Appropriate Use of TAVR - now and in the future

A Surgeon's Perspective

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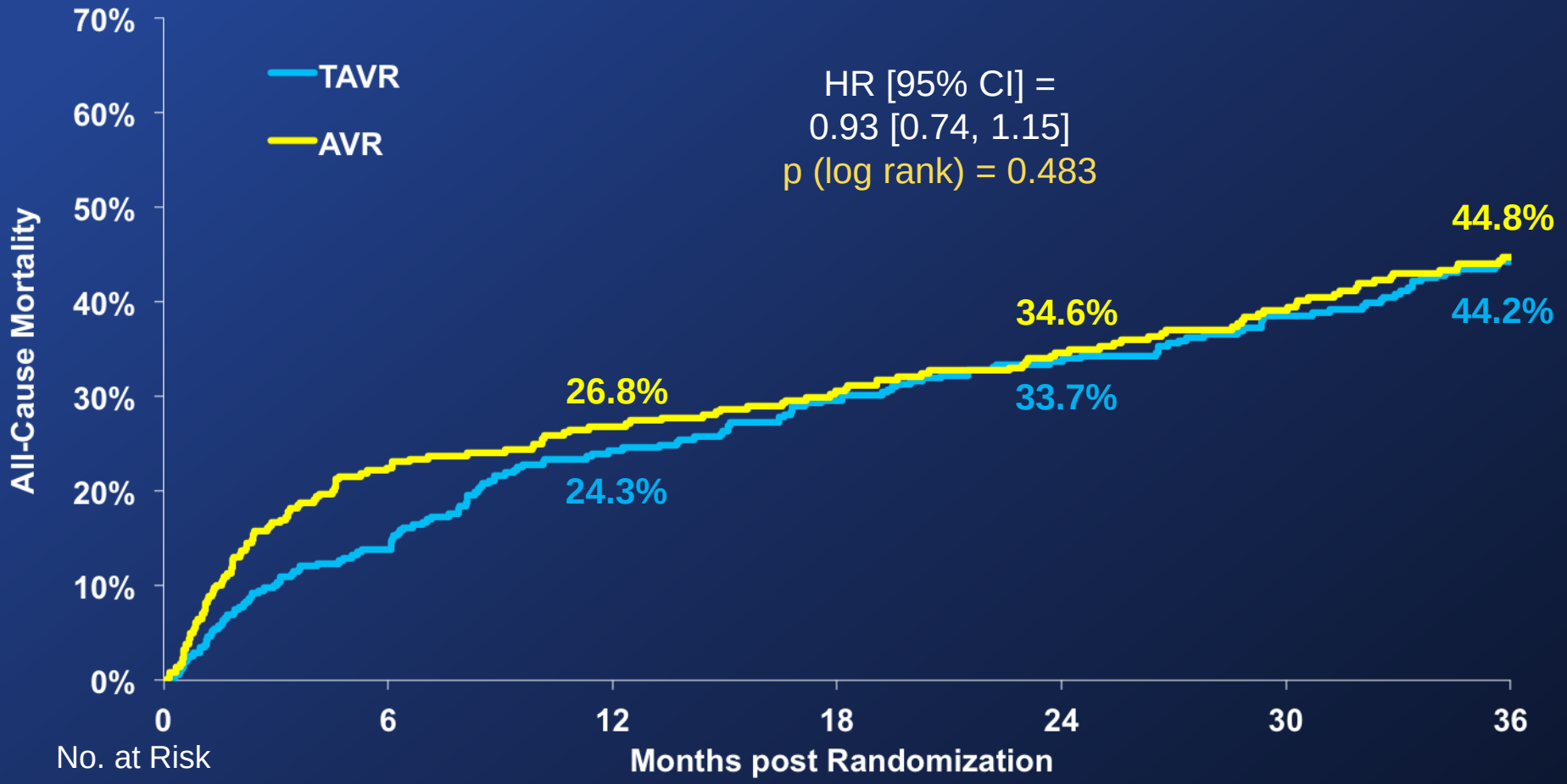
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Consulting Fees/Honoraria	• Medtronic, Abbott, Direct Flow Medical, Edwards

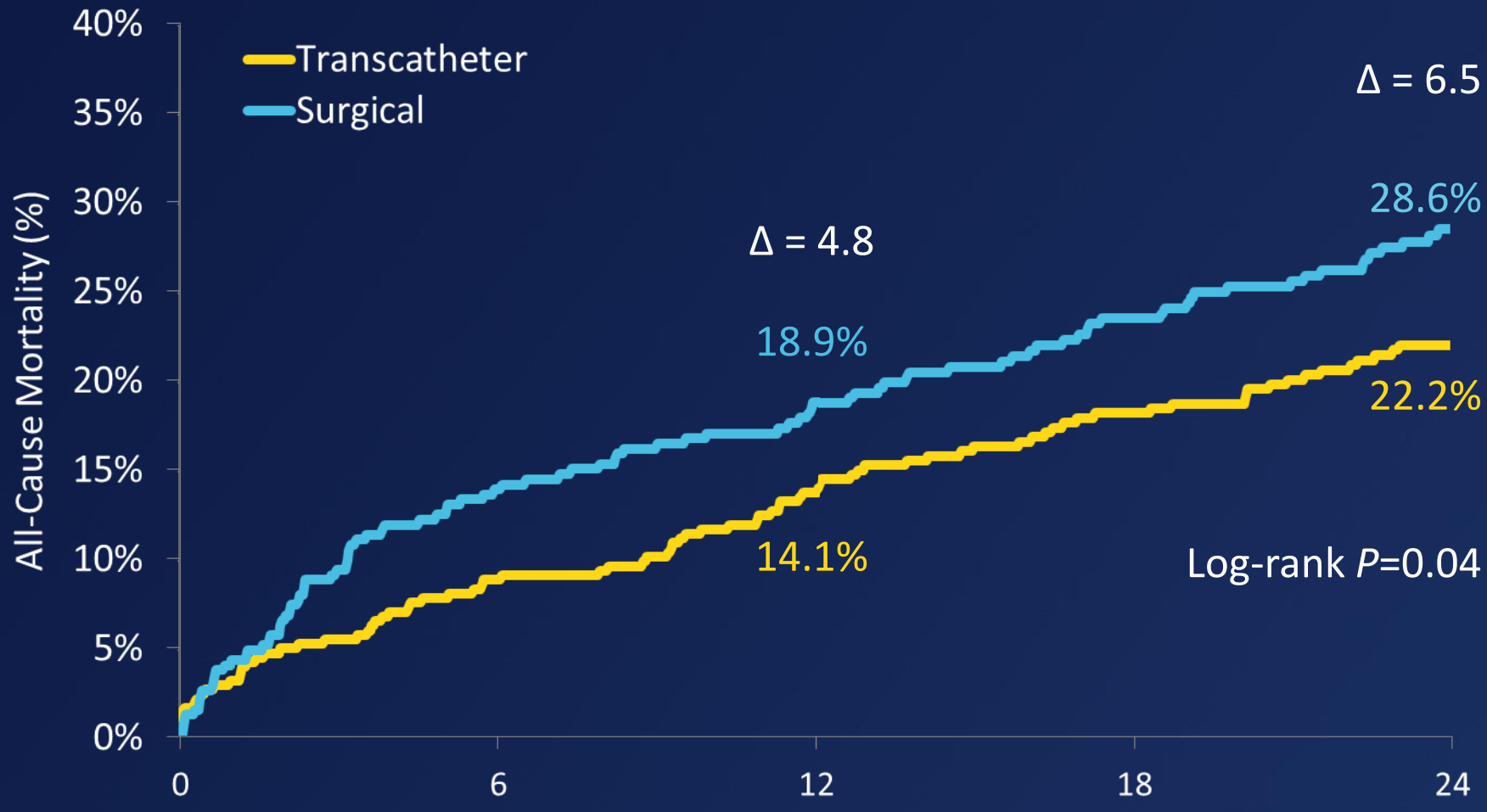
All-Cause Mortality (ITT)



No. at Risk

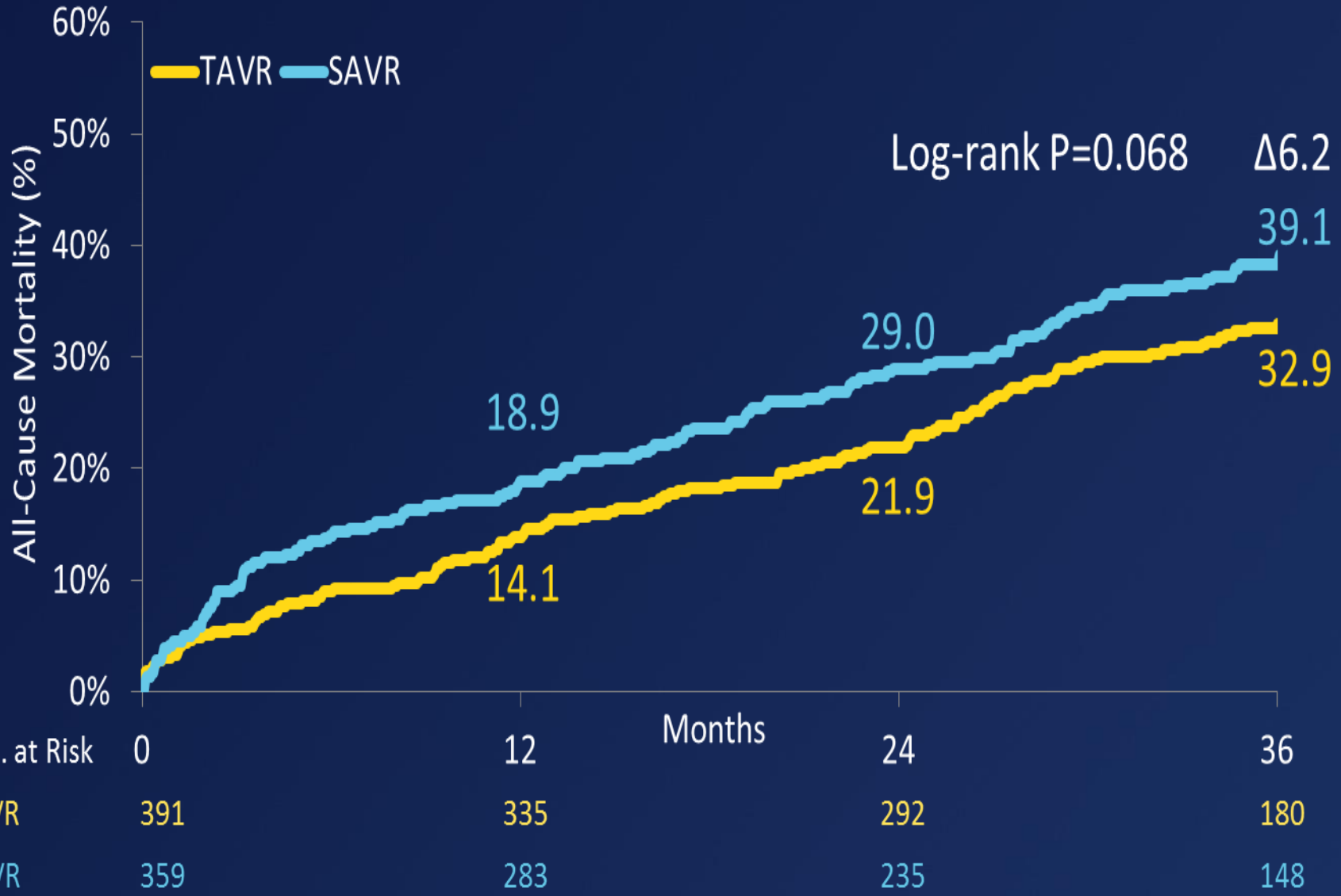
TAVR	348	298	261	239	222	187	149
AVR	351	252	236	223	202	174	142

All-Cause Mortality

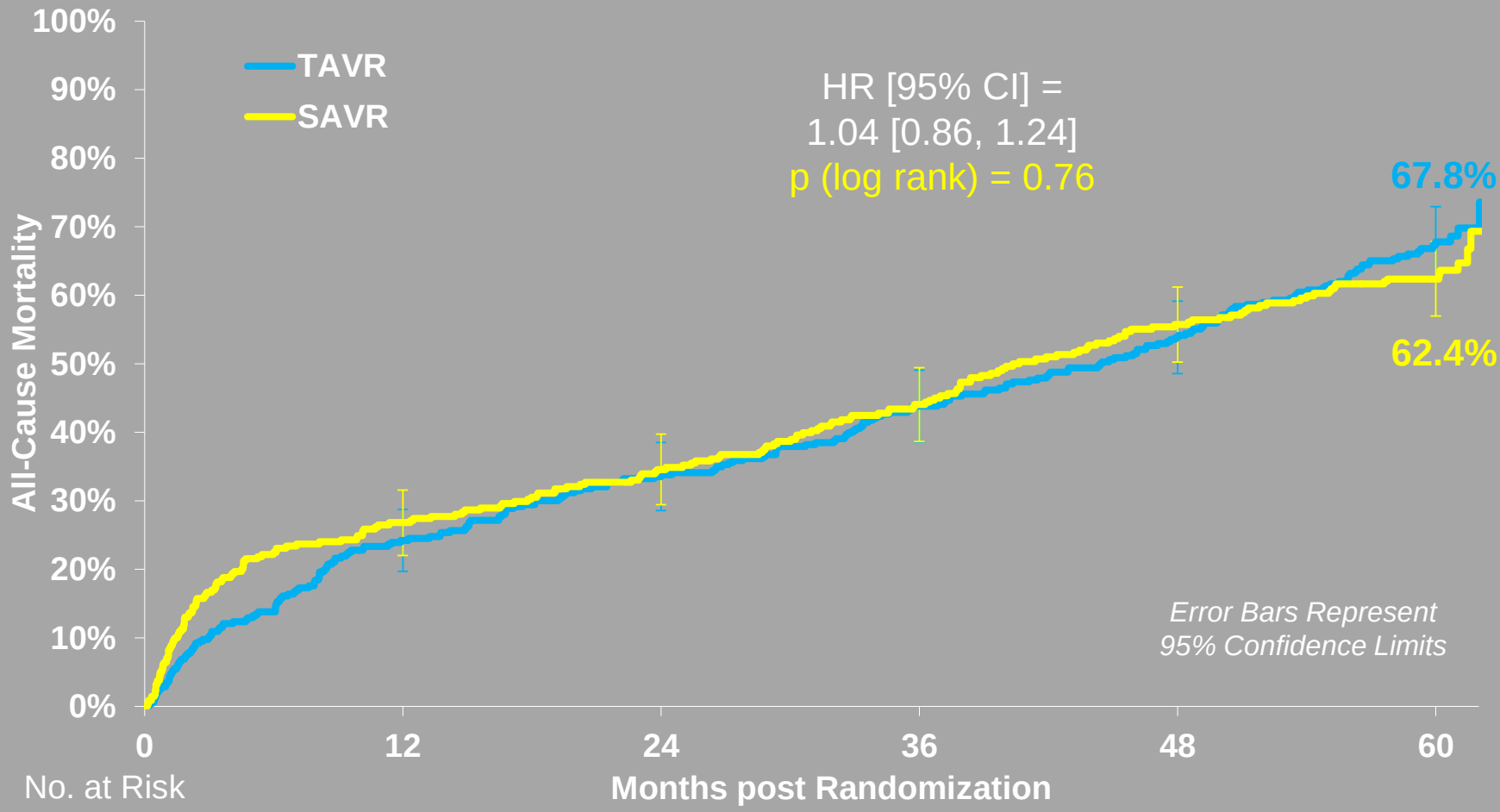


No. at Risk					
Transcatheter	391	378	354	334	219
Surgical	359	343	304	282	191

All-Cause Mortality



All-Cause Mortality (ITT)
All Patients



No. at Risk

TAVR	348	262	228	191	154	61
SAVR	351	236	210	174	131	64

Who are the patients in these trials ?

Baseline Patient Characteristics
Demographics

Characteristic	TAVR (n=348) n		AVR (n=351) n	
Age – years (Mean ± SD)	348	83.6 ± 6.8	349	84.5 ± 6.4
Male	201	57.8%	198	56.7%
NYHA Class III or IV	328	94.3%	328	94.0%
Previous CABG	148	42.5	152	43.6
Cerebrovascular disease	96	29.4	87	26.8
Peripheral vascular disease	149	43.2	142	41.6
STS Score (Mean ± SD)	347	11.8 ± 3.3	349	11.7 ± 3.5

Baseline Demographics

Characteristic	TAVR N=390	SAVR N=357
Age, years	83.1 ± 7.1	83.2 ± 6.4
Men, %	53.1	52.4
STS Predicted Risk of Mortality, %	7.3 ± 3.0	7.5 ± 3.4
Logistic EuroSCORE, %	17.7 ± 13.1	18.6 ± 13.0
NYHA Class III/IV, %	85.6	86.8
Prior Coronary-artery Bypass Surgery	29.5	31.1
Diabetes Mellitus, %	34.9*	45.4*
Insulin Requiring Diabetes, %	11.0	13.2
Prior Stroke, %	12.6	14.0
Modified Rankin 0 or 1, %	74.5	87.2
Modified Rankin > 1, %	25.5	12.8
STS Severe Chronic Lung Disease, %	13.3	9.0

*P < 0.01

25

Baseline Patient Characteristics
Demographics and Vascular Disease

THE PARTNER II TRIAL

Characteristic	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Age - yrs	81.5 ± 6.7	81.7 ± 6.7	0.63
Male - %	54.2	54.8	0.79
STS Score - %	5.8 ± 2.1	5.8 ± 1.9	0.29
NYHA Class III or IV - %	77.3	76.1	0.53
CAD - %	69.2	66.5	0.20
Prior CABG - %	23.6	25.6	0.33
Cerebrovascular Disease - %	32.1	31.0	0.60
PVD - %	27.9	32.9	0.02

In the high risk patient

(top decile of risk for patients undergoing SAVR)

TAVR is the treatment of choice

- TAVI is superior to SAVR in terms of early mortality
- This difference would appear to be sustained out to 2 and 3 years
- TAVI is associated with a lower incidence of early morbidity such as bleeding events, acute kidney injury and new-onset atrial fibrillation
- TAVI is associated with a more rapid recovery that results in shorter durations of stay in critical care and hospital
- TAVI is cost effective in this population

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

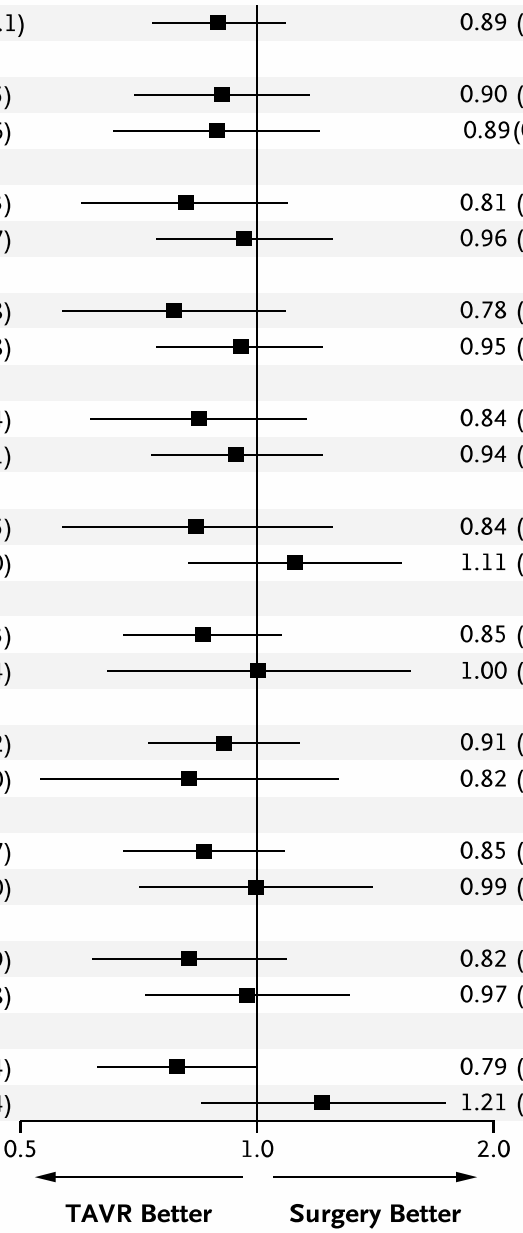
- *Endocarditis and repeat aortic-valve interventions were uncommon*
- *in TAVR vs SAVR groups (at 2 years)*
  - *endocarditis: 1.2% vs. 0.7%, P = 0.22*
  - *re-interventions: 1.4% vs. 0.6%, P = 0.09*

- Re-intervention was more than double in the TAVR arm (NS)

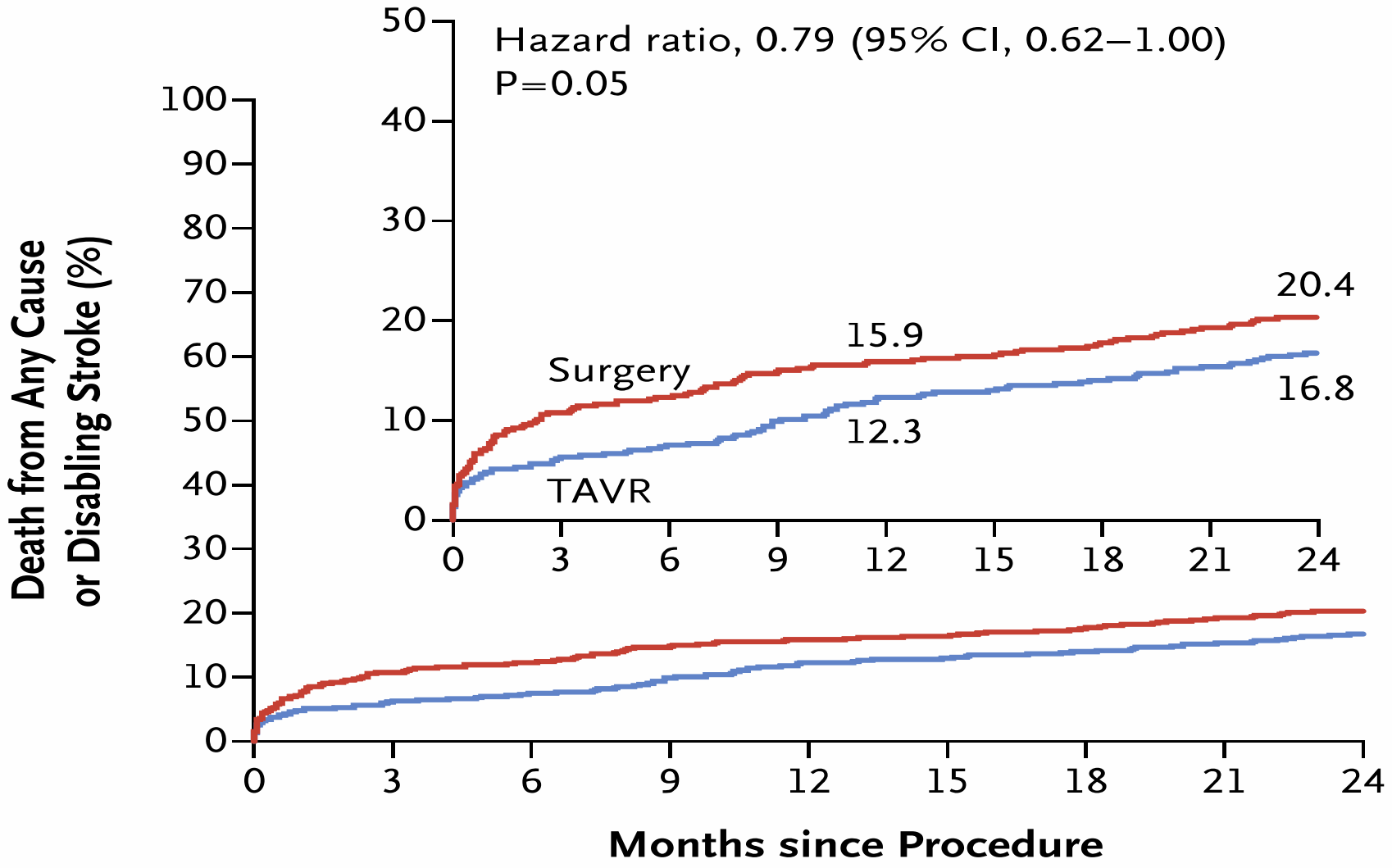
- Endocarditis was almost double in the TAVR arm (NS)

Could leaving behind the bulky native leaflets in addition to the device create an environment that might provide a nidus for infection over the long term ?

Subgroup	No. of Patients	TAVR	Surgery	Hazard Ratio (95% CI)	P Value
		no. of patients with event/total no. of patients (%)			
Overall	2032	192/1011 (19.3)	202/1021 (21.1)	0.89 (0.73–1.09)	0.25
Age					0.96
<85 yr	1245	111/626 (18.0)	114/619 (19.5)	0.90 (0.69–1.17)	
≥85 yr	787	81/385 (21.5)	88/402 (23.6)	0.89(0.65–1.20)	
Sex					0.37
Female	924	77/463 (16.9)	88/461 (20.3)	0.81 (0.59–1.10)	
Male	1108	115/548 (21.4)	114/560 (21.7)	0.96 (0.74–1.25)	
Body-mass index					0.37
≤25	611	66/303 (22.1)	75/308 (26.8)	0.78 (0.56–1.09)	
>25	1421	126/708 (18.1)	127/713 (18.8)	0.95 (0.74–1.22)	
STS score					0.60
≤5	897	73/469 (15.8)	75/428 (18.4)	0.84 (0.61–1.16)	
>5	1134	119/542 (22.4)	127/592 (23.1)	0.94 (0.73–1.21)	
Left ventricular ejection fraction					0.27
≤55	496	44/237 (19.1)	53/259 (21.5)	0.84 (0.56–1.25)	
>55	841	85/426 (20.1)	71/415 (18.0)	1.11 (0.81–1.53)	
Moderate or severe mitral regurgitation					0.53
No	1471	132/748 (17.8)	141/723 (20.3)	0.85 (0.67–1.08)	
Yes	322	38/151 (25.9)	39/171 (24.4)	1.00 (0.64–1.57)	
Previous CABG					0.69
No	1532	156/772 (20.6)	158/760 (22.2)	0.91 (0.73–1.13)	
Yes	500	36/239 (15.3)	44/261 (18.0)	0.82 (0.53–1.27)	
Peripheral vascular disease					0.47
No	1414	130/729 (18.2)	134/685 (20.7)	0.85 (0.67–1.09)	
Yes	618	62/282 (22.3)	68/336 (22.0)	0.99 (0.71–1.40)	
5-Meter walk test					0.43
≤7 sec	1003	91/520 (17.7)	97/483 (20.9)	0.82 (0.62–1.09)	
>7 sec	834	85/416 (20.7)	82/418 (20.8)	0.97 (0.71–1.31)	
Access route					0.06
Transfemoral	1550	128/775 (16.8)	149/775 (20.4)	0.79 (0.62–1.00)	
Transthoracic	482	64/236 (27.7)	53/246 (23.4)	1.21 (0.84–1.74)	



C Transfemoral-Access Cohort, Intention-to-Treat Analysis



No. at Risk

TAVR	775	718	709	685	663	652	644	634	612
Surgery	775	643	628	604	595	577	569	557	538

Low profile Delivery Systems will increase the proportion of patients that can have trans-femoral access

14F Equivalent for all valve sizes

It is not known what the outcomes will be in those patients who previously would have required a trans-thoracic approach when they are able to be treated transfemorally.

Where are we now in patients with a degree of equipoise ?

TAVI

- Age 80+
- Female
- Small annulus
- TF possible
- Prior CABG
- Prior SAVR

SAVR

- Large annulus
- Large volume +/- dense calcification
- Bicuspid valve
- Low lying cor ostia
- Narrow sinuses
- TT access needed

Deeb GM et al JACC 2016, 2016:2565–74

PERSPECTIVES

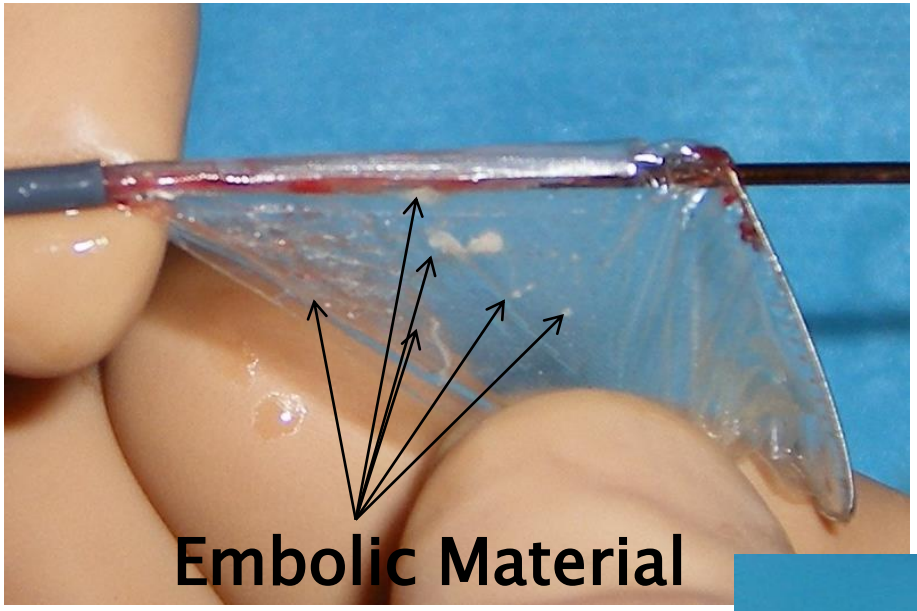
COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: TAVR with self-expanding prostheses has sustained benefit in patients with severe aortic stenosis at high surgical risk for ≥3 years compared to surgical valve replacement.

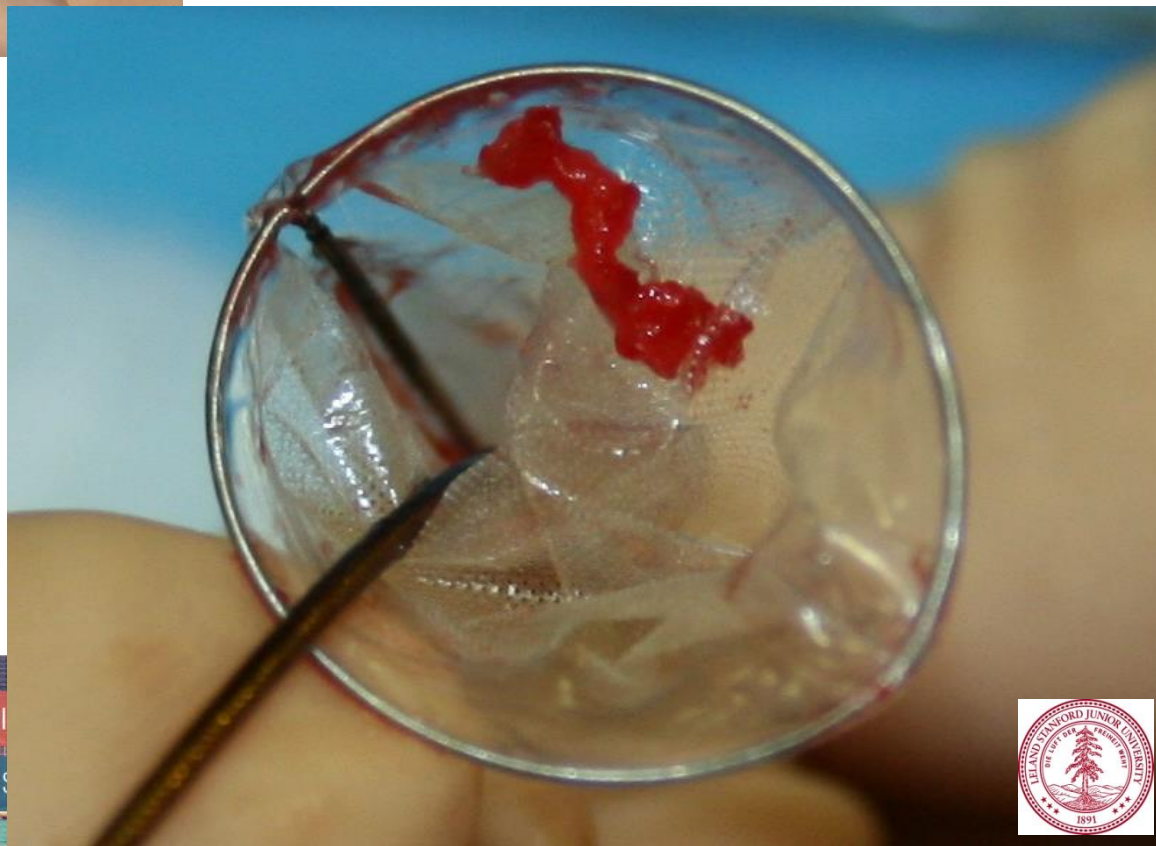
TRANSLATIONAL OUTLOOK: Additional studies are needed to validate outcomes of TAVR over even longer follow-up intervals and in lower-risk patients with severe aortic stenosis.

Complications of TAVR that remain of some concern in the lower risk patient

- Paravalvar Regurgitation
- Vascular injury
- Annular rupture
- Coronary occlusion
- Device embolisation
- Macroscopic cerebral emboli

Embolic Material after TAVR





Valve Leaflet Abnormalities

Treatment and Clinical Outcomes of Transcatheter Heart Valve Thrombosis

Azeem Latib, MD*; Toru Naganuma, MD*; Mohamed Abdel-Wahab, MD; Haim Danenberg, MD; Linda Cota, MD; Marco Barbanti, MD; Helmut Baumgartner, MD; Ariel Finkelstein, MD; Victor Legrand, MD; José Suárez de Lezo, MD; Joelle Kefer, MD; David Messika-Zeitoun, MD; Gert Richardt, MD; Eugenio Stabile, MD; Gerrit Kaleschke, MD; Alec Vahanian, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; John G. Webb, MD; Vasileios F. Panoulas, MD; Francesco Maisano, MD; Ottavio Alfieri, MD; Antonio Colombo, MD

- From Jan 2008 to Sept 2013, among 4266 TAVR cases, 26 patients with THV thrombosis (0.61%); 20 Edwards Sapien/Sapien XT , 6 MDT CoreValve
- Median time from TAVR to imaging findings 181 days
- Most common Sx was DOE (65%) and 31% were without Sx
- Echo (TTE usually): mean AV gradient 40.5 mmHG, thickened leaflets 77% and thrombotic mass 23%
- Warfarin for 2 mos: 23 (88%) reduced symptoms and improved gradients

Latib A et al. Circ Cardiovasc Interv 2015 Apr 8

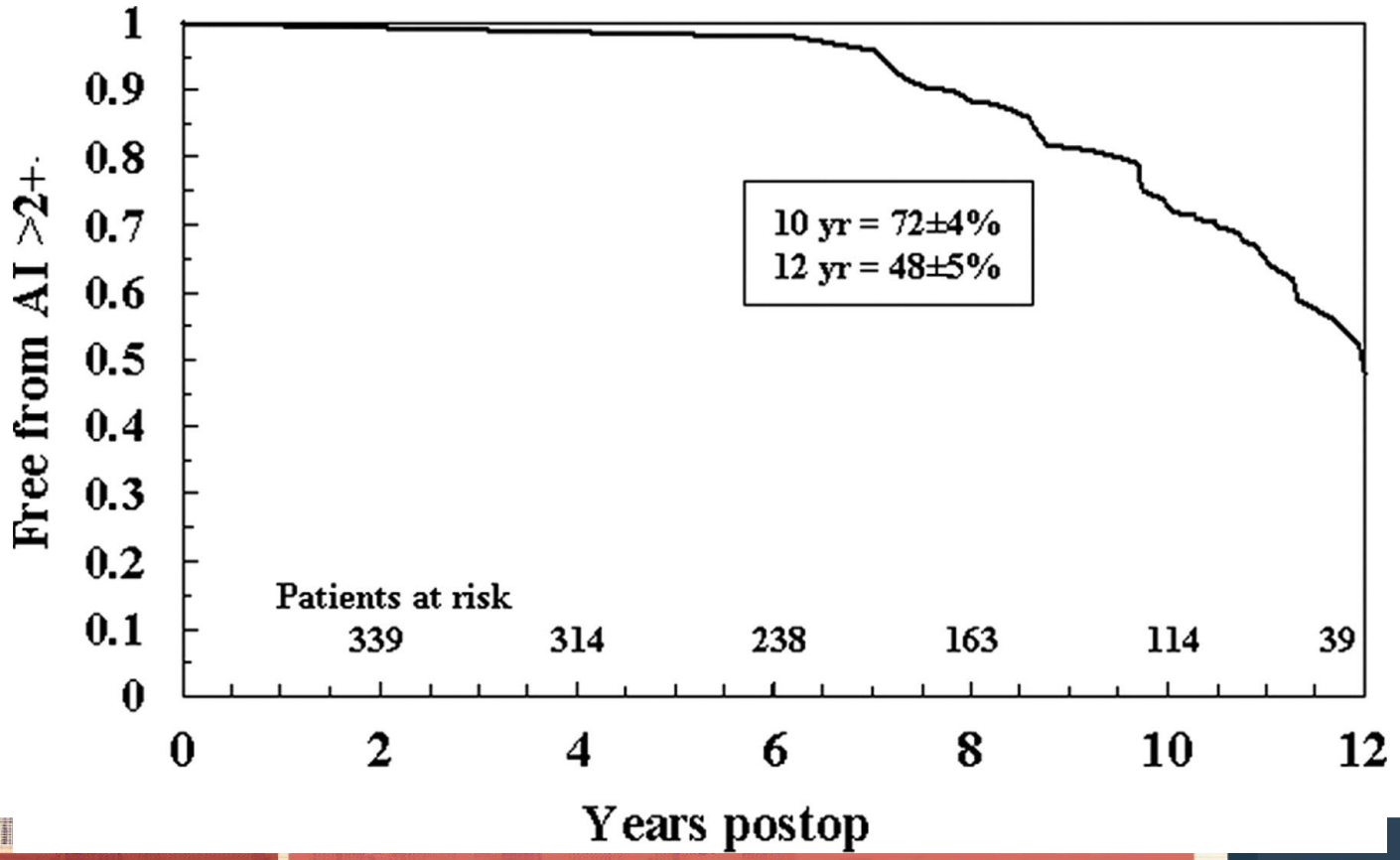
DURABILITY

will be the key determinant of the eventual growth and application of TAVR in the younger and lower risk patient population

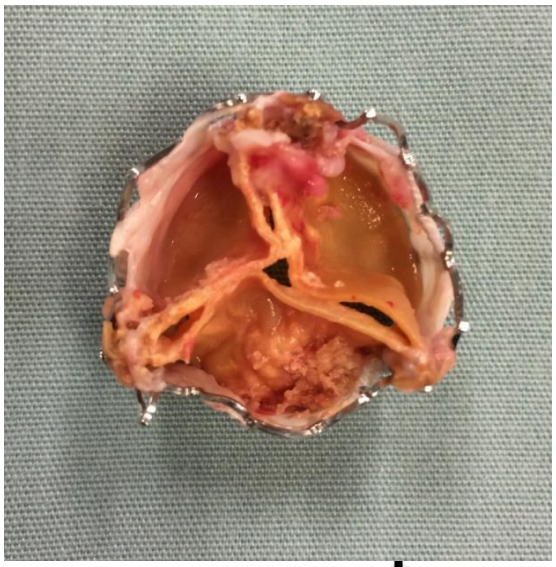
The Toronto Stentless Valve - Freedom from structural valve degeneration

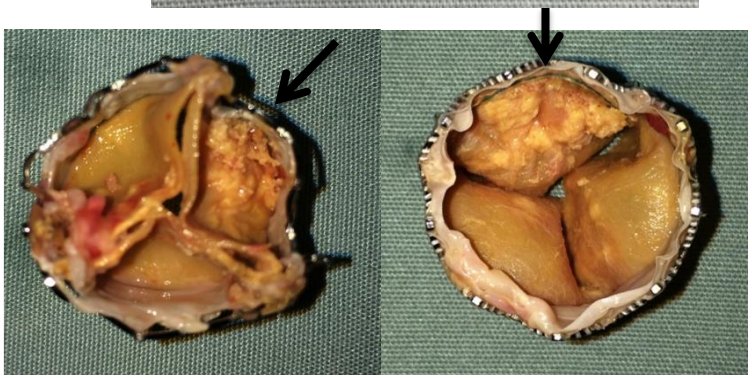
David T. E. et al.; J Thorac Cardiovasc Surg 2008;135:19-24

The "honeymoon period" for aortic bioprostheses



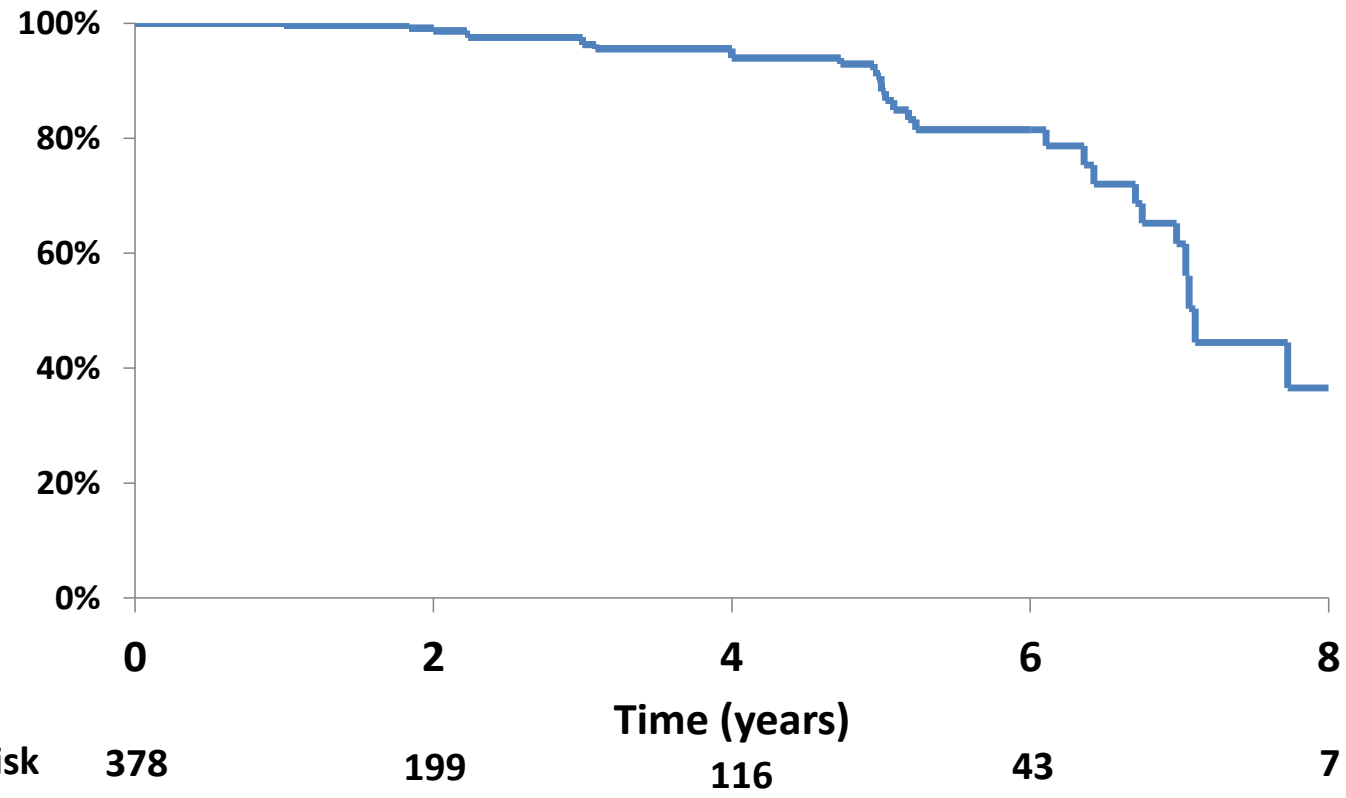
Asymmetric degeneration 5 years after TAVI





Dvir EuroPCR 2016

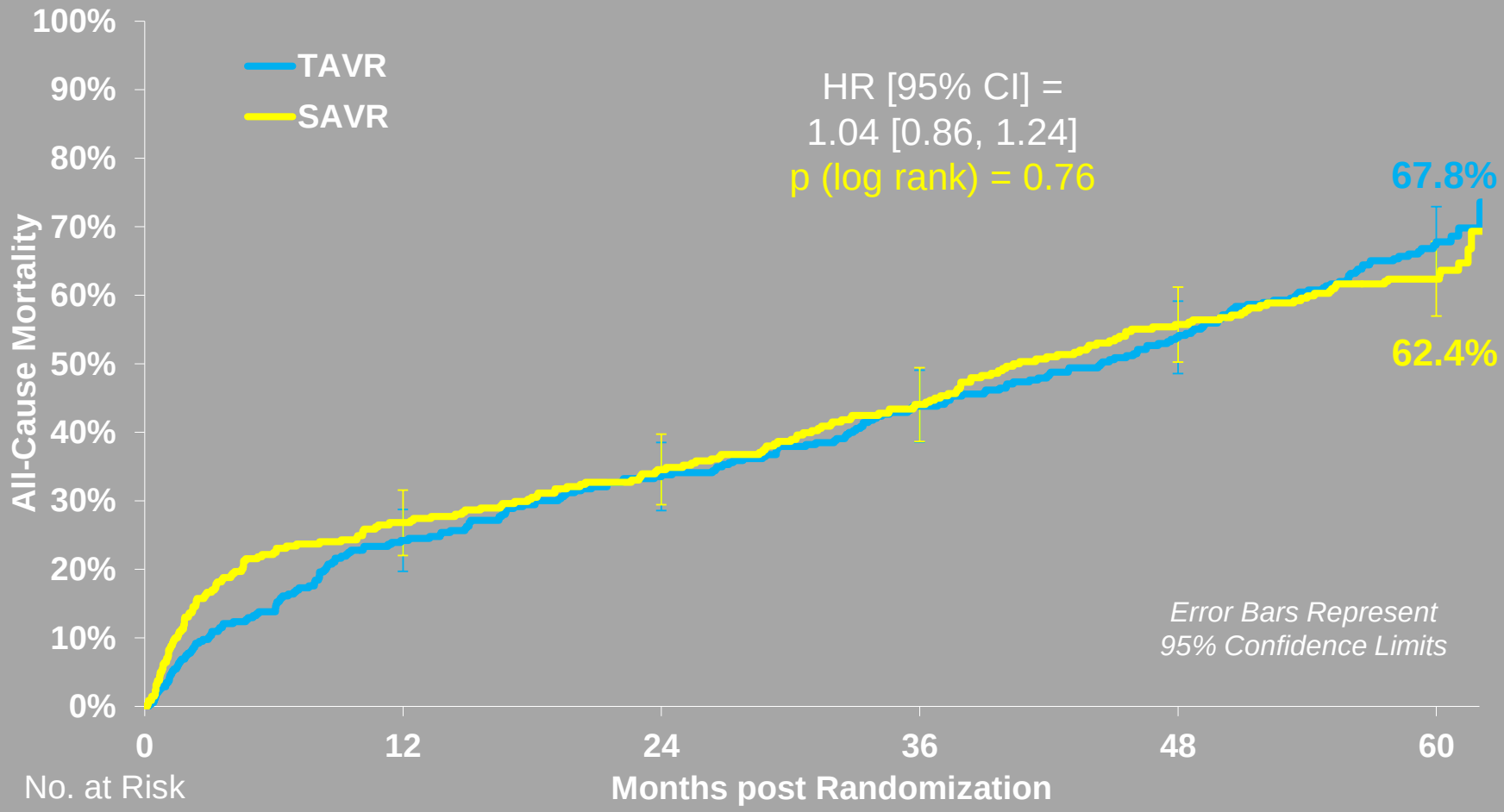
Freedom from THV degeneration



THV degeneration was defined as at least moderate regurgitation AND/OR mean gradient 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.

KM estimate of THV degeneration included censoring of patients at their date of last known THV functioning well without evidence for degeneration per study definition.

All-Cause Mortality (ITT)
All Patients



No. at Risk

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SAVR	351	236	210	174	131	64

A word of caution !

- Let us not forget the lessons learnt by the cardiac surgical community
- Enthusiastic belief and/or trust in a several new prosthetic heart valve designs turned out to be misplaced
- This led to a many patients having sub-optimal outcomes in the mid to long term

The Future

- TAVR will continue to grow and will progressively move down the risk spectrum into younger and lower risk patients
- It is always likely to be superior to SAVR in terms early outcomes such as hospital stay, AF
- It is essential that ongoing studies in lower risk patients (RCT and others) track long term (10+ years) outcomes and durability to ensure that it is non inferior in terms of late outcomes
- Cost may be a major factor in the growth of TAVR in many health economies