TAVR with the SAPIEN 3 Valve

See the Clinical Difference

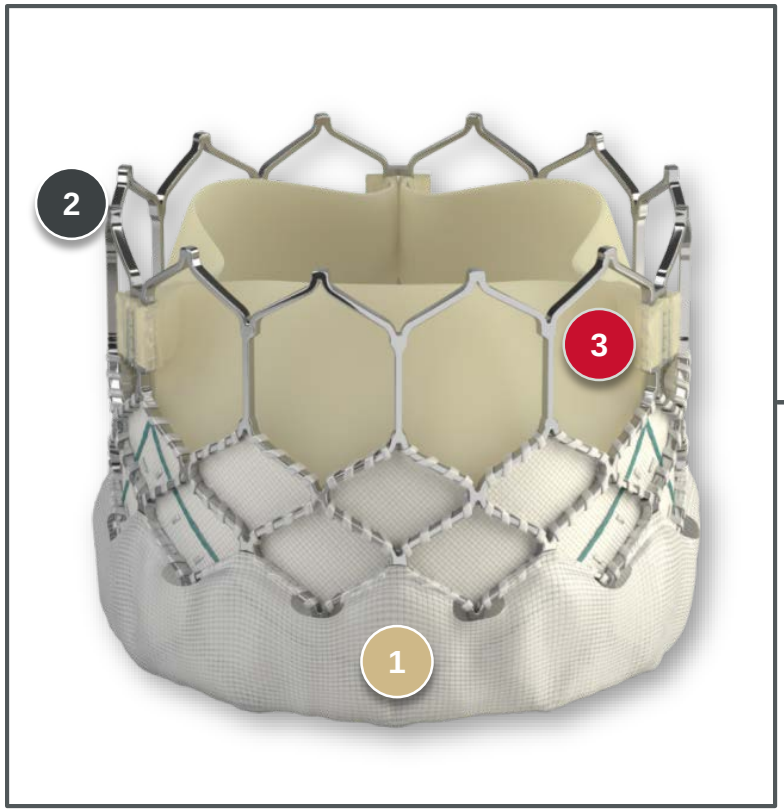
Name:

Title:

Date:

Edwards

SAPIEN 3 Valve



1 **Outer Sealing Skirt**

- Designed to minimize paravalvular (PV) leak

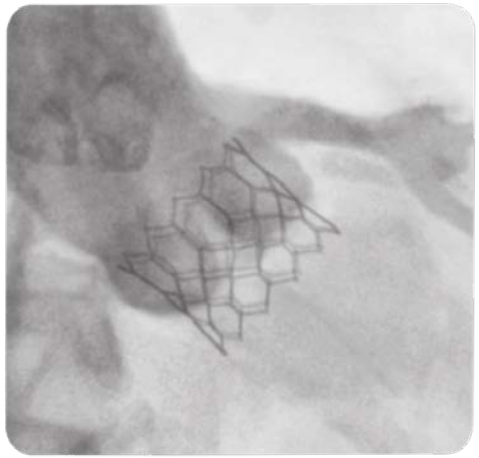
2 **Frame Design**

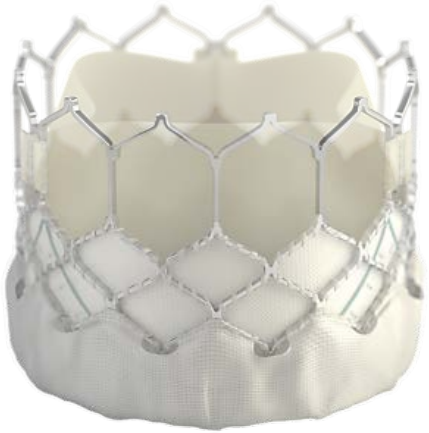
- Enhanced frame geometry for low delivery profile
- Cobalt-chromium

3 **Bovine Pericardial Tissue**

Addition of Outer Sealing Skirt Designed to Minimize PV Leak

Polyethylene Terephthalate (PET) Inner and Outer Sealing Skirt





Inner skirt covers ~1/2 of valve

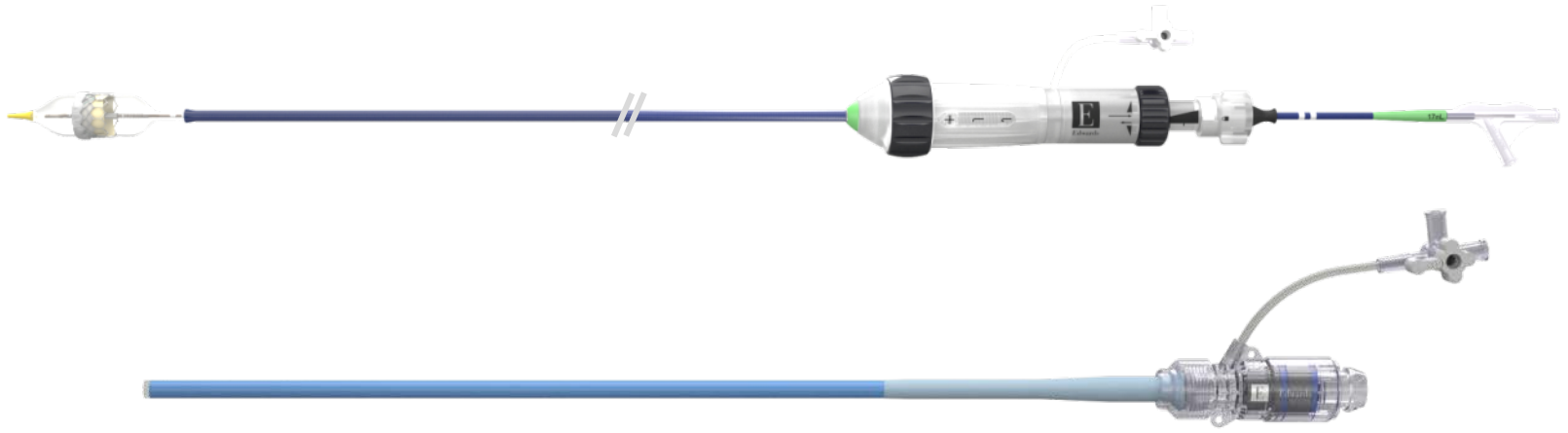
Outer skirt covers ~1/3 of valve

Outer sealing skirt virtually eliminates moderate or greater PV leak*

*The PARTNER II trial intermediate-risk cohort for TAVR with the SAPIEN 3 valve, core lab assessed paravalvular leak, n = 992.

Low Profile Demonstrates Significant Reduction in Major Vascular Complications*

Low Profile 14F / 16F eSheath Introducer Sheath Compatible



SAPIEN 3 Valve Size	20 mm	23 mm	26 mm	29 mm
Edwards eSheath Introducer Set	14F	14F	14F	16F
Minimum Access Vessel Diameter	5.5 mm	5.5 mm	5.5 mm	6.0 mm

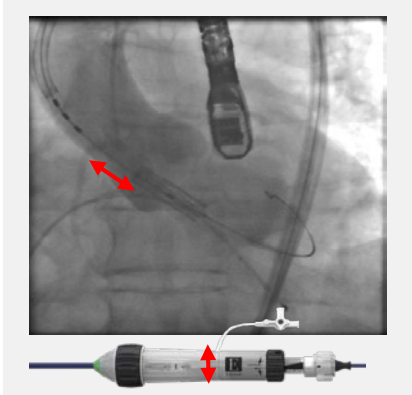
*The PARTNER II S3i trial intermediate-risk SAPIEN 3 valve cohort (VARC II) versus the PARTNER IIA trial intermediate-risk SAPIEN XT valve cohort (VARC I) 30-day unadjusted results.

Optimal Initial Valve Positioning Using Fine Control Features of Edwards Commander Delivery System

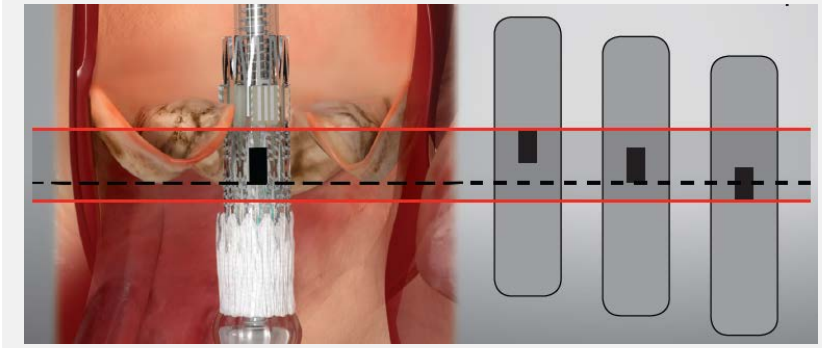
Edwards Commander Delivery System

Dual Articulation

+



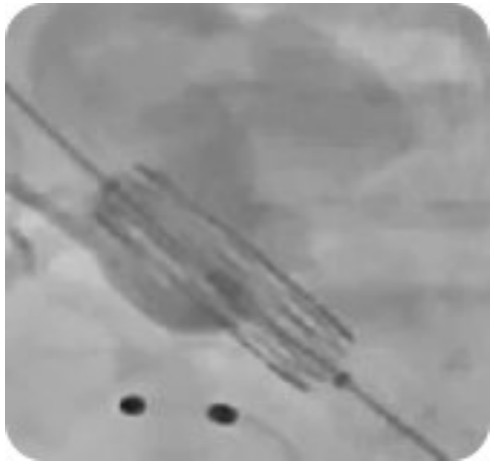
Fine Positioning



Optimal Center Marker Zone (6 mm)

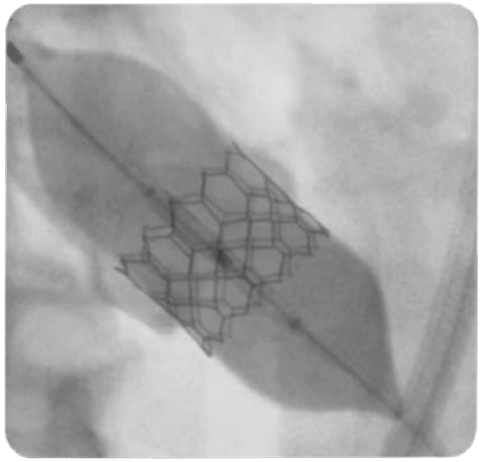
Designed for Precise Deployment and Positioning

Initial Positioning



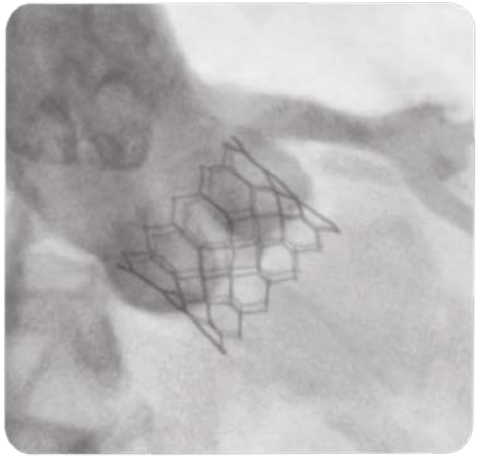
Use Center Marker and fine positioning feature

Deployment



Slow, controlled initial inflation using nominal volume

Final Placement



Precise placement

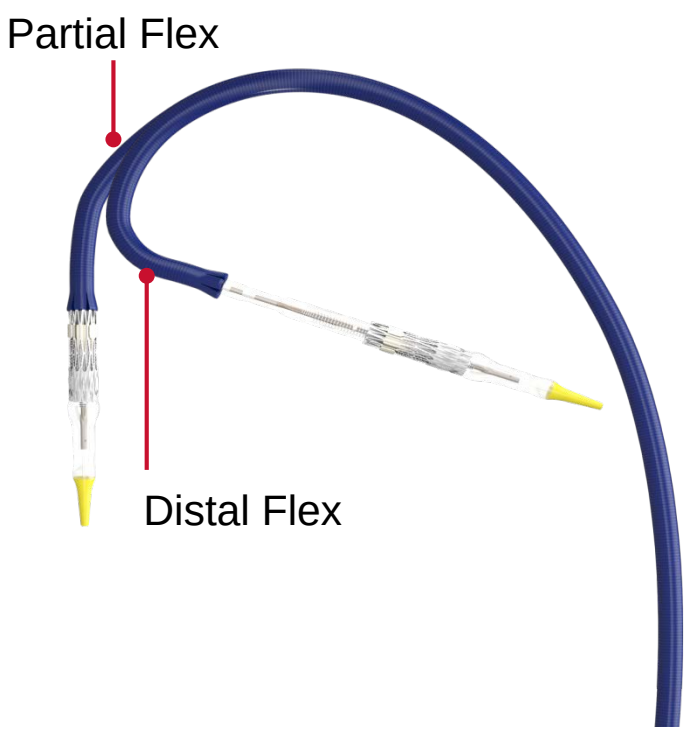
Over 99% of valves placed in the intended location*

*PARTNER II trial intermediate-risk SAPIEN 3 valve cohort.

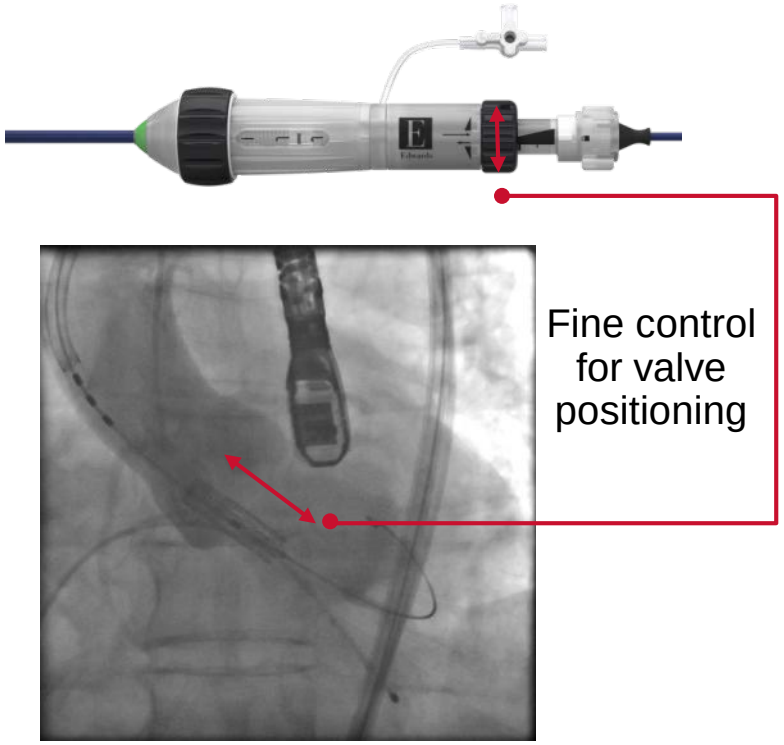
Edwards Commander Delivery System

Dual articulation for coaxiality

Added distal flex to help cross in a variety of anatomies



Improved control and precise valve positioning



Complete Range of Valve Sizes Expands the Treatable Patient Population

Valve Size	20 mm	23 mm	26 mm	29 mm
Native Annulus Size by TEE	16–19 mm	18–22 mm	21–25 mm	24–28 mm
Native Annulus Area (CT)	273–345 mm^2	338–430 mm^2	430–546 mm^2	540–683 mm^2
Area-derived Diameter (CT)	18.6–21 mm	20.7–23.4 mm	23.4–26.4 mm	26.2–29.5 mm

SAPIEN 3 Valve Indication

- The Edwards SAPIEN 3 transcatheter heart valve is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a Heart Team, including a cardiac surgeon, to be at **intermediate or greater risk for open surgical therapy** (i.e., **predicted risk of surgical mortality ≥ 3% at 30 days**, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).
- The SAPIEN 3 valve is also indicated for patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic or mitral valve who are judged by a Heart Team, including a cardiac surgeon, to be at **high or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 8% at 30 days**, based on the STS risk score and other clinical comorbidities unmeasured by the STS risk calculator).

Transcatheter Aortic Valve Replacement (TAVR) with the SAPIEN 3 Valve Compared with Surgery in Intermediate-Risk Patients: A Propensity Score Analysis

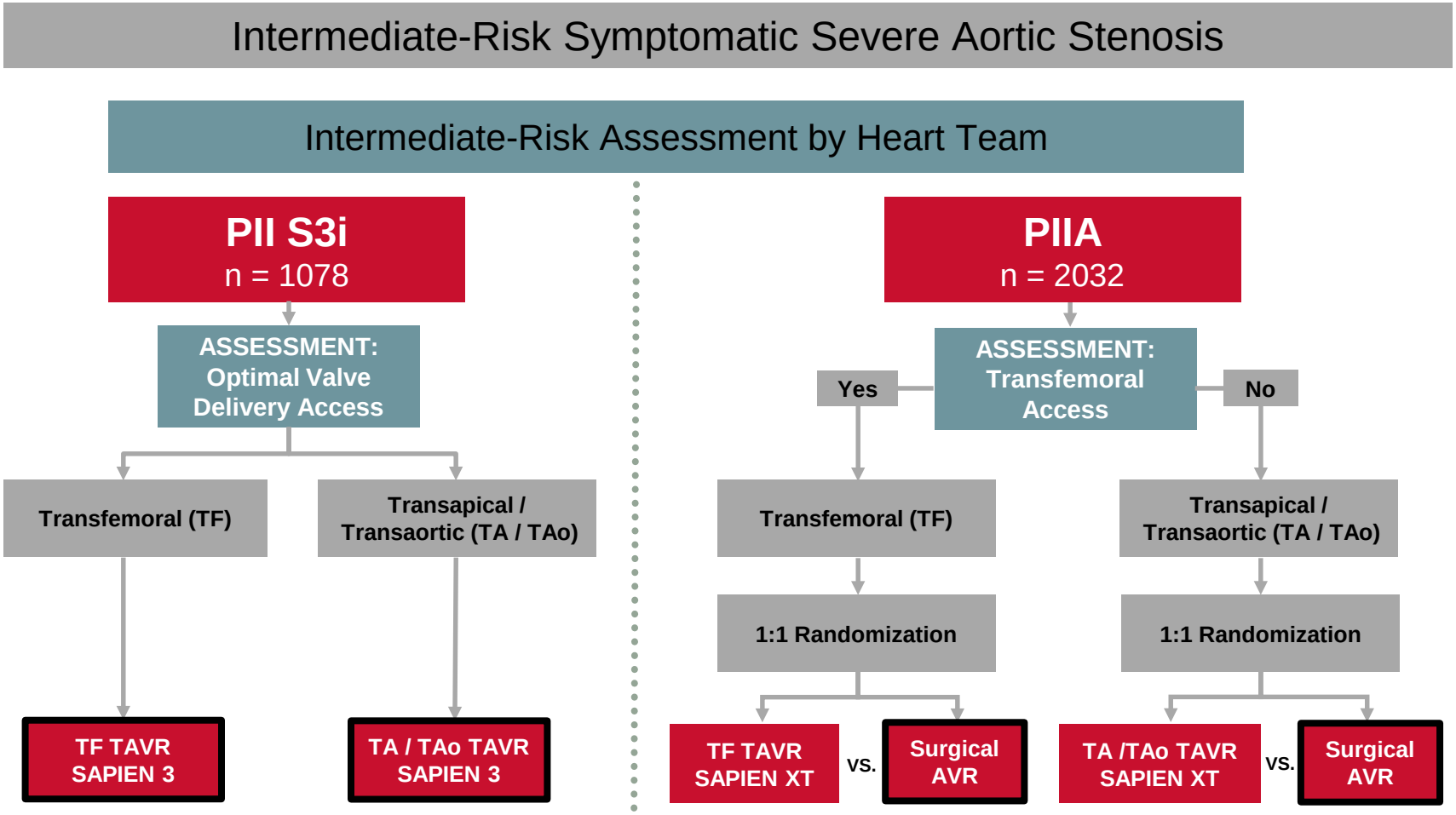
Purpose

- To evaluate the 1-year clinical and echo outcomes of TAVR with the SAPIEN 3 valve in intermediate-risk patients
- To compare these intermediate-risk patient outcomes with surgery results in similar intermediate-risk patients from the PARTNER IIA trial using a **pre-specified propensity score analysis**

The PARTNER II S3i Trial
Participating Sites

1,078 Patients Enrolled at 51 US Participating Sites

The PARTNER IIA and S3i Trial
Study Design



Inclusion Criteria

- ***Severe AS:*** Echo-derived AVA ≤ 0.8 cm2 (or AVA index < 0.5 cm2/m2) and mean AVG > 40 mmHg or peak jet velocity > 4.0 m/s

- ***Cardiac Symptoms***: NYHA Functional Class ≥ II

- ***Intermediate Risk:***
  1. Determined by a multi-disciplinary Heart Team
  2. Using a guideline STS between 4–8%*, and
  3. Adjudicated by case review committee

* PARTNER IIA trial used guideline STS ≥ 4%

Key Exclusion Criteria

- ***Anatomic:***
- Aortic annulus diameter < 18 mm or > 28 mm (echo or CT)
- Bicuspid AV or predominant AR (> 3+)
- Severe LV dysfunction (LVEF < 20%)
- Untreated CAD requiring revascularization with either unprotected LM coronary disease or Syntax score > 32
- Pre-existing surgical valve in any position

- ***Clinical:***
- Serum Cr > 3.0 mg/dL or dialysis dependent
- Acute MI within 1 month
- CVA or TIA within 6 months
- Hemodynamic instability
- Life expectancy < 24 months

The PARTNER II S3i Trial
Primary Endpoint

- Non-hierarchical composite **of all-cause mortality, all stroke, and ≥ moderate aortic regurgitation at one year**
- Propensity score analysis of the valve implant (VI) populations from S3i compared to the surgical arm of the PARTNER IIA trial
- All patients followed for at least 1 year
- Event rates by Kaplan-Meier estimates
- Non-inferiority trial design

Study Methodology

- Every patient reviewed (including imaging studies) by multi-disciplinary Heart Team AND case review committee
- Systematic assessment before and after index procedures for ascertainment of neurologic events
- MDCT evaluation of annulus dimensions for all TAVR S3i patients (with core laboratory analyses)
- In patients with CAD requiring revascularization: treatment (PCI or CABG) allowed (unless unprotected left main disease or Syntax score > 32) at the discretion of the Heart Team
- CEC adjudication of major clinical events (VARC 2 definitions whenever possible)

Baseline Patient Characteristics
Demographics (AT)

Characteristic	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)	p-value
Age (years)	81.9 ± 6.6	81.6 ± 6.8	0.23
Male (%)	61.7	55.0	0.002
BMI – kg/m^2	28.7 ± 6.1	28.4 ± 6.2	0.32
Median STS Score (%)	5.2 [4.3, 6.3]	5.4 [4.4, 6.7]	0.0002
NYHA Class III or IV (%)	72.5	76.1	0.07

Mean ± SD, median [IQR]

Baseline Patient Characteristics
Other Co-morbidities (AT)

Characteristic (%)	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)	p-value
CAD	69.6	66.5	0.14
Previous CABG	27.9	25.7	0.27
Cerebrovascular Disease	9.0	10.3	0.36
PVD	28.2	32.2	0.05
COPD	30.0	30.2	0.92
Cr Level > 2 mg/dL	7.5	5.4	0.06
Atrial Fibrillation	36.0	34.9	0.61
Permanent Pacemaker	13.2	12.0	0.42
15 ft Walk Test > 7s	41.3	45.7	0.06

Quintile Propensity Score Analysis
Primary Endpoint

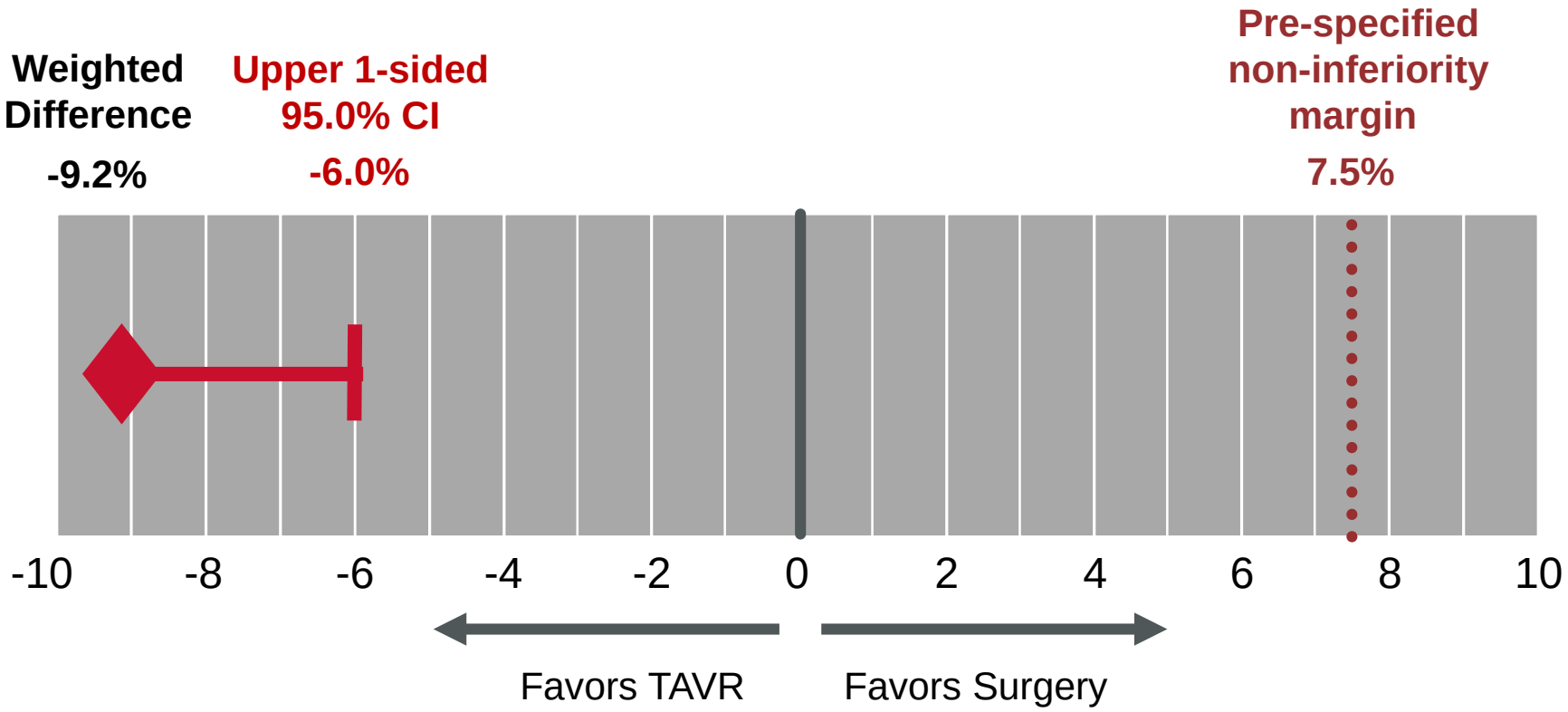
Surgery		TAVR			
Number of Patients	Mortality, Stroke, AR ≥ Mod	Number of Patients	Mortality, Stroke, AR ≥ Mod	Proportional Difference	Weighting
191	28.3%	138	13.8%	-14.5%	0.14
175	22.9%	171	9.9%	-12.9%	0.18
147	**19.7%**	**197**	**10.7%**	**-9.1%**	**0.20**
126	23.0%	219	14.6%	-8.4%	0.23
108	19.4%	238	15.1%	-4.3%	0.25

Overall weighted difference of proportions

-9.2%

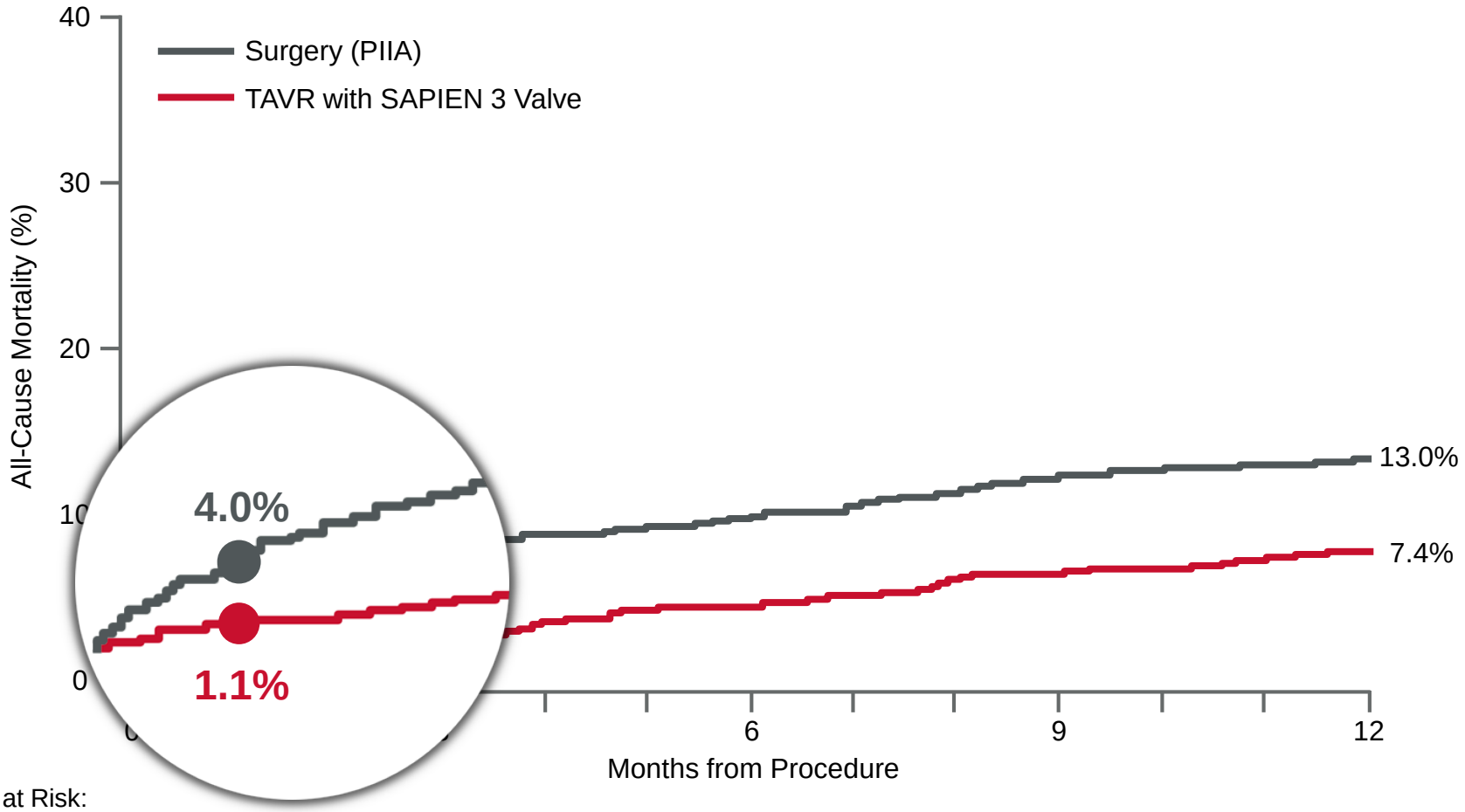
[-12.4%,-6.0%]
Two-sided 90% CI

Primary Endpoint – Non-inferiority Death, Stroke, or AR ≥ Mod at 1 Year (VI)



Primary Non-Inferiority Endpoint Met

All-Cause Mortality*

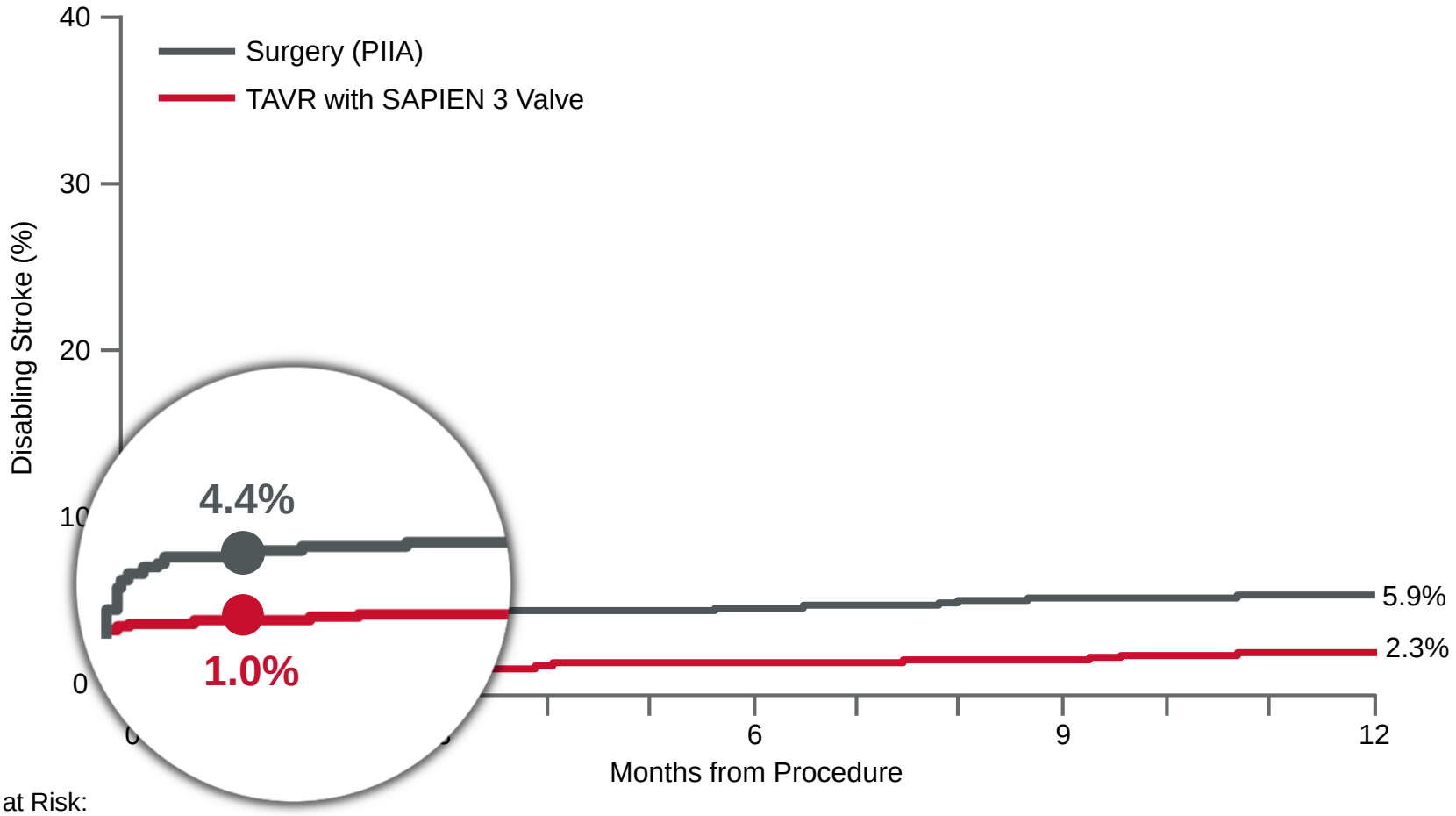


Number at Risk:

Surgery	944	859	836	808	795
SAPIEN 3 TAVR	1077	1043	1017	991	963

*The PARTNER II trial intermediate-risk cohort unadjusted clinical event rates.

Disabling Stroke*



Number at Risk:

Surgery	944	825	806	778	764
SAPIEN 3 TAVR	1077	1033	1008	884	953

*The PARTNER II trial intermediate-risk cohort unadjusted clinical event rates.

Unadjusted Clinical Events
At 30 Days and 1 Year (AT)

Events (%)	30 Days		1 Year	
	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)
Death				
All-Cause	1.1	4.0	7.4	13.0
Cardiovascular	0.9	3.1	4.5	8.1
Neurological Events				
All Stroke	2.7	6.1	4.6	8.2
Disabling Stroke	1.0	4.4	2.3	5.9

KM Estimates

Other Unadjusted Clinical Events
At 30 Days and 1 Year (AT)

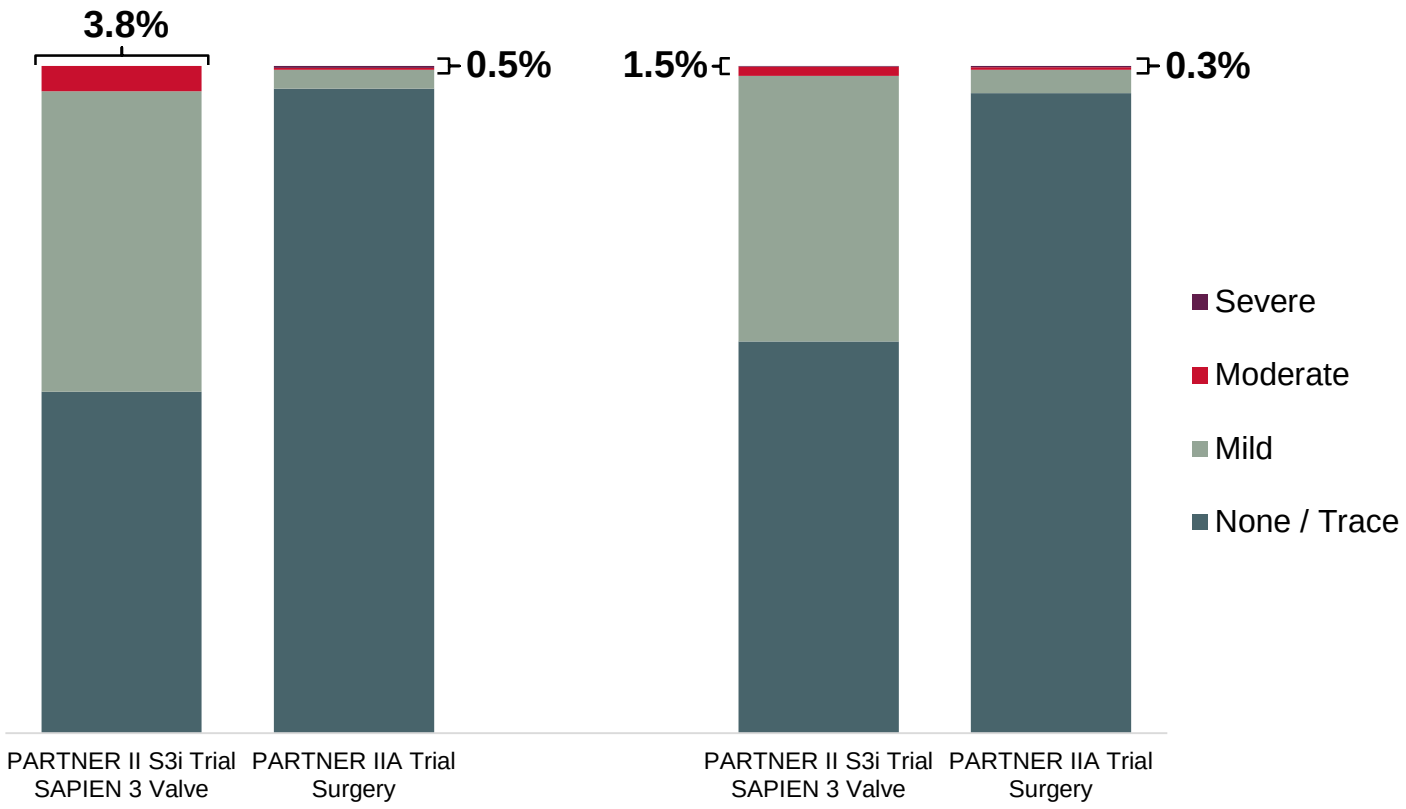
Events (%)	30 Days		1 Year	
	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)
Re-hospitalization	4.6	6.8	11.4	15.1
Myocardial Infarction	0.3	1.9	0.3	3.1
Major Vascular Complication	6.1	5.4	---	---
Life-Threatening / Disabling Bleeding	4.6	46.7	---	---
New Atrial Fibrillation	5.0	28.3	5.9	29.2
New Permanent Pacemaker	10.2	7.3	12.4	9.4
Re-intervention	0.1	0.0	0.6	0.5
Endocarditis	0.2	0.0	0.8	0.7

KM Estimates

Unadjusted Procedural Factors (AT)

	PARTNER II S3i Trial SAPIEN 3 Valve (n = 1,077)	PARTNER IIA Trial Surgery (n = 944)
Mean Total Hospitalization LOS (Days)	5.6	11.9
Mean ICU Stay (Days)	2.7	5.6

Paravalvular Regurgitation (VI)



Number of Echos:		
Surgery	755	610
SAPIEN 3 TAVR	992	875

Key Takeaways

- A propensity score analysis at 1 year demonstrated:
  - Non-inferiority for the primary endpoint (composite of all-cause mortality, all stroke, and AR ≥ moderate)
- TAVR with the SAPIEN 3 valve resulted in low unadjusted clinical event rates of all-cause mortality (1.1%) and disabling stroke (1.0%) at 30 days
  - These rates were 75% lower than surgery

Important Safety Information

Edwards SAPIEN 3 Transcatheter Heart Valve with the Edwards Commander and Certitude Delivery Systems:

Indications: The Edwards SAPIEN 3 transcatheter heart valve, model 9600TFX, and accessories are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a Heart Team, including a cardiac surgeon, to be at intermediate or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 3% at 30 days, based on The Society of Thoracic Surgeons (STS) risk score and other clinical comorbidities unmeasured by the STS risk calculator); and are also indicated for patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic or mitral valve who are judged by a Heart Team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 8% at 30 days, based on the STS risk score and other clinical comorbidities unmeasured by the STS risk calculator).

Contraindications: The valve and delivery systems are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation. There may be an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments in high or greater risk patients. Incorrect sizing of the valve may lead to paravalvular leak, migration, embolization, residual gradient (patient-prosthesis mismatch), and/or annular rupture. Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism. Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve. Caution should be exercised in implanting a valve in patients with clinically significant coronary artery disease. Patients with pre-existing bioprostheses should be carefully assessed prior to implantation of the valve to ensure proper valve positioning and deployment. Do not use the valve if the tamper-evident seal is broken, the storage solution does not completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or if the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting. Valve recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation. Do not add or apply antibiotics to the storage solution, rinse solution, or to the valve. Balloon valvuloplasty should be avoided in the treatment of failing bioprostheses as this may result in embolization of bioprosthesis material and mechanical disruption of the valve leaflets.

Precautions: Safety, effectiveness, and durability have not been established for THV-in-THV procedures. Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve performance. Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Safety Data Sheet available from Edwards Lifesciences. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.

Important Safety Information (cont.)

Precautions (cont.): Additional precautions for transseptal replacement of a failed mitral valve bioprosthesis include the presence of devices or thrombus or other abnormalities in the caval vein precluding safe transvenous femoral access for transseptal approach and the presence of an Atrial Septal Occluder Device or calcium preventing safe transseptal access. Special care must be exercised in mitral valve replacement if chordal preservation techniques were used in the primary implantation to avoid entrapment of the subvalvular apparatus. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: noncalcified aortic annulus; severe ventricular dysfunction with ejection fraction < 20%; congenital unicuspid or congenital bicuspid aortic valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+); pre-existing prosthetic ring in any position; severe mitral annular calcification (MAC); severe (> 3+) mitral insufficiency, or Gorlin syndrome; blood dyscrasias defined as leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesis or coagulopathy; hypertrophic cardiomyopathy with or without obstruction (HOCM); echocardiographic evidence of intracardiac mass, thrombus, or vegetation; a known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately premedicated; significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater, marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe “unfolding” and tortuosity of the thoracic aorta; access characteristics that would preclude safe placement of 14F or 16F Edwards eSheath introducer set, such as severe obstructive calcification, severe tortuosity, or diameter less than 5.5 mm or 6 mm, respectively; excessive calcification at access site; bulky calcified aortic valve leaflets in close proximity to coronary ostia; a concomitant paravalvular leak where the failing bioprosthesis is not securely fixed in the native annulus or is not structurally intact (e.g., wireform frame fracture); or a partially detached leaflet of the failing bioprosthesis that, in the aortic position, may obstruct a coronary ostium. Residual mean gradient may be higher in a THV-in-failing bioprosthesis configuration than that observed following implantation of the valve inside a native aortic annulus using the same size device. Patients with elevated mean gradient post-procedure should be carefully followed. It is important that the manufacturer, model, and size of the pre-existing bioprosthetic valve be determined so that the appropriate valve can be implanted and a prosthesis-patient mismatch is avoided. Additionally, pre-procedure imaging modalities must be employed to make as accurate a determination of the inner diameter as possible.

Potential Adverse Events: Potential risks associated with the overall procedure, including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography: death; stroke/transient ischemic attack, clusters, or neurological deficit; paralysis; permanent disability; respiratory insufficiency or respiratory failure; hemorrhage requiring transfusion or intervention; cardiovascular injury including perforation or dissection of vessels, ventricle, atrium, septum, myocardium, or valvular structures that may require intervention; pericardial effusion or cardiac tamponade; embolization including air, calcific valve material, or thrombus; infection including septicemia and endocarditis; heart failure; myocardial infarction; renal insufficiency or renal failure; conduction system defect which may require a permanent pacemaker; arrhythmia; retroperitoneal bleed; arteriovenous (AV) fistula or pseudoaneurysm; reoperation; ischemia or nerve injury; restenosis; pulmonary edema; pleural effusion; bleeding; anemia; abnormal lab values including electrolyte imbalance; hypertension or hypotension; allergic reaction to anesthesia, contrast media, or device materials; hematoma; syncope; pain or changes at the access site; exercise intolerance or weakness; inflammation; angina; heart murmur; and fever. Additional potential risks associated with the use of the valve, delivery system, and/or accessories include: cardiac arrest; cardiogenic shock; emergency cardiac surgery; cardiac failure or low cardiac output; coronary flow obstruction/transvalvular flow disturbance; device thrombosis requiring intervention; valve thrombosis; device embolization; device migration or malposition requiring intervention; left ventricular outflow tract obstruction; valve deployment in unintended location; valve stenosis; structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis); device degeneration; paravalvular or transvalvular leak; valve regurgitation; hemolysis; injury to the mitral valve; device explants; mediastinitis; mediastinal bleeding; nonstructural dysfunction; mechanical failure of delivery system and/or accessories; and nonemergent reoperation.

Important Safety Information (cont.)

Edwards Crimper:

Indications: The Edwards Crimper is indicated for use in preparing the Edwards SAPIEN 3 transcatheter heart valve for implantation.

Contraindications: There are no known contraindications.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices**. There is no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing.

Precautions: For special considerations associated with the use of the Edwards Crimper prior to valve implantation, refer to the Edwards SAPIEN 3 transcatheter heart valve Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards Crimper.

CAUTION: Federal (United States) law restricts these devices to sale by or on the order of a physician.

Edwards Lifesciences • One Edwards Way, Irvine CA 92614 USA • edwards.com

Edwards

Edwards