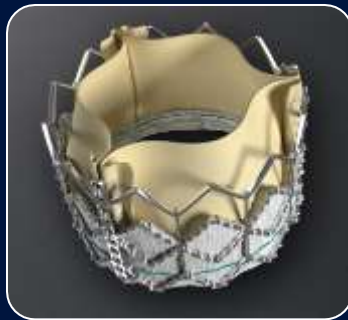


TCT AP 2015

Seoul, Korea

Ultimate Comparison Sapien vs Core Valve



Eberhard Grube MD, FACC, FSCAI

University Hospital, Dept of Medicine II, Bonn, Germany

Stanford University, Palo Alto, California, USA

Eberhard Grube, MD

Physician Name

Company/Relationship

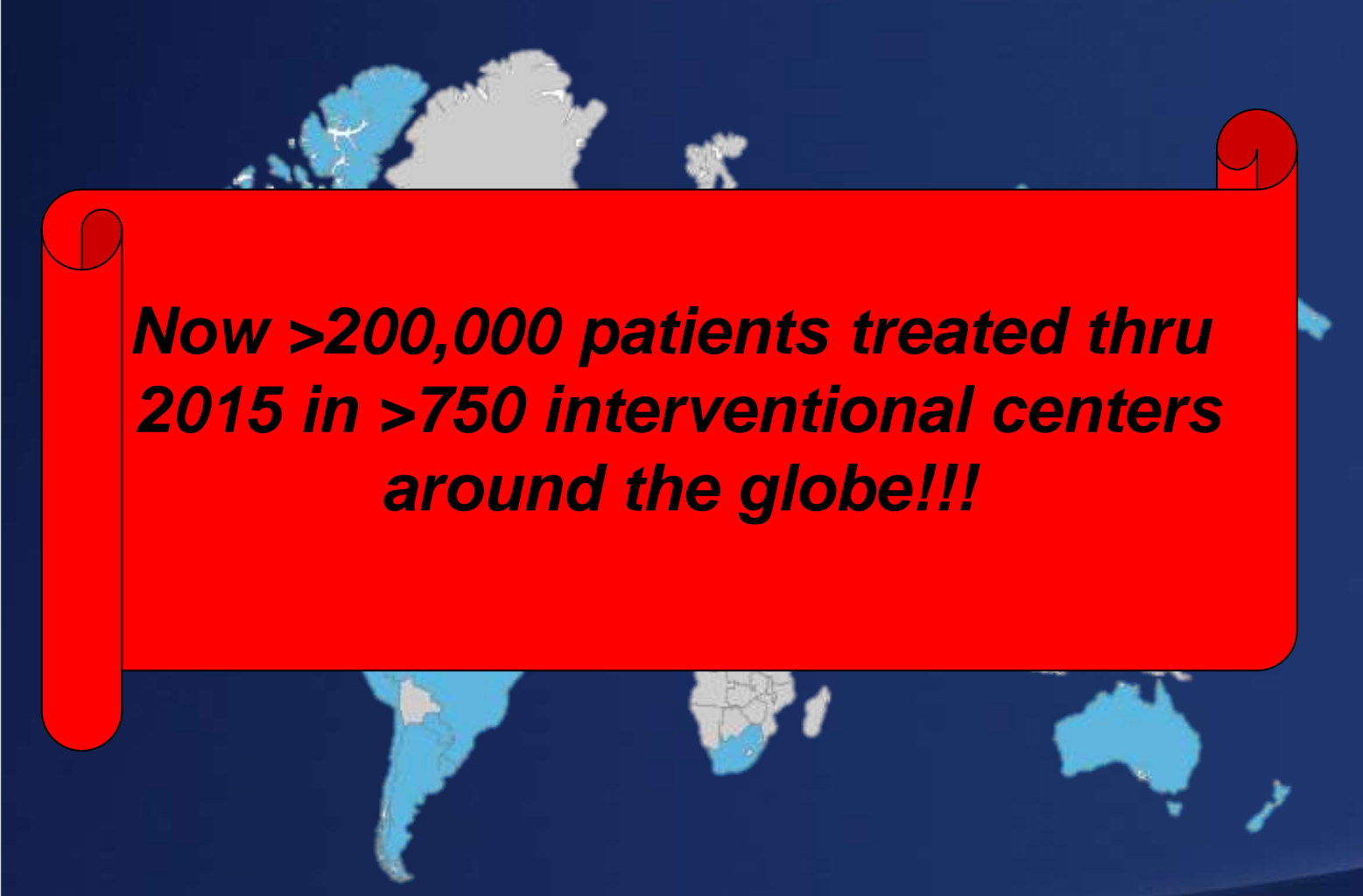
Eberhard Grube, MD

Medtronic, CoreValve: C, SB, AB, OF
Direct Flow: C, SB, AB
Mitralign: AB, SB, E
Boston Scientific: C, SB, AB
Biosensors: E, SB, C, AB
Kona: AB, E
Abbott Vascular: AB
InSeal Medical: AB, E,
Valtech: E, SB,
Claret: SB
Keystone: AB
Shockwave: E, AB

Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits'

TAVI Has Arrived ... And Has Grown fast with Extensive Global Experience

A world map is visible in the background, showing continents in light blue and oceans in dark blue. A large red scroll with rounded corners is positioned in the center, containing the text. The scroll has a white border and a white shadow, giving it a 3D appearance.

Now >200,000 patients treated thru 2015 in >750 interventional centers around the globe!!!

Clinical Evidence

- Over 27,000 patients have been treated with CoreValve and SAPIEN / XT in Europe.

	CoreValve	SAPIEN / XT
CoreValve ADVANCE	1,015	NA
FRANCE 2 Registry	1,298	2,635
GARY	3,627	4,814
UK Registry	1,932	2,051
Italian Registry	1,334	0
Belgian Registry	408	473
Spanish Registry	108	0
Milan Registry	89	132
Ibero-American	1,220	0
Swiss Registry	336	317
Swedish Registry	311	255
SOURCE Registry	NA	2,307
SOURCE XT Registry	NA	2,706
Total Patients	11,678	15,690

Reported Implants of CE-Mark Approved Valves (OUS)

	Medtronic CoreValve	Edwards Sapien /XT/ S3	Symetis ACURATE TA	JenaValve	Portico	Engager	Direct Flow	Lotus	Edwards Sapien 3
FIM	17		50	12	21	10	31	11	15
CE Pivotal	126	353	40	73	103	125	100	250	150
Medtronic ANZ	487	NA	NA	NA	NA	0	NA	0	NA
Medtronic ADVANCE	1,015	NA	NA	NA	NA	NA	NA	NA	NA
FRANCE 2 Registry	1,298	2,635	0	0	0	0	0	0	0
GARY	6,026	8,390	237	161	0	92	0	0	0
UK Registry	1,932	2,051	0	3	35	0	1	0	0
Italian Registry	1,334	0	0	0	0	0	0	0	0
Israel Registry	867	628	0	0	0	0	0	0	0
Belgian Registry	408	473	0	0	0	0	0	0	0
Brazilian Registry	360	58	0	0	0	0	0	0	0
Spanish Registry	108	0	0	0	0	0	0	0	0
Milan Registry	89	132	0	0	0	0	0	0	0
Ibero-American	1,220	0	0	0	0	0	0	0	0
Asia Registry	140	113	0	0	0	0	0	0	0
Swiss Registry	336	317	17	23	1	0	0	0	0
Swedish Registry	311	255	0	0	0	0	0	0	0
Canadian Registry	0	339	0	0	0	0	0	0	0
SOURCE Registry	NA	2,307	NA	NA	NA	NA	NA	NA	NA
SOURCE XT Registry	NA	2,706	NA	NA	NA	NA	NA	NA	NA
Other Post-Market Registries	NA	NA	250	180	NA	NA	153	NA	NA
Total Patients	16,074	20,757	594	452	160	227	285	266	165

Improving Clinical Outcomes: Competitive Landscape



CoreValve



Sapien XT



Direct Flow



Lotus



Portico



Symetis



Sapien 3



Centera



Evolut R



Valve Med

	CoreValve	Sapien XT	Direct Flow	Lotus	Portico	Symetis	Sapien 3	Centera	Evolut R	Valve Med
Survival	Green	Green	Green	Green	Green	Green	Green	Green	Green	TBD
Major Vasc	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	NR	TBD
PPM Rate	Orange	Green	Orange	Orange	Yellow	Yellow	Yellow	Orange	Yellow	TBD
PVL	Yellow	Yellow	Green	Green	Yellow	Yellow	Green	Green	Green	TBD
Durability	200M Valve 600M Frame									TBD
Stroke	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	TBD
Coronary Occlusions	Green	Yellow	Yellow	Yellow	NR	NR	Green	NR	Green	TBD
Annulus Rupture	Green	Orange	Orange	NR	NR	NR	Yellow	NR	Green	TBD
MI	Yellow	Yellow	Yellow	Yellow	Yellow	Green	Yellow	NR	NR	TBD

Green: Near optimal performance

Orange: Performance acceptable but not optimal, competitive disadvantage

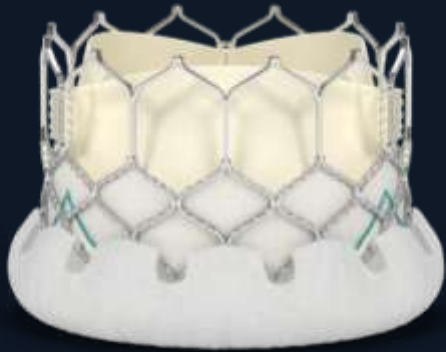
Yellow: Performance acceptable but not optimal yet

Red: Performance not acceptable nor technically feasible

For today, I was asked to discuss only
CoreValve and Edwards ... and clearly these are
Very Different Valves!



CoreValve and EDW continue as the TAVR Workhorses ... and both have released their next Generation Devices



Edwards Lifesciences
Sapien 3



Medtronic CoreValve
Evolut R

Advantages of BE Edwards Sapien

- Short frame design – less interference with peri-valve anatomy (conduction system, CAs)
- Precise positioning in the sub-annular zone (but requires RV pacing for deployment)
- Deflectable delivery system to negotiate arch anatomy and vessel tortuosity
- Circular frame/valve deployment in annular zone
- Full thickness bovine pericardium – good durability (?)
- Access site versatility (TF, TA, TAo)

Advantages of SE MDT CoreValve

- More valve sizes to accommodate full range of annular dimensions (esp. large sizes)
- Slow controlled valve deployment without need for rapid RV pacing
- Partial repositioning features during deployment
- Less trauma to annulus and aorta – reduced risk of rupture
- Circular frame/valve in supra-annular zone (better for small annulus and small V-in-V)
- Access site versatility (TF, SC, T Ao)
- LMA distance from annulus less important

How do you decide what device to use?

Physician Preference

Company Relationship

Ease of Use

Patient Anatomy

*Reduction of
Complications*

*Overall Clinical
Performance*

... it is Data and...



Personal Preference and Experience

SO ... I will not spend time during this presentation on Product Features or Procedural Steps

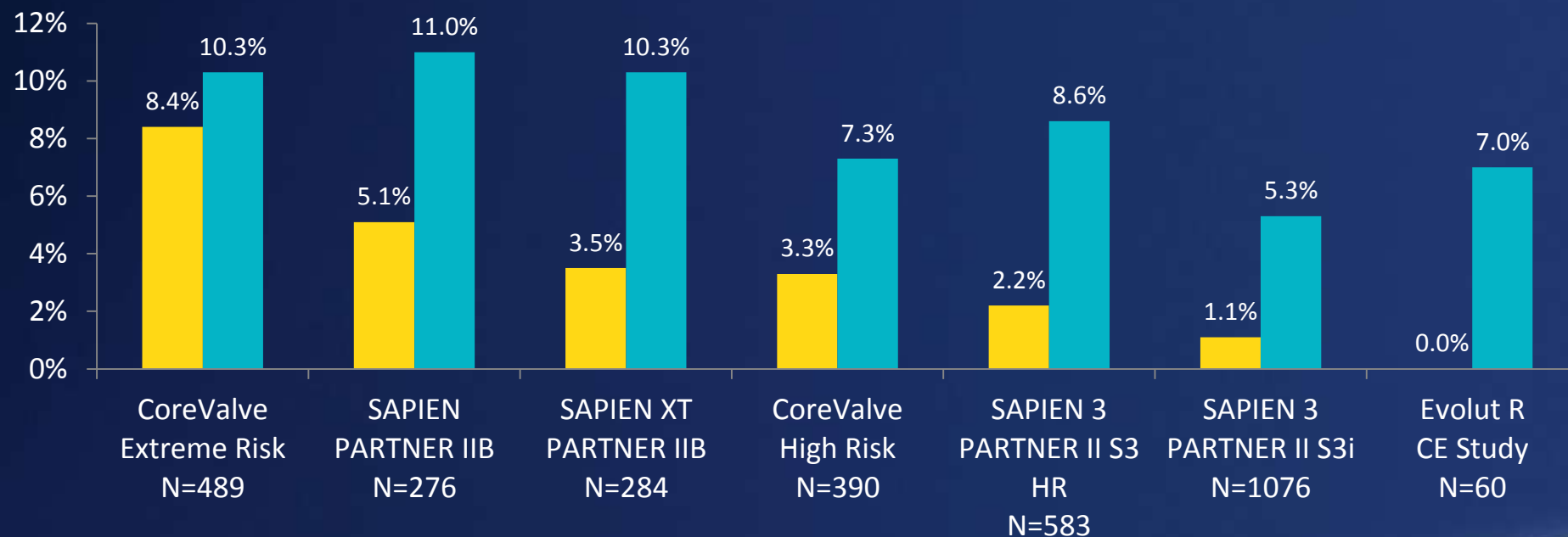
Caveats to This Presentation

- Comparing Trials is Difficult ... But I am trying to do it
- Data from the US pivotal trials represent the most robust data sets that we have on CoreValve and Sapien/XT
 - Randomized, Core Lab Adjudicated, % Follow-Up completed, Monitoring w/Regulatory Oversight, Neuro involvement from the start
- Broad utilization of older registry data does not make sense given retrospective nature, lack of consistency in definitions, generally no core labs, does not represent contemporary practice, etc....
- Early results from Evolut R and Sapien3 are just that ... a bit early. But we can look for signals and trends to see if these next generation devices are achieving their design goals.

30 Day Mortality – Clinical Trial Results

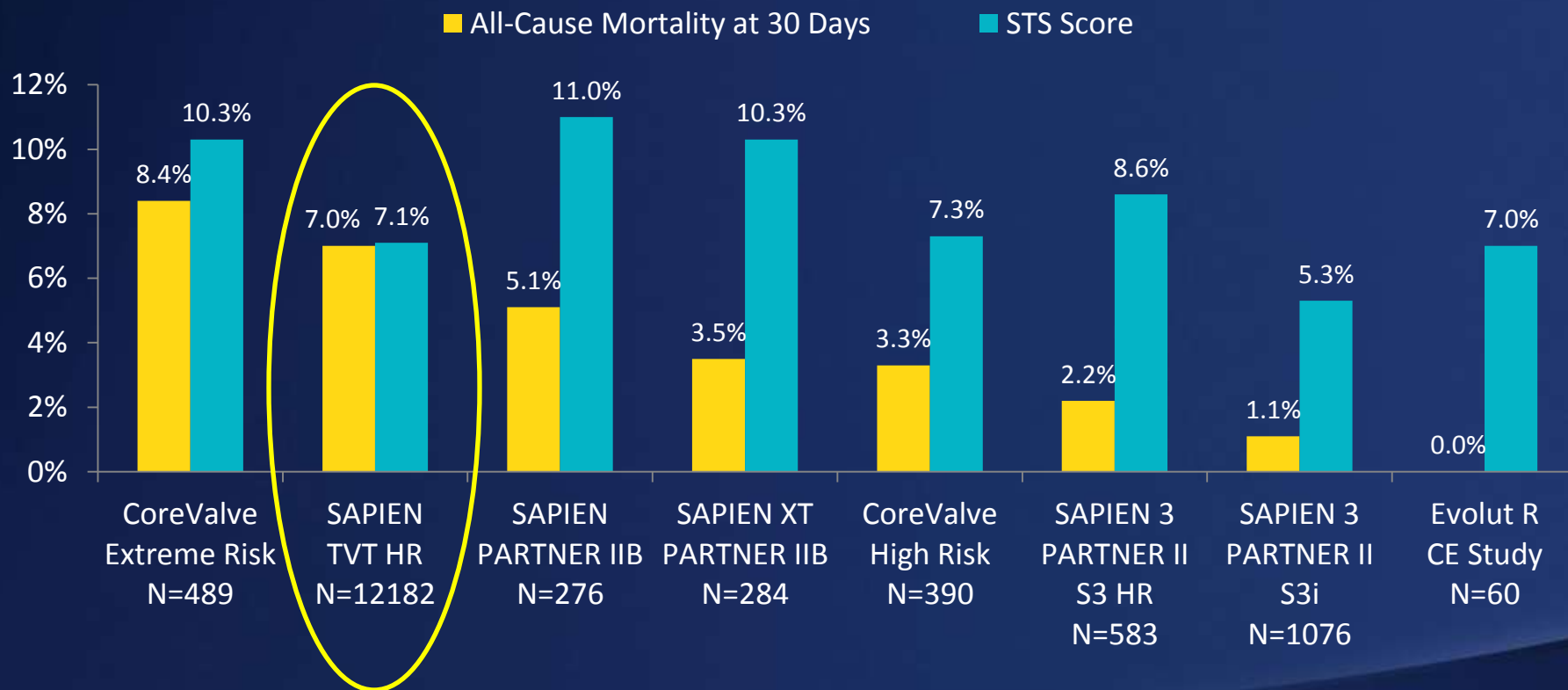
In rigorously controlled clinical trials, 30-day mortality between the valve types tends to track with the clinical status of the patients at baseline (with O/E ratio <1) rather than the valve type that is being implanted.

■ All-Cause Mortality at 30 Days ■ STS Score



30 Day Mortality – Commercial Experience

As we consider commercial experience in the US, we see a relative increase in the 30-day mortality rate with SAPIEN, and the O/E ratio approaches 1.



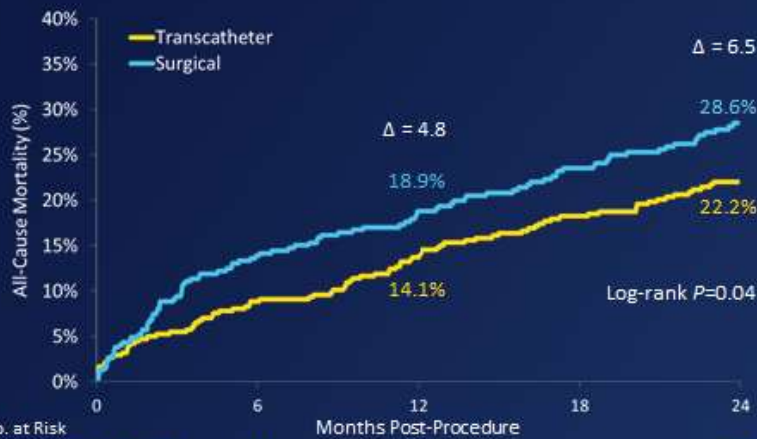
¹Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ²Holmes, et al., *JAMA* 2015; 313: 1019-28; ³Leon, et al. presented at ACC 2013; ⁴Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ⁵Kodali, et al., presented at ACC 2015; ⁶Meredith, et al., presented at ACC 2015

Longer-Term Survival

- Both valves show excellent longer term Survival in the High Risk groups (with widening between TAVR and SAVR mortality curves out to 2 years in the Core Valve trial).

All-Cause Mortality

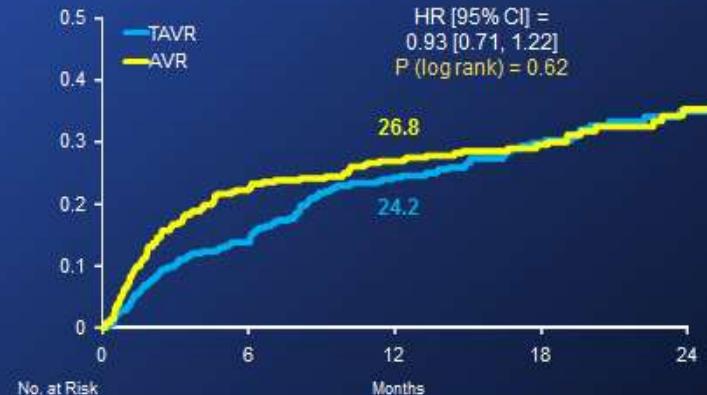
CoreValve US Clinical Trials
ACC 2015



No. at Risk	0	6	12	18	24
Transcatheter	391	378	354	334	219
Surgical	359	343	304	282	191

14

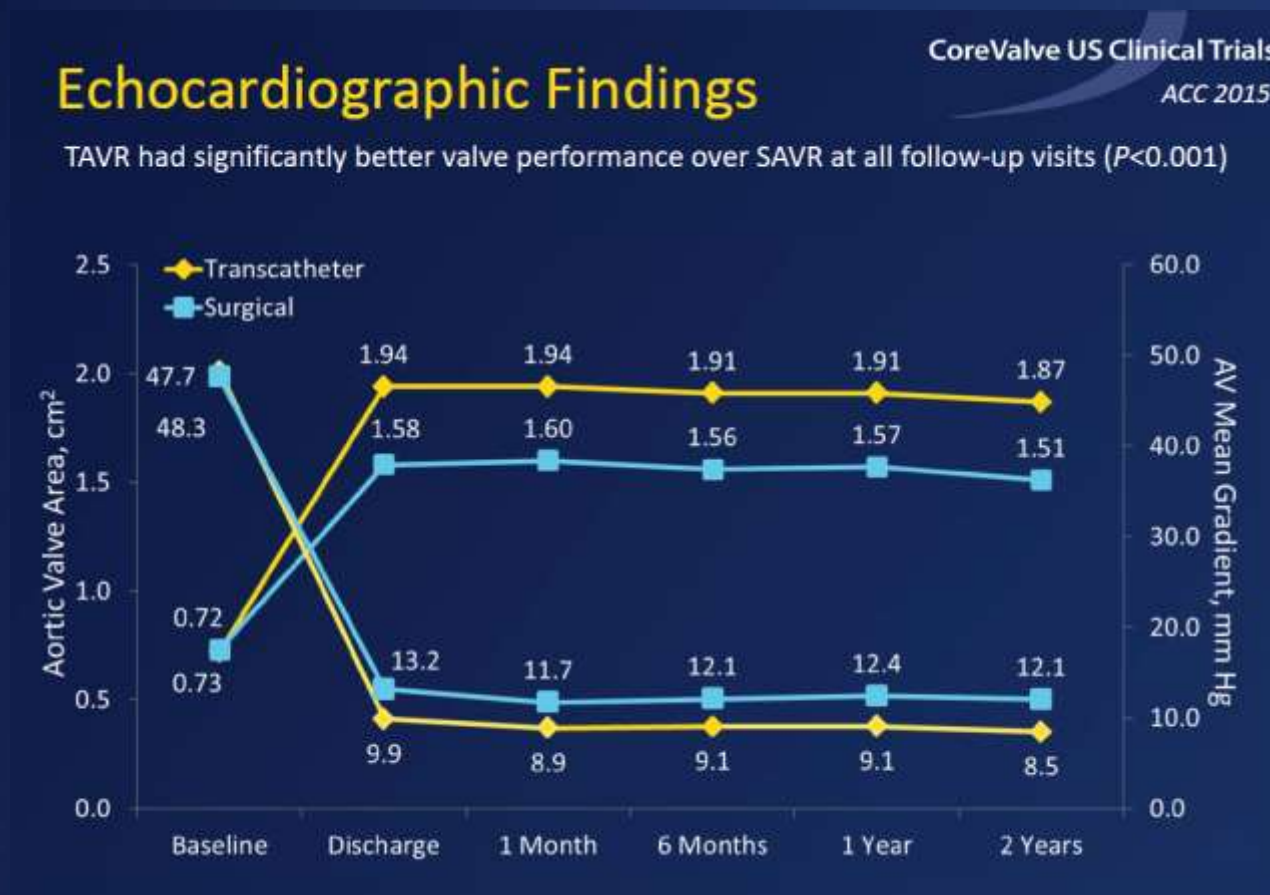
Primary Endpoint: All-Cause Mortality at 1 Year



No. at Risk	0	6	12	18	24
TAVR	348	296	260	147	67
AVR	351	252	236	139	65

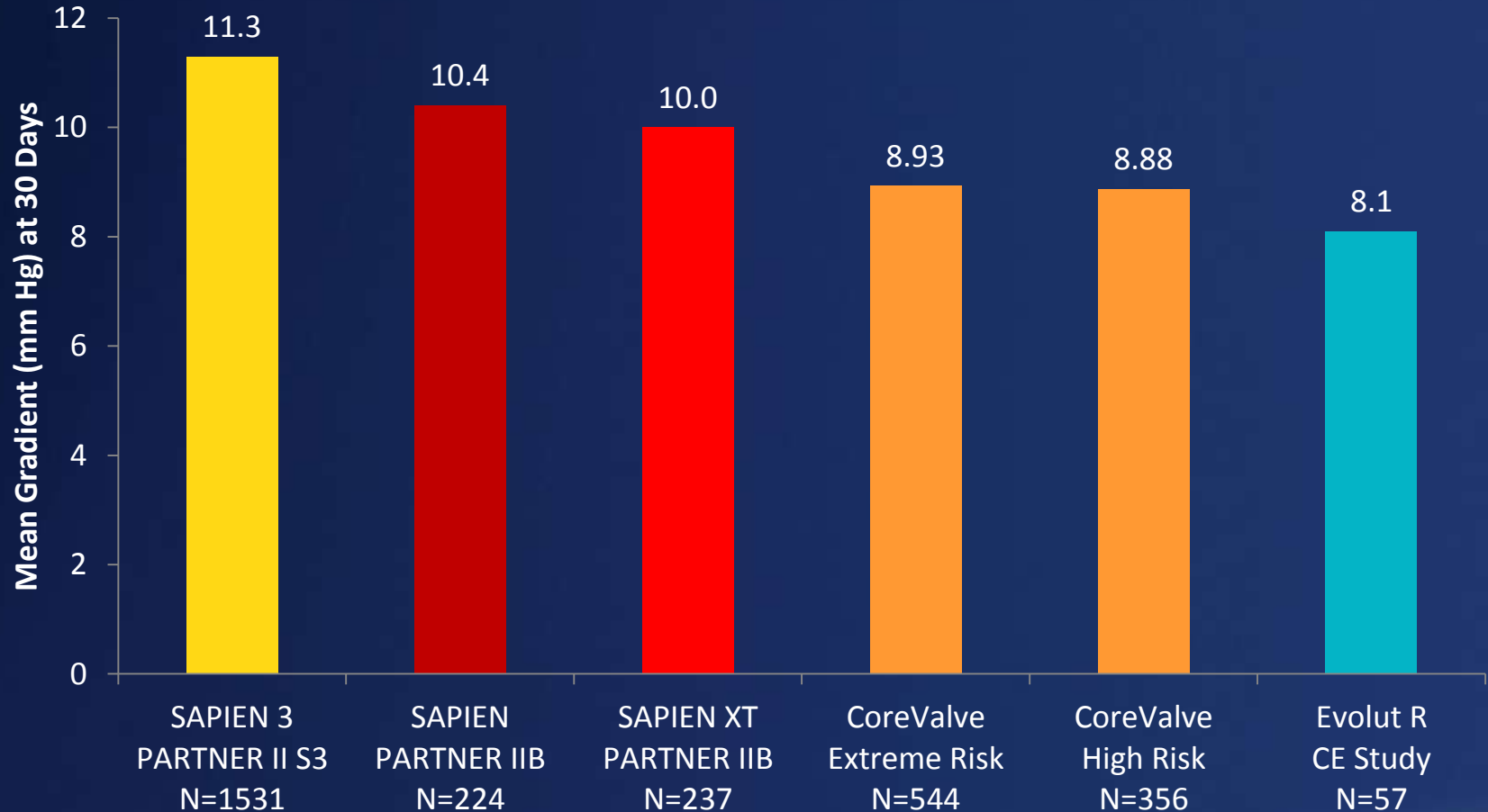
Hemodynamics

- As issues with PVL are solved and the field treats more patients at lower surgical risk, optimal forward flow should take priority
 - Both TAVs have outperformed SAVs in randomized trials



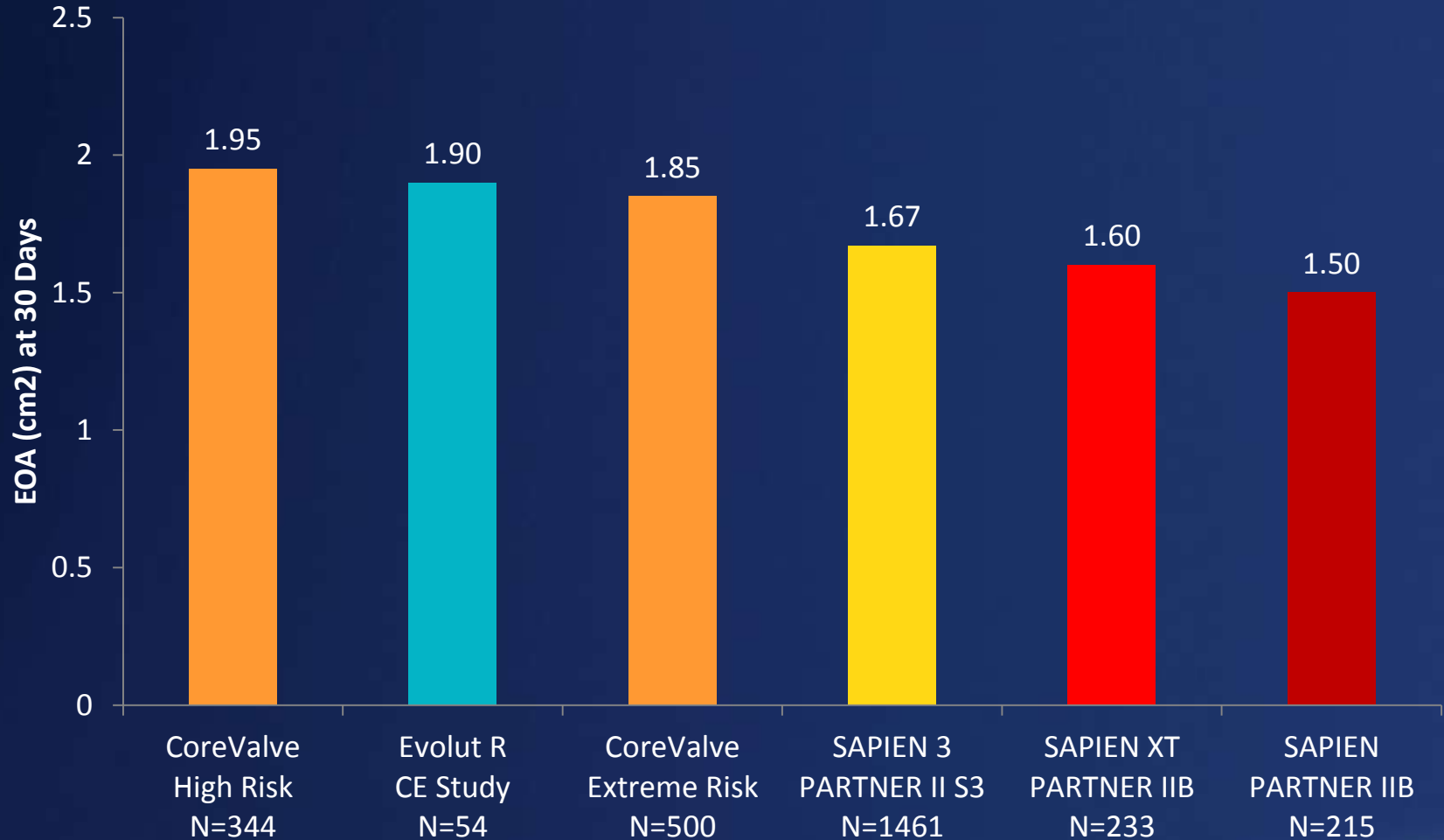
Hemodynamics – Mean Gradients

...with excellent forward flow characteristics of TAVs



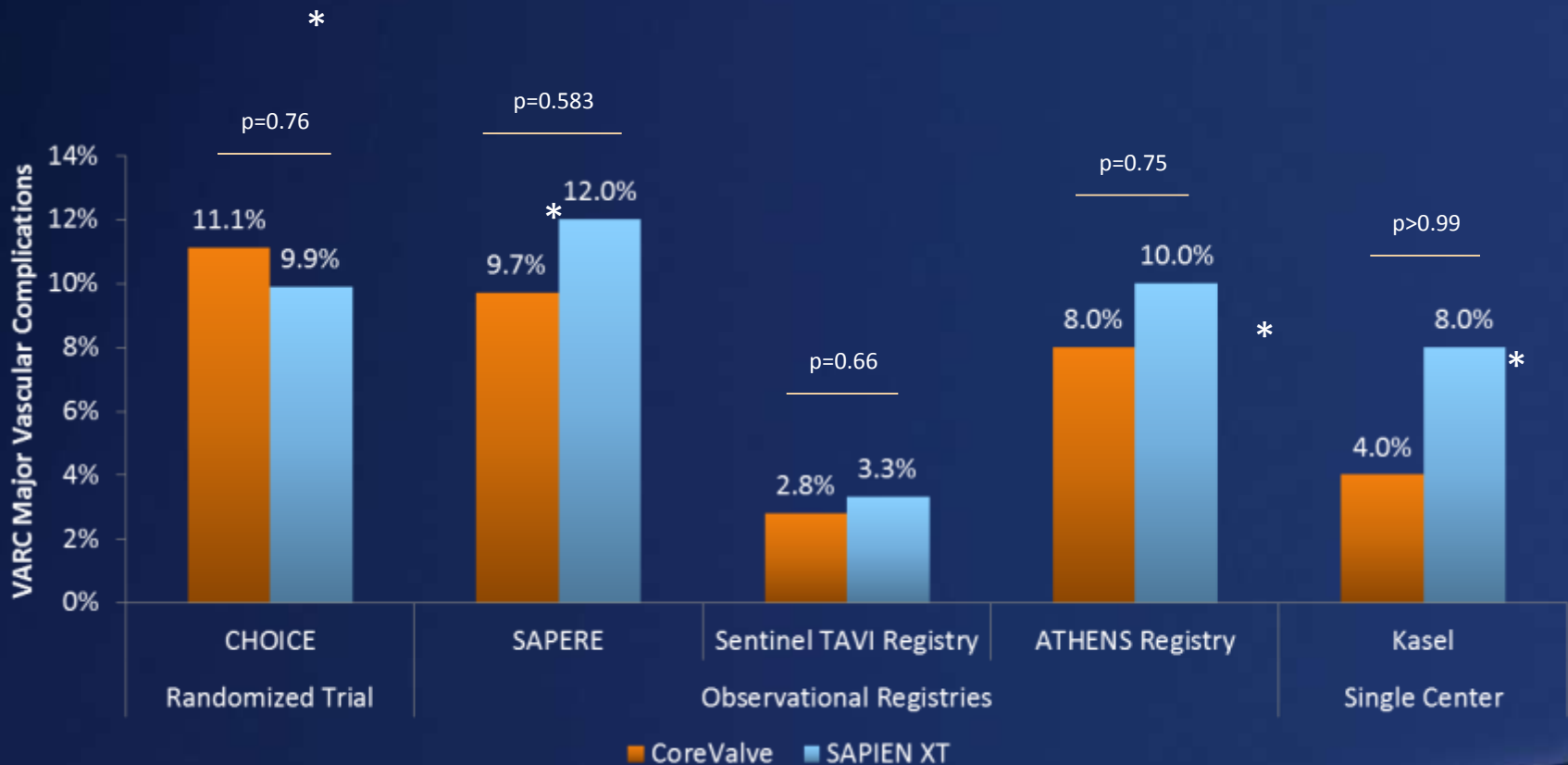
Hemodynamics - EOA

...and excellent EOA of both valves



Vascular Complications

- 5 reports have directly compared TF-TAVI outcomes between CoreValve and SAPIEN XT¹⁻⁵. No study has shown a statistically significant difference between the devices.

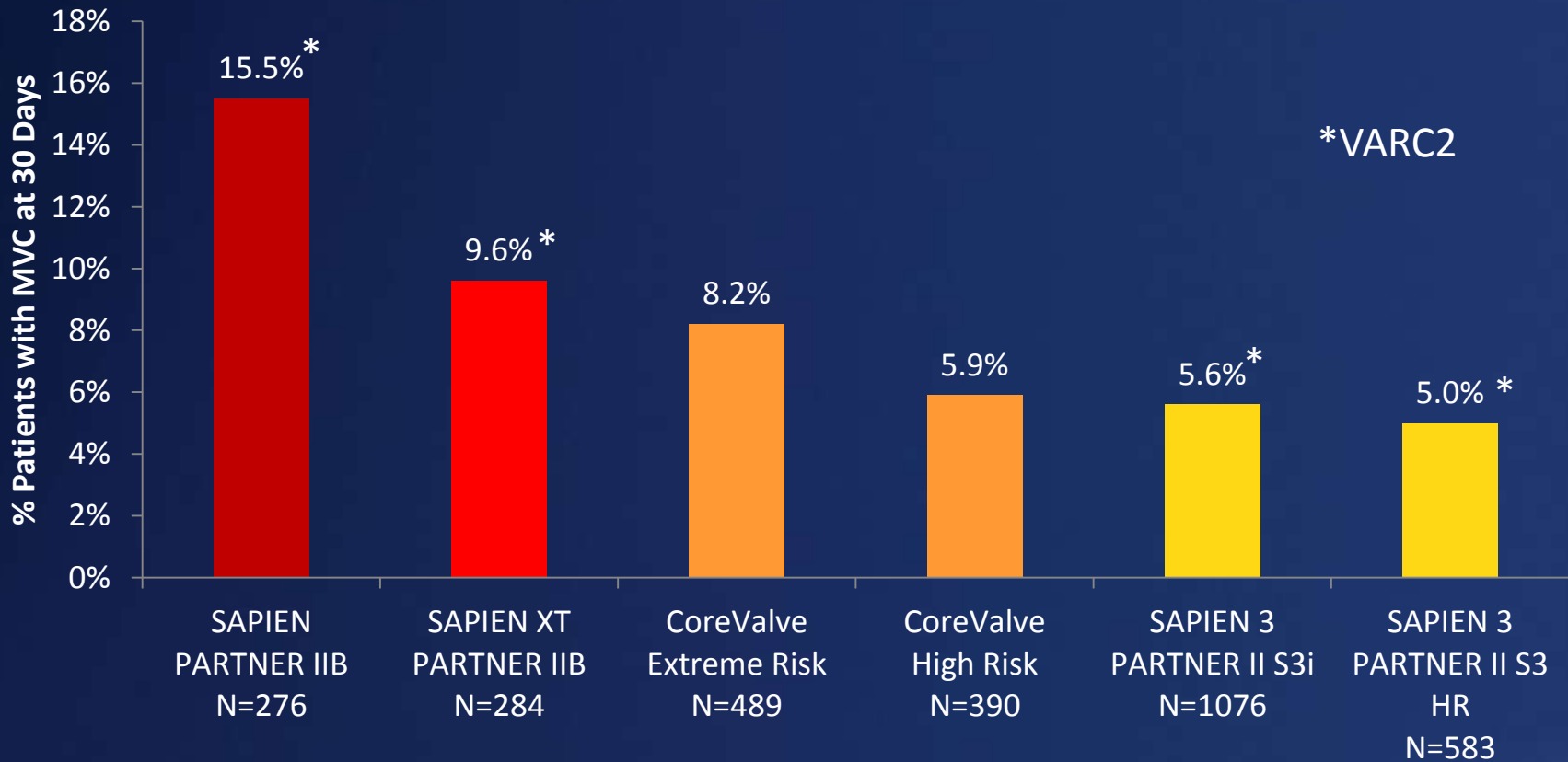


¹Abdel-Wahab, et al., *JAMA* 2014; 311(15): 1503-14; ²Buchanan, et al., presented at EuroPCR 2012; ³Di Mario, et al., *EuroIntervention* 2013; 8(12): 1362-71; ⁴Spargias, et *Hellenic J Cardiol* 2013; 54: 18-24; ⁵Kasel, et al., *Am J Cardiovasc Dis* 2014; 4(2): 87-99

Vascular Complications

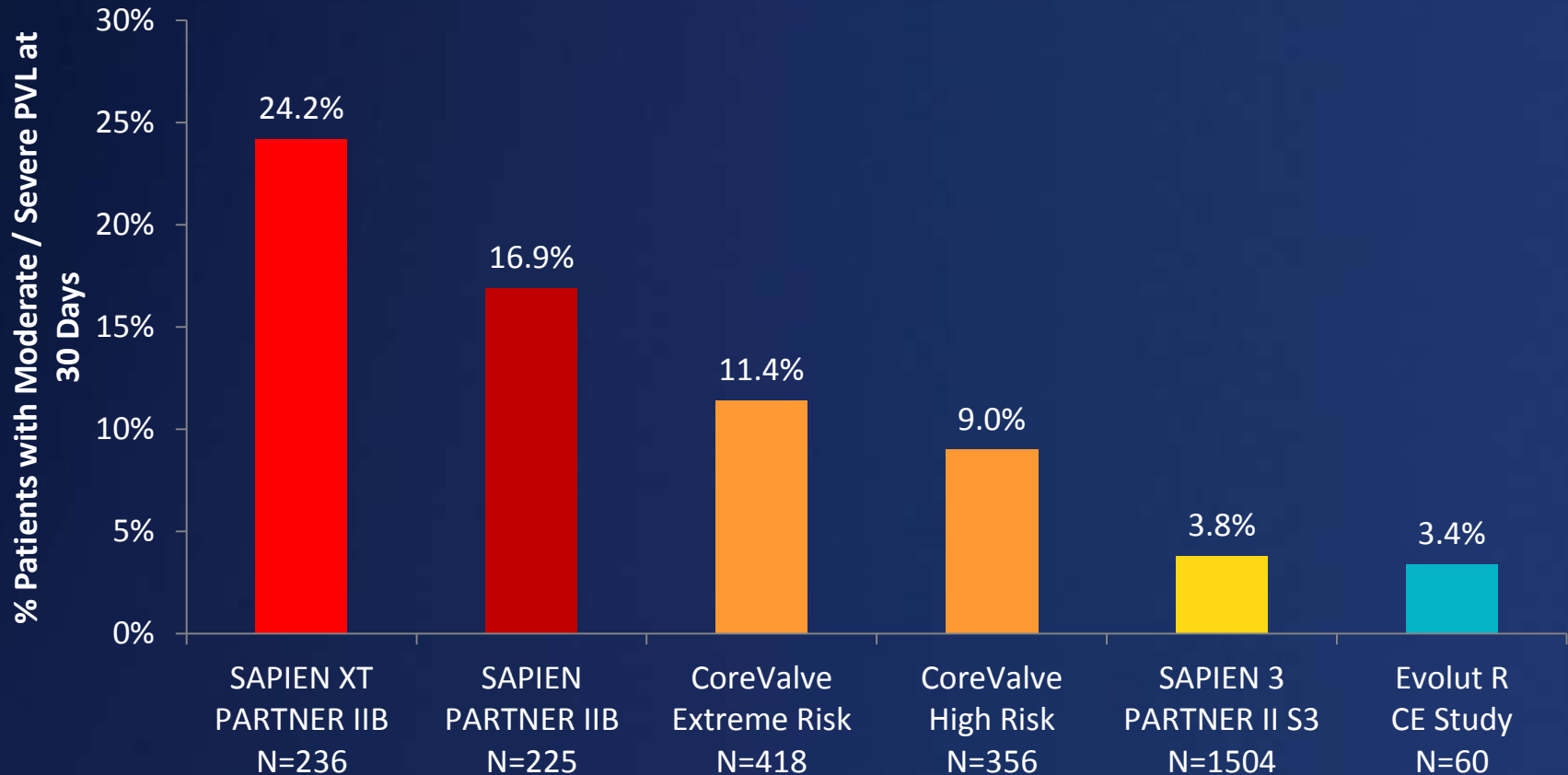
Data from rigorous controlled trials begin to show

the positive impact that smaller sheath size has on major vascular complications



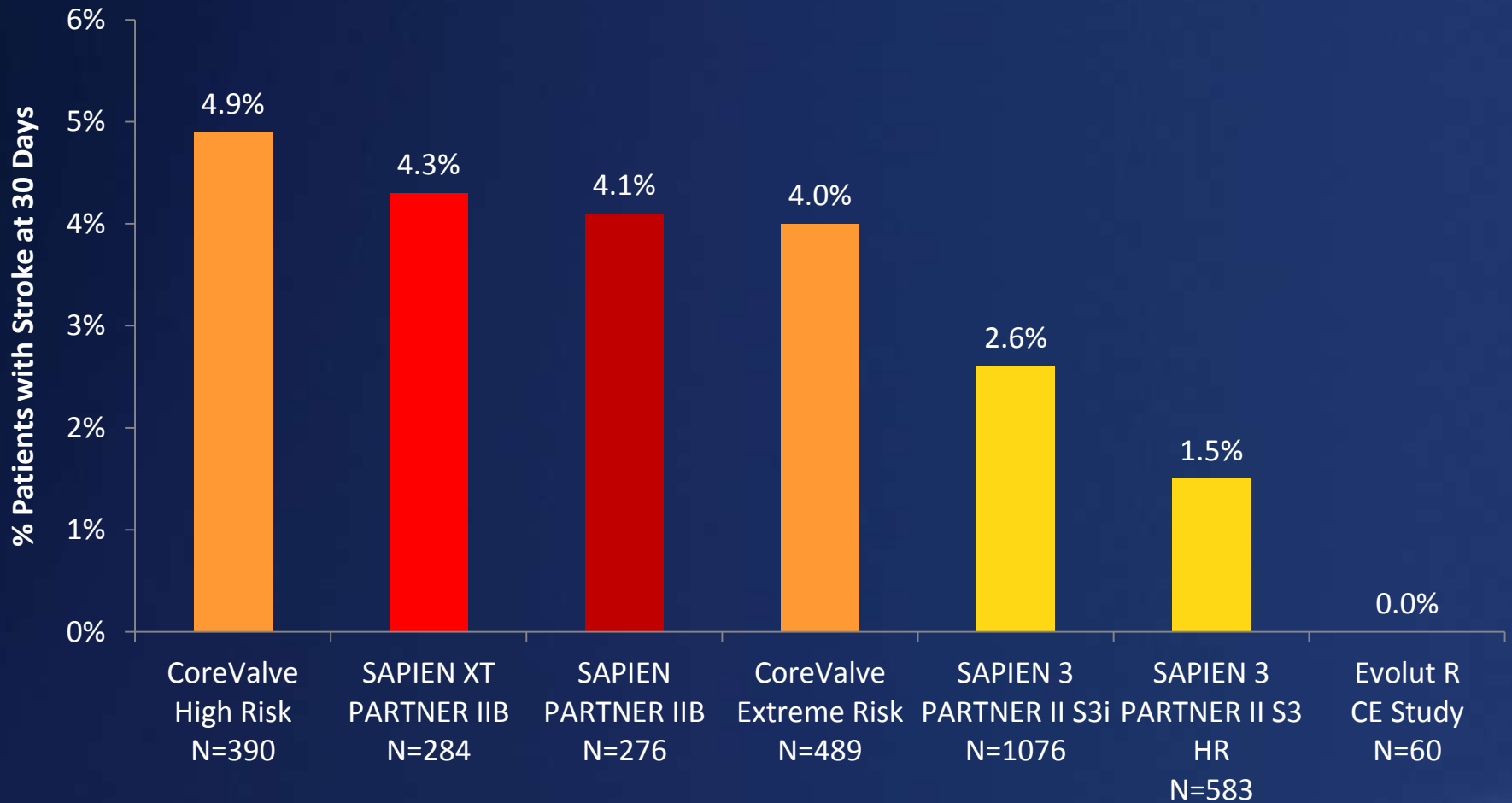
30 Day Moderate and Severe PVL

Newer technologies are clearly driving a decrease in early PVL rates



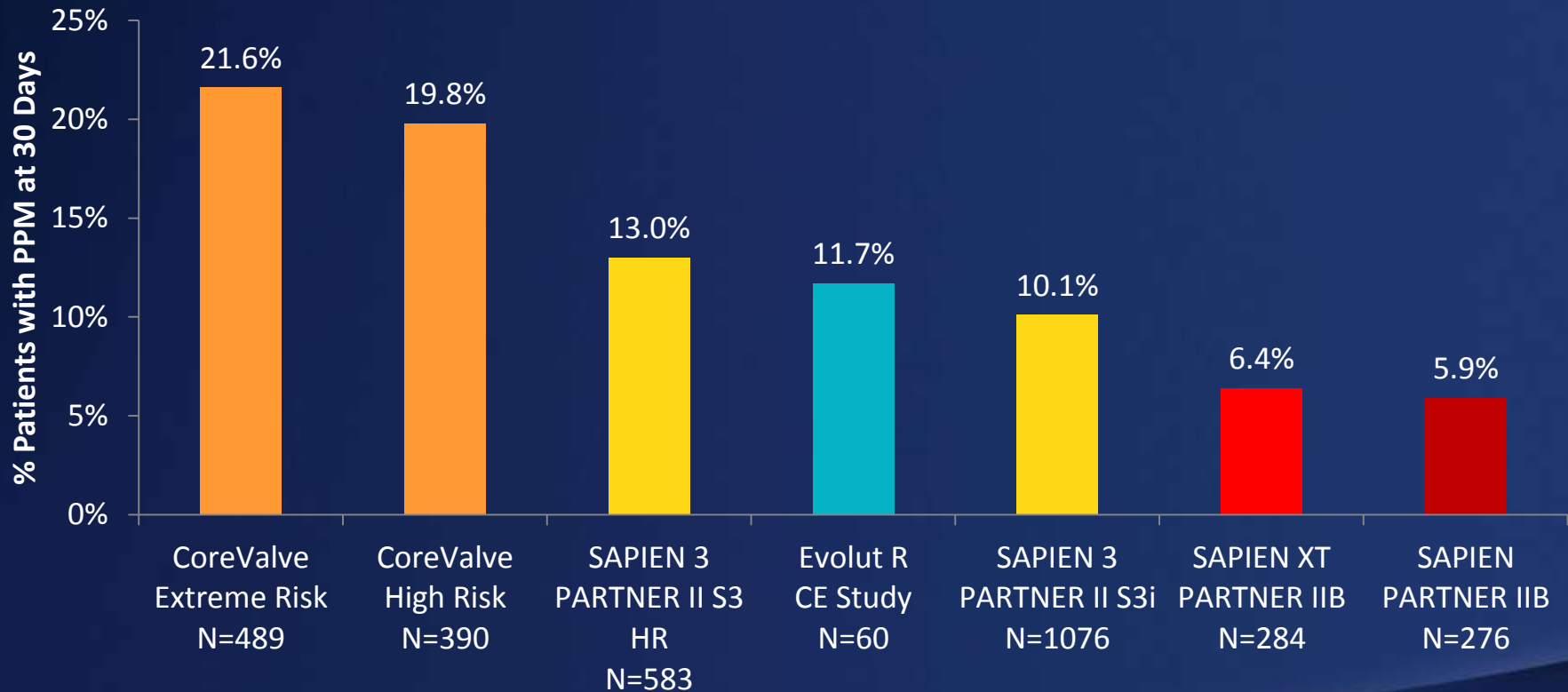
30 Day Stroke

Stroke rates are decreasing, but monitoring/assessment differs between studies. And no one is at 0% yet.



Post-TAVI Permanent Pacemakers

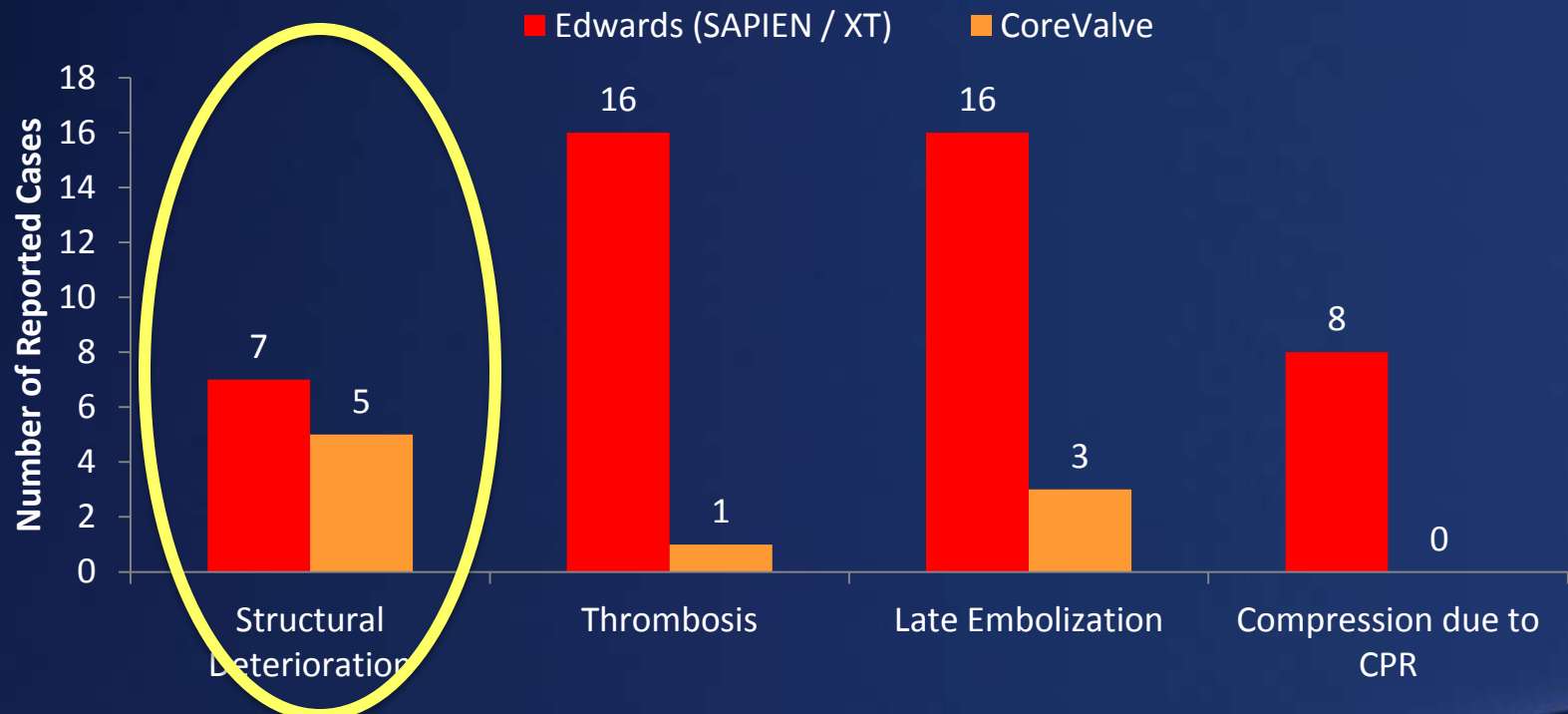
SAPIEN and SAPIEN XT have consistently had lower pacemaker rates compared to CoreValve. This gap is closing with newer generation devices.



¹Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ²Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ³Kodali, et al., presented at ACC 2015 ; ⁴Meredith, et al., presented at ACC 2015; ⁵Leon, et. al. presented at ACC 2013

Late Complications

- Long term durability and safety will be of paramount importance as TAVI is applied to patients with longer life expectancy. The overall outlook so far however is very positive



Conclusion

We and Our Patients are Lucky:
Two Great THV Platforms in 2016



Conclusion

The biggest issue is not which valve to use,
but getting patients who can benefit from
TAVR, the therapy they deserve!