



고려대학교의료원  
KOREA UNIVERSITY MEDICINE

11th  
**AP VALVES & 2022**  
**STRUCTURAL HEART**

*Sapien 3 Ultra : Engineered for the Future*

# SAPIEN 3 Ultra multidimensional analysis: From Frame to outerskirt



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ENABLING  
FUTURE MEDICINE



# Elevating the expectations of what is possible

TAVI is built upon:

Clinical study

**25,000+**

patients studied in  
Edwards clinical trials

Real world experience

**450,000+**

patients treated worldwide  
with Edwards TAVI valves



**SAPIEN valve**



**SAPIEN XT valve**



**SAPIEN 3 valve**



**SAPIEN 3 Ultra valve**

Data on file at Edwards Lifesciences



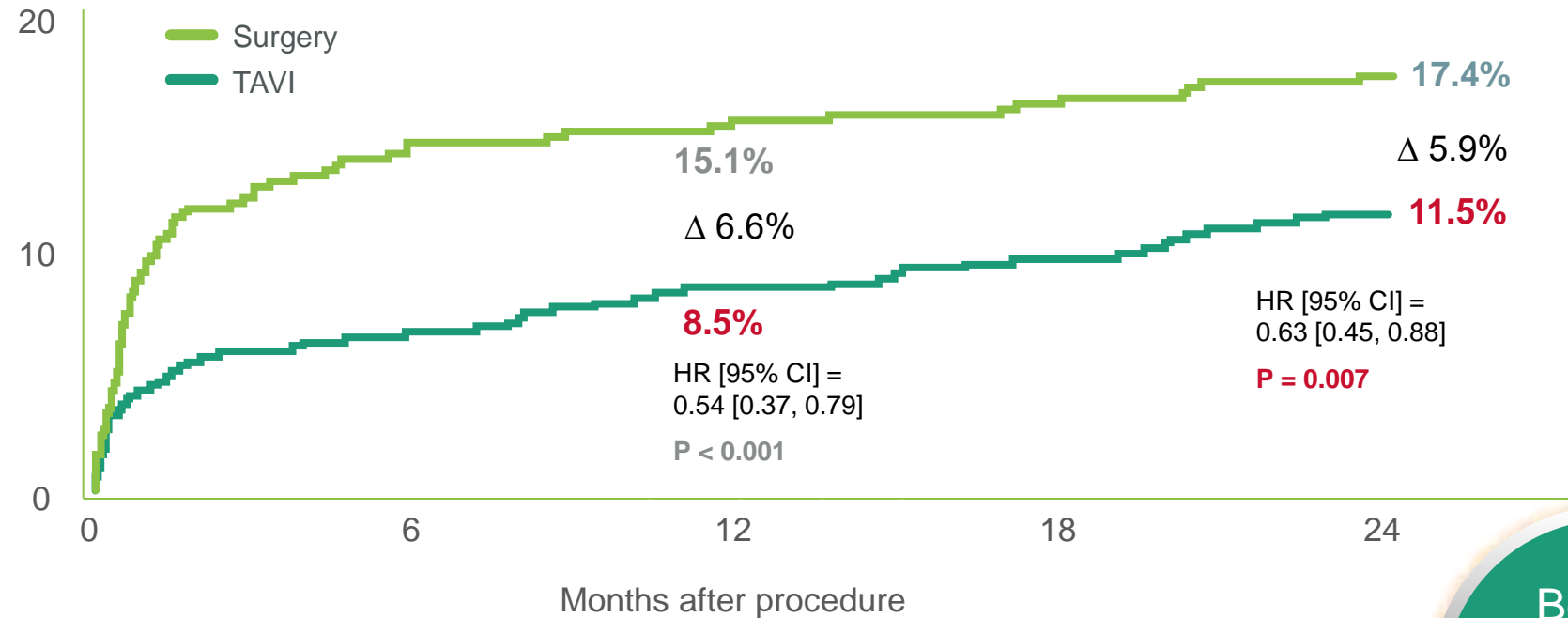
# Sapien 3 first-in-human, Jan 27, 2012



# Only SAPIEN 3 TAVI is proven superior to surgery in low-risk severe aortic stenosis patients

## PARTNER 3 Low Risk Trial:

Primary endpoint<sup>1</sup>  
Death, stroke, or  
rehospitalization



Benefit  
of TAVI  
sustained at  
2 years<sup>2</sup>

### Number at risk:

Surgery	454	381	374	352	339
<b>TAVI</b>	<b>496</b>	<b>462</b>	<b>451</b>	<b>436</b>	<b>422</b>

1. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019.

2. Mack, M. (2020). Two-year Clinical and Echocardiographic Outcomes from the PARTNER 3 Low-risk Randomized Trial. Presented at ACC 2020 March. Virtual ACC.



# SAPIEN 3 TAVI is designed to deliver the outcomes you demand

	30 days		1 year		
	TAVI (n=496)	Surgery (n=454)	TAVI (n=496)	Surgery (n=454)	P-value
<b>All-cause mortality</b>	0.4%	1.1%	1.0%	2.5%	0.09
<b>All-stroke</b>	0.6%	2.4%	1.2%	3.1%	0.04
<b>Rehospitalization</b>	3.4%	6.5%	7.3%	11.0%	0.046
<b>Life-threatening/disabling or major bleeding*</b>	3.6%	24.5%	7.7%	25.9%	<0.001
<b>New-onset Afib*</b>	5.0%	39.5%	7.0%	40.9%	<0.001
<b>AKI*</b>	0.4%	1.8%	0.4%	1.8%	0.05

Delivering outcomes better than surgery in your low-risk patients:

- **Mortality**
- **Stroke**
- **Rehospitalization**
- **Bleeding**

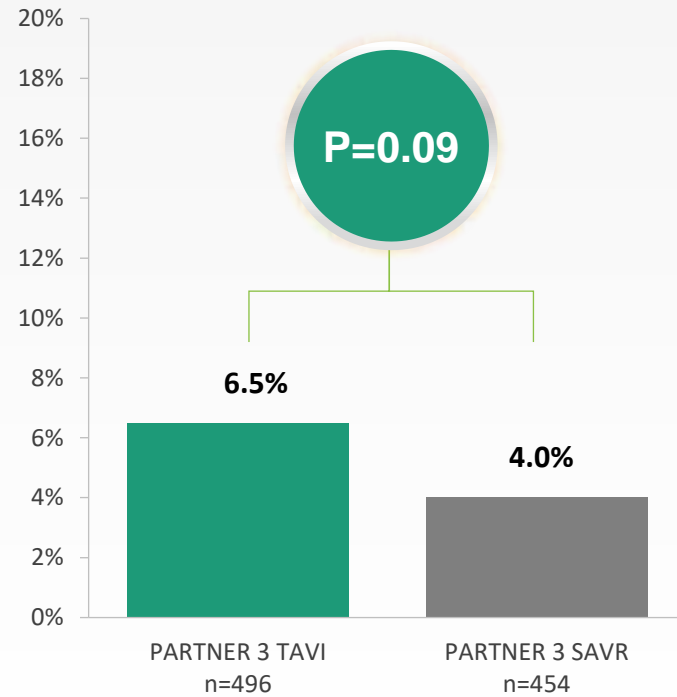
\*These endpoints were not subject to multiplicity adjustment

Mack M, Leon M, Thourani R, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695-705.  
Leon MB, Mack MJ, PARNTER 3 Transcatheter or Surgical Aortic Valve Replacement in Low Risk Patients with Aortic Stenosis. Presented at ACC 2019. New Orleans, LA

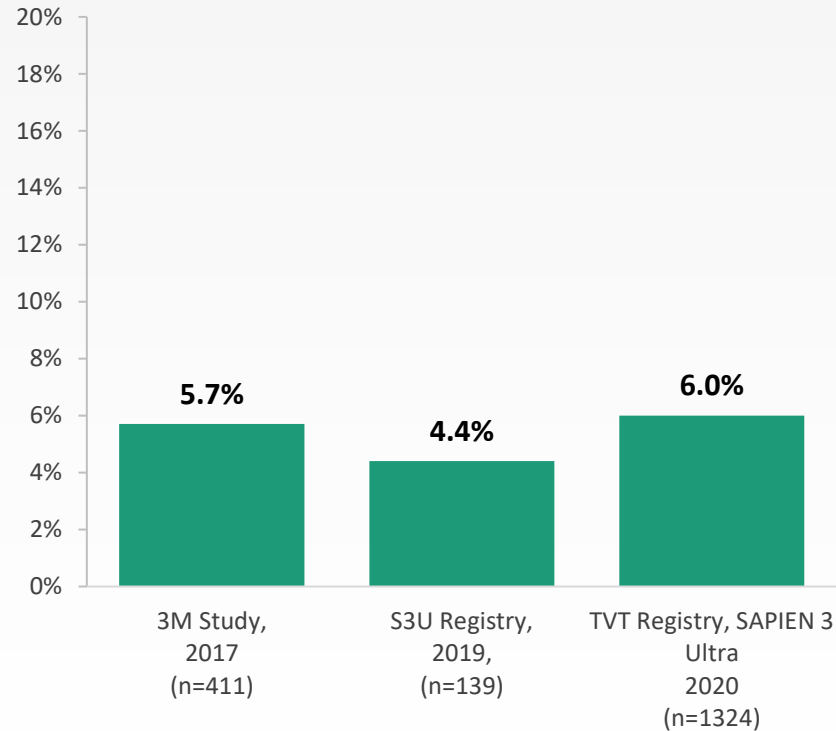


# Globally consistent, single-digit new permanent pacemaker implantation rates

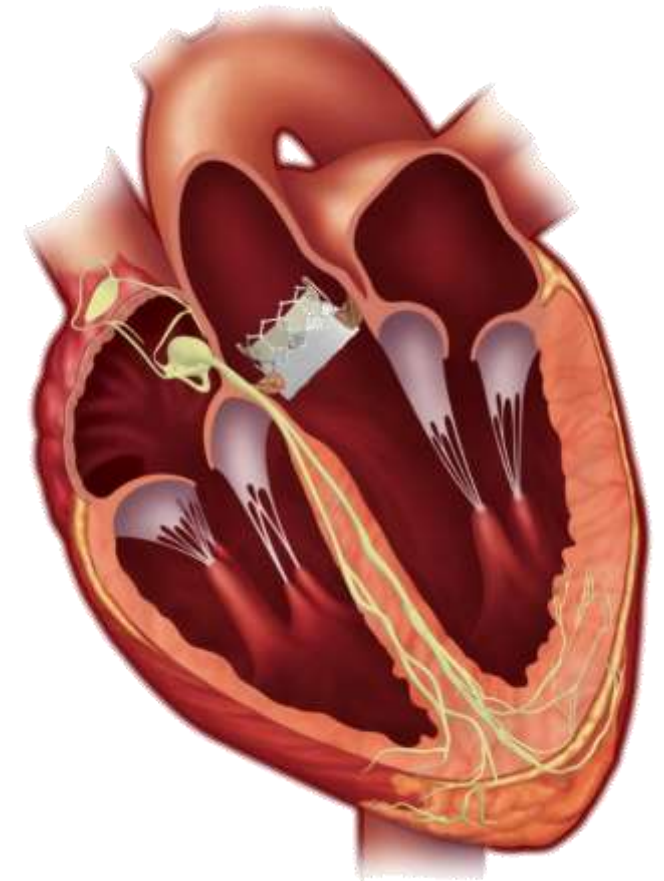
## Equivalent to SAVR<sup>1</sup>



## Consistent single digit outcomes<sup>2-4</sup>



## 30-day outcomes

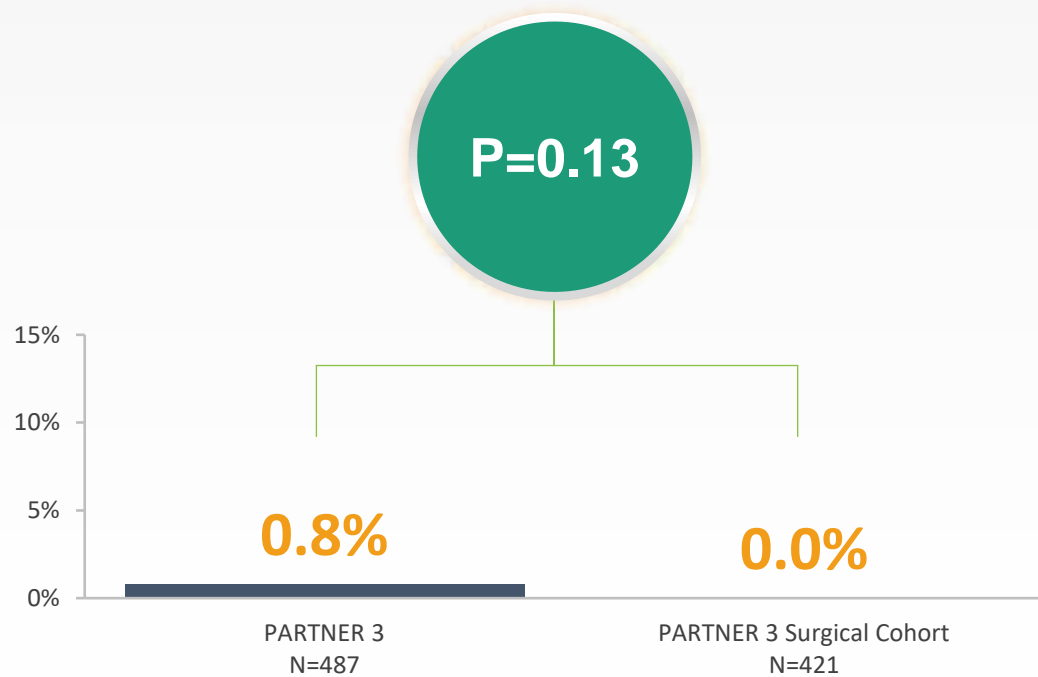


1. Mack M, Leon M, Thourani R, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695-705.
2. Wood et al. The Vancouver 3M Clinical Pathway Facilitates Safe Next-Day Discharge Home at Low, Medium and High Volume TAVR Centers *JACC*. Published on Mar, 2019.
3. Saia F, et al. In-hospital and thirty day outcomes of the SAPIEN 3 Ultra balloon-expandable TAVR: the S3U registry. *Eurointervention* 2020.
4. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020

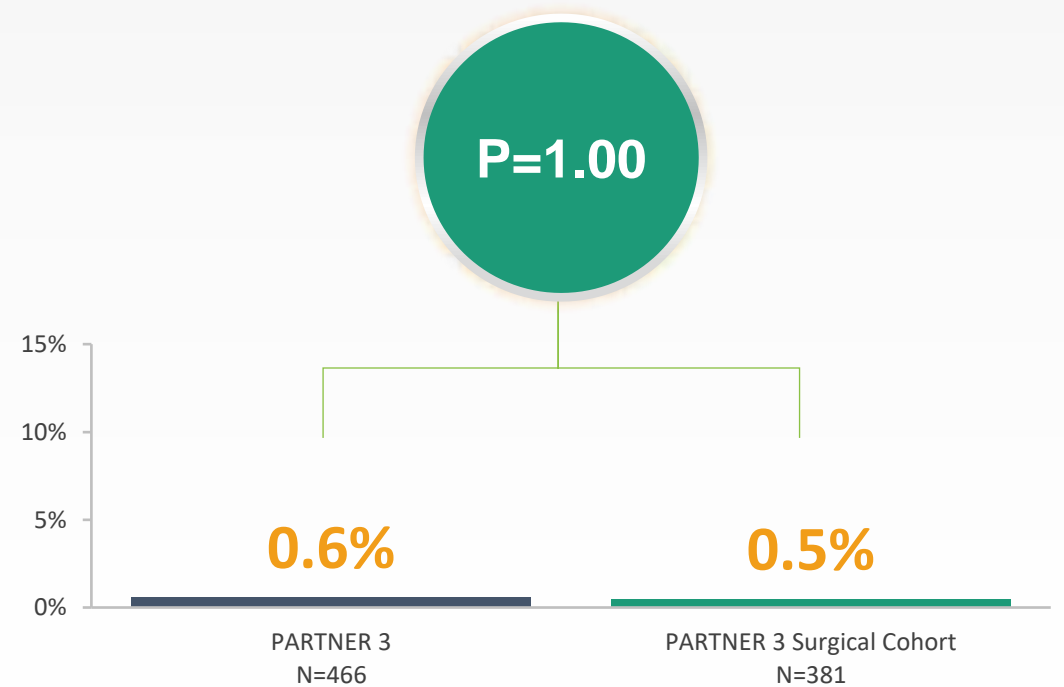


# Demonstrated equivalence to SAVR in $\geq$ moderate PVL: Outcomes at 30 days and 1 year

## 30-day outcomes



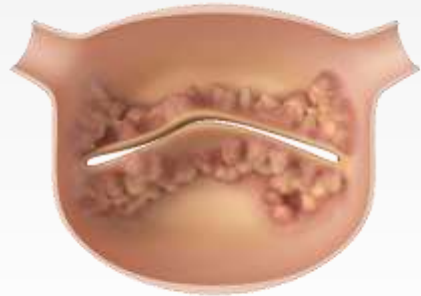
## 1-year outcomes



Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019.  
Leon MB, Mack MJ, PARTNER 3 Transcatheter or Surgical Aortic Valve Replacement in Low Risk Patients with Aortic Stenosis. Presented at ACC 2019. New Orleans, LA

# Controlling for the future of TAVI patients

Patients with longer life expectancies require additional considerations for TAVI procedures



**Bicuspid morphology has a higher prevalence in younger patients<sup>1</sup>**



**Younger patients need a durable valve<sup>2</sup>**



**Secondary interventions will be more common in patients with longer life expectancies<sup>2</sup>**



**Future coronary interventions may be required<sup>3</sup>**

1. Roberts WC, Janning KG, Ko JM, et al. Frequency of Congenitally Bicuspid Aortic Valves in Patients >80 Years of Age Undergoing Aortic Valve Replacement for Aortic Stenosis (With or Without Aortic Regurgitation) and Implications for Transcatheter Aortic Valve Implantation. *Am J Cardiol.* 2012;109(11):1632-1636.
2. Pasala TKR, Ruiz CE. Transcatheter Aortic Valve Replacement for All-comers With Severe Aortic Stenosis: Could It Become a Reality?. *Rev Esp Cardiol (Engl Ed).* 2018;71(3):141-145.
3. Yudi MB, et al. Coronary Angiography and percutaneous coronary intervention after transcatheter aortic valve replacement. *JACC Vol 71, No 12, 2018.*



# The Challenge is Making a System Better than the SAPIEN 3 THV System

**SAPIEN 3 THV System**



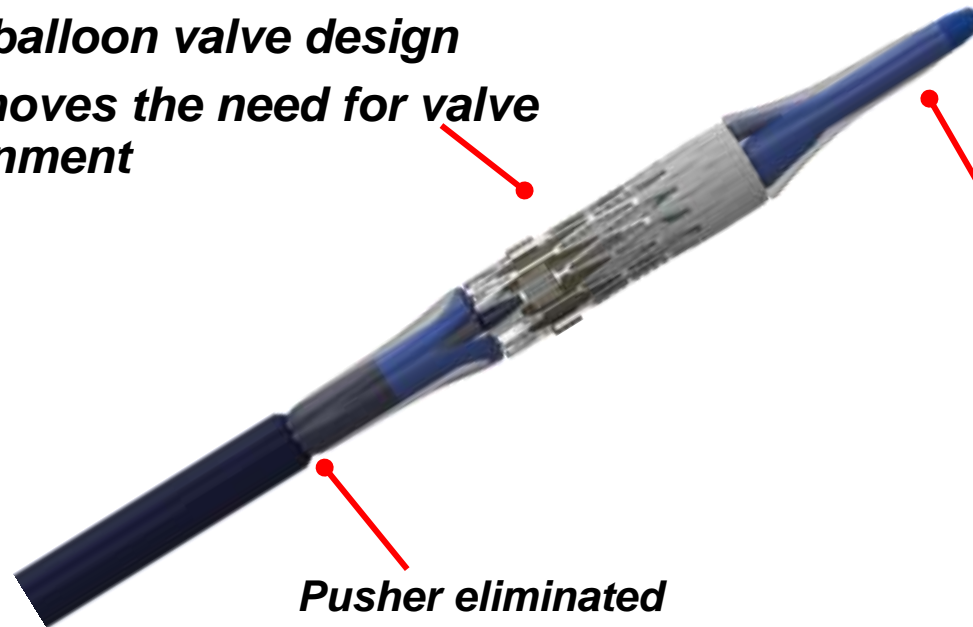
	Accurate Positioning	Outer Sealing Skirt	Low Profile
Stroke	↓	↓	↓
AKI	↓	↓	
Major Vasc & Bleeding Complications			↓

## ***Next Generation: Design Goals***

- ***Same SAPIEN 3 Valve***
- ***Improved delivery system to further streamline the procedure***
- ***Seamless sheath design with a single, low profile sheath for all valve sizes***

# Edwards SAPIEN 3 Ultra System

***On-balloon valve design  
Removes the need for valve  
alignment***



***Atraumatic, short tip  
Further improved  
crossability and less  
material in the ventricle***

***Pusher eliminated  
Reduces steps required during  
deployment***

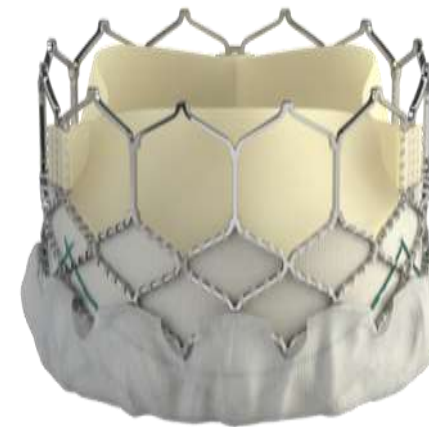
***14F compatible for all valve sizes  
including the 29mm***



Edwards' SAPIEN 3 Ultra Transcatheter Heart Valve Receives FDA Approval

IRVINE, Calif., Dec. 28, 2018 -- Edwards Lifesciences Corporation (NYSE: EDO), the global leader in patient-focused innovations for structural heart disease and critical care monitoring, today announced that the SAPIEN 3 Ultra system has received U.S. Food and Drug Administration (FDA) approval for transcatheter aortic valve replacement in severe, symptomatic aortic stenosis patients who are determined to be at intermediate or greater risk of open-heart surgery.

**SAPIEN 3 Valve**



# Burst Balloons With Series 2

## Ultra

## Safe

## Rec

Edward  
have le

by [Shelley](#)

# FDA: Class I Recall for Burst

## ra

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Valve alignment markers

Tapered tip

Center marker

Triple marker



Note

The center marker is only visible under fluoroscopy



Flex tip

# Edwards Lifesciences Symposium : New Product *SAPIEN 3 ULTRA*



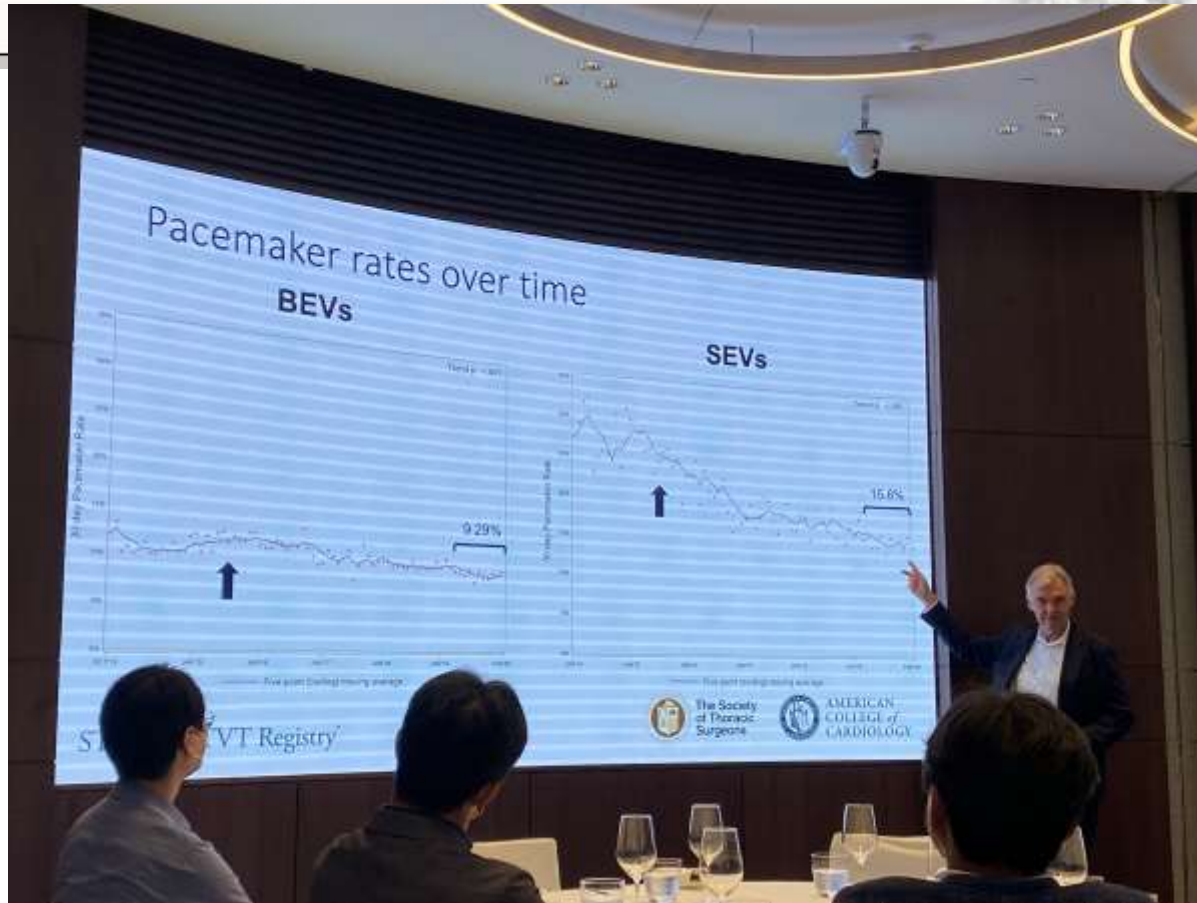
*Speaker : Prof. John G. Webb (University of British Columbia, Canada)*

*Date : 2022. 07. 11(Mon) / 18:30 ~*

*Venue : Park Hyatt Seoul*

## **What' new**

- Approximately 40% increased outer skirt height
- Textured PET fabric
- Enhanced PVL management

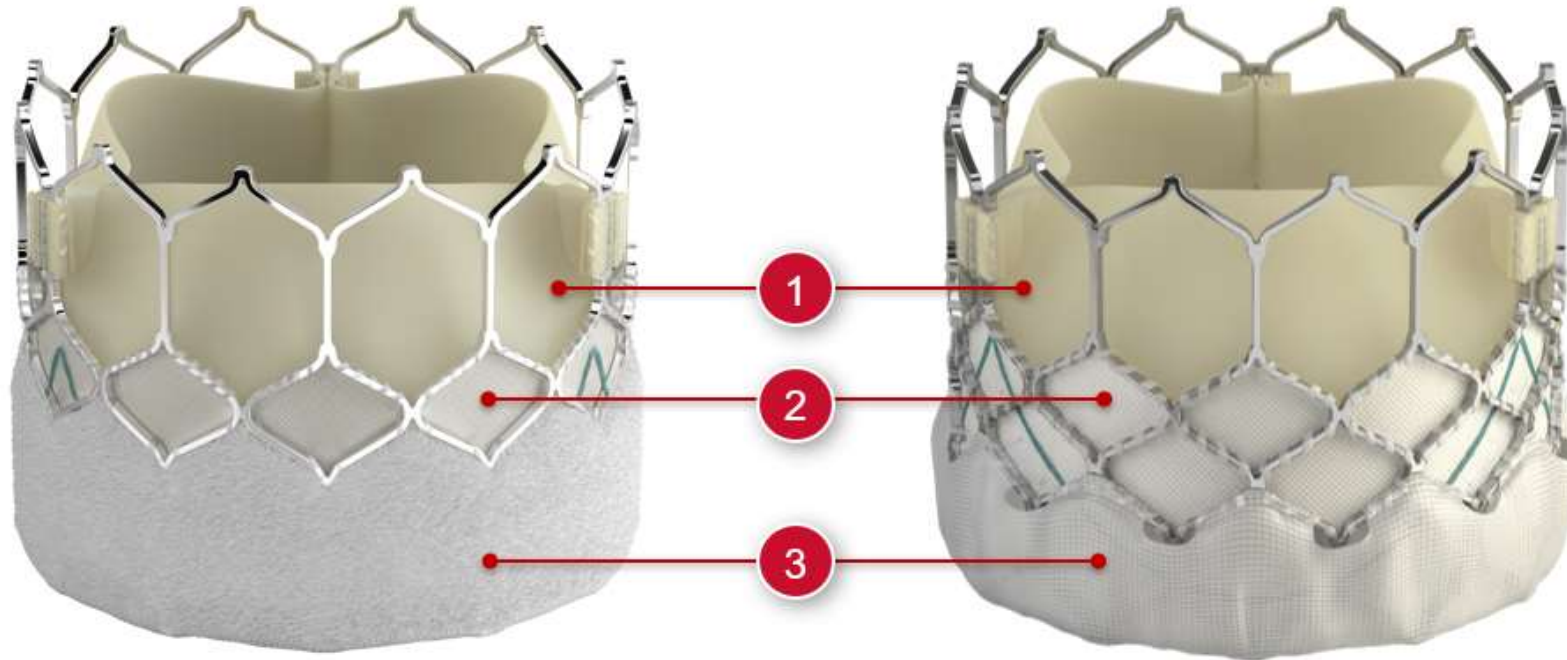


# 'Sapien 3 Ultra' Finally Launched in Korea



## Edwards SAPIEN 3 Ultra Transcatheter Heart Valve

## Edwards SAPIEN 3 Transcatheter Heart Valve



1

### Bovine pericardial tissue

- Scalloped leaflet shape
- Utilizes the same bovine pericardial tissue and processes as Edwards surgical valves

2

### Inner skirt

- Polyethylene terephthalate (PET) material

3

### Outer sealing skirt

- PET outer sealing skirt designed to minimize paravalvular leak

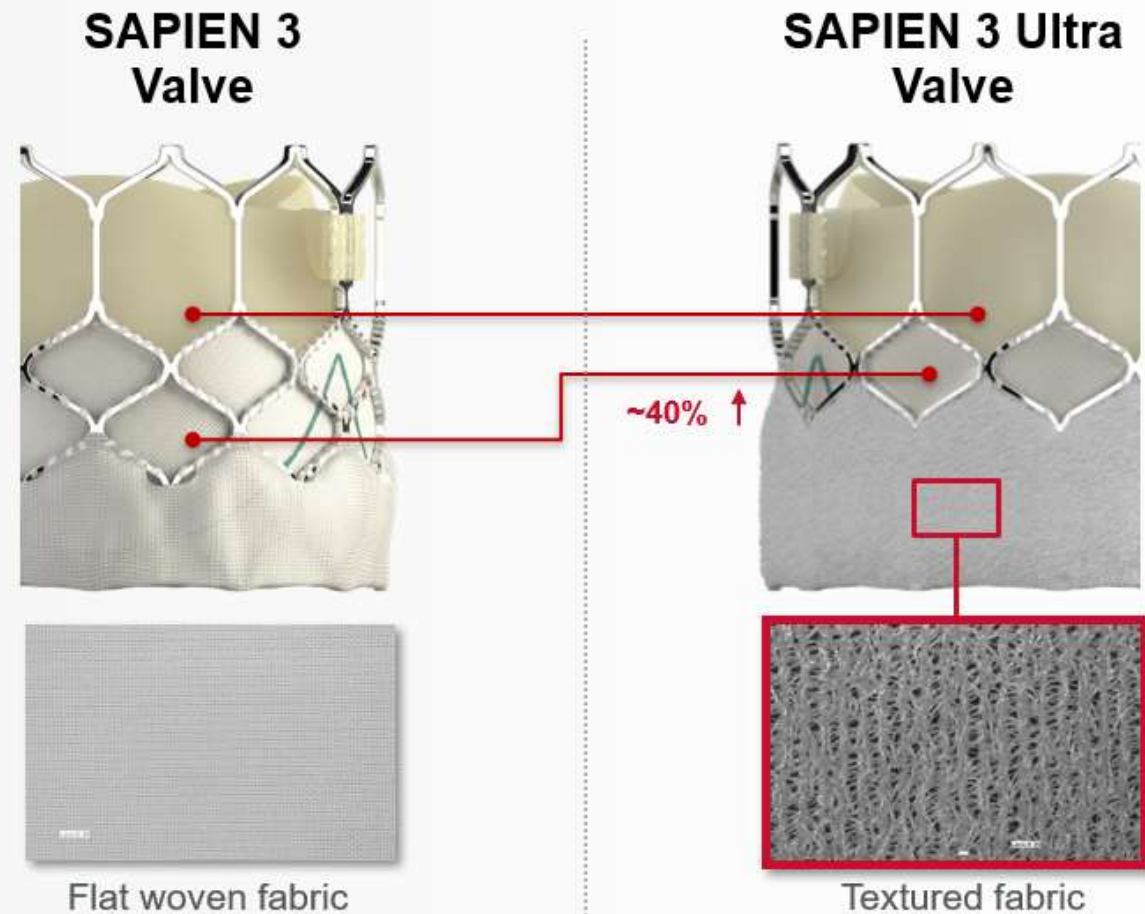
# Edwards SAPIEN 3 Ultra Transcatheter Heart Valve inner and outer skirt comparison

## Outer skirt

- ~40% outer skirt height increase versus SAPIEN 3 valve (From ~1/3 to ~1/2 of valve height)
- Textured outer skirt material designed to aid in sealing
- Same biocompatible PET material as SAPIEN 3 valve outer skirt

## Inner skirt

- Same inner skirt as SAPIEN 3 valve





# Summary of Product Differences

## What is the same as SAPIEN 3 on Commander System?

- Commander Delivery System
- eSheath Introducer set
- 29mm SAPIEN 3 may still include a balloon catheter in the kit if currently providing it in your region
- Valve Crimping components (crimper, qualcrimp, crimp stopper)

## What is different with SAPIEN 3 Ultra System?

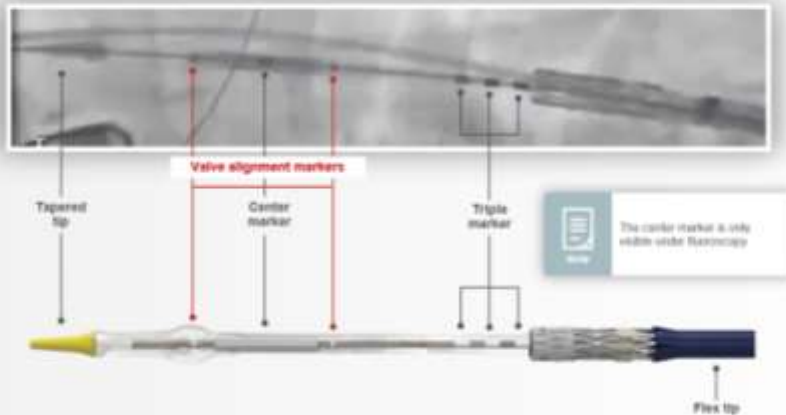
- THV: the SAPIEN 3 Ultra Valve System configuration is the same as SAPIEN 3 except for:
  - SAPIEN 3 Ultra Valve: Taller outer skirt – ~50% of valve height from a skirt height perspective, same material, but “textured” to aid in sealing
- The SAPIEN 3 Ultra Valve System currently comes with a (SAPIEN 3 “like”) Ultra Peel Away Loader
  - Balloon catheter is no longer provided as part of the kit for 20-26mm valves

# Summary of Procedure Differences

## What is the same as SAPIEN 3?

- Valve sizing
- THV orientation/confirmation
- Nominal inflation volumes
- THV alignment in the straight portion of the descending aorta

### Edwards Commander Delivery System – distal end



## What is different for SAPIEN 3 Ultra?

- Initial Valve Positioning
- The SAPIEN 3 Ultra Valve System currently comes with a (SAPIEN 3 “like”) Ultra Peel Away Loader

## Preparation, Procedural Overview, Intraprocedural, and Post-Procedure Considerations:

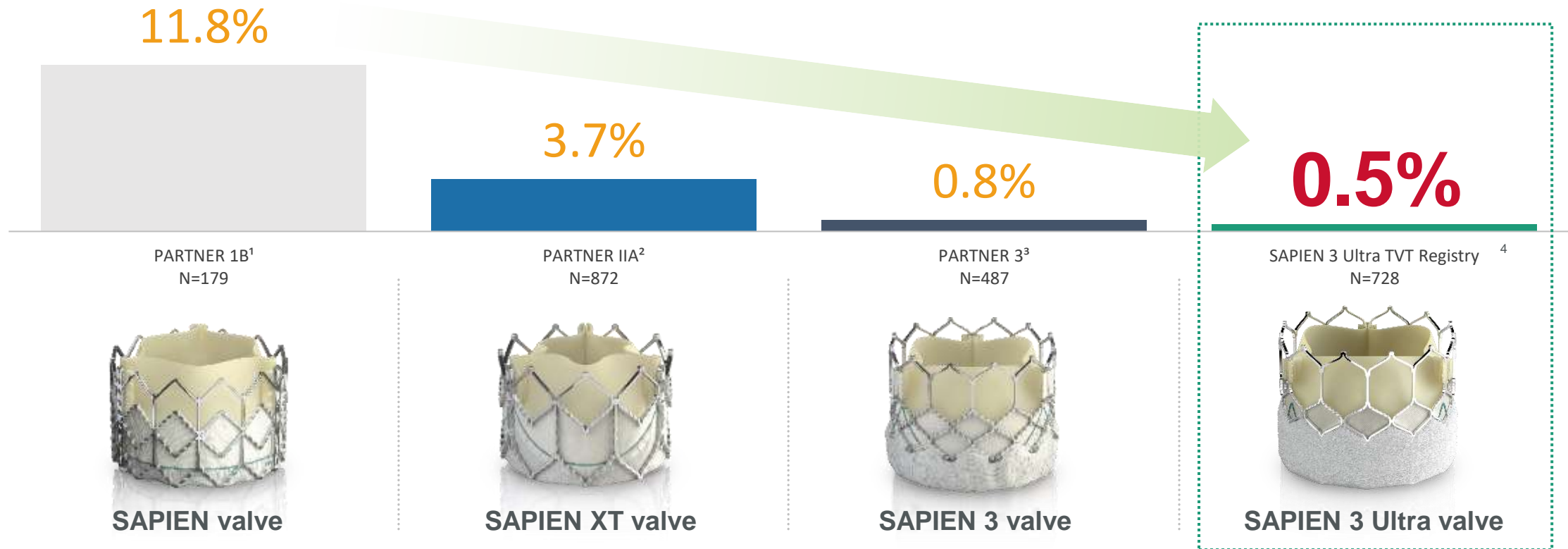
- Updates to clinical best practices
- New content around:
  - Ultrasounds guided access
  - System Advancement Force Best Practices
  - Post Procedure Care on conduction management best practices that align with Edwards Benchmark Program

# How better is Sapien 3 Ultra compared to Sapien 3?



# Delivering on the changing expectations of TAVI

Moderate or severe PVL at 30 days



1. Leon MB, Smith CR, Mack MJ, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363(17):1597-1607.

2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2016;374(17):1609-1620.

3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med.* 2019;380(18):1695-1705.

4. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020.

# SAPIEN 3 Ultra vs SAPIEN 3 TAVR Study Population

40,740 S3U and S3 Patients in  
TVT Registry  
(Jan 2019 – February 2020)

1164 Non-Native;  
2055 Non-Transfemoral;  
3196 Non-Elective;  
19 < 30 Days from Procedure

**SAPIEN 3 Ultra**  
N = 1324

**SAPIEN 3**  
N = 32982

**1:1 Propensity Score Matching**  
(27 Covariates)

**SAPIEN 3 Ultra**  
N = 1324

**SAPIEN 3**  
N = 1324

**Echocardiographic and clinical outcomes at discharge and 30 days**



# Baseline Characteristics Propensity-Matched

Characteristic Mean ± SD or %	SAPIEN 3 Ultra (N = 1324)	SAPIEN 3 (N = 1324)	p-value
Age (years)	79.5 ± 8.47	79.9 ± 7.98	0.21
Male	44.2	44.0	0.91
BMI (kg/m <sup>2</sup> )	29.1 ± 6.84	28.9 ± 6.22	0.51
STS Risk Score (%)	4.3 ± 3.12	4.4 ± 3.35	0.68
PAD	21.9	20.6	0.4
Carotid Stenosis	25.3	26.7	0.48
Atrial Fibrillation/Flutter	33.7	33.5	0.9
Prior Stroke	9.3	8.8	0.64
Chronic Lung Disease	35.3	35.4	0.95
Prior PCI	31.0	27.6	0.058
Prior CABG	11.0	11.0	1
Porcelain Aorta	2.3	2.1	0.79
GFR (mL/min/1.73 m <sup>2</sup> )	61.8 ± 25.28	62.6 ± 31.29	0.45
NYHA III/IV	57.4	57.8	0.83
KCCQ	48.2 ± 24.51	50.1 ± 24.30	0.05



# Baseline ECHO Propensity-Matched

Characteristic Mean ± SD or %	SAPIEN 3 Ultra (N = 1324)	SAPIEN 3 (N = 1324)	p-value
<b>LVEF</b>	<b>59.4 ± 11.69</b>	<b>59.8 ± 10.07</b>	<b>0.34</b>
<b>Mean Gradient (mmHg)</b>	<b>42.5 ± 14.07</b>	<b>43.1 ± 13.26</b>	<b>0.22</b>
<b>AV Area (cm<sup>2</sup>)</b>	<b>0.73 ± 0.21</b>	<b>0.74 ± 0.23</b>	<b>0.65</b>
<b>Aortic Regurgitation</b>			
<b>None/Trace</b>	<b>48.7</b>	<b>48.8</b>	<b>0.95</b>
<b>Mild</b>	<b>40.8</b>	<b>39.6</b>	<b>0.55</b>
<b>Moderate/Severe</b>	<b>10.6</b>	<b>11.6</b>	<b>0.40</b>
<b>Mitral Regurgitation (mod/sev)</b>	<b>12.6</b>	<b>12.7</b>	<b>0.95</b>
<b>Tricuspid Regurgitation (mod/sev)</b>	<b>11.7</b>	<b>12.4</b>	<b>0.57</b>

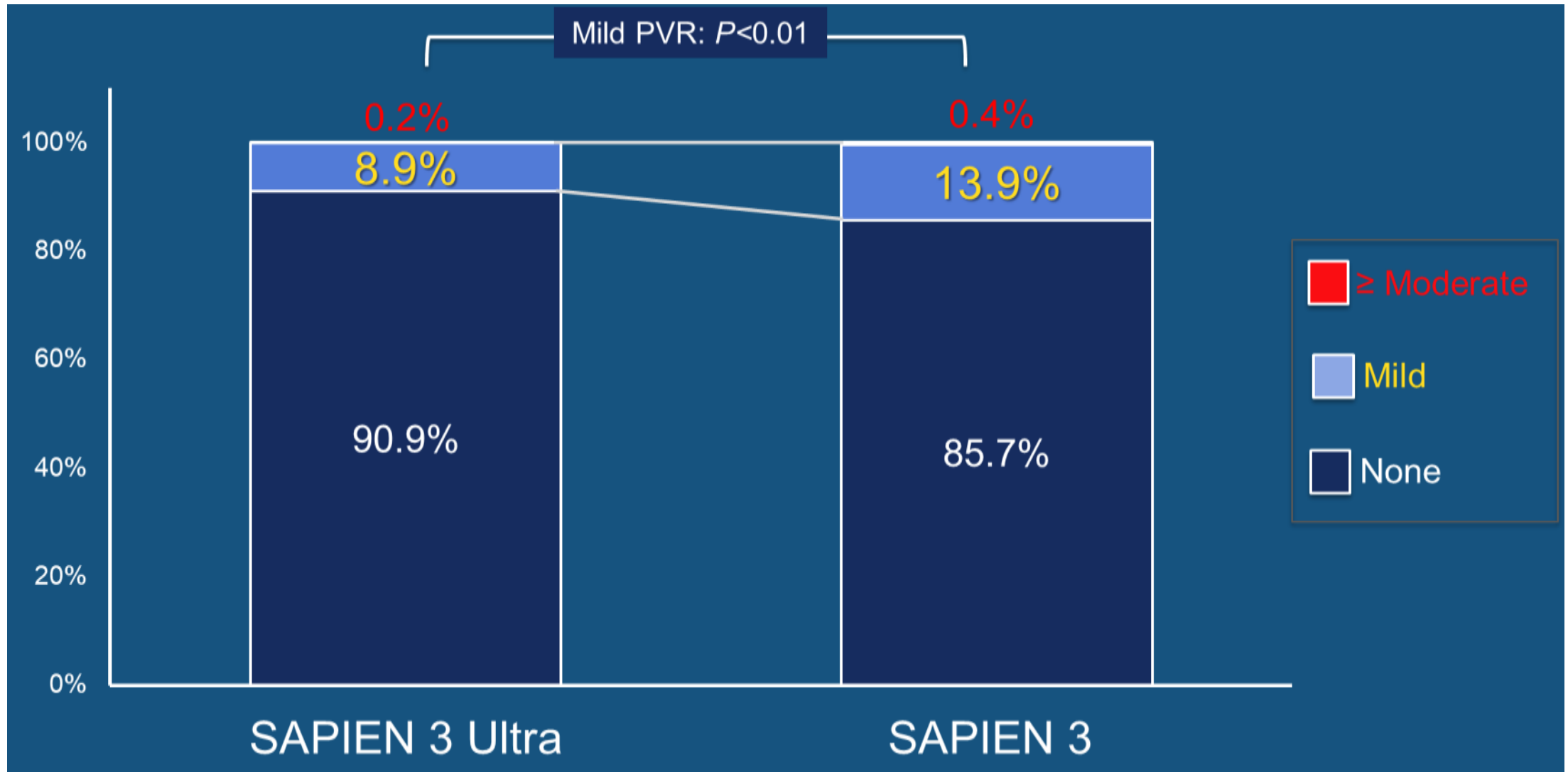
# Procedural Outcomes Propensity-Matched

Outcome Mean ± SD or %	SAPIEN 3 Ultra (N = 1324)	SAPIEN 3 (N = 1324)	p-value
Conscious Sedation	73.5	75.6	0.22
Valve Size			
20 mm	1.5	1.7	0.64
23 mm	45.5	46.1	0.73
26 mm	53.0	52.1	0.64
Procedure Time (min)	75.3 ± 36.63	81.7 ± 40.57	<0.01
Fluoroscopy Time (min)	13.2 ± 10.32	14.7 ± 8.48	<0.01
Device Success	97.1	98.0	0.11
Conversion to Open Heart Surgery	0.2	0.1	1.00
Coronary Compression/Obstruction	0.1	0.0	1.00
Annulus Rupture	0.0	0.0	N/A

# Index Hospitalization Propensity-Matched

Outcome Median [IQR] or %	SAPIEN 3 Ultra (N = 1324)	SAPIEN 3 (N = 1324)	p-value
ICU LOS (hours)	2.4 [0.0, 26.0]	7.0 [0.0, 26.0]	0.41
% with No ICU Stay	40.6	39.7	0.63
Hospital LOS (days)	2.0 [1.0, 2.0]	1.0 [1.0, 2.0]	0.02
≤ 1 day	48.4	52.2	0.05
2 days	29.6	29.7	0.97
≥ 3 days	22.0	18.1	0.01
Discharge Location			
Home	94.0	92.6	0.16
Extended Care/TCU/Rehab	3.4	4.3	0.23
Other	2.6	3.1	0.48

# Discharge Paravalvular Regurgitation Propensity-Matched



# 30-Day Clinical Outcomes Propensity-Matched

Outcome Mean ± SD or %	SAPIEN 3 Ultra (N = 1324)	SAPIEN 3 (N = 1324)	p-value
All-cause Mortality	0.9	1.3	0.34
Cardiac Death	0.5	0.3	0.63
Stroke	1.2	1.7	0.38
All-cause Mortality or Stroke	1.9	2.9	0.11
Aortic Valve Re-intervention	0.0	0.0	N/A
Life-threatening Bleeding	0.0	0.3	0.10
Major Vascular Complication	1.1	0.9	0.66
New Requirement for Dialysis	0.4	0.2	0.35
New Pacemaker (including baseline)	6.0	5.7	0.66
Any Readmission	4.4	6.8	0.02
NYHA III/IV	4.6	5.5	0.42
KCCQ	79.2 ± 20.83	77.6 ± 21.02	0.12

# Clinical Outcomes Are Comparable to S3 Ultra Prospective, Multicenter Study

2019 PCR london valves

Secondary Endpoints to 30 Days

Outcome	N = 83
Mortality	1 (1.2)*
Stroke	2 (2.4)
Disabling Stroke	2 (2.4)
AKI – Stage 2 or 3	1 (1.2)
New PPMI (incl baseline)	8 (9.6)
New LBBB (incl baseline)	10 (12.0)
Coronary Obstruction	1 (1.2)
AV Re-intervention	0
Endocarditis	0
Valve Thrombosis	0

n (%)  
\*Cause of death was terminal renal failure

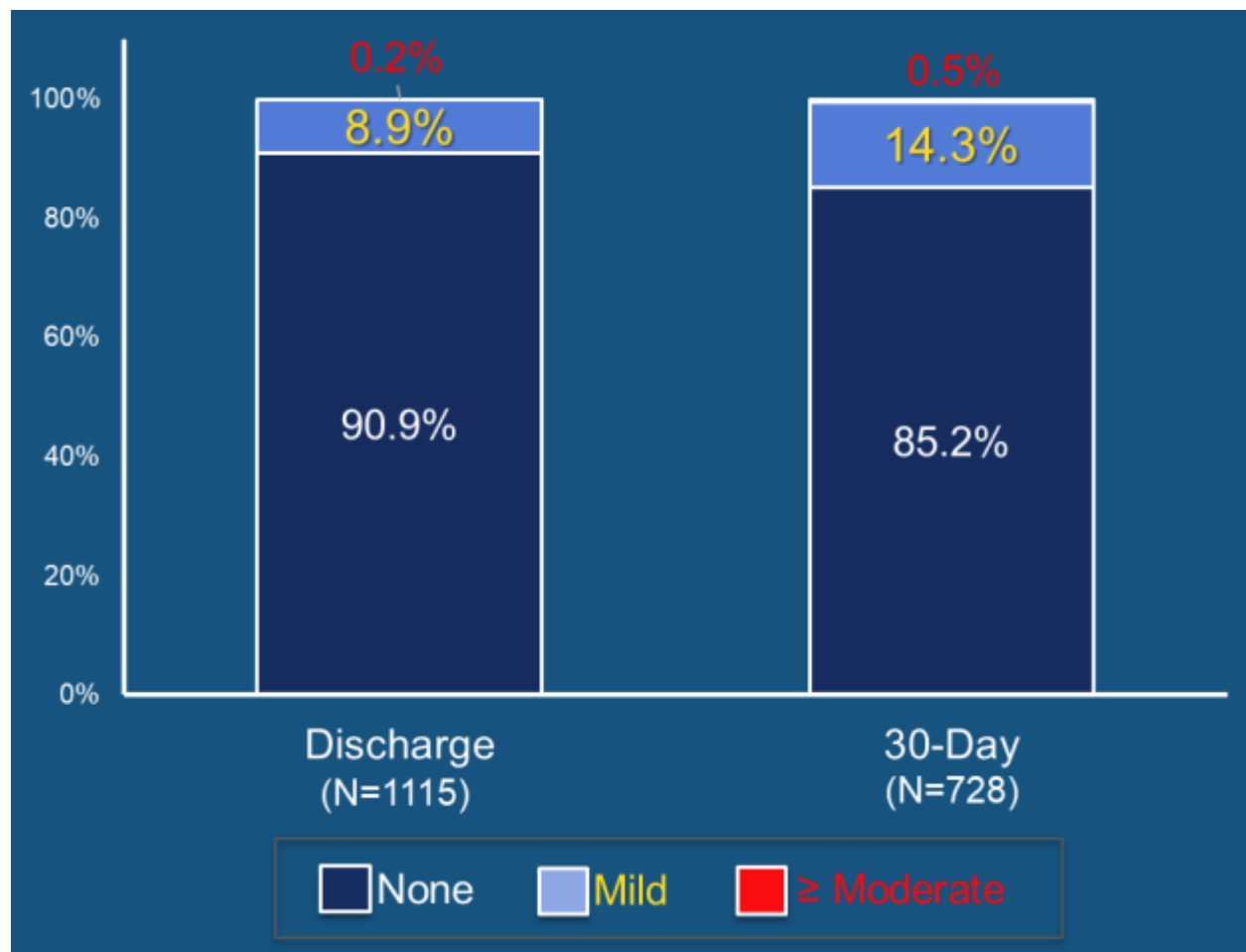
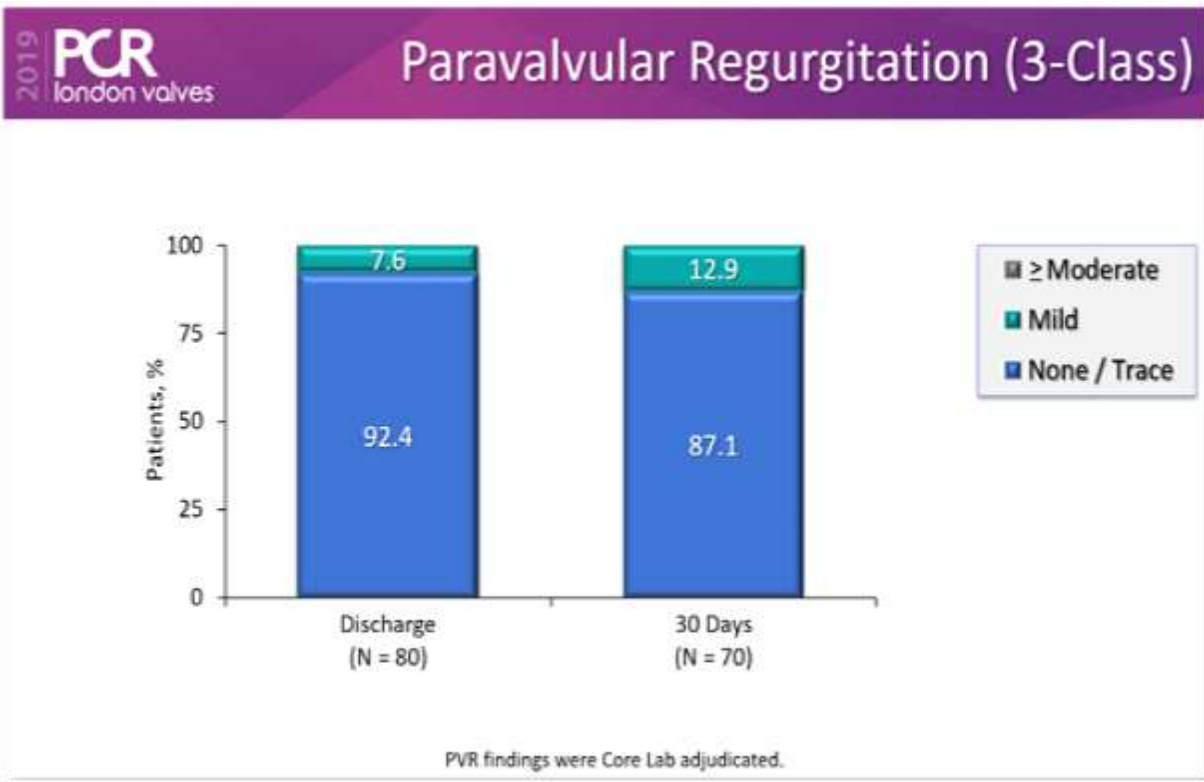
Outcome %	SAPIEN 3 Ultra (N = 1324)
All-cause Mortality	0.9
Stroke	1.2
New Pacemaker (inc baseline)	6.0
Coronary Obstruction	0.1
Aortic Valve Re-intervention	0.0
Endocarditis	0.0
Valve Thrombosis	0.1

Webb J. PCR London Valves; November 18, 2019; London, England.





# PVR Rates Are Comparable to SAPIEN 3 Ultra Prospective, Core Lab Adjudicated, Multicenter Study

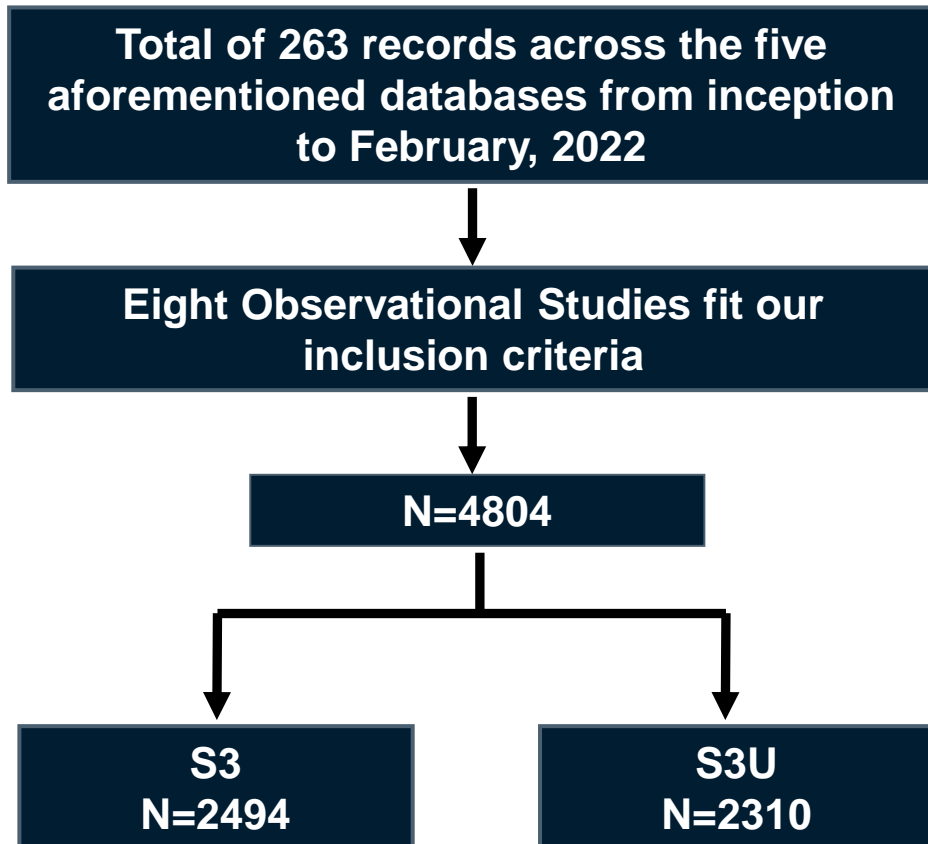


Webb J. PCR London Valves; November 18, 2019; London, England.



# Short-term Outcomes of TAVI Using the Sapien 3 vs Sapien 3 Ultra: Updated Meta-Analysis

## PRISMA Flowchart



## Baseline Characteristics

- Mean age was 79.9 years (S3U:79.8 vs S3:80.0)
- Male Sex: 48.8% (S3U:48.3% vs S3:49.3%)
- Mean STS score was 4.4 (S3U:4.2 vs S3:4.5)
- The primary endpoint: all-cause mortality
- Secondary endpoints: stroke, major bleeding, PPMI, mild/moderate/severe PVL

# Primary Endpoint: All-Cause Mortality

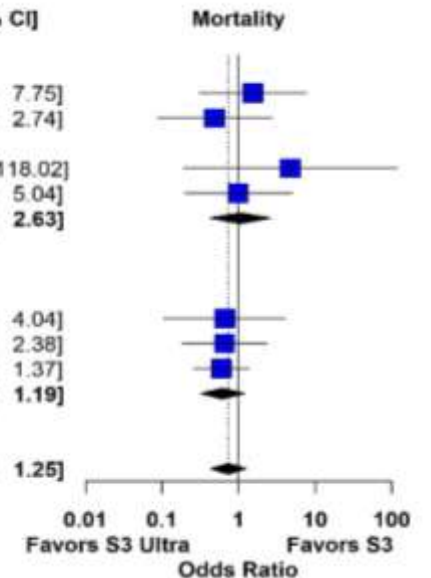


VS



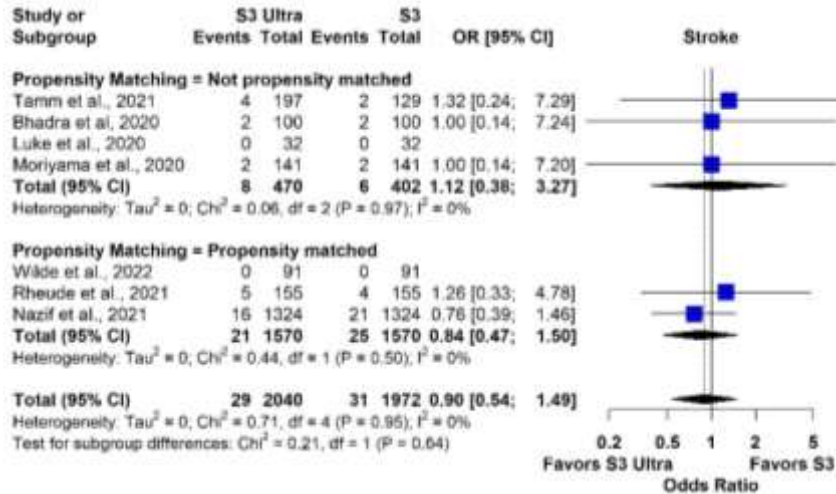
- There were **no** statistically significant differences between S3 Ultra and S3 with respect to all-cause mortality (1.16% vs. 1.55%; OR: 0.74; 95% CI: 0.43-1.25)

Study or Subgroup	S3 Ultra		S3		OR [95% CI]
	Events	Total	Events	Total	
<b>Propensity Matching = Not propensity matched</b>					
Tamm et al., 2021	3	129	3	197	1.54 [0.31; 7.75]
Bhadra et al., 2020	2	100	4	100	0.49 [0.09; 2.74]
Luke et al., 2020	0	32	0	32	
Weile et al., 2020	1	101	0	159	4.76 [0.19; 118.02]
Moriyama et al., 2020	3	141	3	141	1.00 [0.20; 5.04]
<b>Total (95% CI)</b>	<b>9</b>	<b>503</b>	<b>10</b>	<b>629</b>	<b>1.05 [0.42; 2.63]</b>
Heterogeneity: Tau <sup>2</sup> = 0; Chi <sup>2</sup> = 0.92, df = 3 (P = 0.82); I <sup>2</sup> = 0%					
<b>Propensity Matching = Propensity matched</b>					
Wilde et al., 2022	2	91	3	91	0.66 [0.11; 4.04]
Rheude et al., 2021	4	155	6	155	0.66 [0.18; 2.38]
Nazif et al., 2021	9	1324	15	1324	0.60 [0.26; 1.37]
<b>Total (95% CI)</b>	<b>15</b>	<b>1570</b>	<b>24</b>	<b>1570</b>	<b>0.62 [0.32; 1.19]</b>
Heterogeneity: Tau <sup>2</sup> = 0; Chi <sup>2</sup> = 0.02, df = 2 (P = 0.99); I <sup>2</sup> = 0%					
<b>Total (95% CI)</b>	<b>24</b>	<b>2073</b>	<b>34</b>	<b>2199</b>	<b>0.74 [0.43; 1.25]</b>
Heterogeneity: Tau <sup>2</sup> = 0; Chi <sup>2</sup> = 1.42, df = 6 (P = 0.96); I <sup>2</sup> = 0%					
Test for subgroup differences: Chi <sup>2</sup> = 0.86, df = 1 (P = 0.35)					

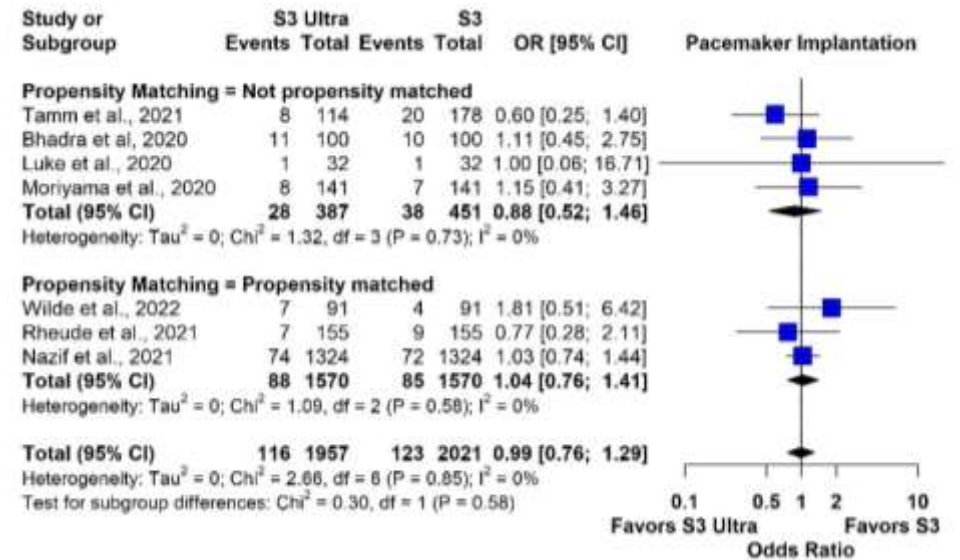


# Secondary Clinical Endpoints

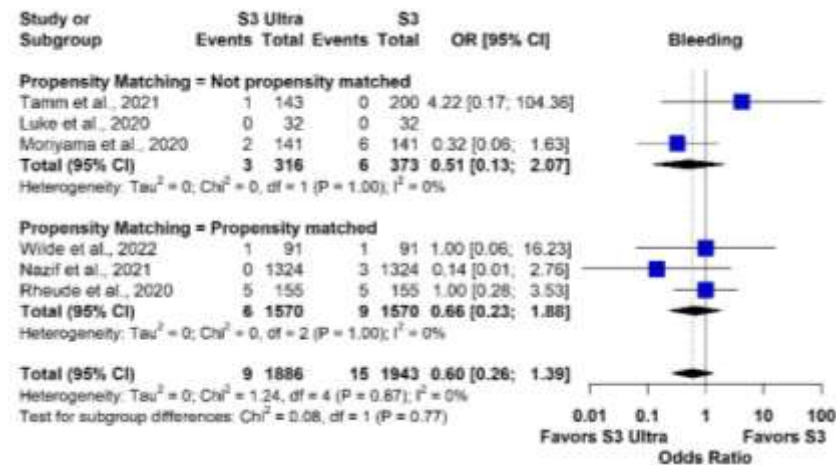
## Stroke



## Pacemaker at 30-days



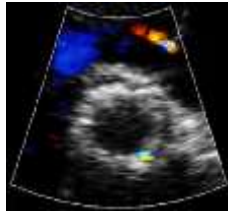
## Bleeding



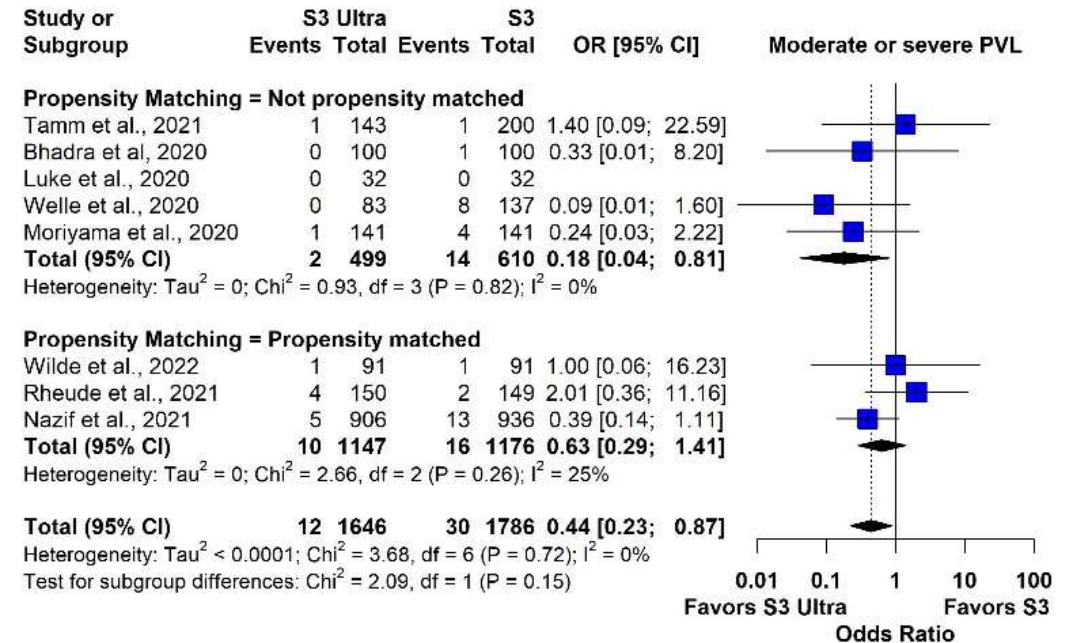
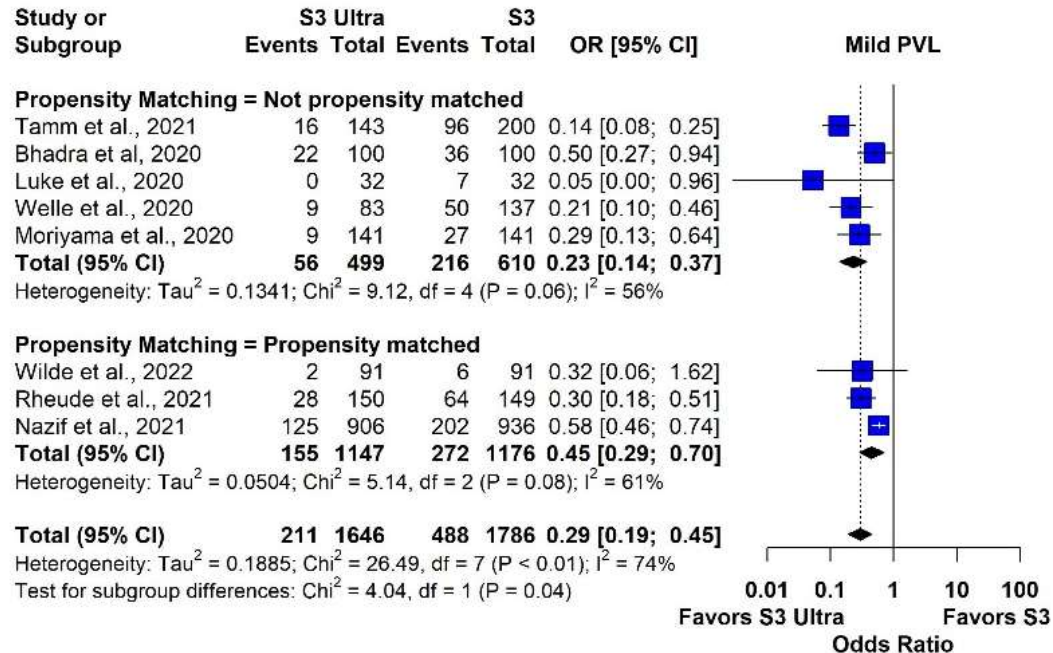
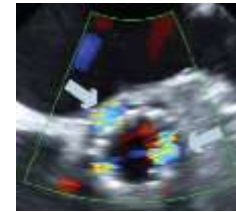


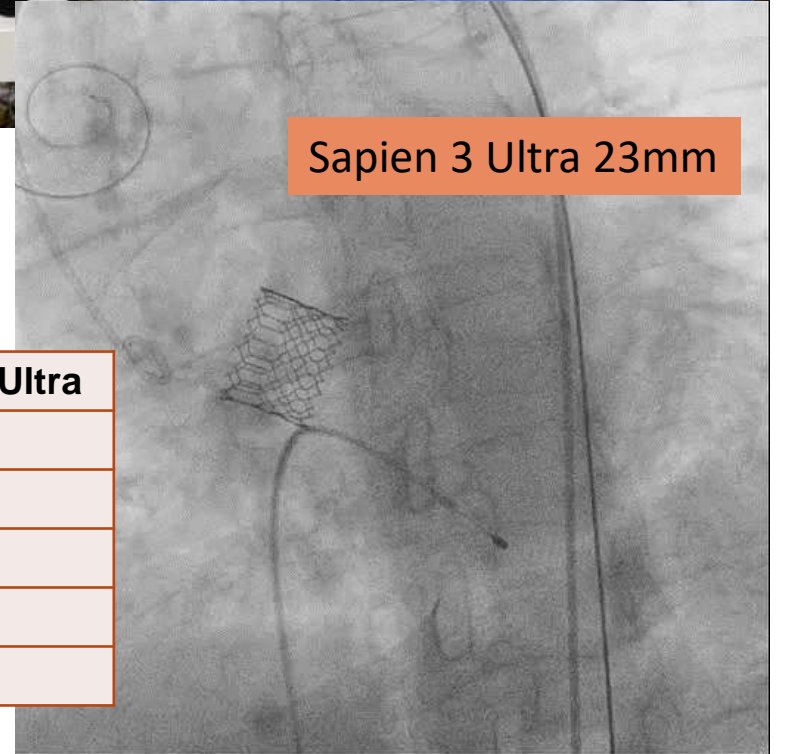
# Secondary Hemodynamic Endpoints

## Mild PVL



## Moderate/Severe PVL





Sapien 3 Ultra 23mm

Recent cases	Sapien 3	Sapien 3 Ultra
case (N)	10	4
PVL		
None	7	4
Mild	3	0
≥Moderate	0	0



# Summary

- **Same system**
  - Edward Commander delivery system
- **Same procedure**
- **But upgrade valve (Sapien 3 Ultra)**
  - Outer skirt
  - More advanced to reduce PVL

