Five-year Results from the COMPASSION S3 Trial

Treatment of Patients with a Dysfunctional RVOT Conduit or Previously Implanted Pulmonic Valve with the SAPIEN 3 Transcatheter Heart Valve

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Disclosures

- As a faculty member for this program, I disclose the following relationships with industry:
    - Proctor and Consultant – Medtronic
    - Proctor – Edwards Lifesciences
    - Research Funding- Venus Medtech
    - Consultant- Siemens
    - Editorial Board Member - Int J Cardiol CHD, American Journal of Cardiology, JSCAI

COMPASSION S3 Clinical Trial

- **Design**: Prospective, Single-arm, Multicenter
- **Objective**: To evaluate the safety and effectiveness of SAPIEN 3 valve in patients with a dysfunctional RVOT conduit or previously implanted surgical valve in the pulmonic position and at least moderate-to-severe PR and/or a mean RVOT gradient ≥ 35 mmHg.
- **Follow-up:** Discharge, 30 days, 6 months, & annually for 5 years

Clinical Endpoints

Primary Endpoint

THV dysfunction at 1 year, defined as a non-hierarchical composite of:

- RVOT re-intervention
- Moderate or greater total PR
- Mean RVOT gradient > 40 mmHg

1 Year Outcomes*

Primary Endpoint

- THV dysfunction at 1 year– 4.3%

Additional Outcomes

- Single THV implanted successfully in the desired location - 98.2%
- RV-PA peak-to-peak gradient < 35 mmHg - 100%
- < moderate PR by discharge, assessed via TTE - 100%
- Free of explant at 24 hours post implantation - 100%
- At 30 days, there were no major adverse clinical events

This presentation is the 5-year follow-up data

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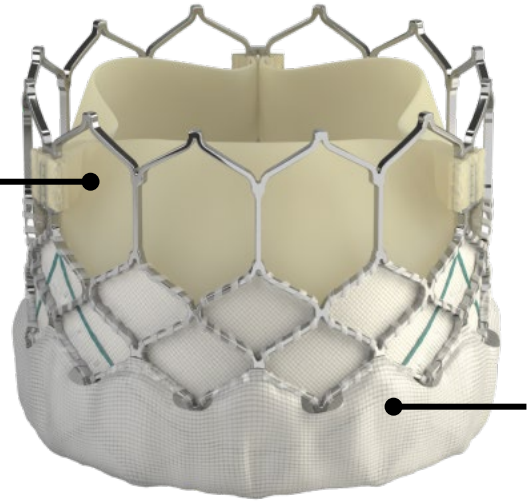
* Presented at SCAI 2020 and published Lim *et al., Am J Cardiol* 2023 190:102-109. doi: 10.1016/j.amjcard.2022.12.010.

SAPIEN 3 Valve & Commander Delivery System

SAPIEN 3 Valve



Bovine pericardium leaflets

Sealing skirt designed to minimize PVR

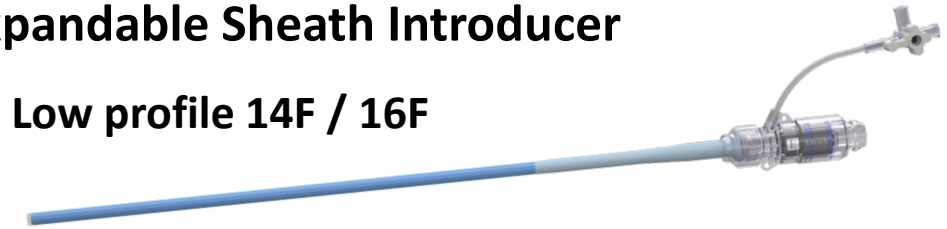
Balloon-expandable cobalt-chromium frame

Commander Delivery System

- Dual articulation
- 14F / 16F eSheath compatible

Expandable Sheath Introducer

- Low profile 14F / 16F



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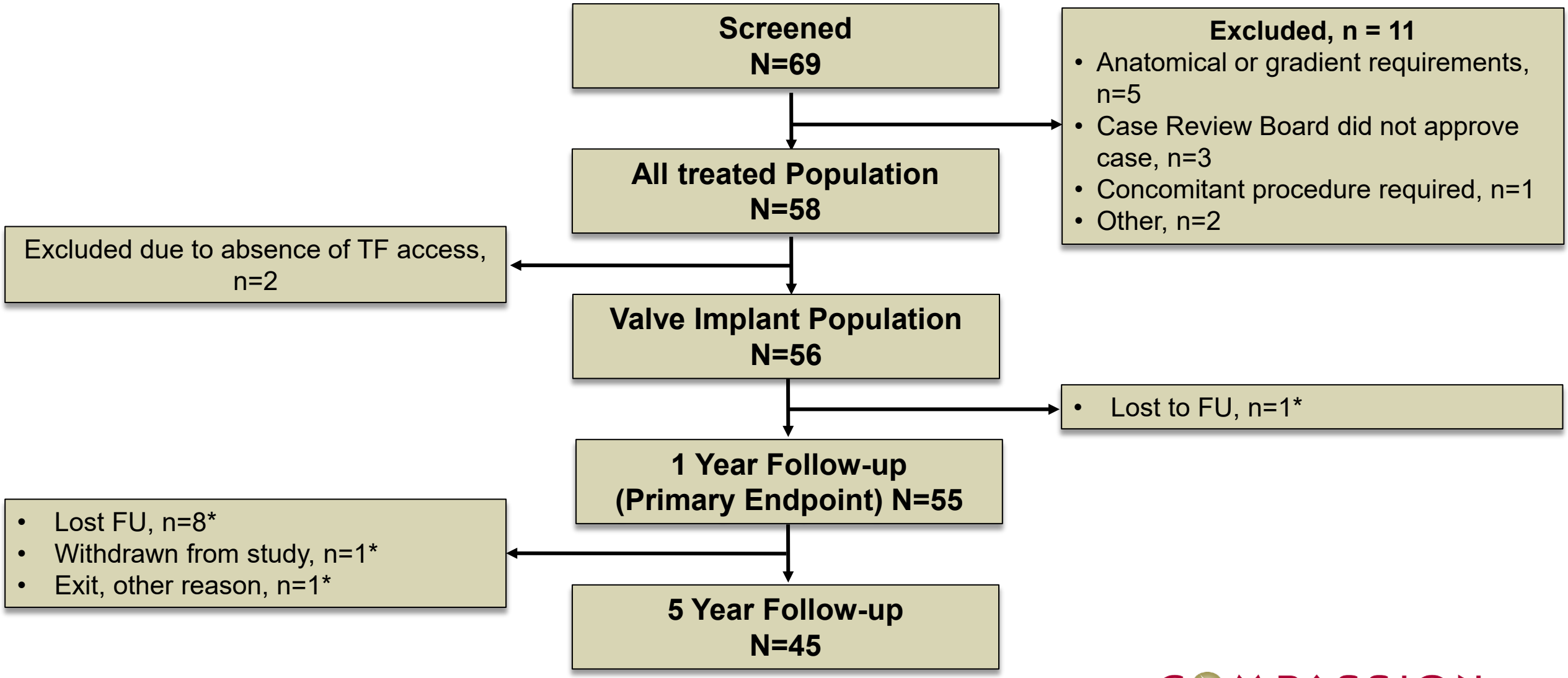
Study Flow Chart



*All patients confirmed alive at 5Y, as determined by a vital status sweep

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Baseline Characteristics

Demographics (All Treated N=58)	Summary Statistics
Age (years)	**32.0** (22.0, 38.0)
Age group	
<12 years (child)	**8.6%** (5/58)
12-21 years (adolescent)	**13.8%** (8/58)
>21 years (adult)	**77.6%** (45/58)
Sex	
Female	**31.0%** (18/58)
Body mass index (kg/m^2)	**25.1** (21.1, 30.2)
Weight (kg)	**74.7** (58.5, 89.1)
Height (cm)	**170.2** (161.5, 175.3)

Clinical Characteristics (All Treated N=58)	Summary Statistics
NYHA class grouped	
Class I/II	**89.5%** (51/57)
Class III/IV	**10.5%** (6/57)
Primary Indication	
Pulmonary stenosis	**12.3%** (7/57)
Pulmonary regurgitation	**19.3%** (11/57)
Both	**68.4%** (39/57)
Most recent RVOT/PV Repair/Replacement	
Homograft/valved Conduit	**65.5%** (38/58)
Bioprosthetic heart valve	**34.5%** (20/58)

median (IQR) or % (n/N)

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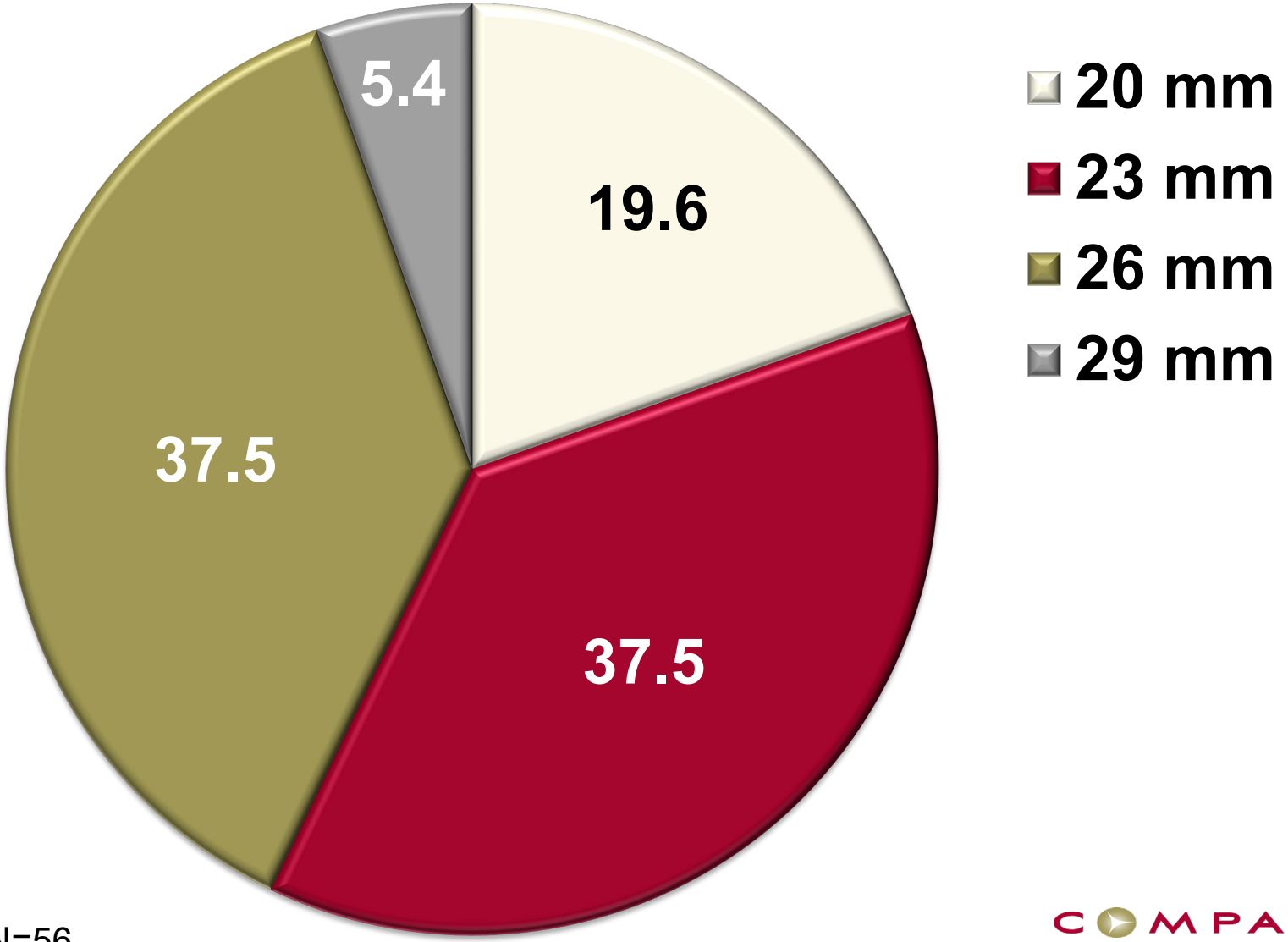
SAPIEN 3 Valve Sizes



% VI population, N=56

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Primary Endpoint

	1 Year VI population, % (n/N at risk)	5 Years VI population, % (n/N at risk)
THV dysfunction	**4.3%** (2/47)	**10.0%** (4/40)
RVOT re-intervention	**0%** (0/56)	**2.1%** (1/49)
Moderate or greater PR	**2.1%** (1/47)	**5.0%** (2/40)
Mean RVOT gradient >40 mmHg	**2.1%** (1/48)	**2.5%** (1/40)

PR: pulmonary regurgitation, RVOT: right ventricular outflow tract, THV: transcatheter heart valve

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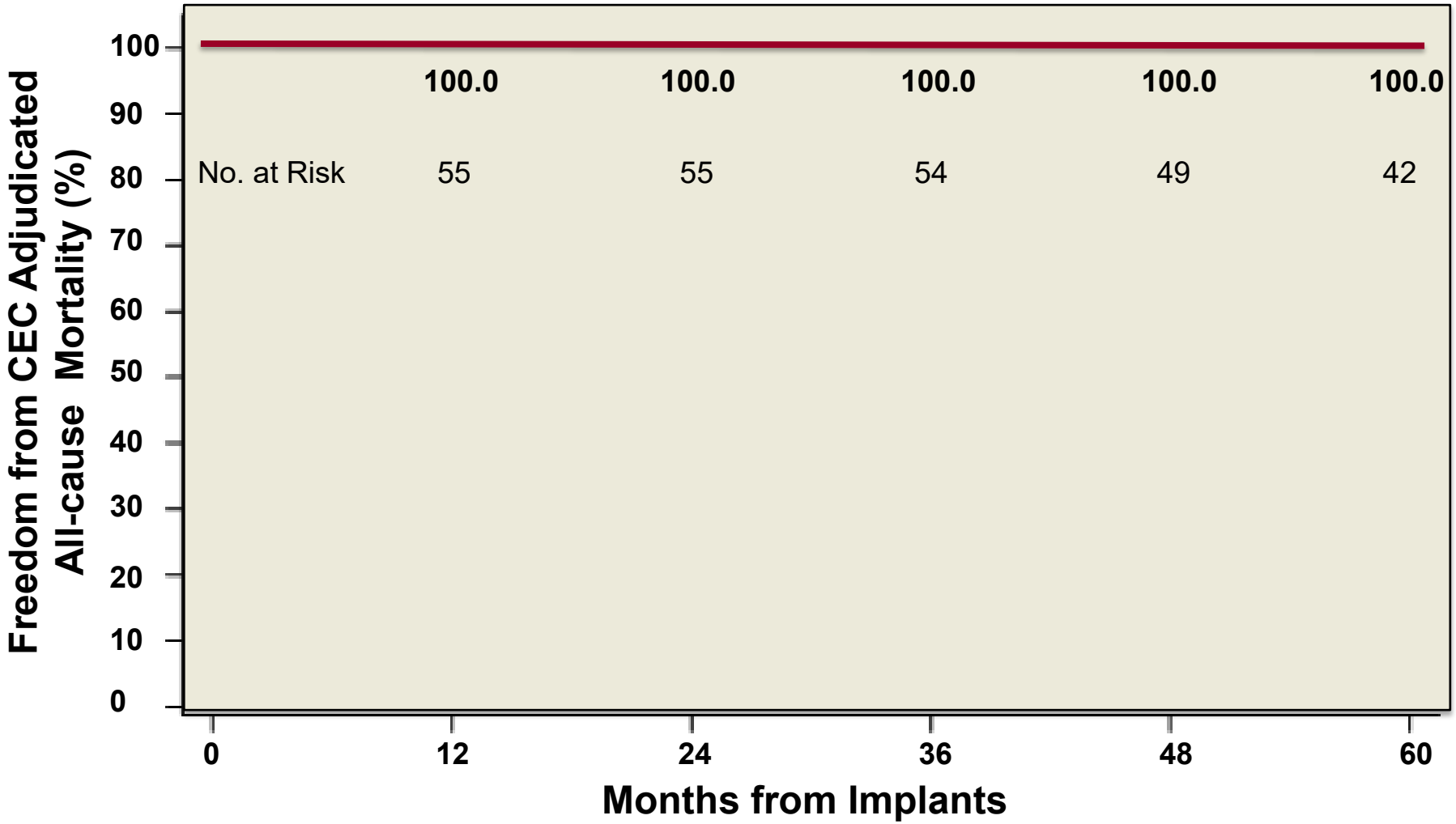
All-cause Mortality



VI population

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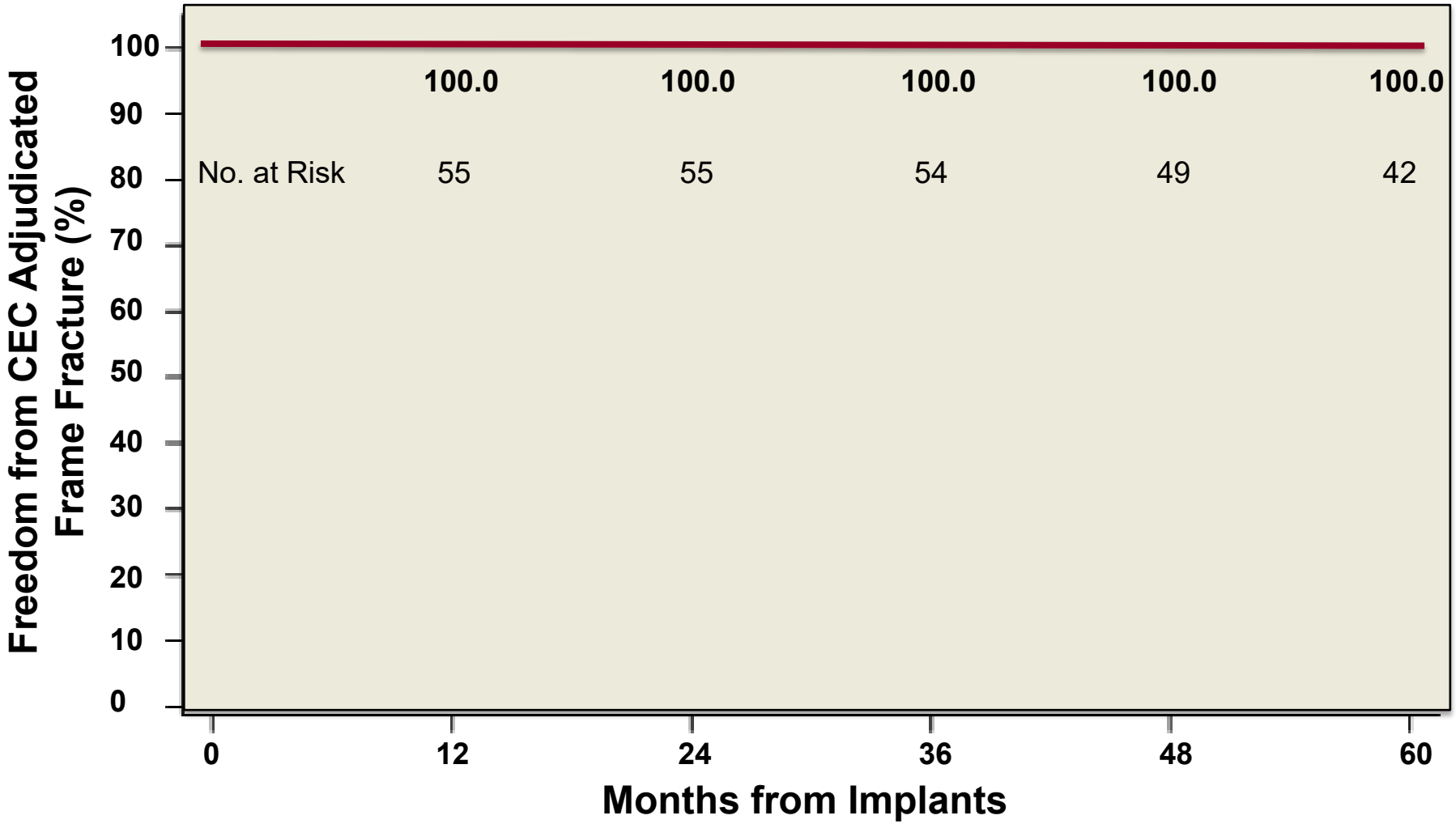
Frame Fracture



VI population

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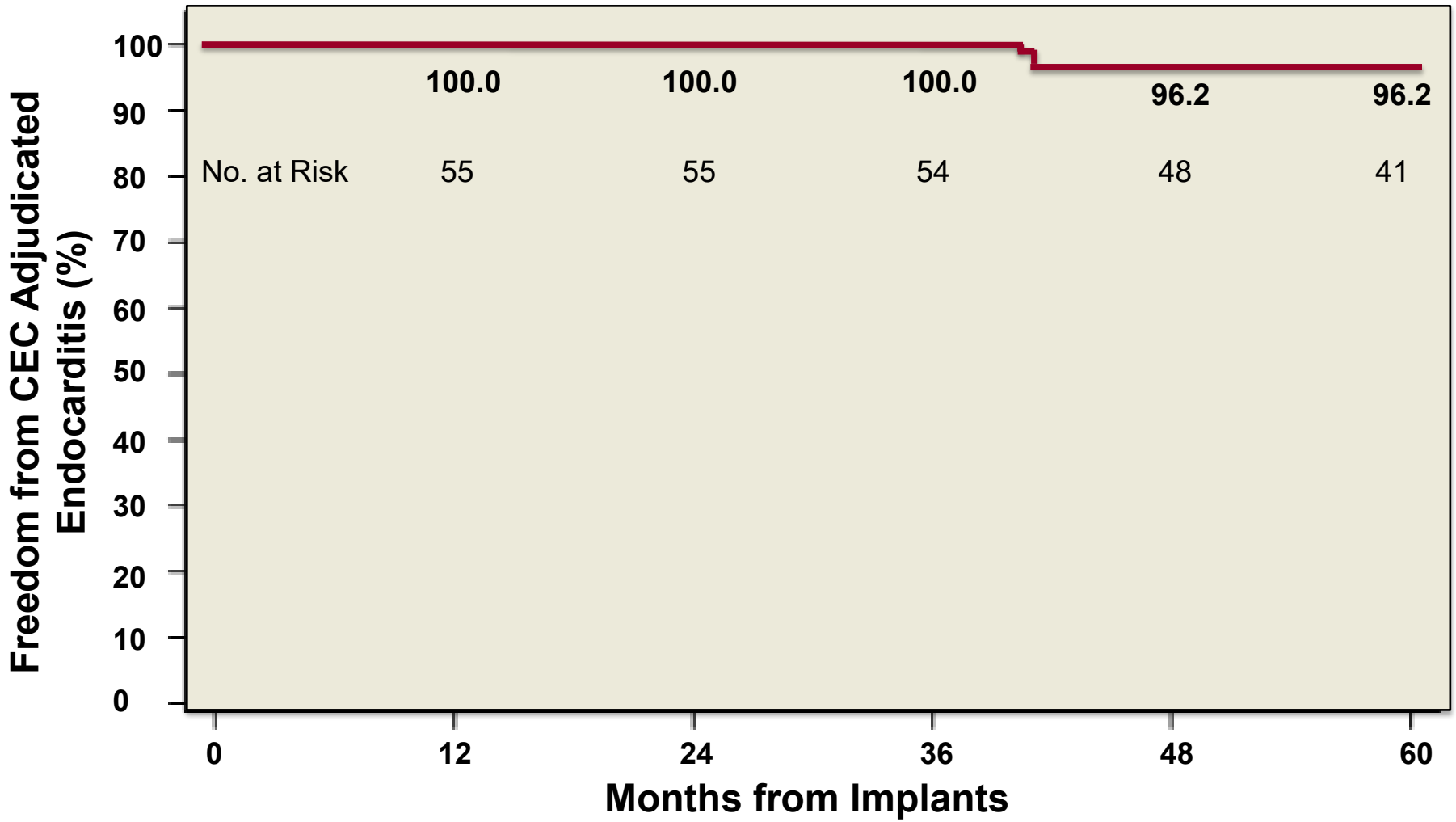
Endocarditis



VI population

1 of 2 cases was not device related (tricuspid endocarditis)

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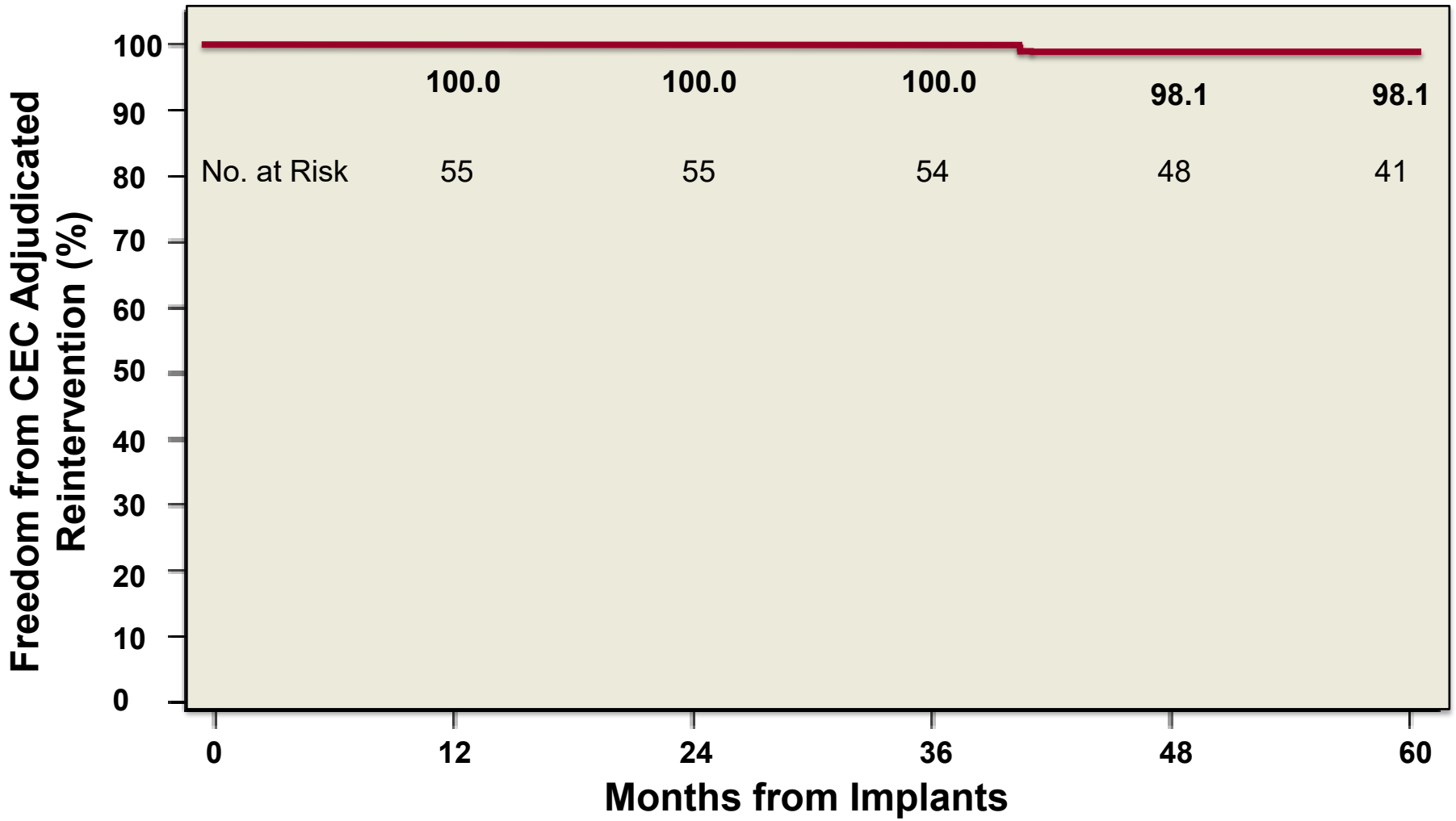
Reintervention



VI population

Day 1129: balloon valvuloplasty of the SAPIEN 3 valve due to moderate valve stenosis. Patient was discharged next day. No other AEs for this patient.

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Additional Outcomes

Event, KM estimates % (n, N events)	30 days	1 year	5 years
Death	**0%**	**0%**	**0%**
Reintervention	**0%**	**0%**	**1.9%** (1,1)
Arrhythmia, including conduction abnormalities†	**5.2%** (3,3)	**8.7%** (6,5)	**16.2%** (11,9)
Permanent Pacemaker	**0%**	**1.8%** (1,1)	**1.8%** (1,1)
Endocarditis	**0%**	**0%**	**3.8%** (2,1)
Valve Thrombosis*	**0%**	**0%**	**4.3%** (2,2)
Myocardial Infarction#	**0%**	**0%**	**1.9%** (1,1)
Pulmonary Embolism	**0%**	**0%**	
Stroke / Transient Ischemic Attack	**0%**	**0%**	
Coronary Artery Compression	**0%**		

† 2 VT, 2 AVB, 2 AFib, 2 atrial flutter, 2 SVT and 1 atrial tachycardia.
9/11 resolved, 8/9 with medication or intervention, 1 without treatment.
*Site-reported values only (not CEC-adjudicated)
#CEC adjudicated only out to 30 days

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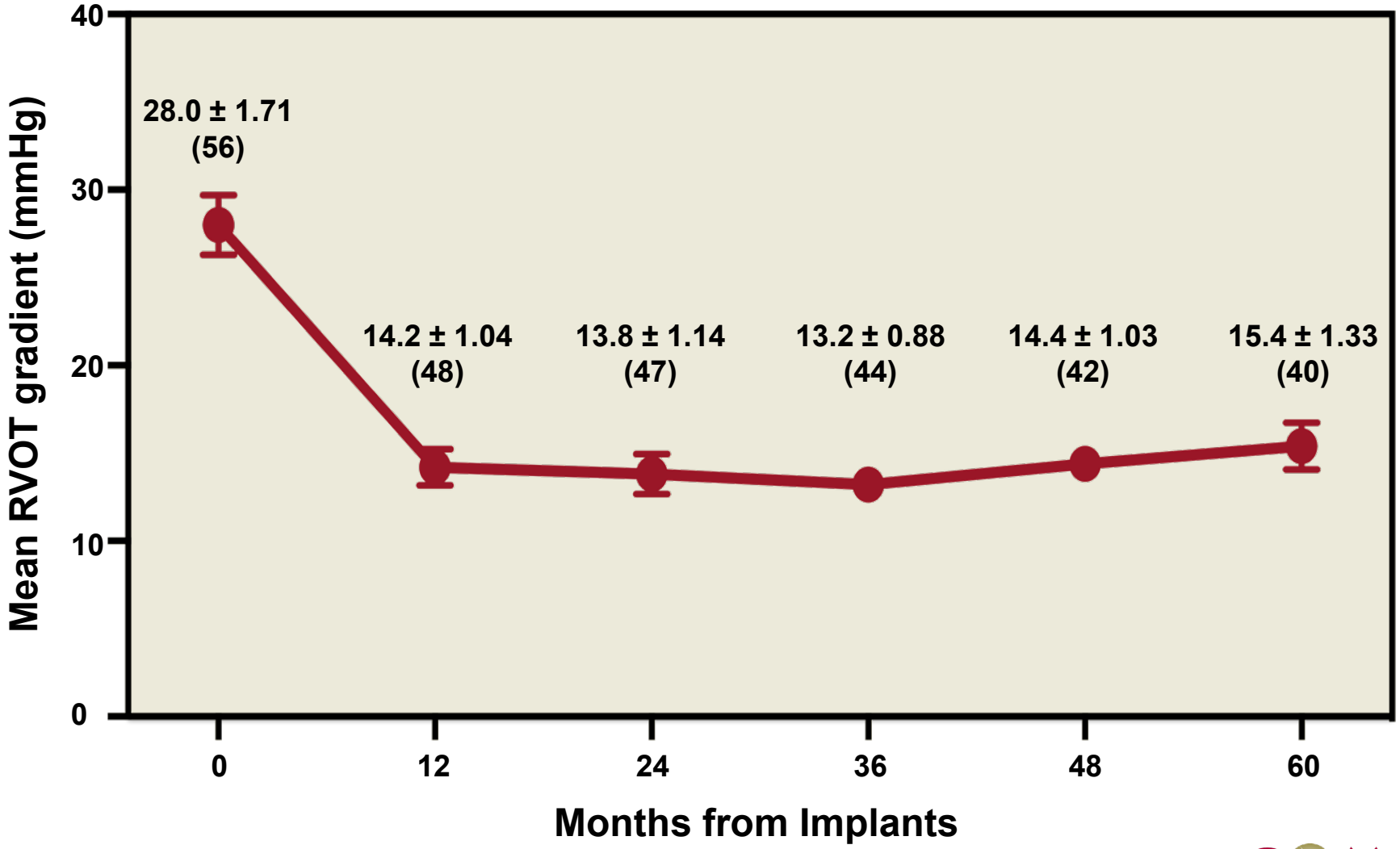
Mean RVOT Gradient over Time



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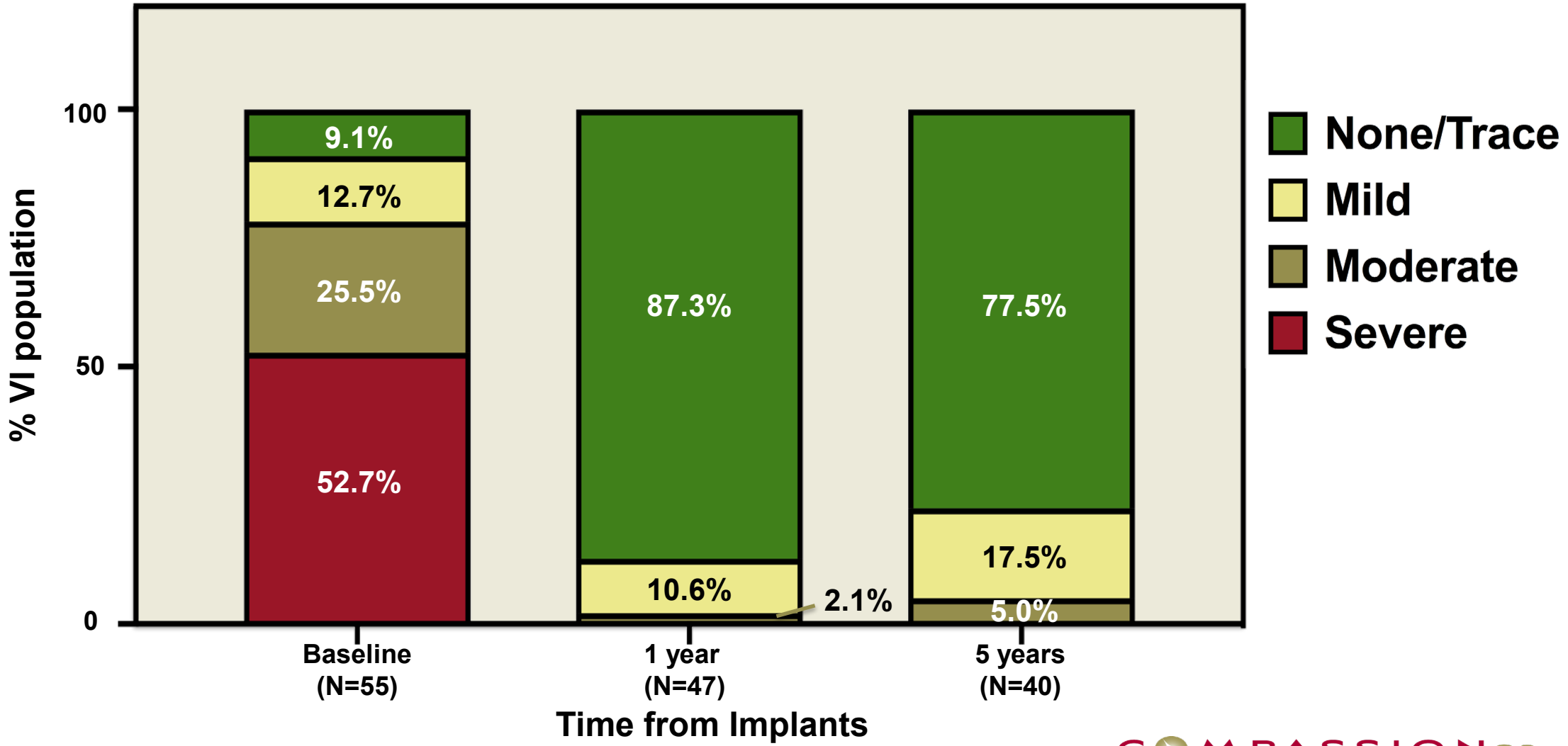
Total PR to 5 Years



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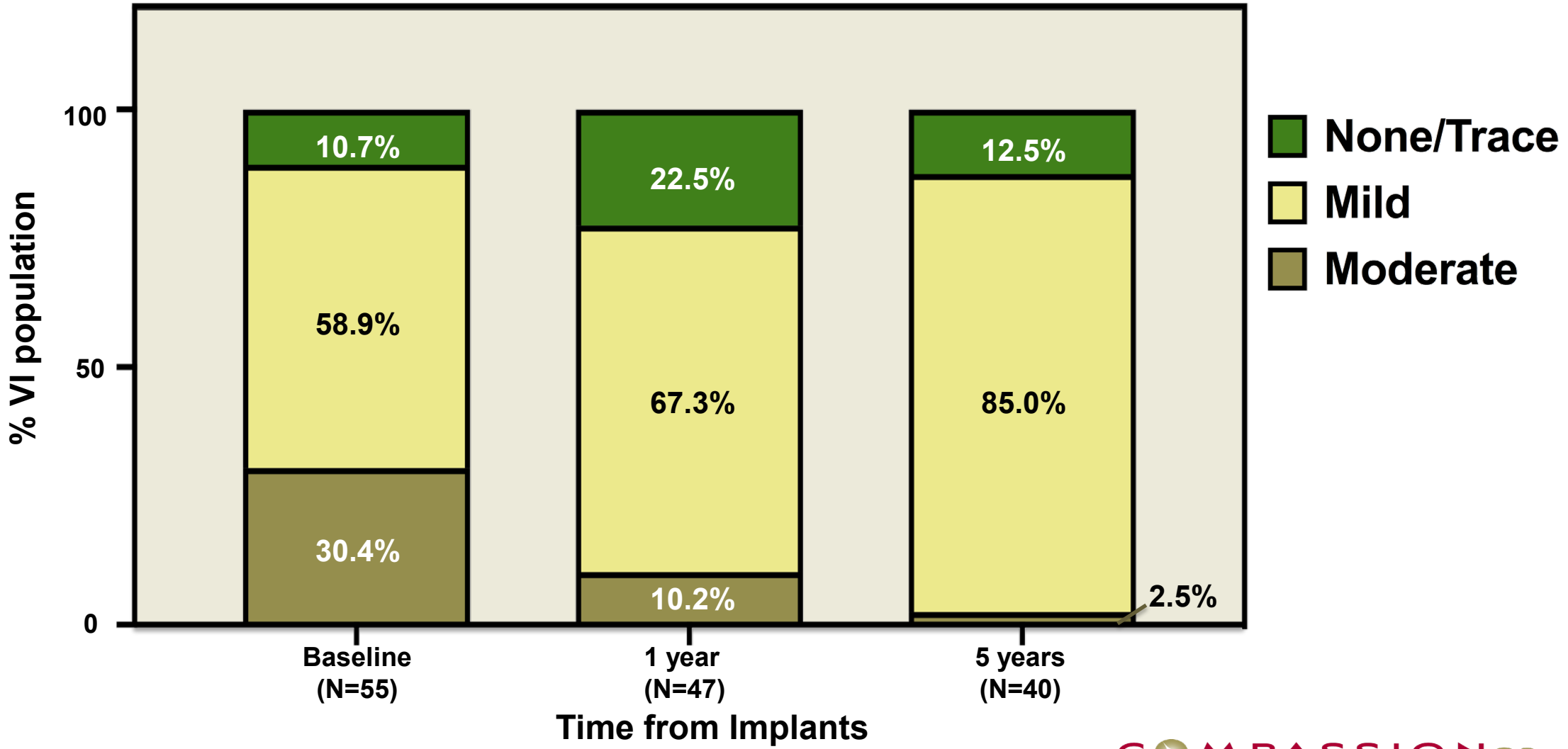
Total TR to 5 Years



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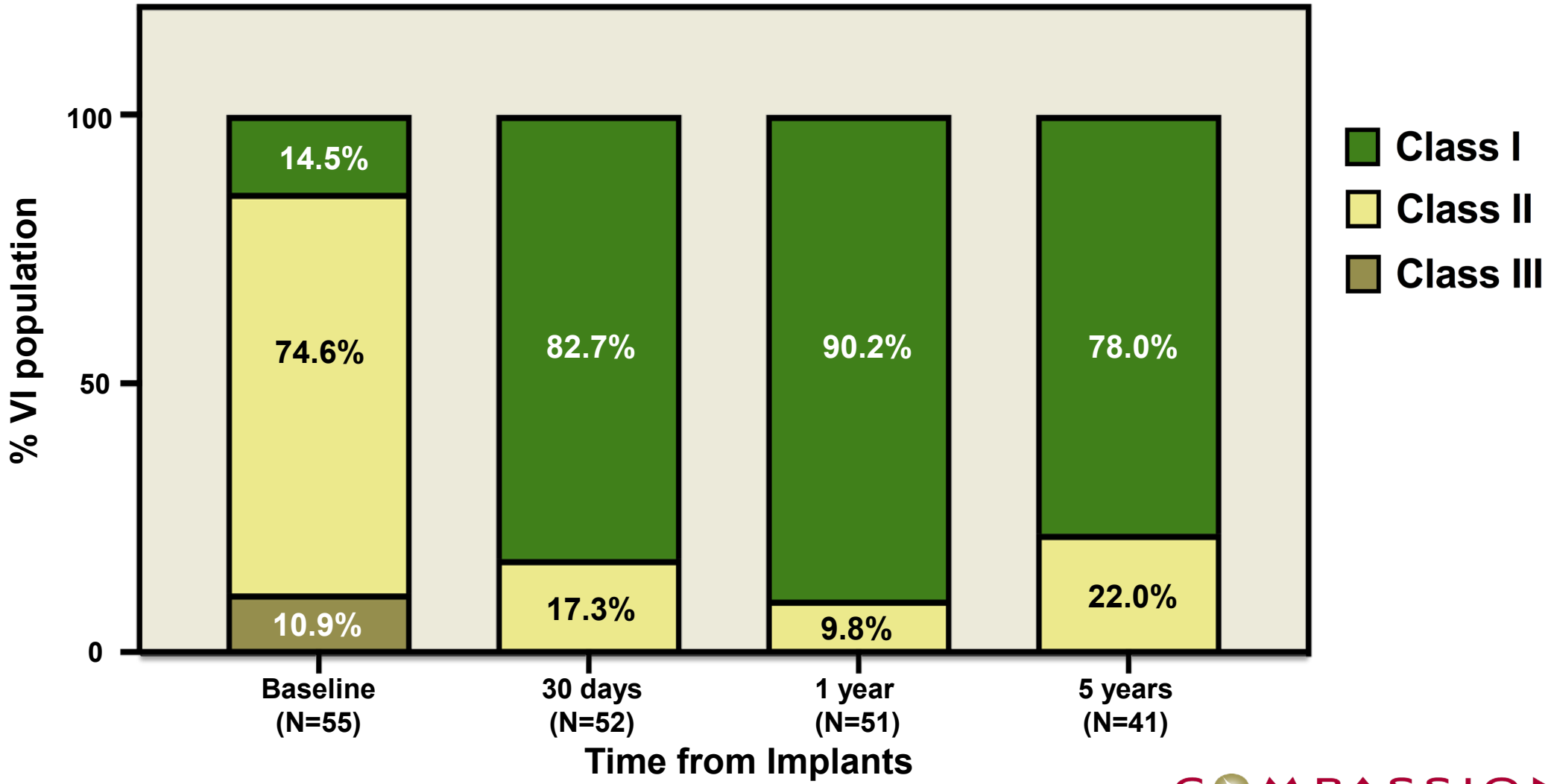
NYHA Functional Classifications



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Conclusion

- Here, we report the longest follow-up of the COMPASSION S3 trial
- Excellent clinical and hemodynamic outcomes were sustained out to 5 years
  - No deaths, frame fractures or surgical explants
  - Only 1 case of reintervention and 1 case of possibly device related endocarditis
  - 95.0% of patients had none, trace, or mild total PR
  - Mean RVOT gradient decreased from 28.0 mmHg to 15.4 mmHg between baseline and 5 years

Thanks and Recognition

Participating Sites

Emory University, GA
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Alejandro Torres, Robert Sommer

University of California, Los Angeles, CA
Jamil Aboulhosn, Daniel Levi

Duke University Medical Center
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Clinical Events Committee

Cardiovascular Research Foundation, New York, NY

CT Core Laboratory

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Directors: Jonathon Leipsic, Philipp Blanke

Echocardiographic Core Laboratory

Children's Mercy, Kansas City, MO
Directors: Girish Shirali

Sponsor

Edwards Lifesciences, Irvine, CA

* Dr Leventhal is now located at the University of Kentucky, KY
† Dr Shahanavaz is now located at Cincinnati Children's Hospital, OH.

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Important Safety Information

Edwards SAPIEN 3 Transcatheter Heart Valve System – Pulmonic

Indications: The Edwards SAPIEN 3 Transcatheter Heart Valve (THV) System with Edwards Commander Delivery System is indicated for use in the management of pediatric and adult patients who have a clinical indication for intervention on a dysfunctional right ventricular outflow tract (RVOT) conduit or surgical bioprosthetic valve in the pulmonic position with ≥ moderate regurgitation and/or a mean RVOT gradient of ≥ 35 mmHg.

Contraindications: The Edwards SAPIEN 3 THV System with Edwards Commander Delivery System is contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices**. There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. Correct sizing of the valve into the non-compliant RVOT conduit or failing bioprosthesis (landing zone) is essential to minimize risks. Too small of a valve may result in paravalvular leak, migration, or valve embolization; whereas too large of a valve may result in residual gradient (patient-prosthesis mismatch) or RVOT rupture. Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism. Assessment for coronary compression risk prior to valve implantation is essential to prevent the risk of severe patient harm. The physician must verify correct orientation of the valve prior to its implantation; the inflow (outer skirt end) of the valve should be oriented toward the proximal end (handle) of the delivery system to prevent the risk of severe patient harm. 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. 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 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. It is recommended that all prosthetic heart valve recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection. 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 solutions or to the valve.

Precautions: 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 Material 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. Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device. Patient should be heparinized to maintain the ACT at ≥ 250 sec prior to introduction of the delivery system in order to prevent thrombosis. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: Blood dyscrasias defined as: leukopenia, acute anemia, thrombocytopenia, or history of bleeding diathesis or coagulopathy. A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated. Positive urine or serum pregnancy test in female subjects of child-bearing potential. Residual mean gradient may be higher in a "THV-in-failing bioprosthesis" configuration than that observed following implantation of the valve inside a native 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 preexisting bioprosthetic valve be determined, so that the appropriate valve can be implanted and a prosthesis-patient mismatch be 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 anesthesia, interventional procedure and imaging include but are not limited to: death; stroke/transient ischemic attack; respiratory insufficiency or respiratory failure; cardiovascular or vascular injury, such as perforation or damage (dissection) of vessels, myocardium or valvular structures including rupture of the RVOT that may require intervention; pericardial effusion/cardiac tamponade; embolic event: air, calcific material, thrombus, device fragments; infection including incisional site infection, septicemia and endocarditis; myocardial infarction; renal insufficiency or renal failure; conduction system injury, arrhythmia, arteriovenous (AV) fistula; systemic or peripheral nerve injury, systemic or peripheral ischemia, pulmonary edema, pneumothorax, pleural effusion, atelectasis; blood loss requiring transfusion; anemia; radiation injury; electrolyte imbalance; hypertension or hypotension; allergic reaction to anesthesia, contrast media, antithrombotic therapy, device materials; hematoma or ecchymosis, syncope, pain, exercise intolerance or weakness, inflammation; angina; fever; cardiac failure. Potential risks associated with the valve, delivery system and/or accessories include, but may not be limited to, the following: cardiac arrest; cardiogenic shock; coronary flow obstruction/transvalvular flow disturbance, device thrombosis requiring intervention; injury to tricuspid valve; device embolization requiring intervention; device acute migration or malposition requiring intervention; endocarditis; hemolysis/hemolytic anemia; THV dysfunction resulting in pulmonary valve symptoms; mechanical failure of delivery system, and/or accessories; emergent and non-emergent re-intervention; dyspnea.

Important Safety Information (continued)

Edwards Crimper

Indications: The Edwards crimper is indicated for use in preparing the Edwards SAPIEN 3 Ultra transcatheter heart valve and the Edwards SAPIEN 3 transcatheter heart valve, for implantation.

Contraindications: There are no known contraindications.

Warnings: The device is designed, intended, and distributed for single use only. **Do not resterilize or reuse the device.** There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing. Do not mishandle the device. Do not use the device if the packaging or any components are not sterile, have been opened or damaged, or the expiration date has elapsed.

Precautions: For special considerations associated with the use of the Edwards crimper prior to THV implantation, refer to the THV 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.

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