SAPIEN 3:
PARTNER 2 and Real World Registries

John Webb MD

Director interventional cardiology, St Paul's Hospital
McLeod Professor of heart valve intervention, University of British Columbia
Medical director transcatheter heart valve program, Province of BC
Vancouver, Canada

Centre for
Heart Valve Innovation
St. Paul's Hospital, Vancouver

UBC

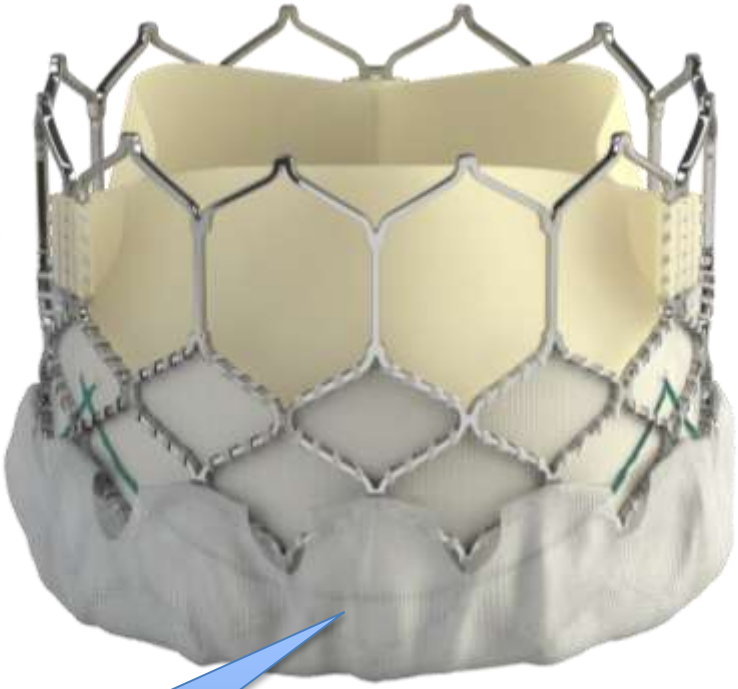
Consultant:

- Abbott
- Edwards Lifesciences
- Gore
- Medtronic
- Mitralign
- Orford
- St Jude Medical
- Transverse Medical
- Siemens
- Valtech
- Vivitro

SAPIEN 3

Lower profile

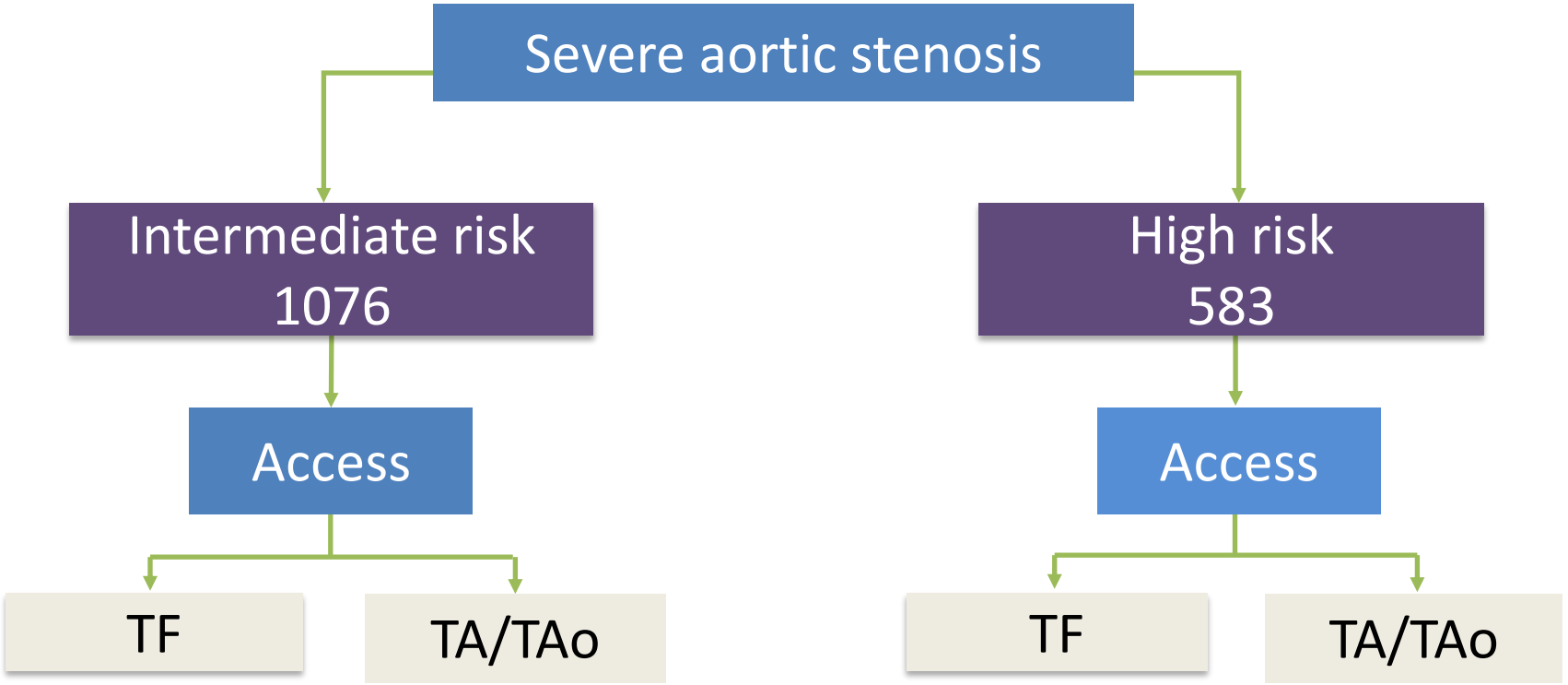
3mm longer



Outer sealing skirt

PARTNER II SAPIEN 3 Trial

Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis



Hemodynamic function was excellent

Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis

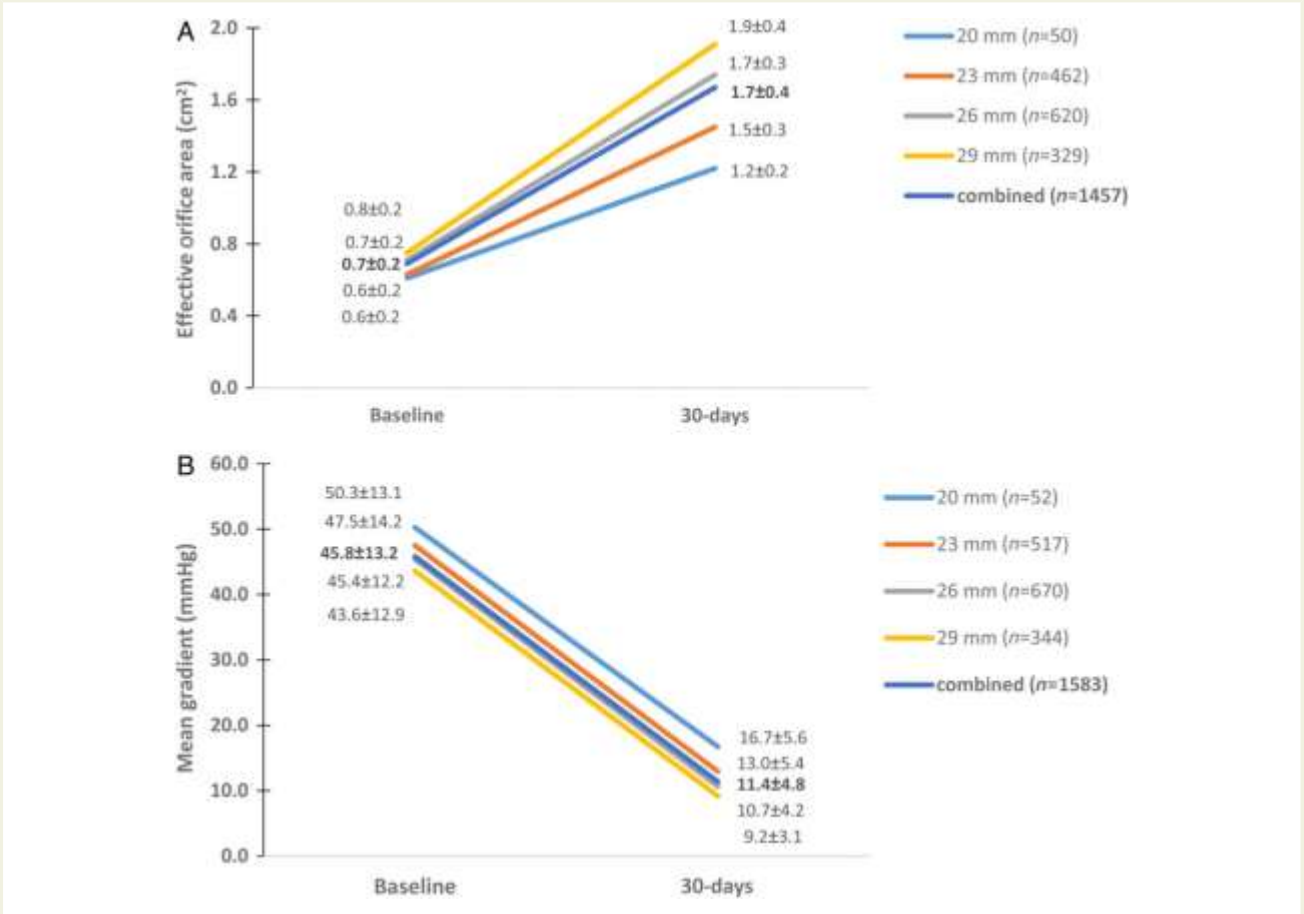
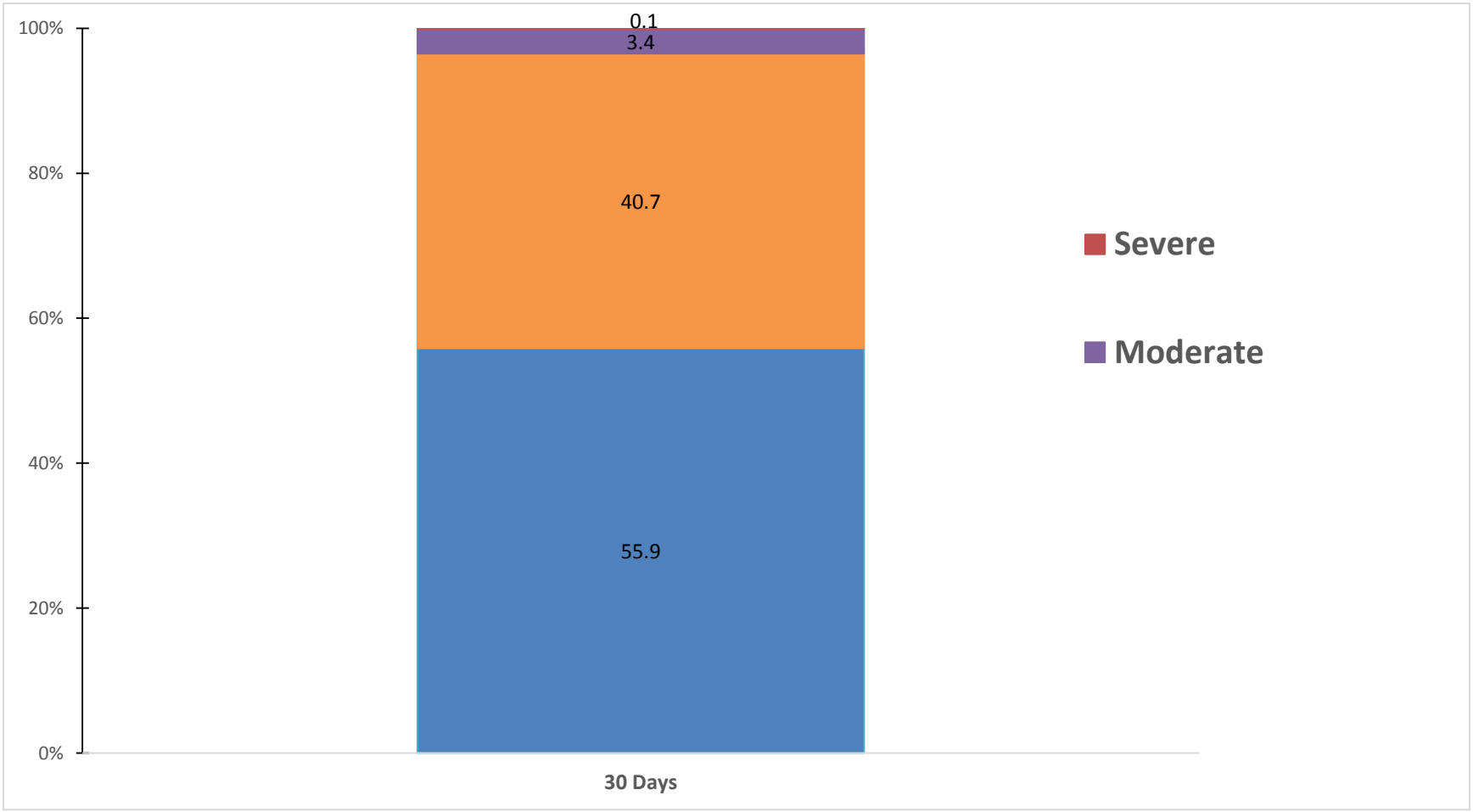


Figure 3 Change in effective orifice area and mean gradient stratified by transcatheter heart valve size. The effective orifice area (*A*) and mean aortic valve gradient (*B*) stratified by valve size are shown at baseline and 30-day follow-up.

Paravalvular leaks none or mild in 97.5%



PARTNER II: High and Intermediate risk

NYHA functional status improved dramatically

Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis

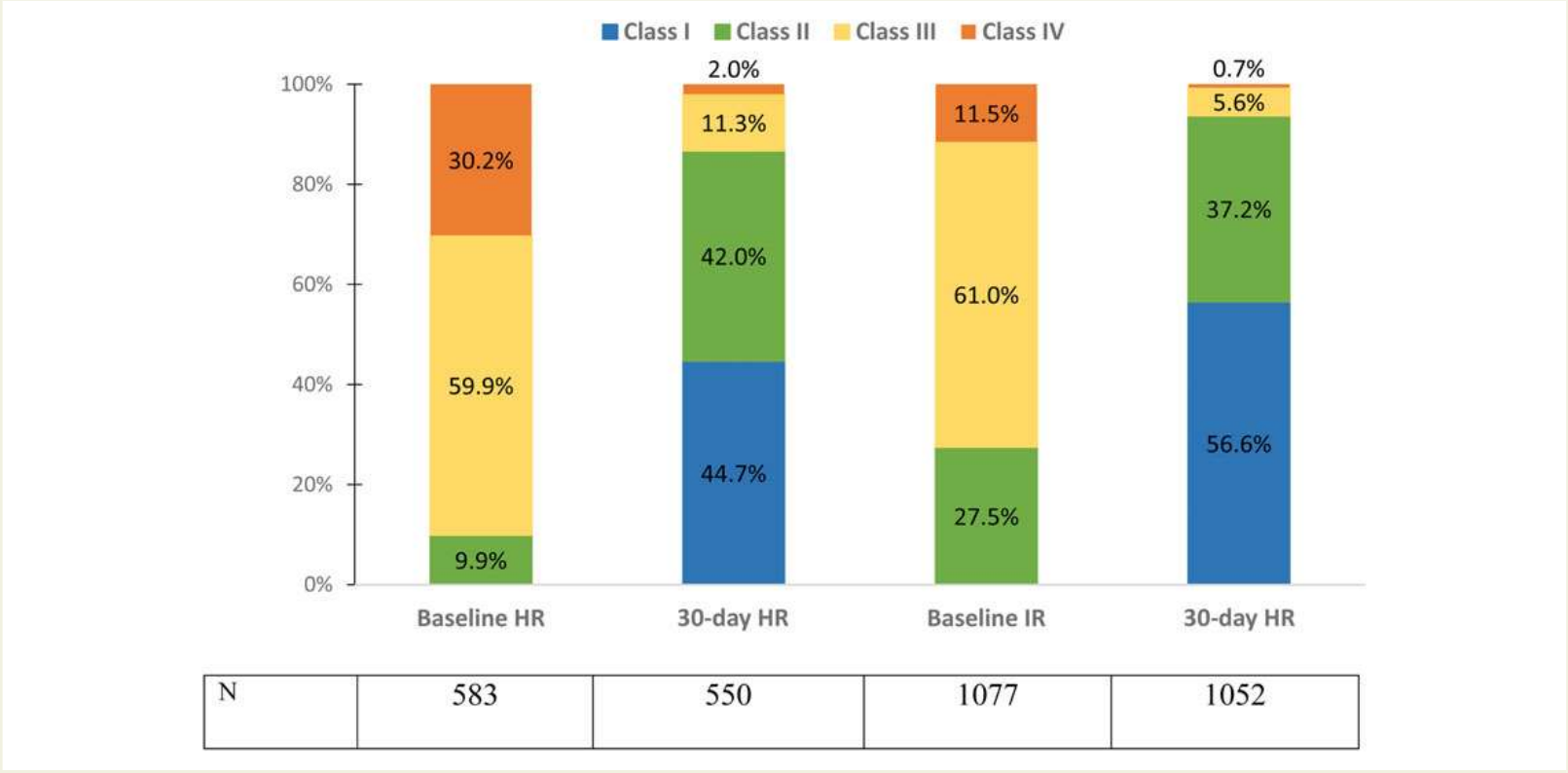
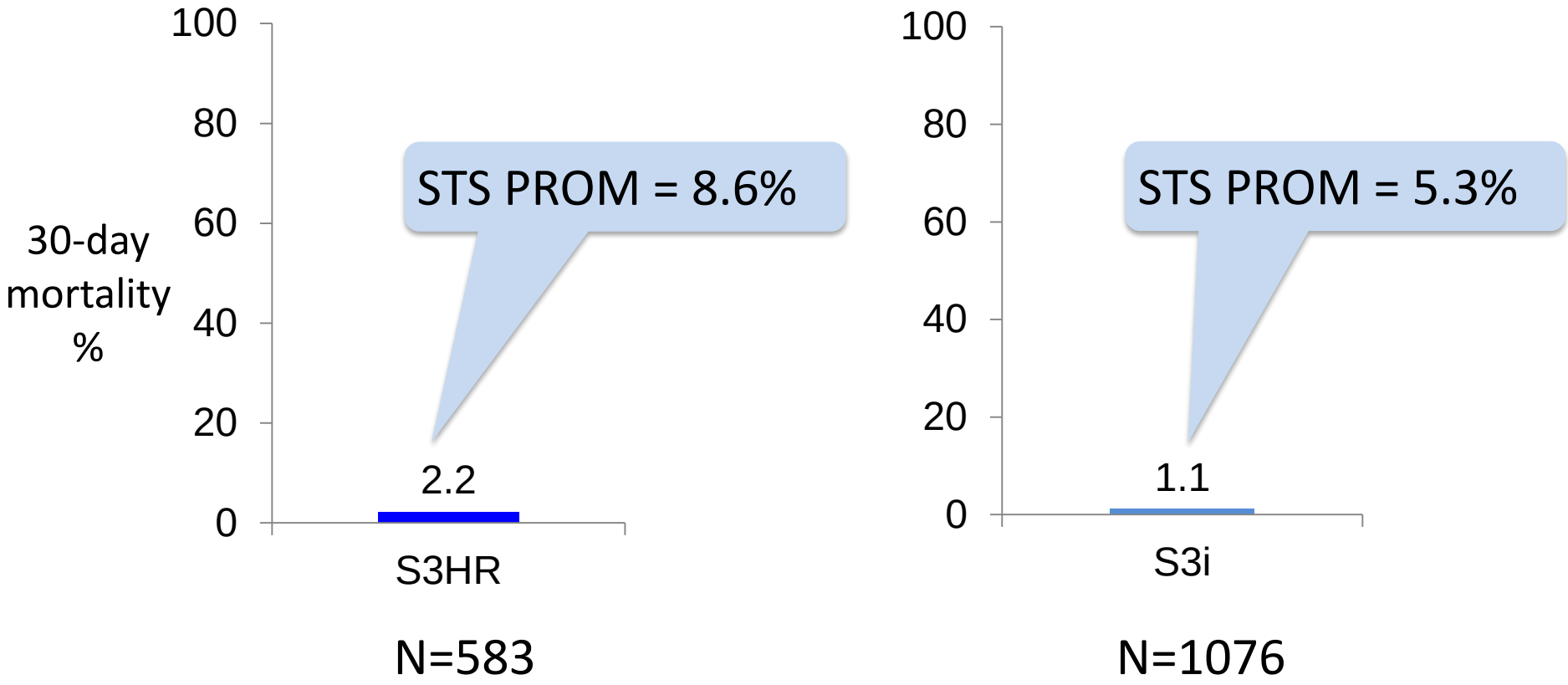


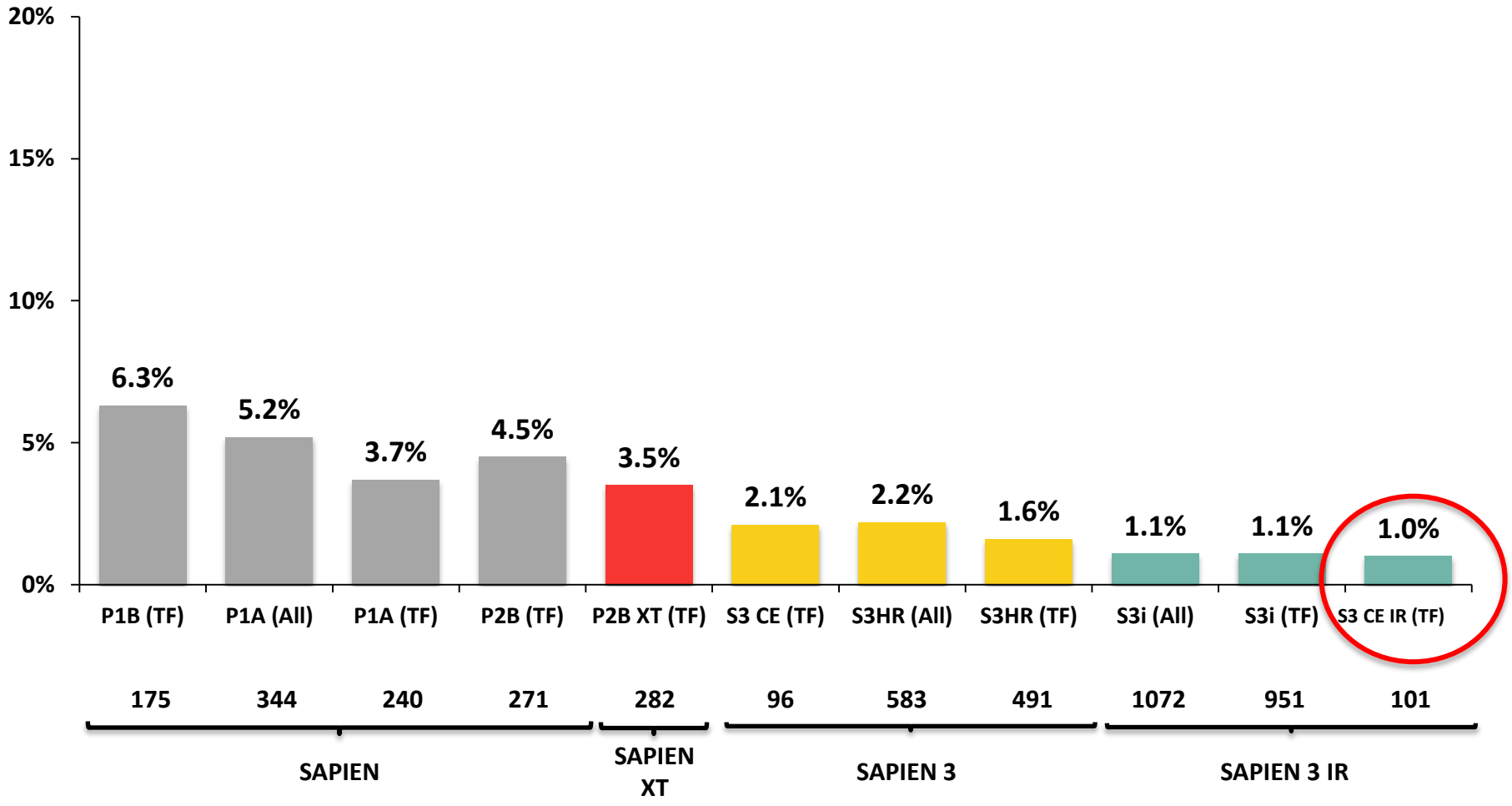
Figure 2 Symptom status by New York Heart Association functional class. Symptom status according to New York Heart Association class is shown at baseline and at 30 days among patients in both HR/inoperable and intermediate risk cohorts.

PARTNER II SAPIEN 3 Trial

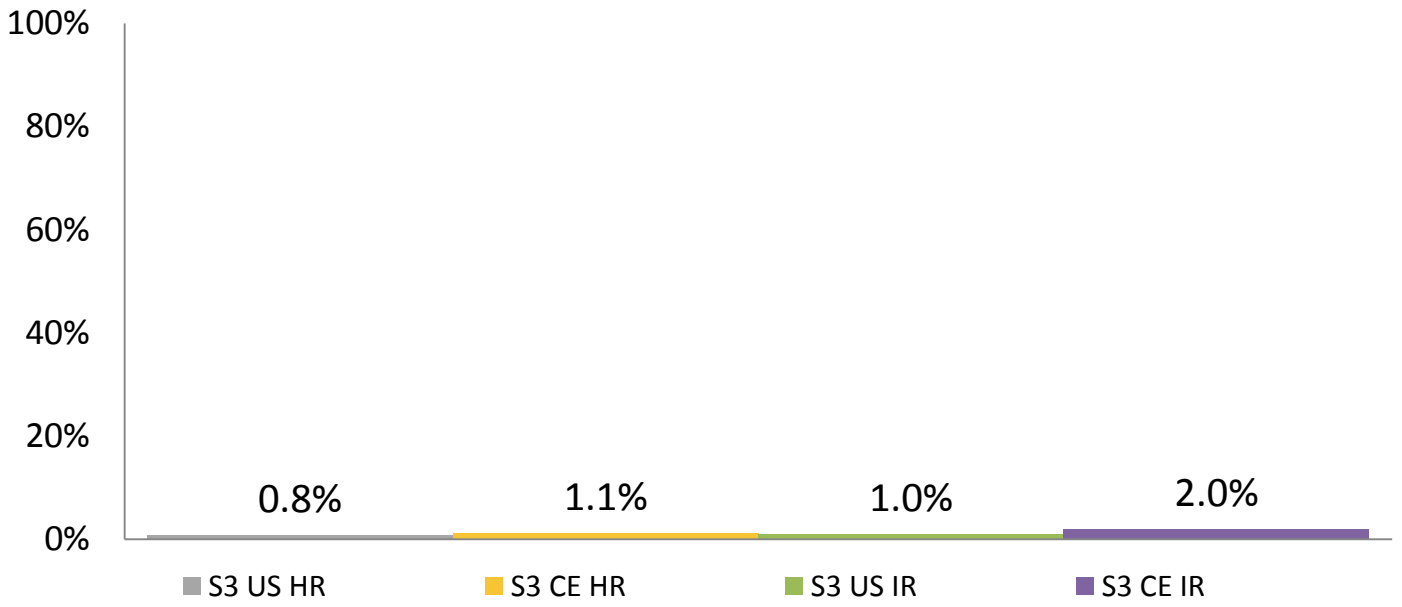


ACC 2015

Edwards SAPIEN valve studies
Mortality at 30 Days



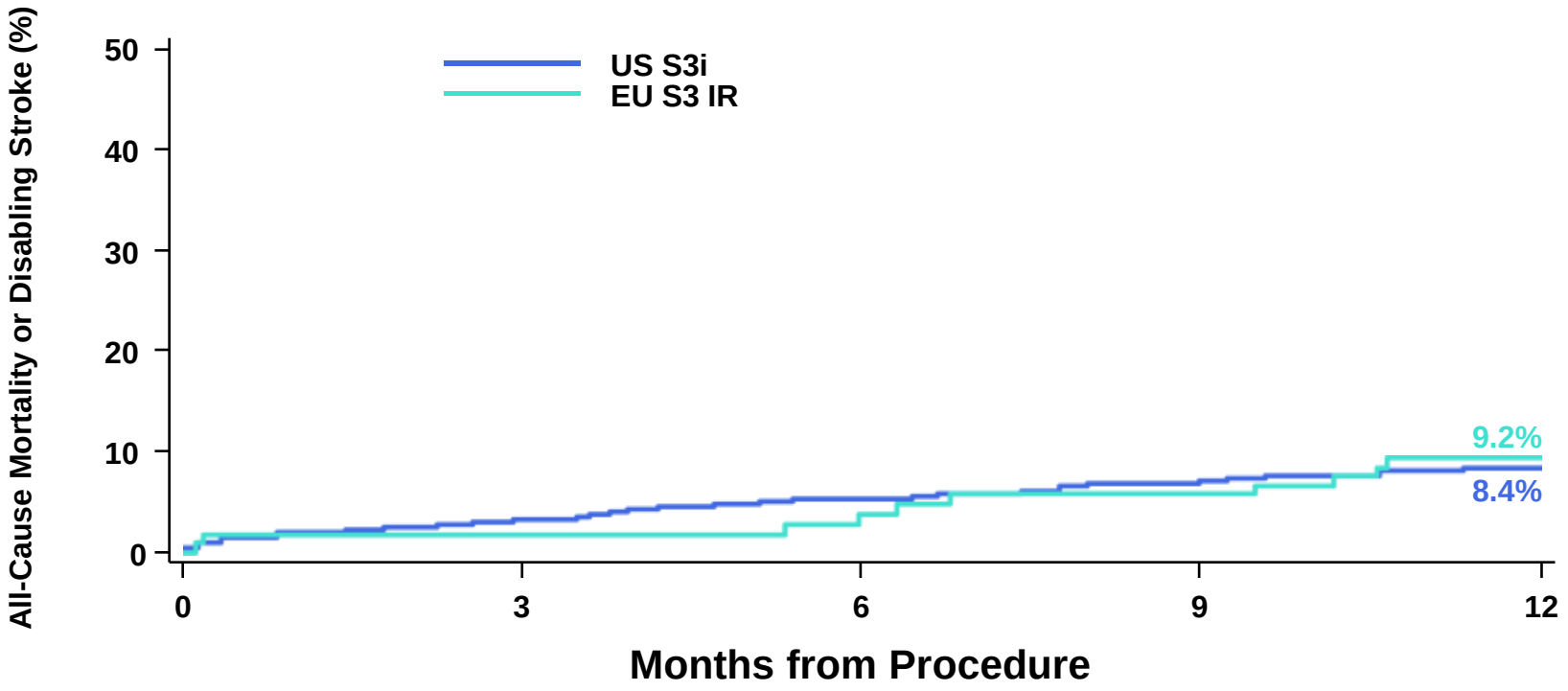
SAPIEN 3 trials: disabling stroke



"disabling stroke" defined as stroke, with <u>any</u> permanent disability

All-Cause Mortality and Disabling Stroke at 1 year

Intermediate risk EU and PARTNER studies



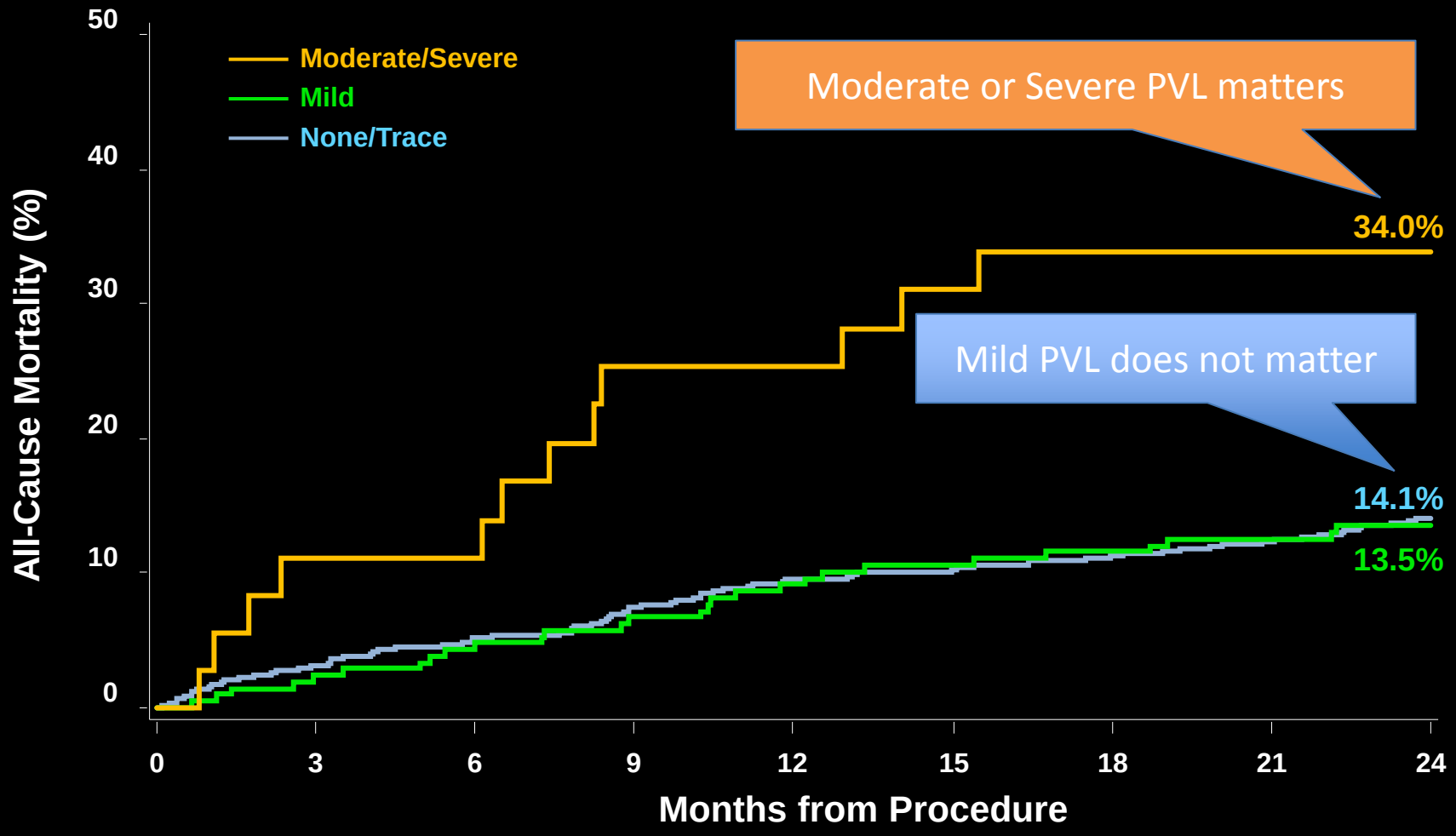
Number at risk:

US S3i	1,077	1,033	1,008	984	953
EU S3IR	109	107	105	103	85

The NEW ENGLAND JOURNAL of MEDICINE

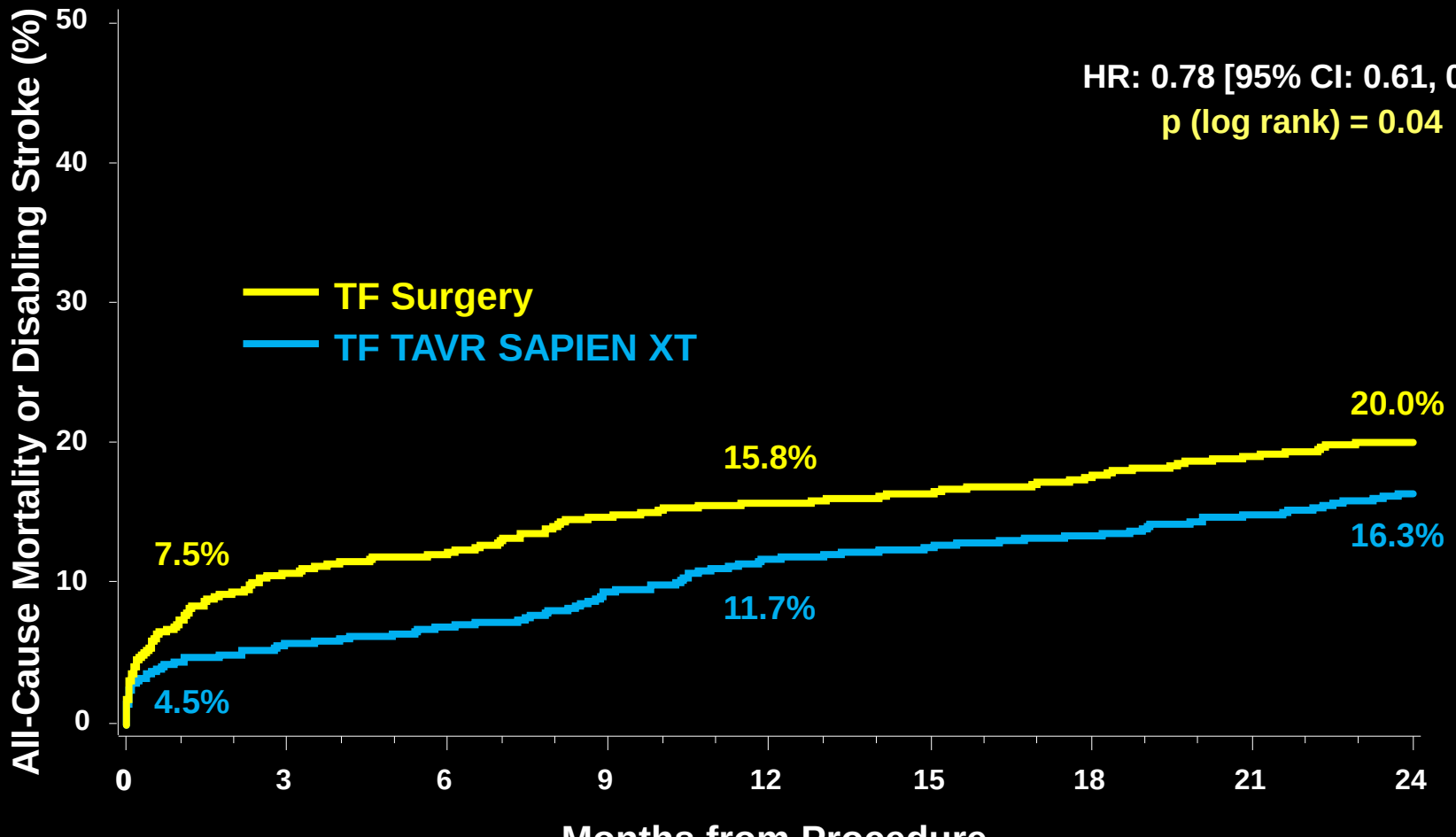
PARTNER 2A

All-cause Mortality and Severity of PVR at 30 Days



PARTNER 2: TF Primary Endpoint (AT)

All-Cause Mortality or Disabling Stroke



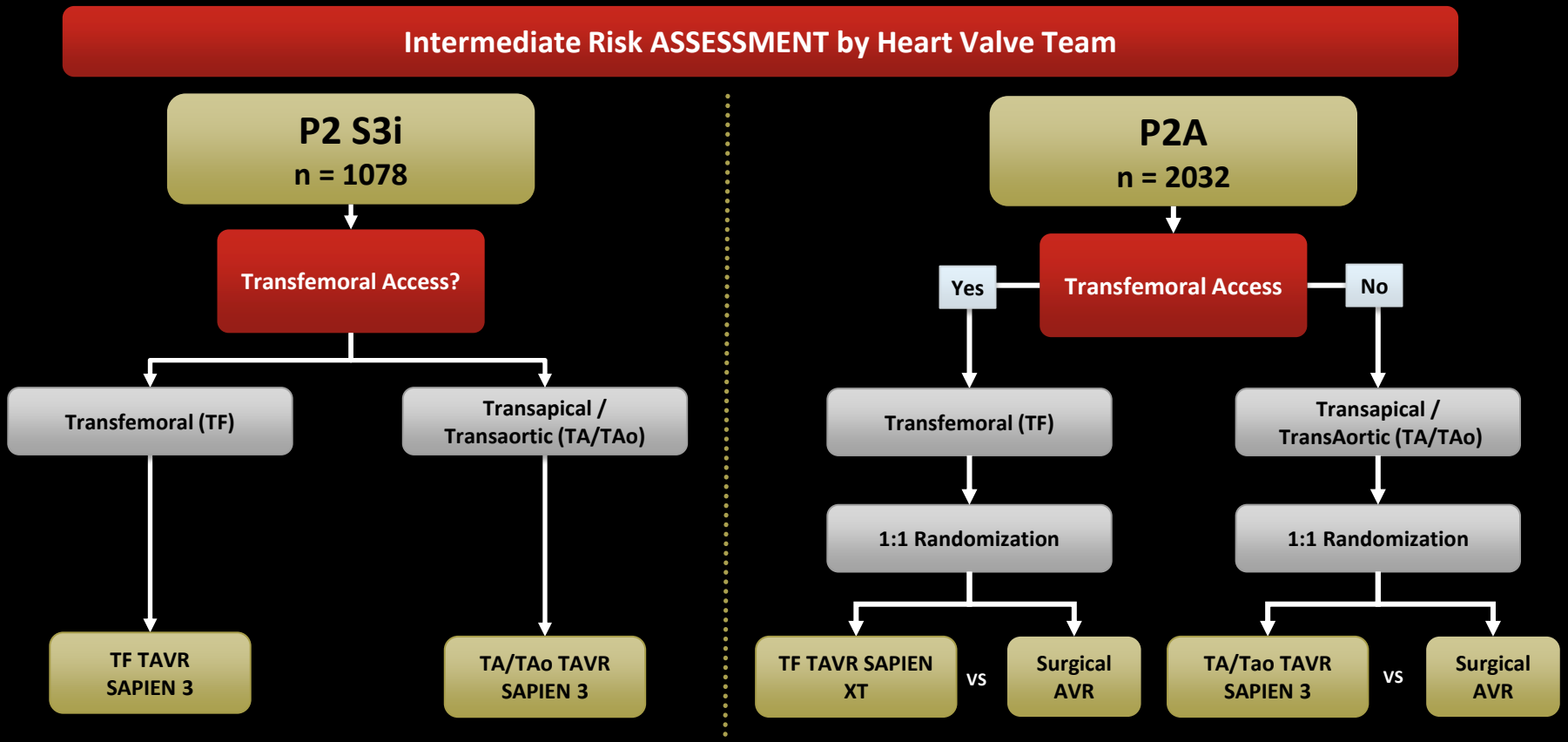
Number at risk:									
TF Surgery	722	636	624	600	591	573	565	555	537
TF TAVR	762	717	708	685	663	652	644	634	612

The PARTNER 2A and S3i Trials

Study Design

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Lancet 2016

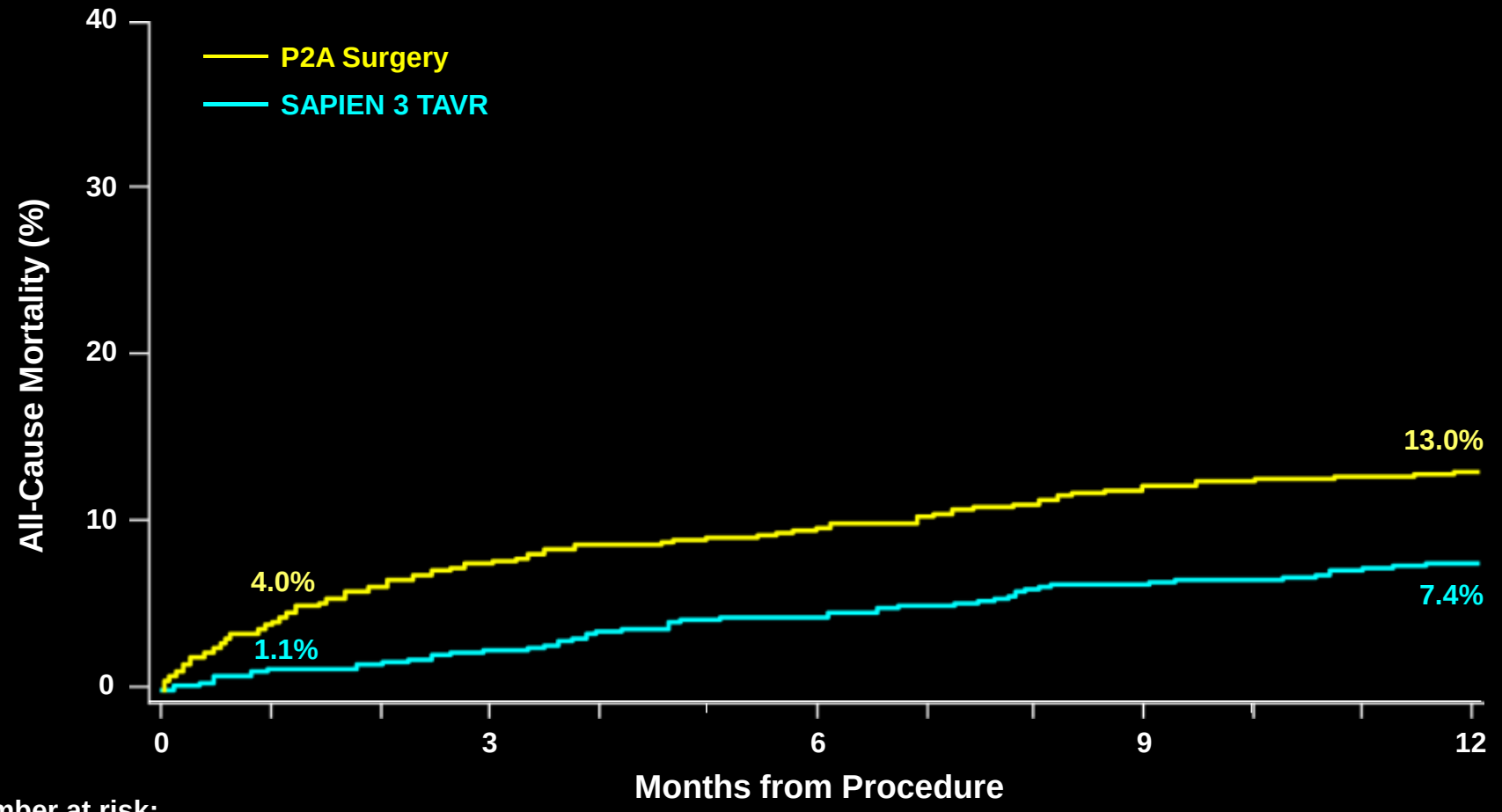


All-Cause Mortality

PARTNER 2A and S3i Propensity Analysis

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Lancet 2016



Number at risk:

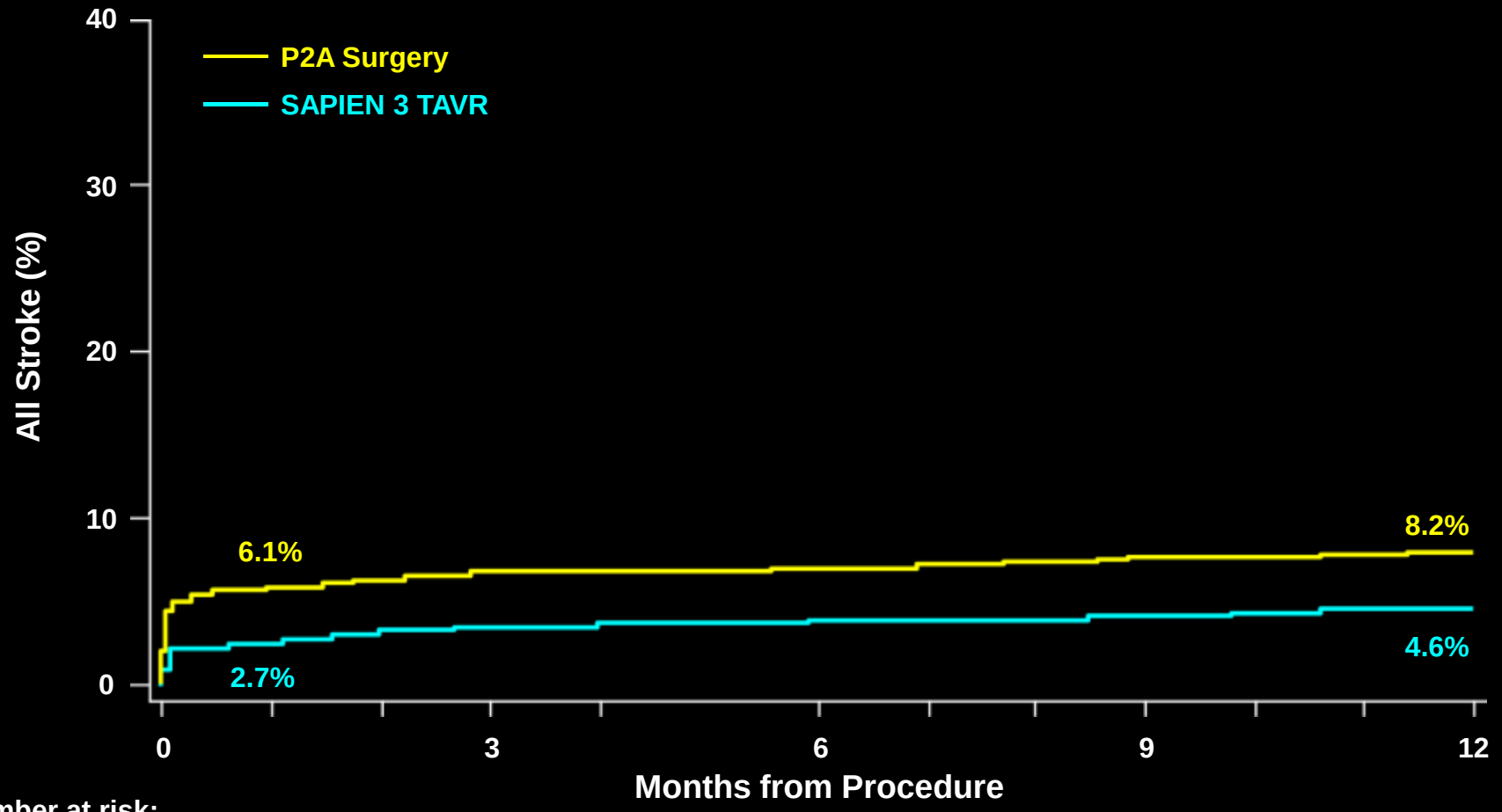
P2A Surgery	944	859	836	808	795
S3 TAVR	1077	1043	1017	991	963

All Stroke

PARTNER 2A and S3i Propensity Analysis

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Lancet 2016



Number at risk:

P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

PARTNER III:
Low risk trial approved: Jan 15th 2016

FDA Approves Expanded Indication Study for Edwards' Sapien 3 TAVR Device

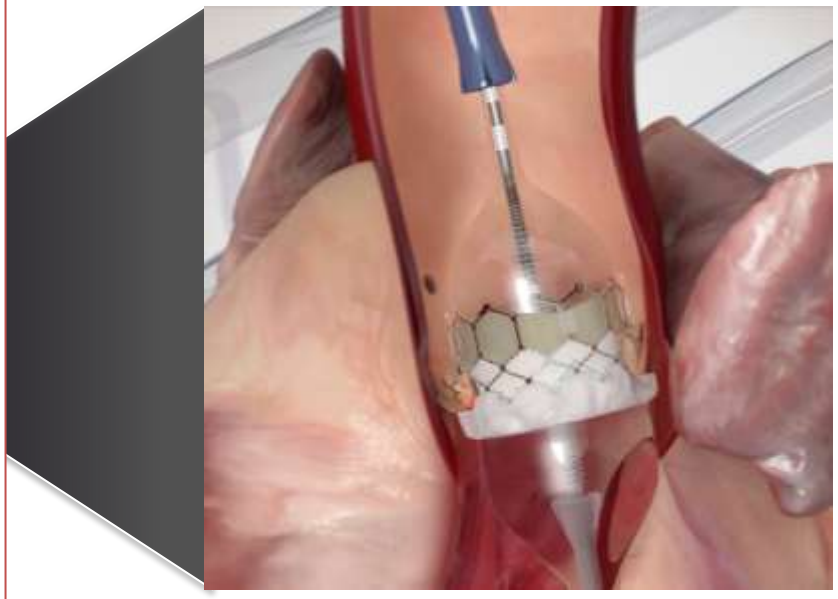
SHARE | E-MAIL | PRINT | BOOKMARK

January 15, 2016--Edwards Lifesciences Corporation announced that the US Food and Drug Administration (FDA) has approved an expanded indication study of the Edwards Sapien 3 valve, the company's most advanced transcatheter aortic valve replacement (TAVR) device. The Edwards Sapien 3 valve was approved by the FDA in 2015 for the treatment of high-risk patients with severe, symptomatic aortic stenosis (AS) in the United States.

According to Edward Lifesciences, the investigational device exemption study will enroll elderly patients with severe, symptomatic AS who have been determined by a heart team to be at low risk for mortality if they were to undergo surgical aortic valve replacement (SAVR).

Patients enrolled in the new PARTNER III trial will be randomized to receive either TAVR with Sapien 3 or SAVR. To be eligible for the trial, patients must be at least 65 years of age, exhibit symptoms of severe AS, and be determined by a heart team to have a surgical risk score of less than 4% per the Society of Thoracic Surgeons adult cardiac surgery risk calculator. The trial is a noninferiority study with a 1-year composite endpoint that includes death, stroke, and rehospitalization.

Enrollment of approximately 1,300 patients at up to 50 sites in the United States is expected to begin during the second quarter. Edwards Lifesciences advised that the trial will also include a 400-patient substudy using advanced imaging to evaluate leaflet motion in tissue heart valves.



SAPIEN 3 deployment

Commander balloon expansion characteristics

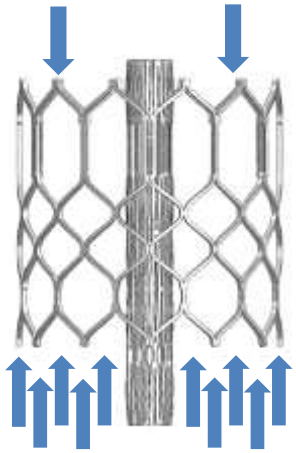
- Coil under balloon allows fluid to pass to distal end of balloon
- Symmetric dog bone balloon shape during initial inflation
- Slow controlled inflation during initial deployment important for stability

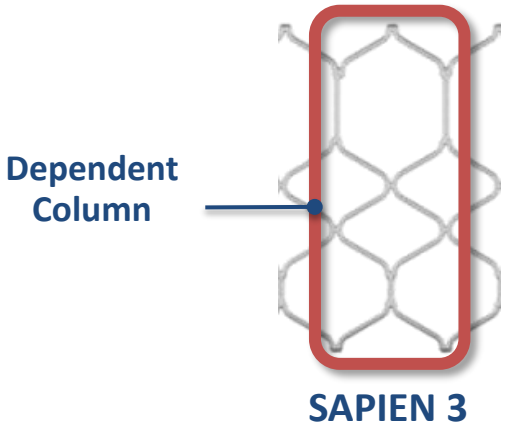
Initial inflation should be slow

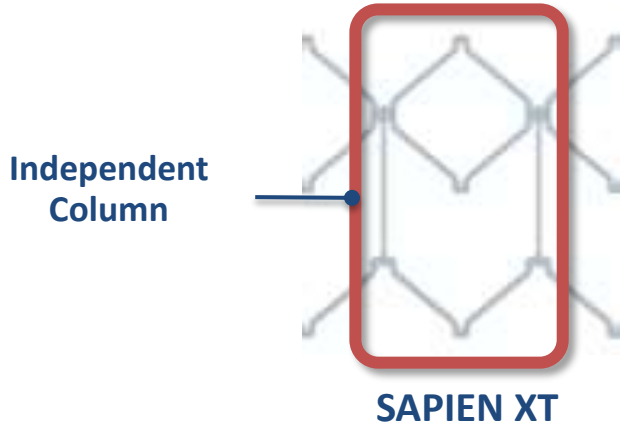
Fast inflation

Slow inflation

SAPIEN 3 Cell Geometry Impacts Foreshortening

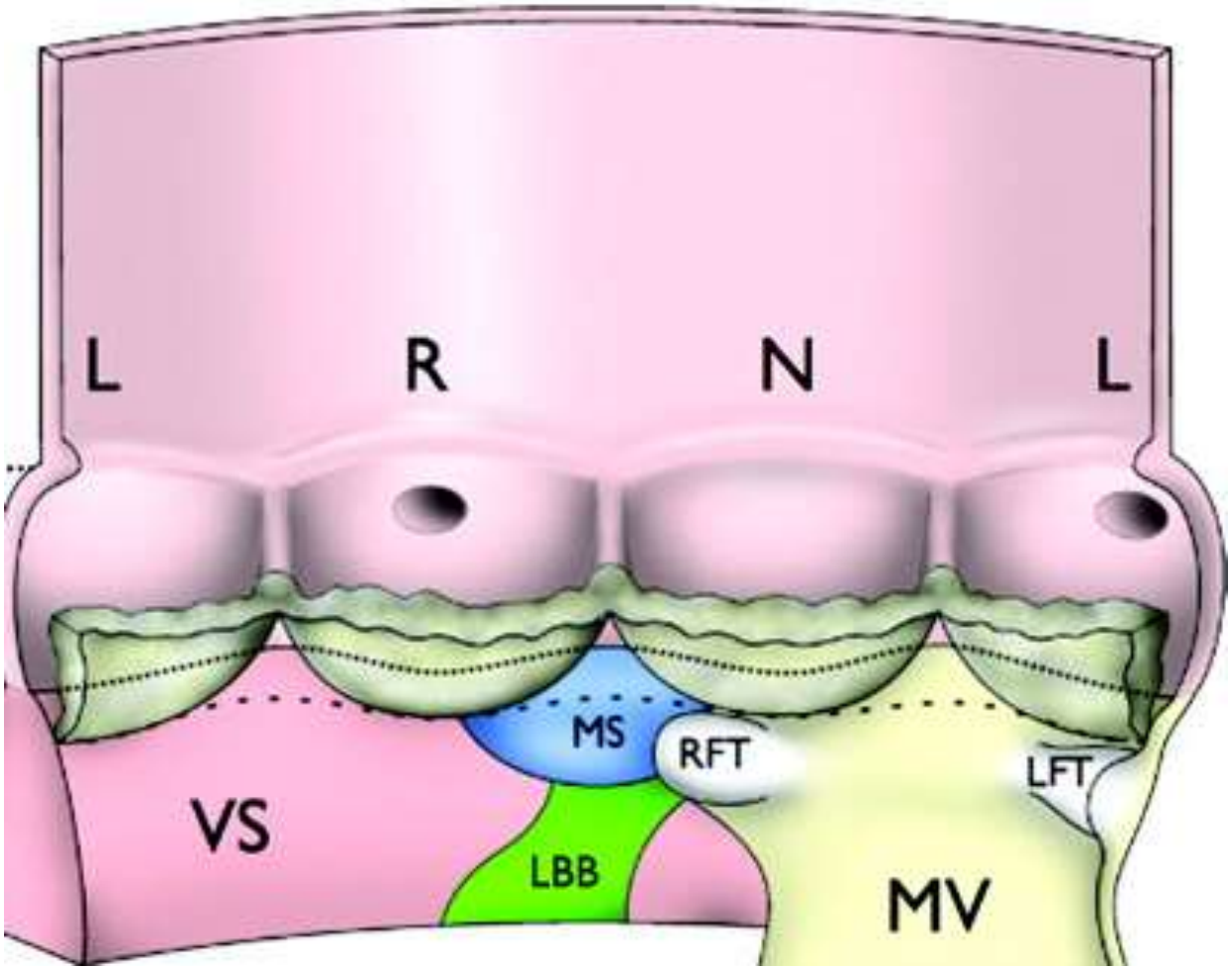




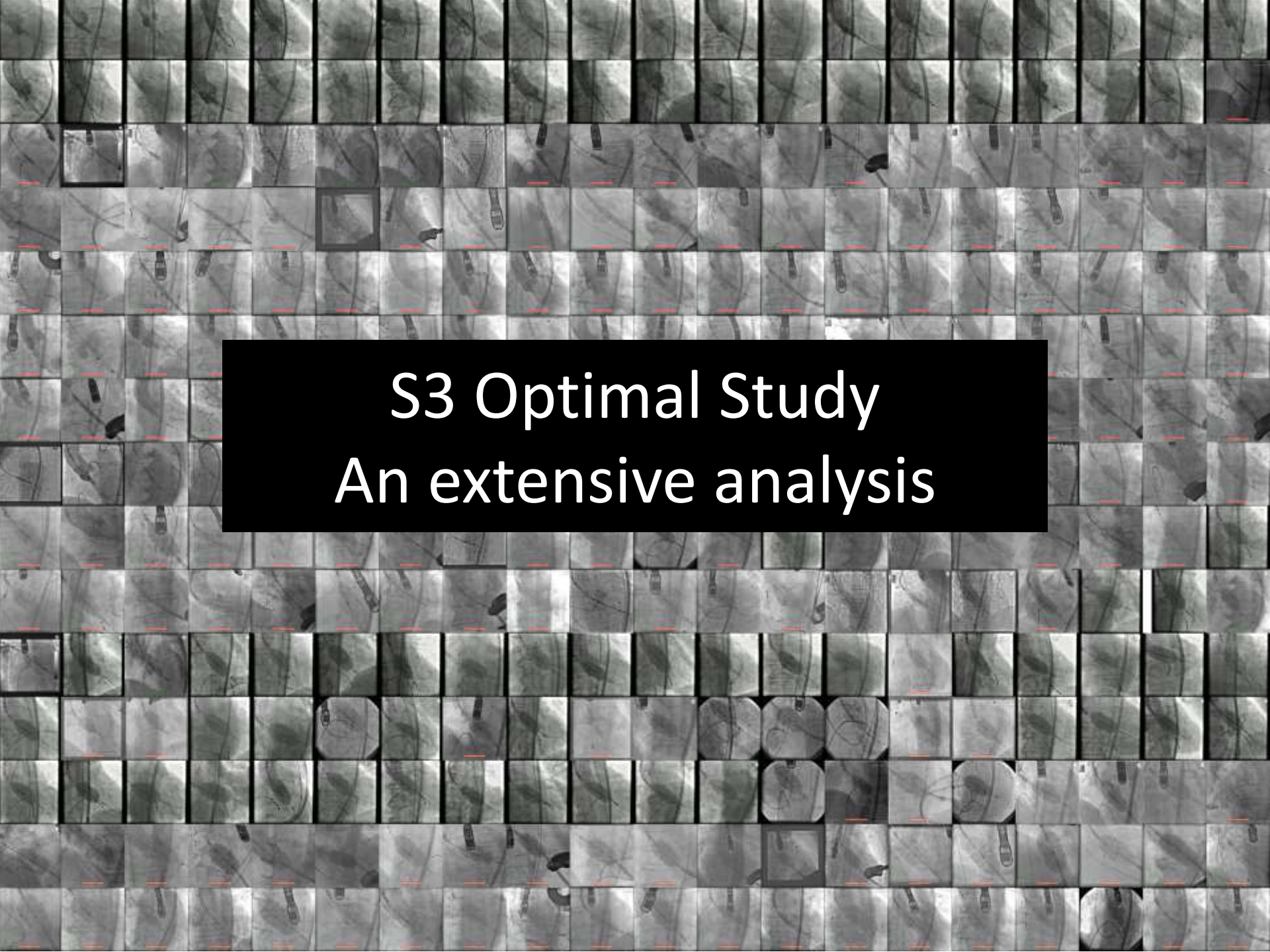


- Outflow does not move much
- The inflow shortens up
- Shortening mainly occurs late

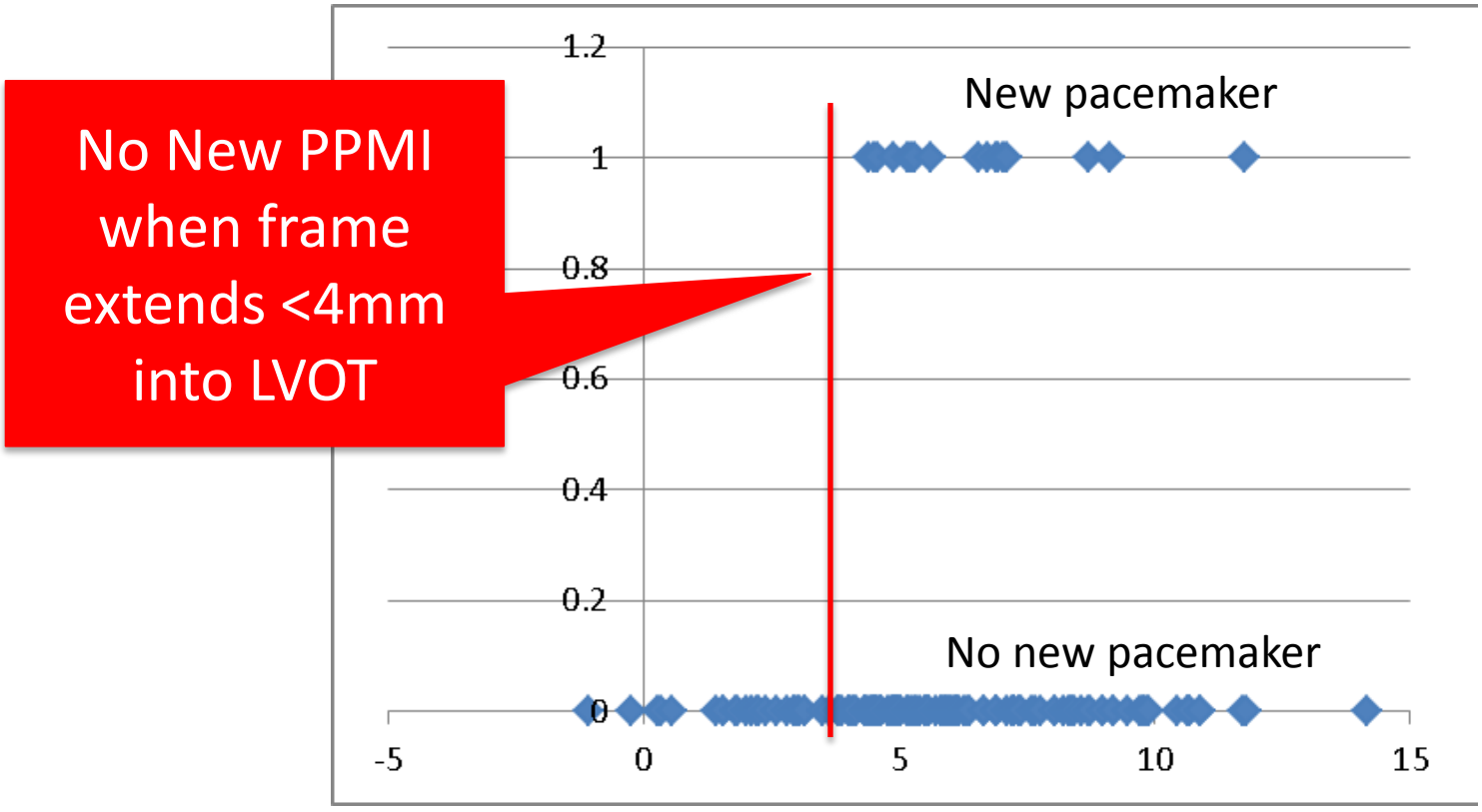
Conduction disturbances are related to THV implant depth



Khawaja M et al. Circulation. 2011;123:951-960

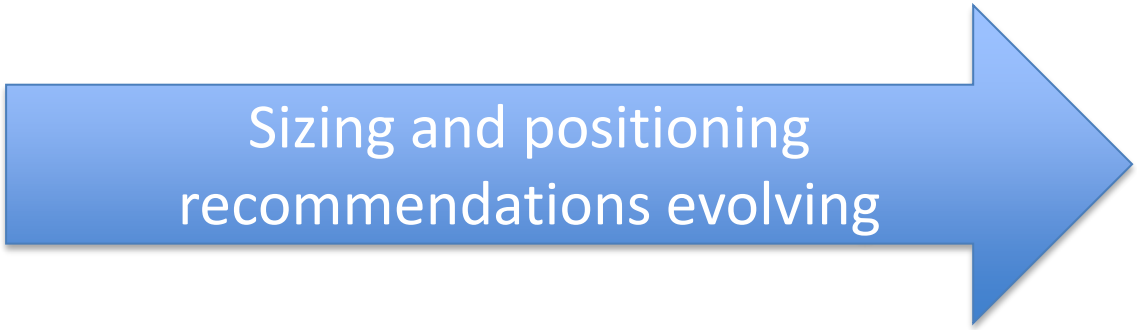

S3 Optimal Study
An extensive analysis

New Pacemaker According to Frame Depth

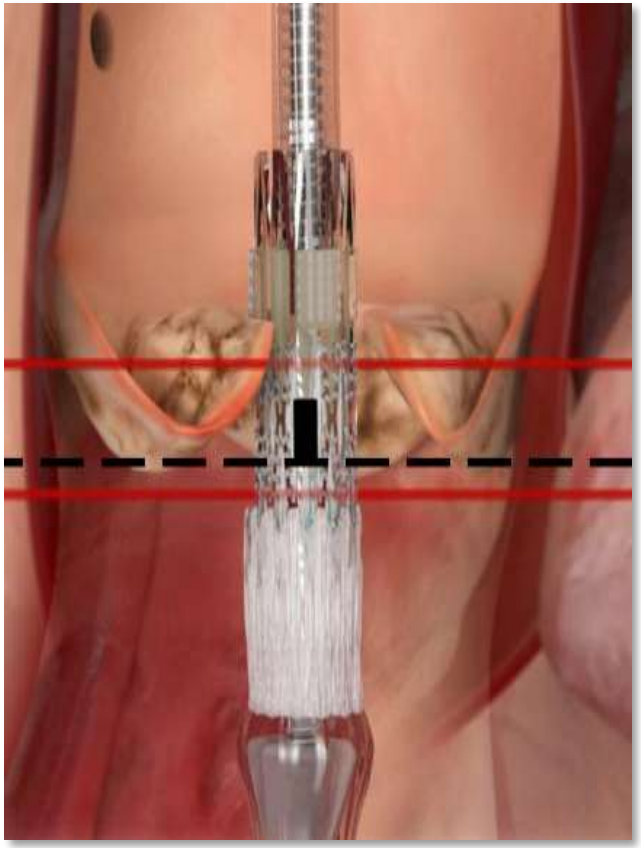


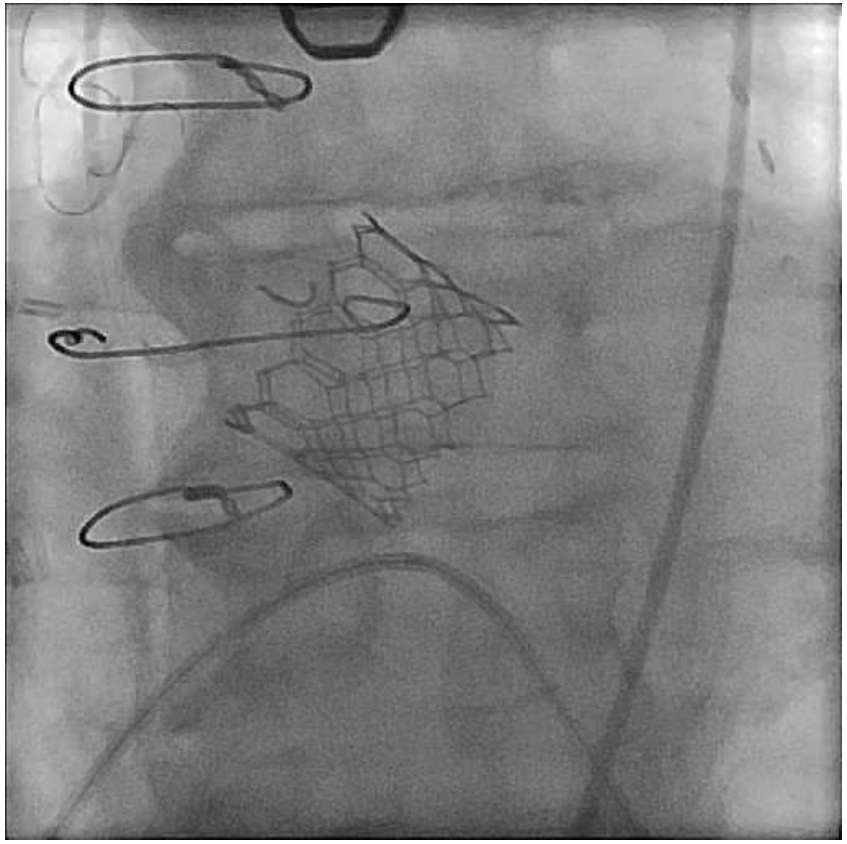
New Pacemakers and SAPIEN 3

	EU HR	PII HR	PII IR	EU IR
Pacemaker	13.3%	13.0%	10.1%	4%



Optimal SAPIEN 3 Positioning





FIH S3, Vancouver 5 years ago

Feb 11, 2016 email

- “The new pacemaker rate for all aortic pts was SXT 6.3% vs S3 4.1%.

- For native aortic valve pts SXT 5.1% vs S3 3.4%.

- Our pacer rate was lower with S3”

SAPIEN 3 Sizing

20 mm

23 mm

26 mm

29 mm

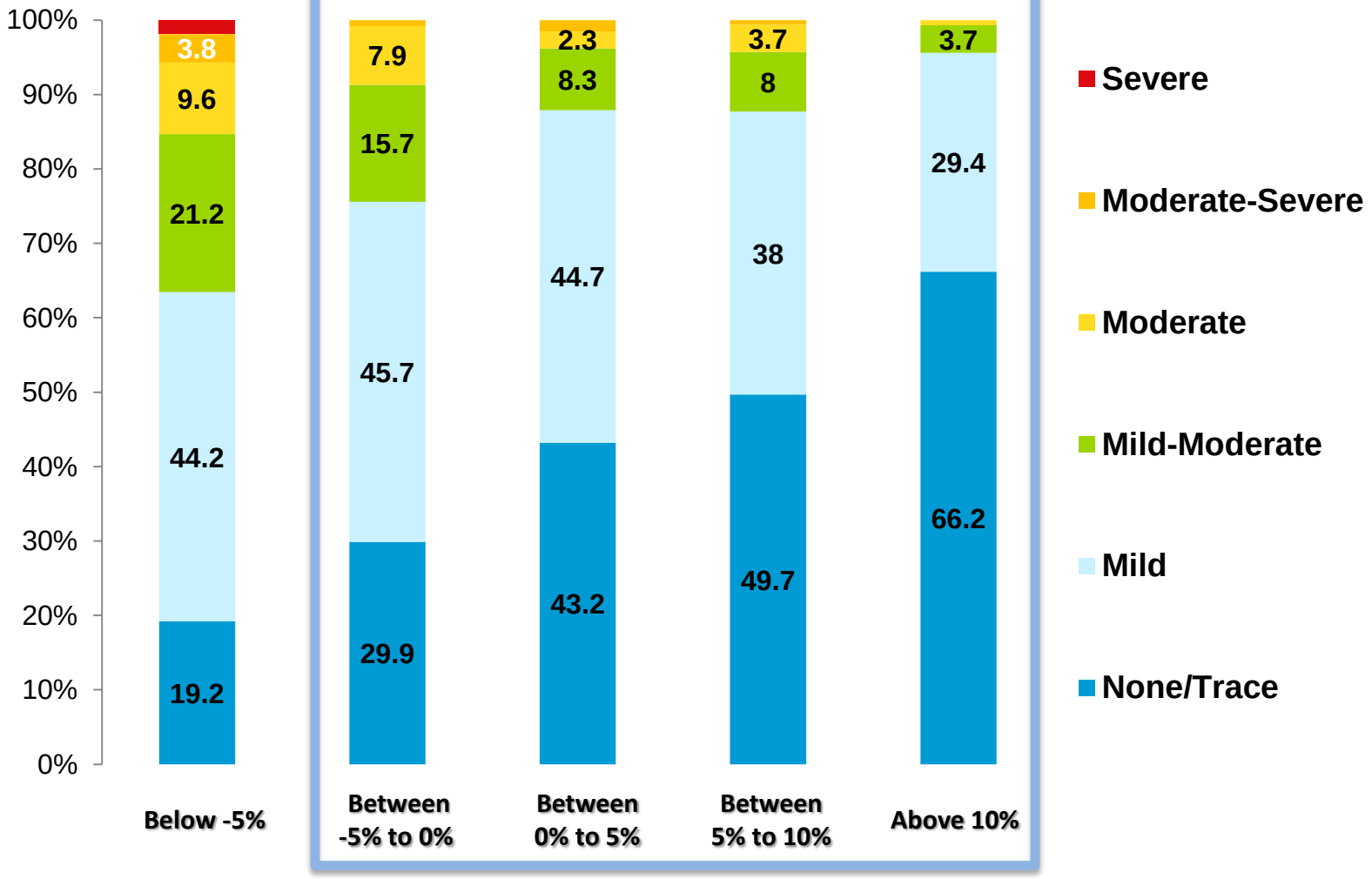
Area Oversizing Calculations: Nominal SAPIEN 3 is Different than SAPIEN XT

THV Size	20 mm	23 mm	26 mm	29 mm
				
Nominal Area	328 mm^2	409 mm^2	519 mm^2	649 mm^2
Nominal Diameter	20.44 mm	22.75 mm	25.71 mm	28.75 mm

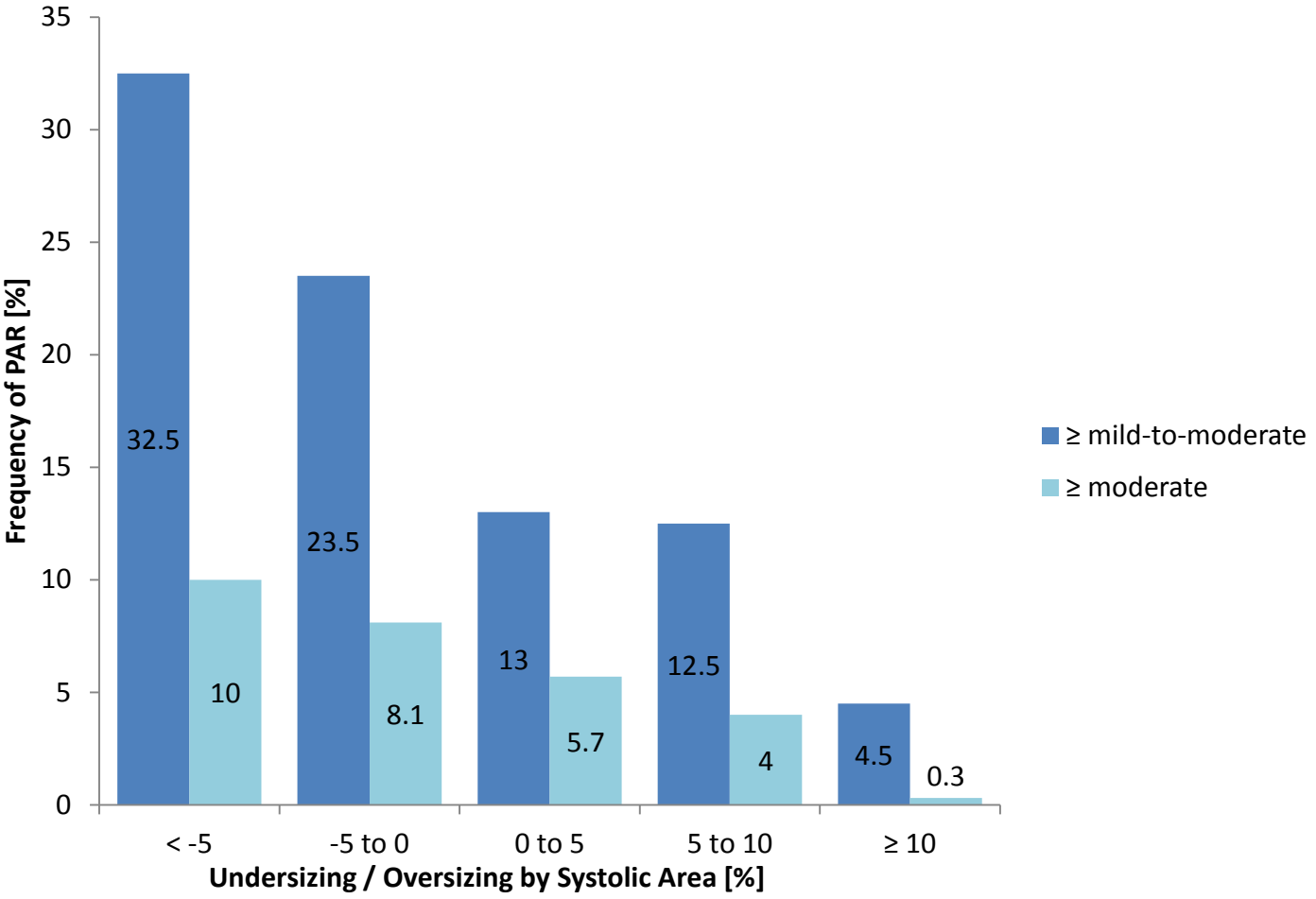
Yang et. al, *Incidence and Severity of Paravalvular Aortic Regurgitation With Multidetector Computed Tomography Nominal Area Oversizing or Undersizing After Transcatheter Heart Valve Replacement With the Sapien 3*. JACC Card Int Vol 8: 3, 2015

PAR Stratified by % Area Oversizing

Recommend:
-5% undersizing to
+20% oversizing



Extent and frequency of PAR stratified by degree area undersizing or oversizing



SAPIEN 3 sizing recommendations

Annulus diameter 20-25mm

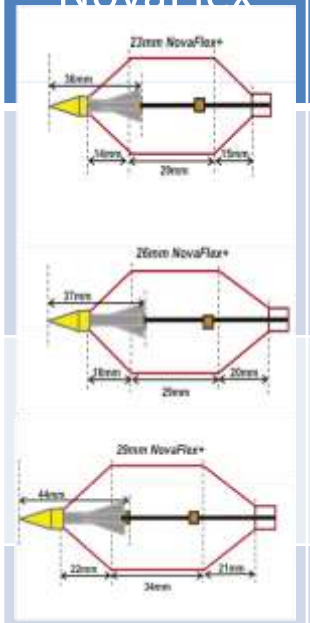
3D Area - derived Diameter (mm)		20.0	20.2	20.5	20.7	21.0	21.1	21.4	21.7	22.0	22.3	22.6	22.8	23.0	23.1	23.4	23.7	23.9	24.0	24.2	24.7
3D Annular Area (mm^2)		314	320	330	338	346	350	360	370	380	390	400	410	415	420	430	440	450	452	460	480
% Annular Area Over (+) or Under (-) Nominal by 3D CT	23mm	29.3	26.9	23.0	**20.1**	**17.3**	**16.0**	**12.8**	**9.7**	**6.8**	**4.0**	**1.5**	**-1.0**	**-2.2**	**-3.3**	**-5.6**	-7.7	-9.8			
	26mm											29.8	26.6	25.1	23.6	**20.7**	**18.0**	**15.3**	**14.8**	**12.8**	**8.1**
	29mm																				

Annulus diameter 25-30mm

3D Area - derived Diameter (mm)		25.0	25.2	25.5	25.7	26.0	26.2	26.4	26.5	26.7	26.9	27.2	27.4	27.6	27.9	28.0	28.1	28.3	28.5	28.8	29.0	29.2	29.4	29.5	29.6	29.9	30.1	30.3
3D Annular Area (mm^2)		490	500	510	520	530	540	546	550	560	570	580	590	600	610	615	620	630	640	650	660	670	680	683	690	700	710	720
% Annular Area Over (+) or Under (-) Nominal by 3D CT	23mm																											
	26mm	**5.9**	**3.8**	**1.8**	**-0.2**	**-2.1**	**-3.9**	**-4.9**	-5.6	-7.3	-8.9																	
	29mm		29.8	27.3	24.8	22.5	**20.2**	**18.9**	**18.0**	**15.9**	**13.9**	**11.9**	**10.0**	**8.2**	**6.4**	**5.5**	**4.7**	**3.0**	**1.4**	**-0.2**	**-1.7**	**-3.1**	**-4.6**	**-5.0**	-5.9	-7.3	-8.6	-9.9

“Adjustable valve sizing strategy”


Underexpansion and Ad Hoc Post-Dilation in Selected Patients Undergoing Balloon-Expandable Transcatheter Aortic Valve Replacement

NovaFlex	SAPIEN XT	Nominal Volume	Under fill ~ 10%
	23 mm	17 ml	1.5 ml
	26 mm	22 ml	2 ml
	29 mm	33 ml	3 ml

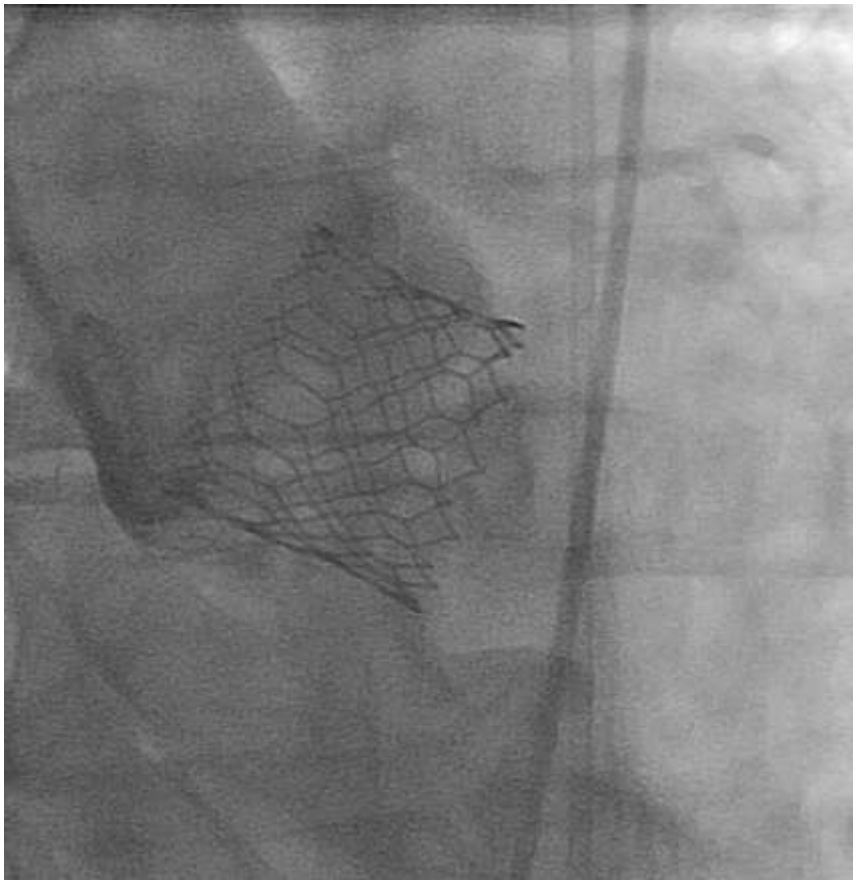
- Pick a valve larger than the annulus
- Under fill the balloon 10%
- Redilate if necessary

What are the concerns with SAPIEN 3 under-expansion?

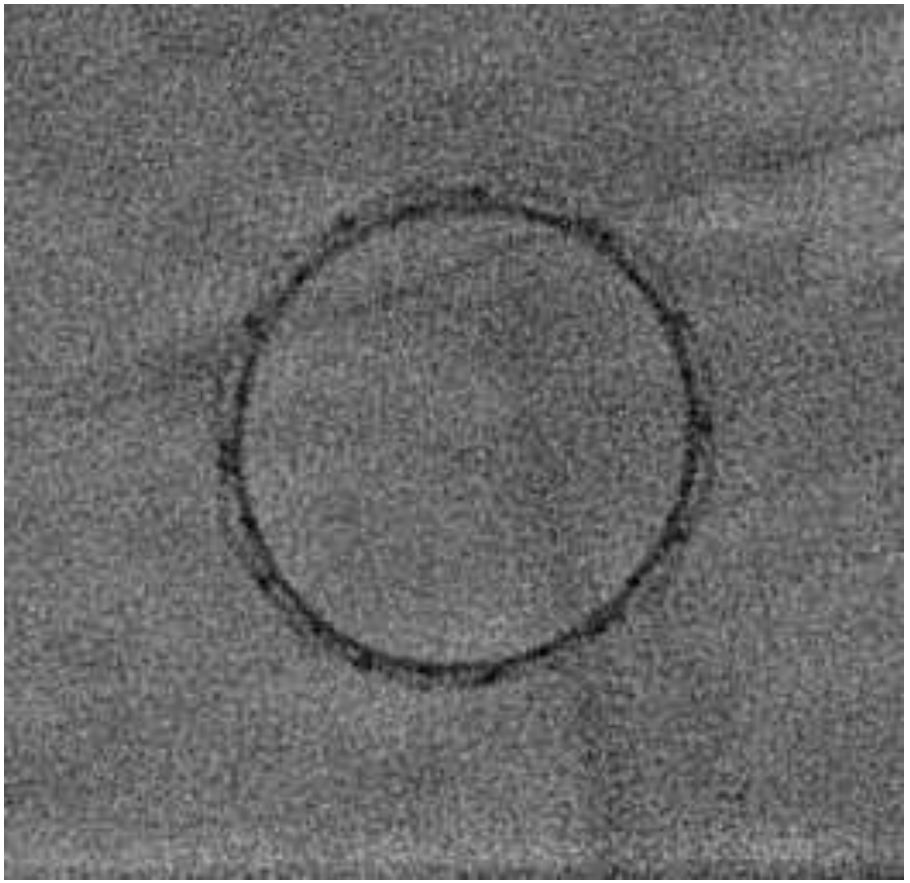
- Reduced durability
  - Longer SAPIEN 3 leaflets result in suboptimal coaptation
  - Leaflets may contact stent frame
  - Asymmetric deployment
- Paravalvular leaks
- More frequent post-dilation

Under deployment

SAPIEN 3, 29mm, under-filled 2ml, ~5%

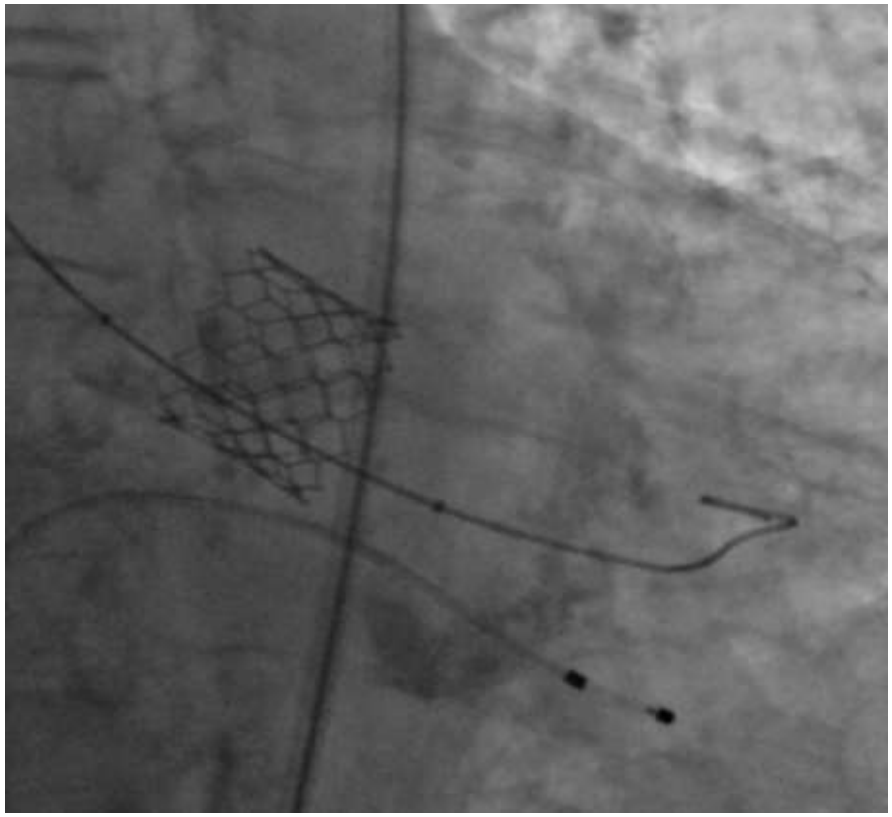


Asymmetric, no leak

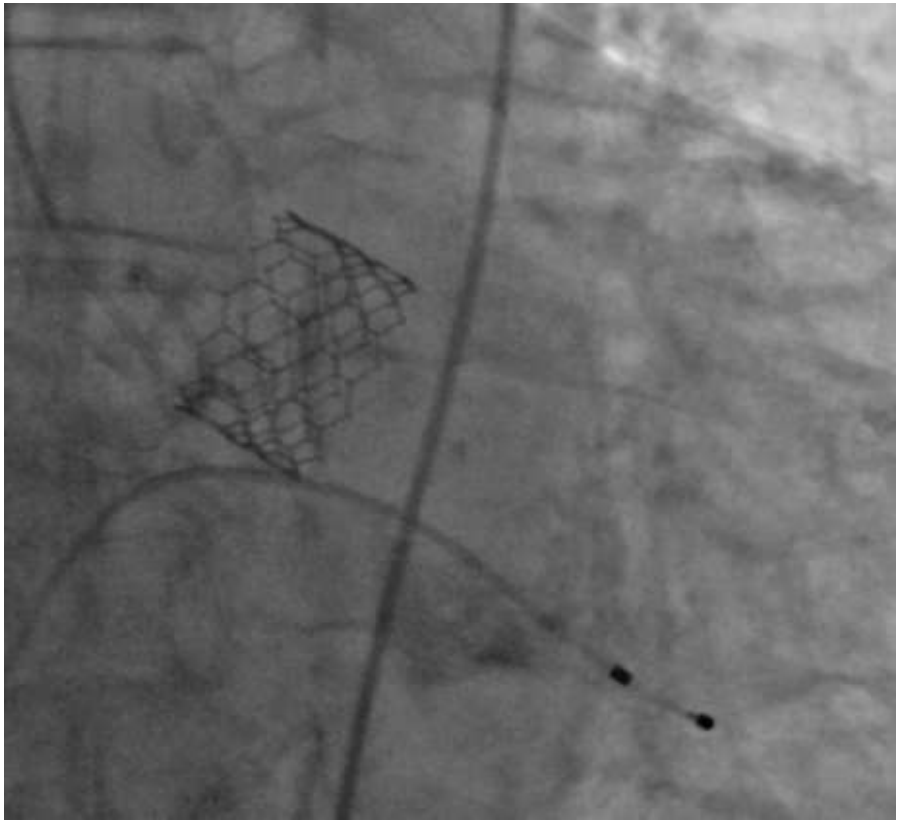


Still circular

SAPIEN 3 can be dilated larger



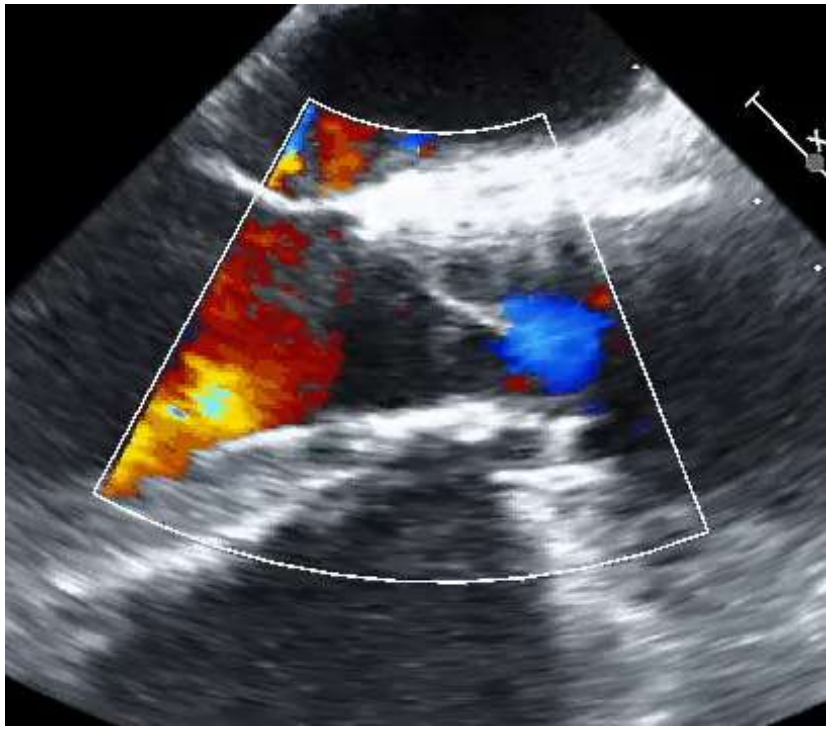
SAPIEN 3, 23mm



True balloon, 24mm

New indications?

SAPIEN 3 bicuspid registry

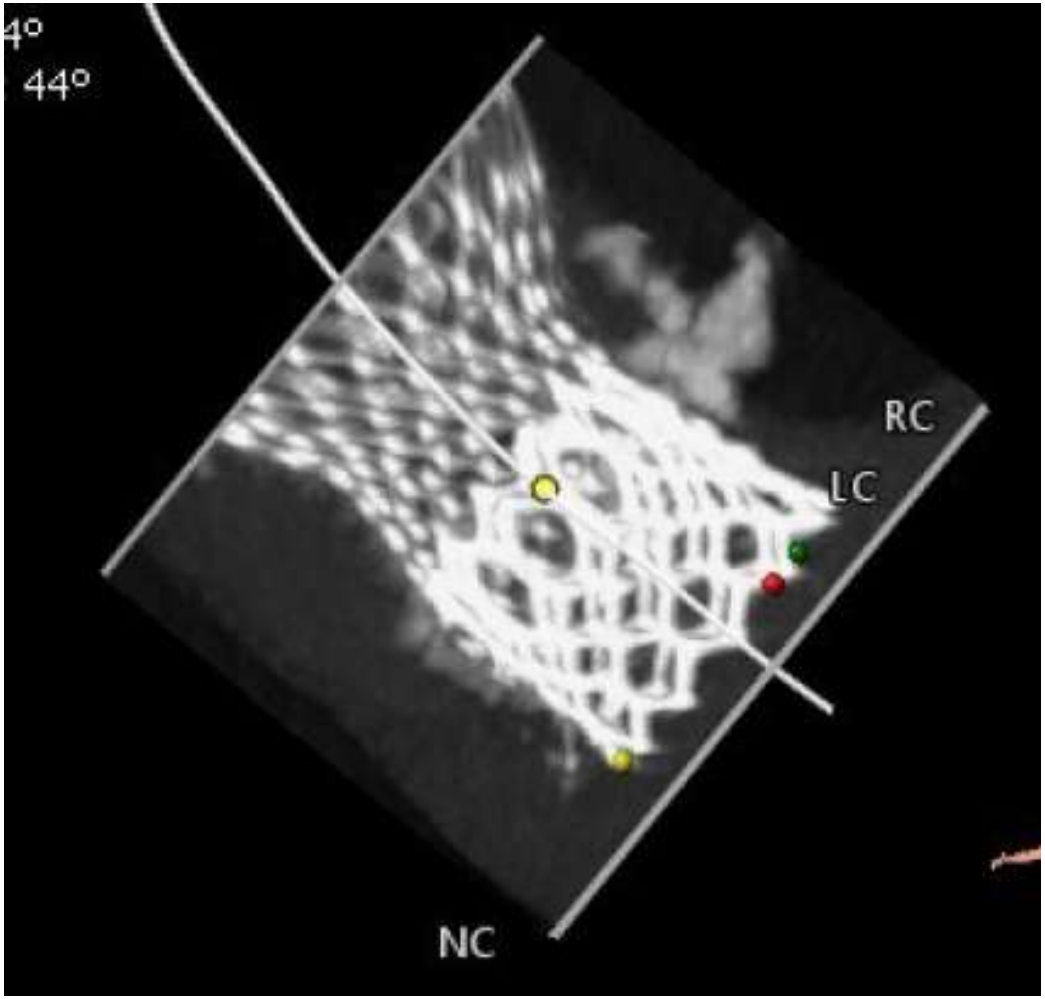


Bicuspid, 0% oversizing, no leak

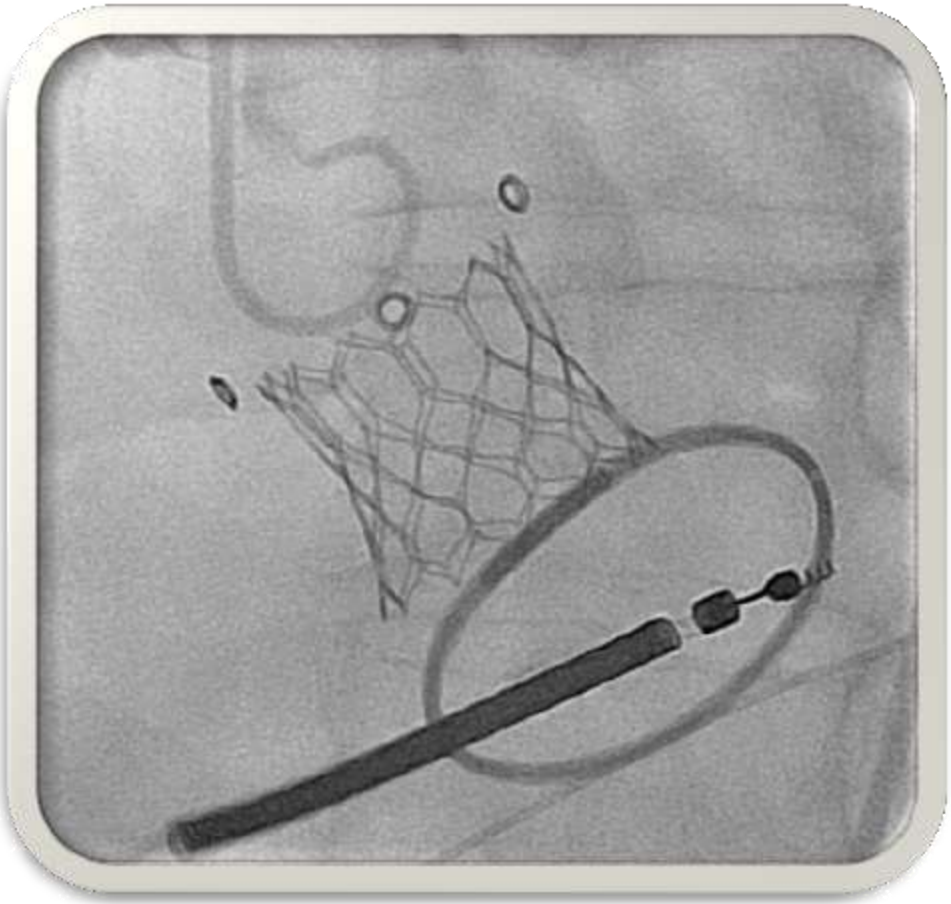
Complications	N=51
Valve embolization	0%
Second valve	0%
Annular rupture	0%
Coronary occlusion	0%
AR >mild	0%

Perlman JACC CVI 2016

SAPEN 3 in undersized CoreValve in bicuspid native valve



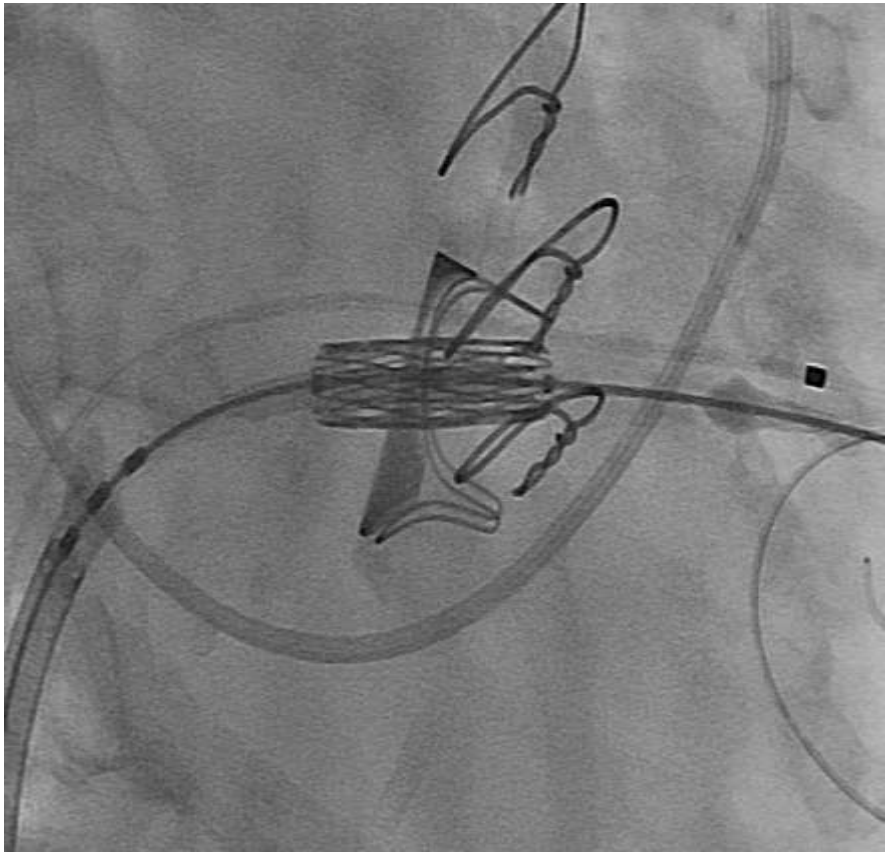
SAPIEN 3 Valve-inValve

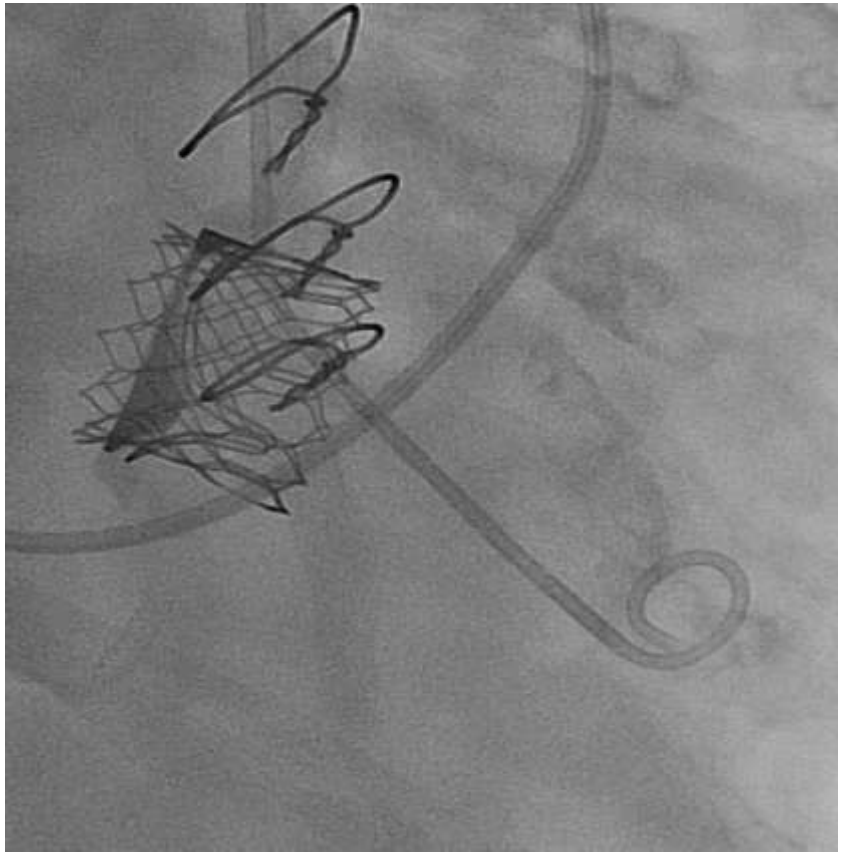


Mosaic aortic valve and mitral ring

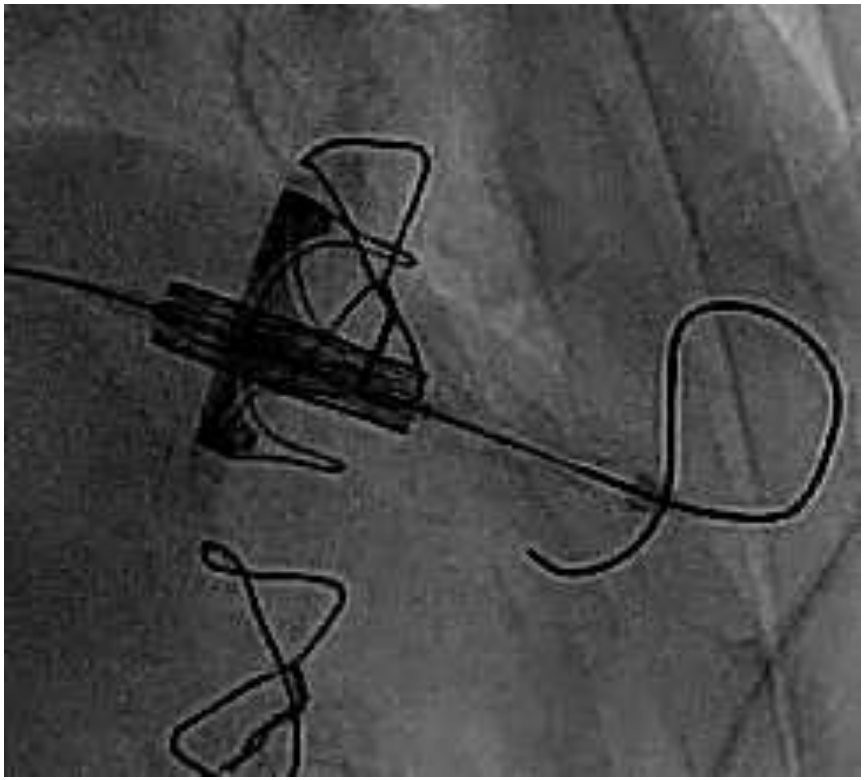
- Conscious sedation
- No TEE
- Contrast not necessary
- Pre-dilation not necessary
- Negligible risk of
  - AV block
  - annular rupture
  - PV leak
- Next day discharge

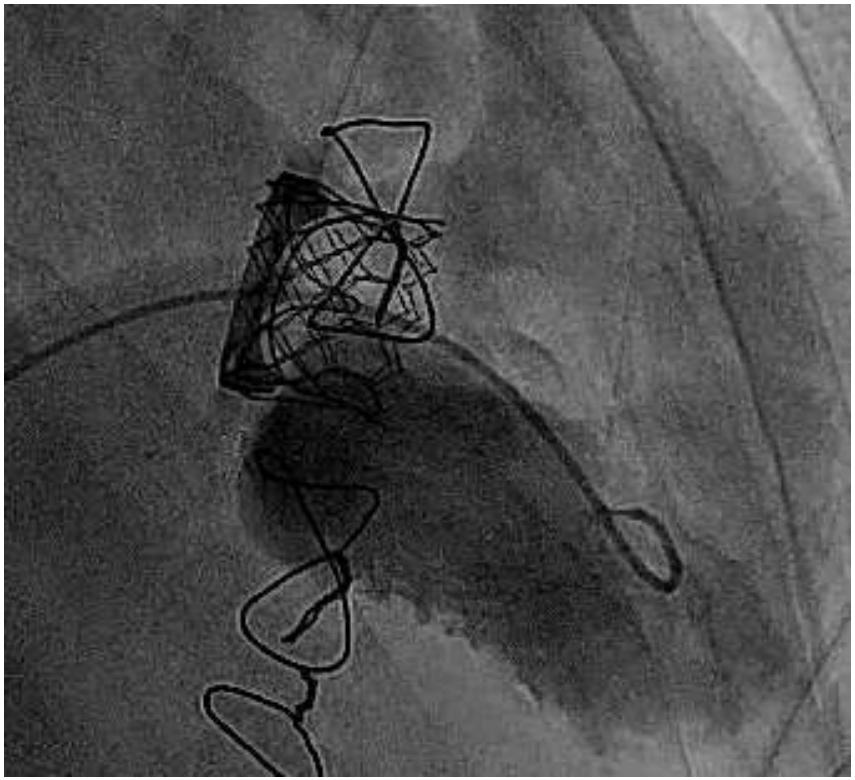
Transseptal mitral valve-in-valve implant





Tricuspid valve in valve with Sapien 3

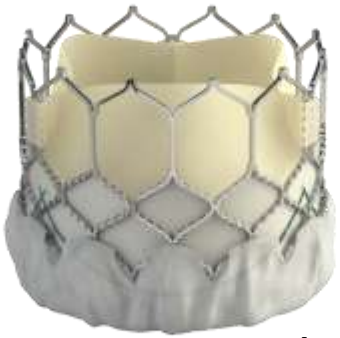




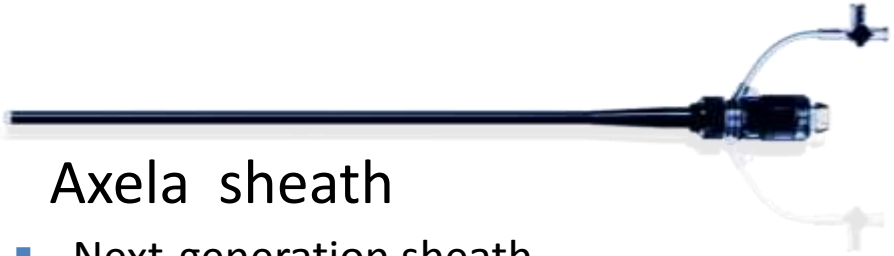
The Edwards SAPIEN 3 Ultra system

Ultra delivery catheter

- No alignment step
- No predilation
- No Flex cath withdrawal prior to deployment



SAPIEN 3 valve



Axela sheath

- Next-generation sheath
- Facilitates dynamic expansion and contraction
- 14F for all sizes of valve

End