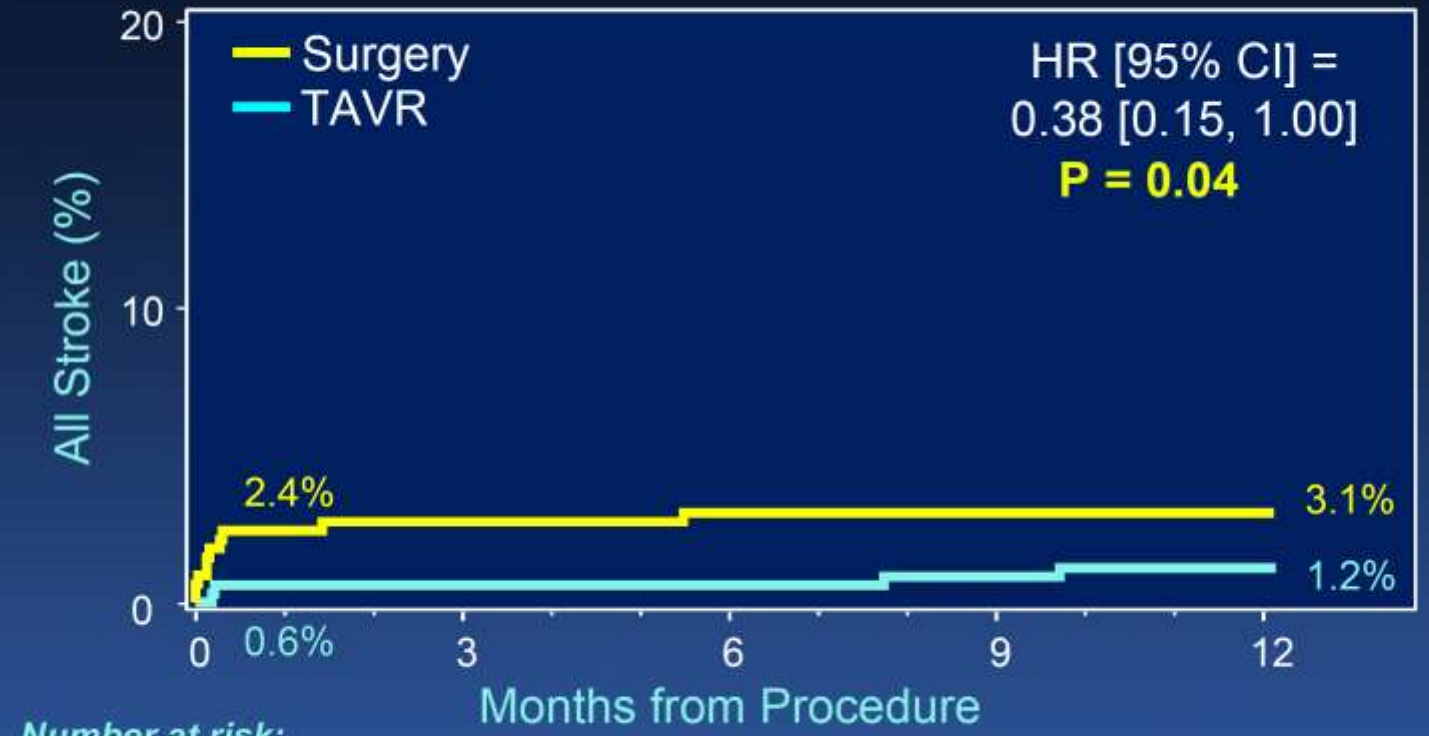


Number at risk:

Surgery	454	445	438	433	431	427
TAVR	496	494	494	493	492	488

THE PARTNER 3 TRIAL

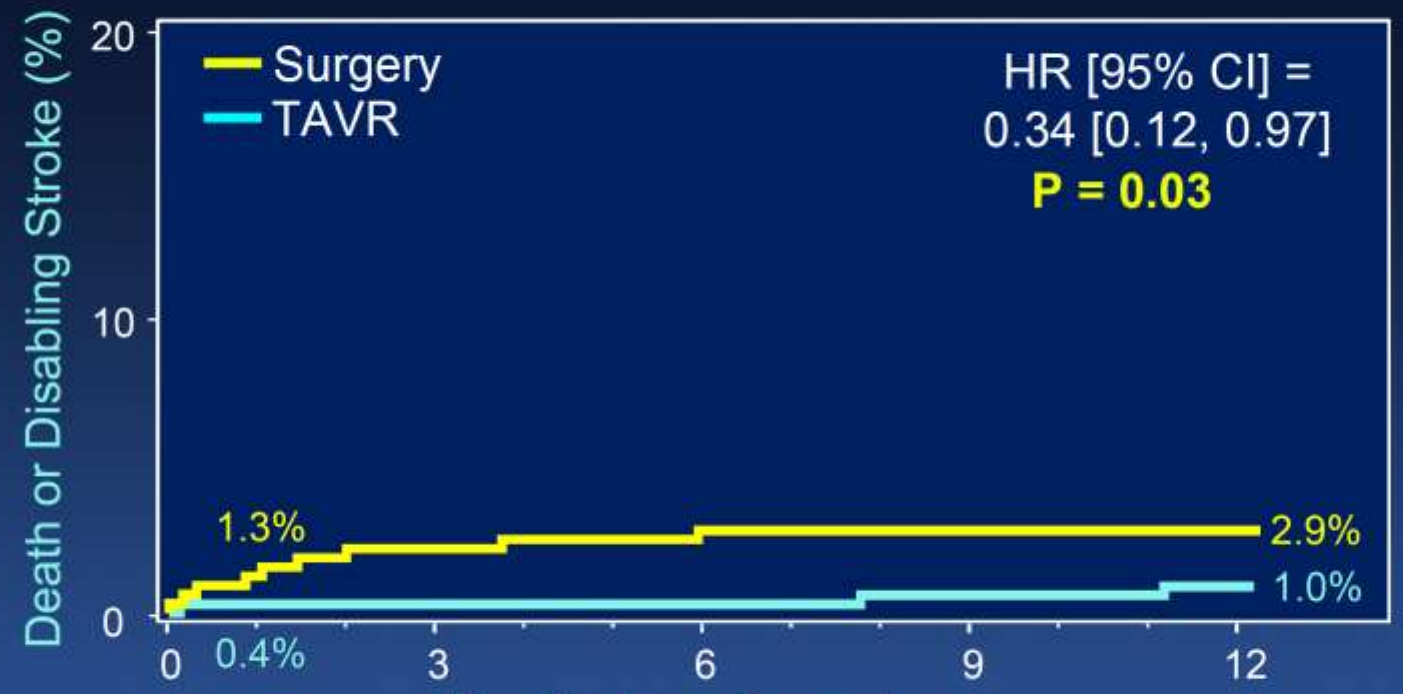
All Stroke



Number at risk:

Surgery	454	435	427	423	421	417
TAVR	496	491	491	489	487	484

THE PARTNER TRIAL Death or Disabling Stroke

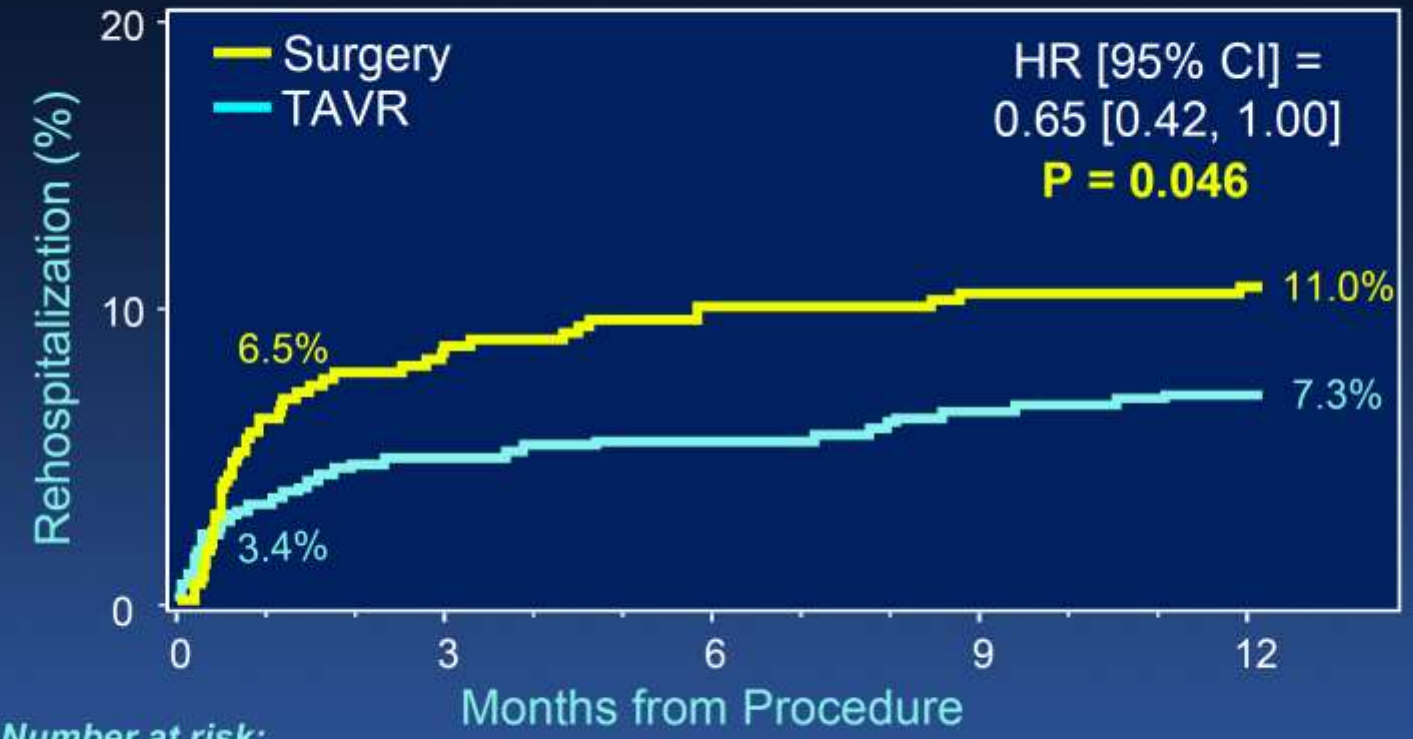


Number at risk:

Surgery	454	444	436	432	430	426
TAVR	496	494	494	493	491	488

THE PARTNER 3 TRIAL

Rehospitalization

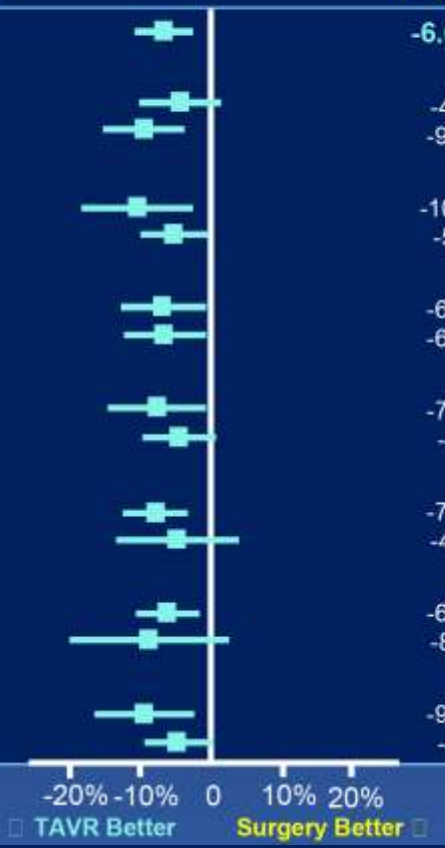


Number at risk:

Surgery	454	416	399	389	385	382
TAVR	496	477	469	465	459	453

Primary Endpoint - Subgroup Analysis

Subgroup	TAVR	Surgery	Diff [95% CI]	P-value*
Overall	**8.5**	**15.1**	**-6.6 [-10.8, -2.5]**	
Age				
≤ 74 (n=516)	10.6	14.9	-4.3 [-10.1, 1.5]	**0.21**
> 74 (n=434)	5.8	15.3	-9.5 [-15.3, -3.7]	
Sex				
Female (n=292)	8.1	18.5	-10.4 [-18.3, -2.5]	**0.27**
Male (n=658)	8.7	13.8	-5.1 [-9.9, -0.3]	
STS Score				
≤ 1.8 (n=464)	9.1	15.7	-6.7 [-12.6, -0.7]	**0.98**
> 1.8 (n=486)	8.0	14.5	-6.5 [-12.2, -0.8]	
LV Ejection Fraction				
≤ 65 (n=384)	9.6	17.2	-7.6 [-14.5, -0.7]	**0.48**
> 65 (n=524)	8.0	12.4	-4.4 [-9.6, 0.7]	
NYHA Class				
I/II (n=687)	6.8	14.5	-7.8 [-12.4, -3.2]	**0.54**
III/IV (n=263)	12.3	16.9	-4.7 [-13.5, 4.1]	
Atrial Fibrillation				
No (n=786)	7.9	14.0	-6.1 [-10.5, -1.7]	**0.67**
Yes (n=163)	11.6	20.3	-8.7 [-19.9, 2.5]	
KCCQ Overall Summary Score				
≤ 70 (n=407)	10.5	19.9	-9.4 [-16.5, -2.4]	**0.27**
> 70 (n=536)	6.5	11.2	-4.6 [-9.4, 0.2]	



Event rates are KM estimates (%)

* P-value is for interaction

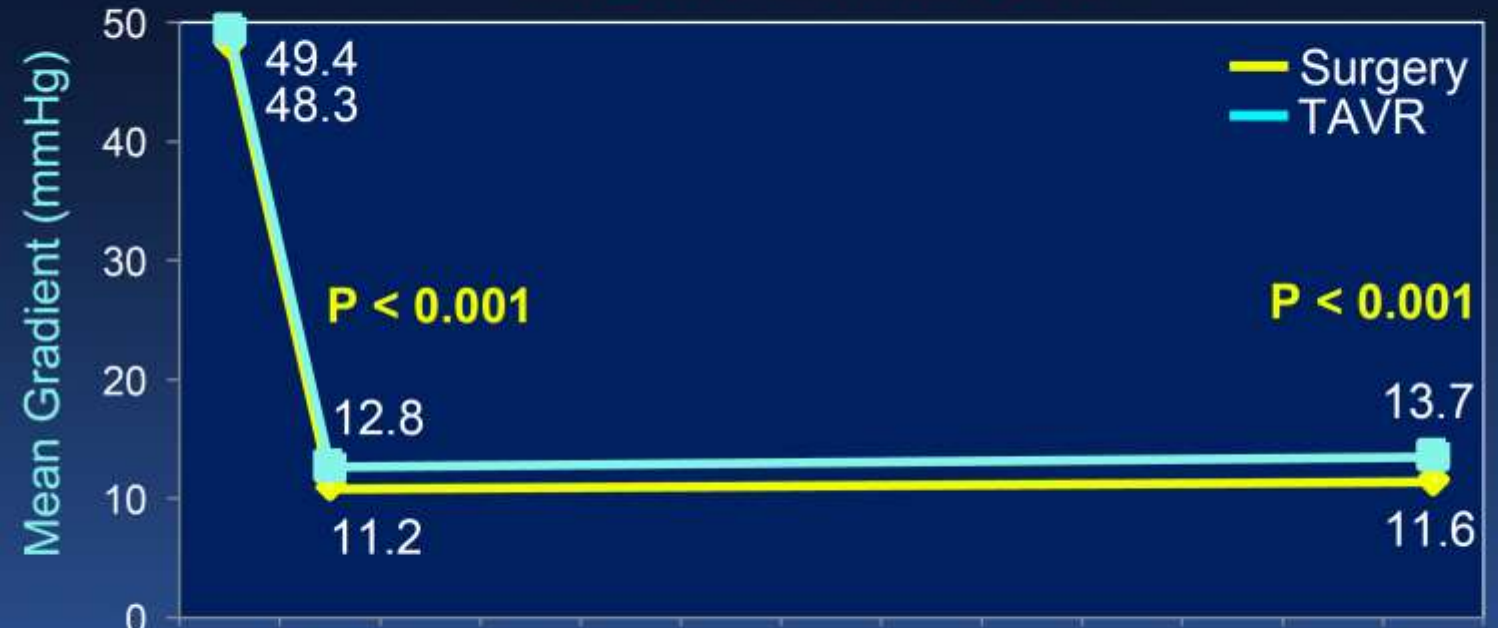
Other Secondary Endpoints

Outcomes	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
Bleeding - Life-threat/Major	3.6% (18)	24.5% (111)	<0.001	7.7% (38)	25.9% (117)	<0.001
Major Vascular Complics	2.2% (11)	1.5% (7)	0.45	2.8% (14)	1.5% (7)	0.19
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21
New LBBB	22.0% (106)	8.0% (35)	<0.001	23.7% (114)	8.0% (35)	<0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0% (0)	0% (0)	NA	0.6% (3)	0.5% (2)	0.76
Endocarditis	0% (0)	0.2% (1)	0.29	0.2% (1)	0.5% (2)	0.49
Asymp Valve Thrombosis	0.2% (1)	0% (0)	0.34	1.0% (5)	0.2% (1)	0.13

Event rates are KM estimates (%) and p-values are based on Log-Rank test
* Event rates are incidence rates and p-value is Fisher's Exact test

Echocardiography Findings

Mean Gradient

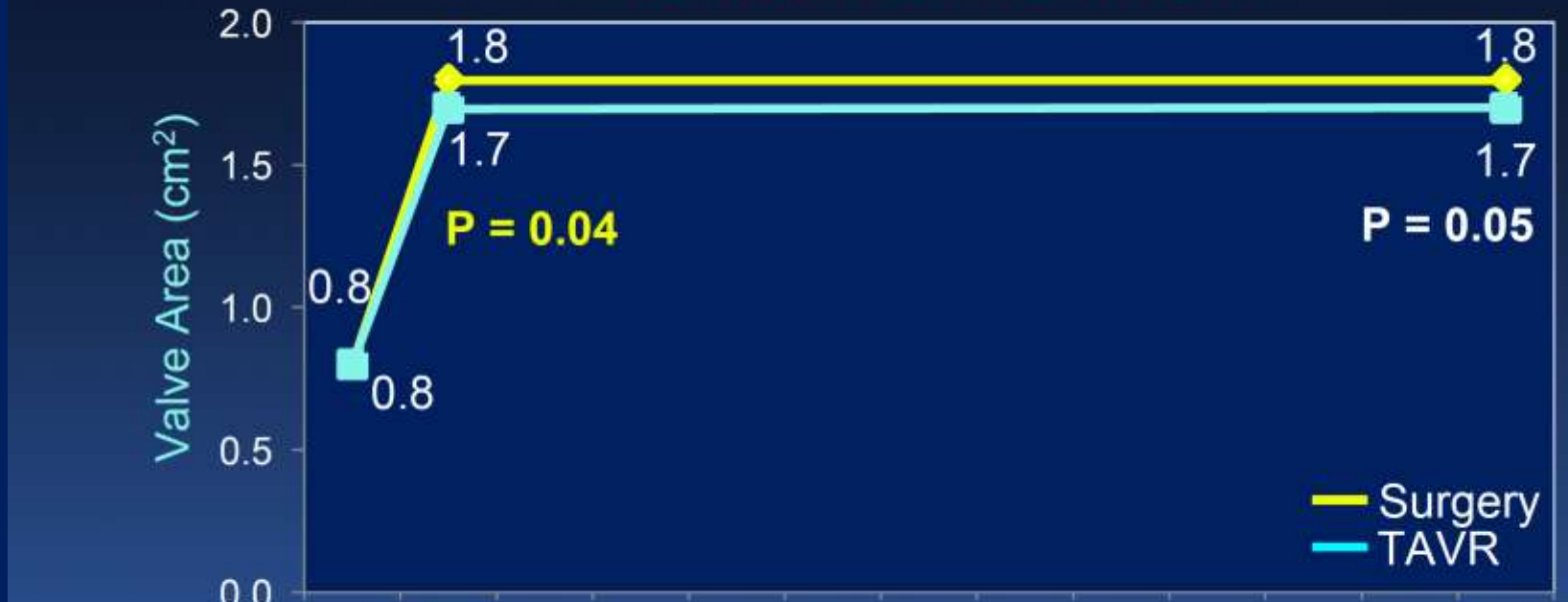


No. of Echos			
Surgery	441	426	390
TAVR	483	490	469

P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

Echocardiography Findings

Aortic Valve Area



No. of Echos	Baseline	30D	1 Year
Surgery	423	395	371
TAVR	458	470	446

P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

The PARTNER 3 Trial
Study Limitations

- Results only reflect 1-year outcomes; long-term assessment of structural valve deterioration is required
  - § 10-year clinical and echocardiographic FU planned in all patients
- Results only apply to the enrolled AS population (e.g. bicuspid aortic valves, non-suitable for TF, and complex CAD excluded)

The PARTNER 3 Trial
Conclusions (1)

In a population of severe symptomatic aortic stenosis patients who were at low surgical risk, TAVR (using the SAPIEN 3 valve) compared to surgery:

- Significantly reduced the primary endpoint of death, stroke, or rehospitalization by 46% at 1-year.
  - § Components of the primary endpoint favored TAVR, both at 30 days and 1 year
  - § Multiple sensitivity analyses confirmed robustness of the primary endpoint findings

The PARTNER 3 Trial
Conclusions (2)

- Secondary endpoints adjusted for multiple comparisons indicated that TAVR reduced new-onset AF, index hospitalization days, and a measure of poor treatment outcome (death or low KCCQ score at 30 days).
- Other secondary endpoint analyses also showed reduced bleeding after TAVR and no differences in the need for new permanent pacemakers, major vascular complications, coronary obstruction, and mod-severe PVR.
- Some secondary endpoints favored surgery, including reduced new LBBB, reduced mild PVR, and lower aortic valve gradients.

The PARTNER 3 Trial
Conclusions (3)

- TAVR had more rapid post-procedure improvement in patient-oriented functional indices, including NYHA class, 6-minute walking distance, and KCCQ scores.

The PARTNER 3 Trial
Clinical Implications

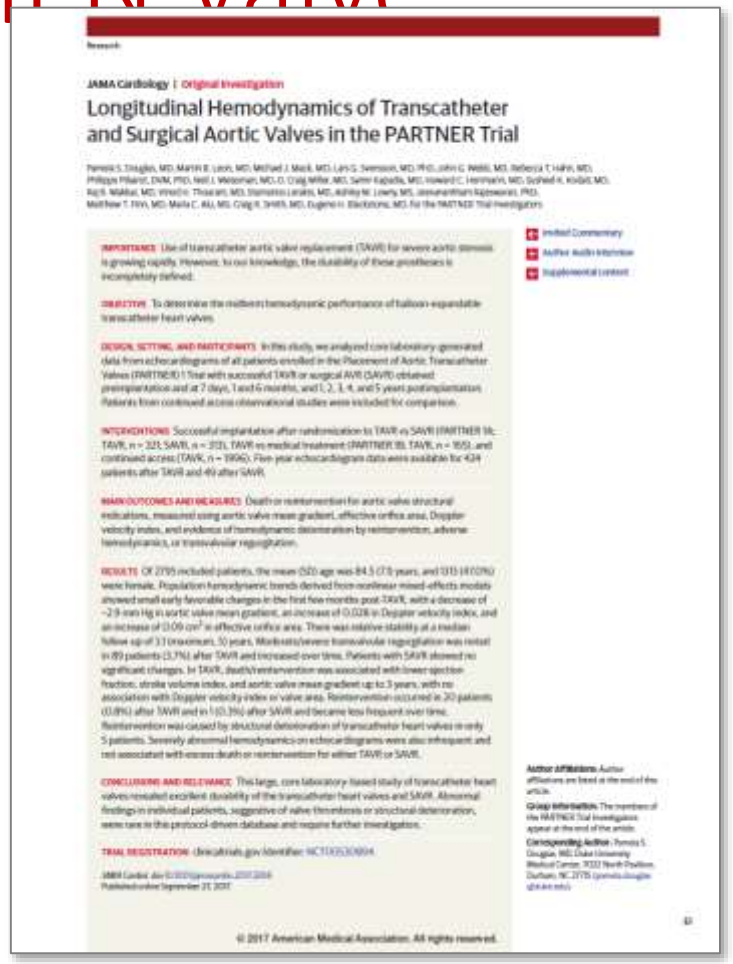
- *Based upon these findings, TAVR, through 1-year, should be considered the preferred therapy in low surgical risk aortic stenosis patients!*
- *PARTNER randomized trials over the past 12 years, clearly indicate that the relative value of TAVR compared with surgery is independent of surgical risk profiles.*
- *The choice of TAVR vs. surgery in aortic stenosis patients should be a shared-decision making process, respecting patient preferences, understanding knowledge gaps (esp. in younger patients), and considering clinical and anatomic factors.*

TAVR 5-Year Clinical Results

Douglas, et al. Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trail. JAMA Cardiol 2017

Echo Analysis Demonstrates Excellent Mid-term Durability of the SAPIEN Valve

- 2482 TAVR patients in the PARTNER I trial
  - largest, core-lab based study of transcatheter heart valves
- Excellent mid-term durability of the SAPIEN transcatheter heart valve
  - comparable to surgical bioprostheses
- Five (0.2%) TAVR patients received a reoperation as a result of structural valve deterioration at 5 years

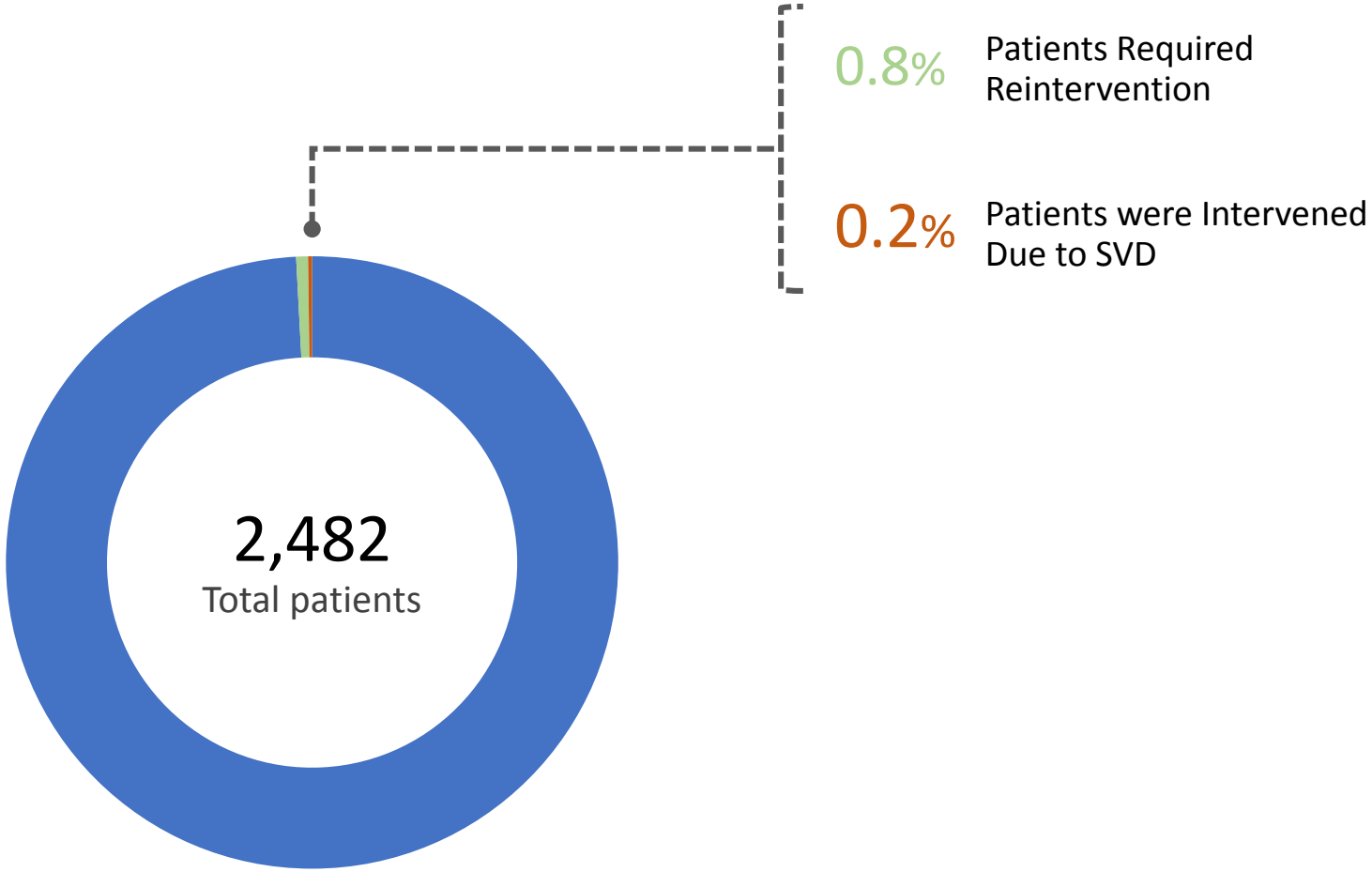


JAMA Cardiology | Original Investigation

Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trial

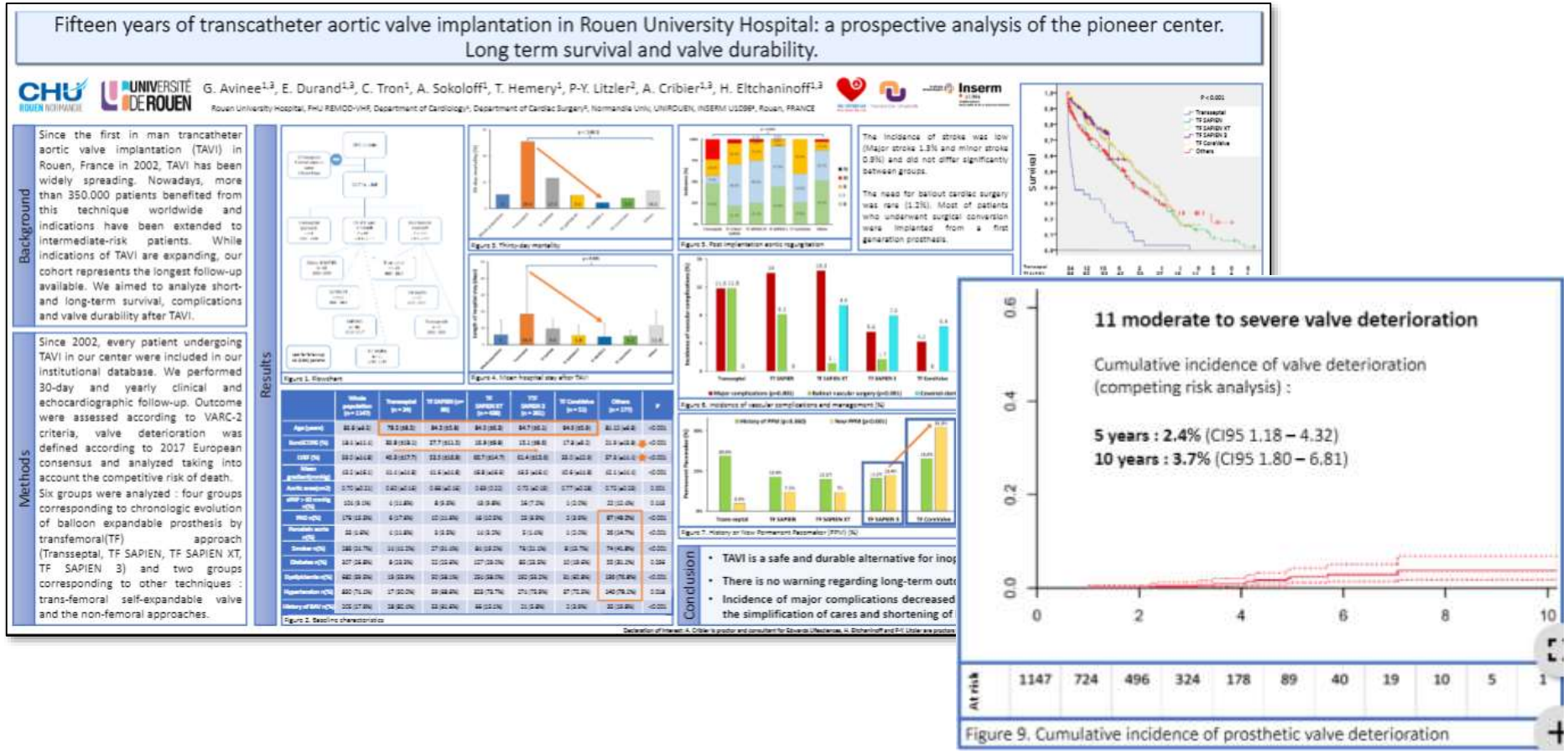
*Douglas, et al. Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trail JAMA Cardiol 2017

Low Rates of Reintervention for SVD Through 5 Years



Douglas, et al. Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trail JAMA Cardiol 2017

15-year TAVR Experience – Rouen (Cribier)



Summary

- TAVR is first line treatment of choice for most patients in the Intermediate, high and extreme risk cohort
- Durability is similar to reported SAVR experience
- Low risk trial results will shift more patients to TAVR, especially with its association with early discharge and a clear economic advantage
- Simplicity and predictability of the Sapien 3 platform has made a major impact on this therapy area and it continues to evolve further

Changing algorithm ?