TAVR Will Be a Standard Treatment for All Patients with Aortic Stenosis : How Much Younger?

Duk-Woo Park, MD., PhD.

Division of Cardiology, University of Ulsan College of Medicine,
Heart Institute, Asan Medical Center, Seoul, Korea

Conflict of Interest Statement

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	Edwards LifeSciences
Consulting Fees/Honoraria	Medtronic Inc
Consulting Fees/Honoraria	Boston Scientific

Clinical Trials

Trial Name	STS Score	Age
Inoperable Population		
PARTNER IB Trial (***2010***)	11.6	83
High Risk Population (>8)		
PARTNER IA Trial (***2011***)	11.8	84
CoreValve US Pivotal Trial (***2014***)	**7.4**	**83**
Intermediate Risk Population (4-8)		
PARTNER II Trial (***2016***)	5.8	82
Low Risk Population (<4)		
NOTION Trial (***2015***)	3.0	79
PARTNER III (***2019***)	1.9	73
Evolut Low Risk Trial (***2019***)	1.9	74

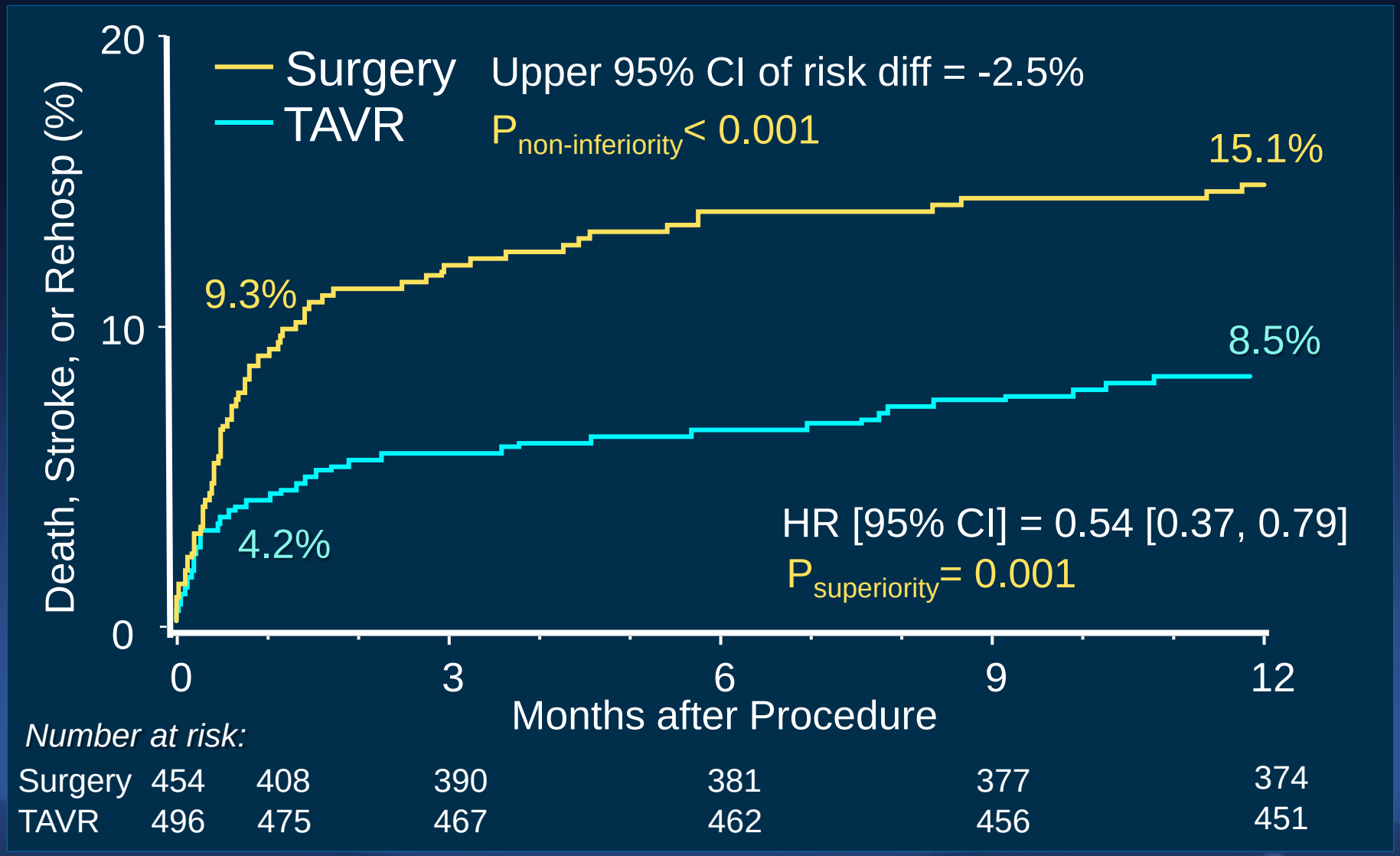
Low Risk Patients (Balloon Expandable)

PARTNER 3 Trial

	TAVR (N=496)	SAVR (N=454)
Age, years	73.5 ± 5.8	73.6 ± 6.1
STS PROM, %	1.9 ± 0.7	1.9 ± 0.6
Male sex	335 (67.5)	323 (71.1)
Diabetes mellitus	155 (31.2)	137 (30.2)
Serum creatinine >2 mg/dl	1 (0.2)	1 (0.2)
Prior Myocardial infarction	28 (5.7)	26 (5.8)
Prior Stroke	17 (3.4)	23 (5.1)
Peripheral vascular disease	34 (6.9)	33 (7.3)

Low Risk Patients (Balloon Expandable)

Death, Stroke, or Rehospitalization at 1 Year



Mack MJ et al, N Engl J Med 2019

Low Risk Patients (Self-expanding)

Evolut Low Risk Trial

	TAVR (N=725)	SAVR (N=678)
Age, years	74.1 ± 5.8	73.6 ± 5.9
STS PROM, %	1.9 ± 0.7	1.9 ± 0.7
Male sex	464 (64.0)	449 (66.2)
Diabetes mellitus	228 (31.4)	207 (30.5)
Serum creatinine >2 mg/dl	3 (0.4)	1 (0.2)
Prior Myocardial infarction	48 (6.6)	33 (4.9)
Cerebrovascular disease	74 (10.2)	80 (11.8)
Peripheral vascular disease	54 (7.5)	56 (8.3)

Popma JJ et al, N Engl J Med 2019

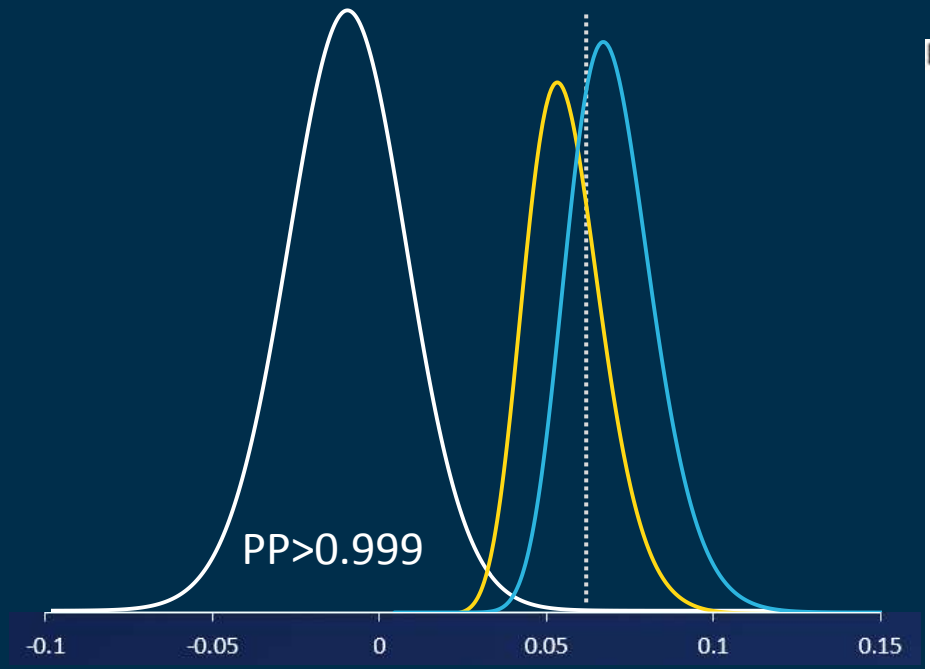
Low Risk Patients (Self-Expanding)

Death or Disabling Stroke at 24 Months

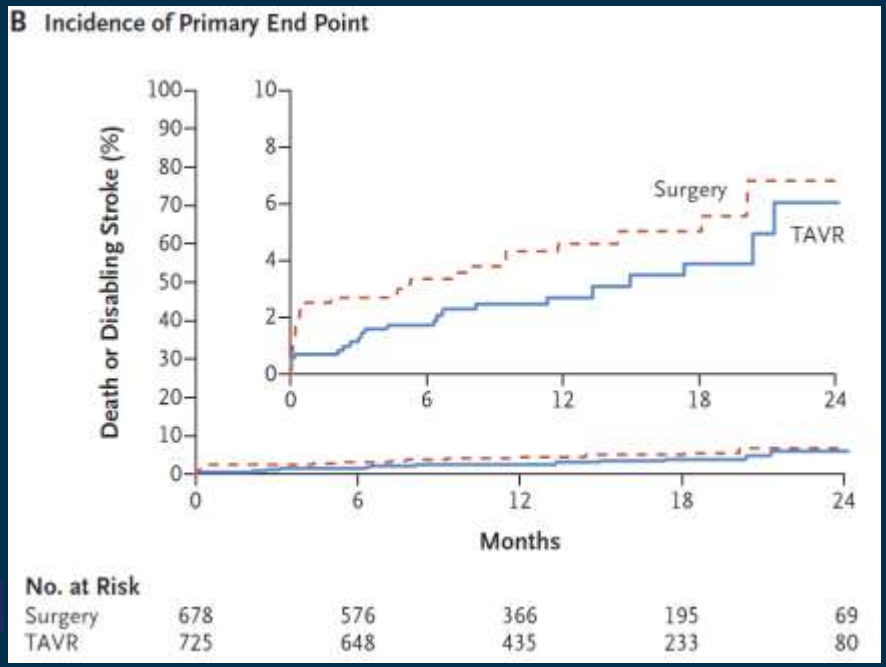
Primary Endpoint Met
TAVR is noninferior to SAVR

TAVR 5.3% **SAVR 6.7%**

Posterior probability of noninferiority > 0.999



TAVR –SAVR difference
= -1.4% (95% BCI; -4.9, 2.1)



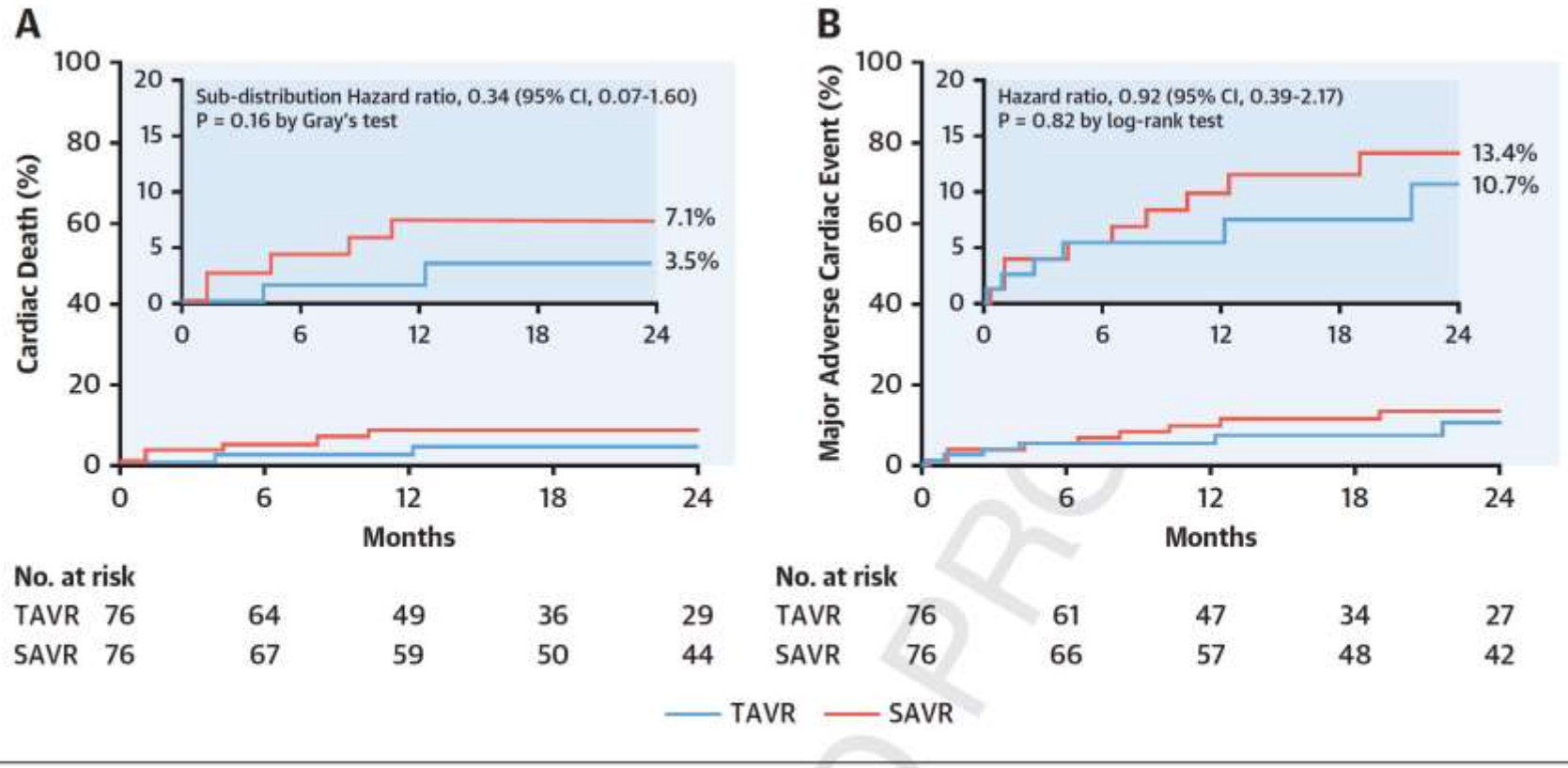
All things being equal, less-invasive therapies will always reign supreme!

TAVR in Old Age and Low Risk

TAVR Wins!

TAVR in Low-Risk, Octogenarian

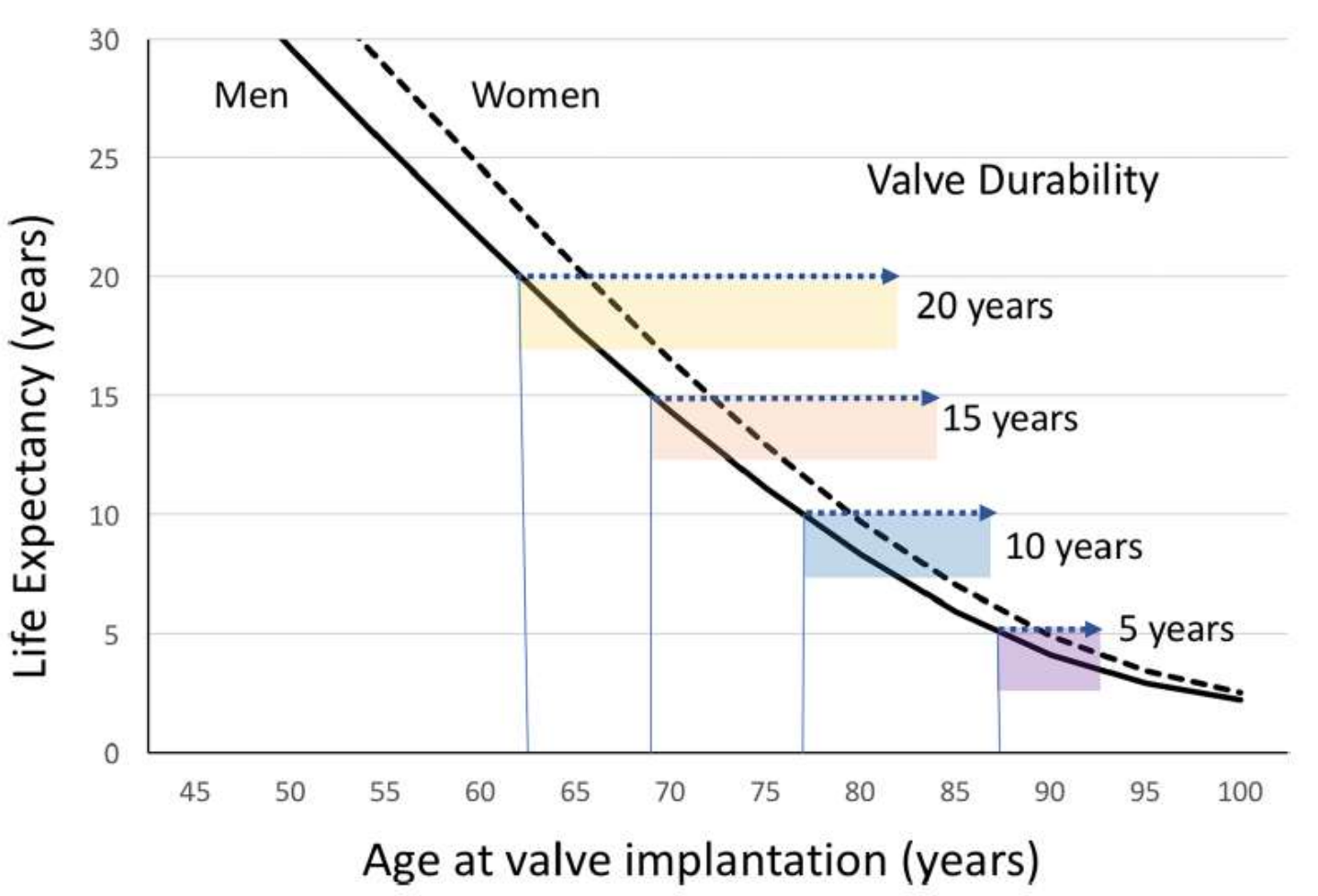
FIGURE 1 Time-to-Event Curves for the Primary and Secondary Endpoints in the Propensity Score-Matched Cohort



Cumulative incidence curves for cardiac death **(A)** and major adverse cardiac events **(B)**. The **insets** show the same data on an enlarged y-axis. CI = confidence interval; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

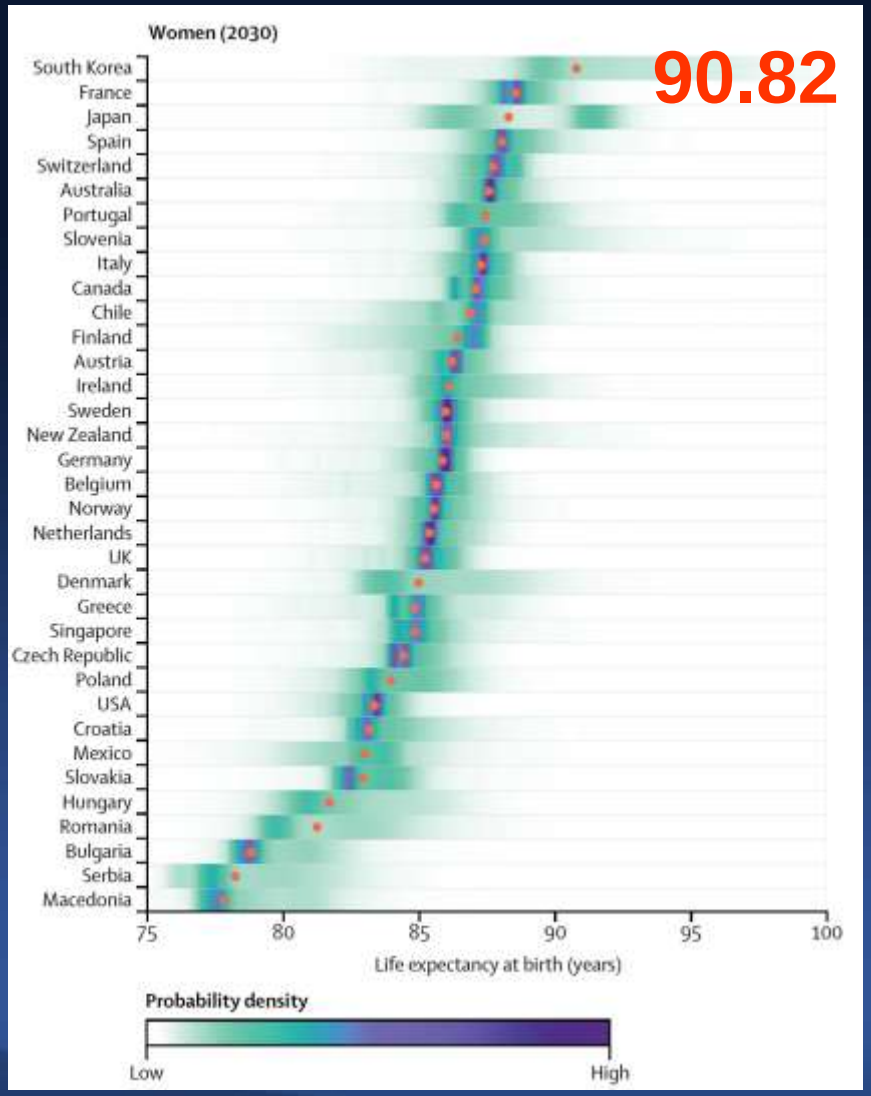
Younger Patients With Low Risk With *Long Life Expectancy*

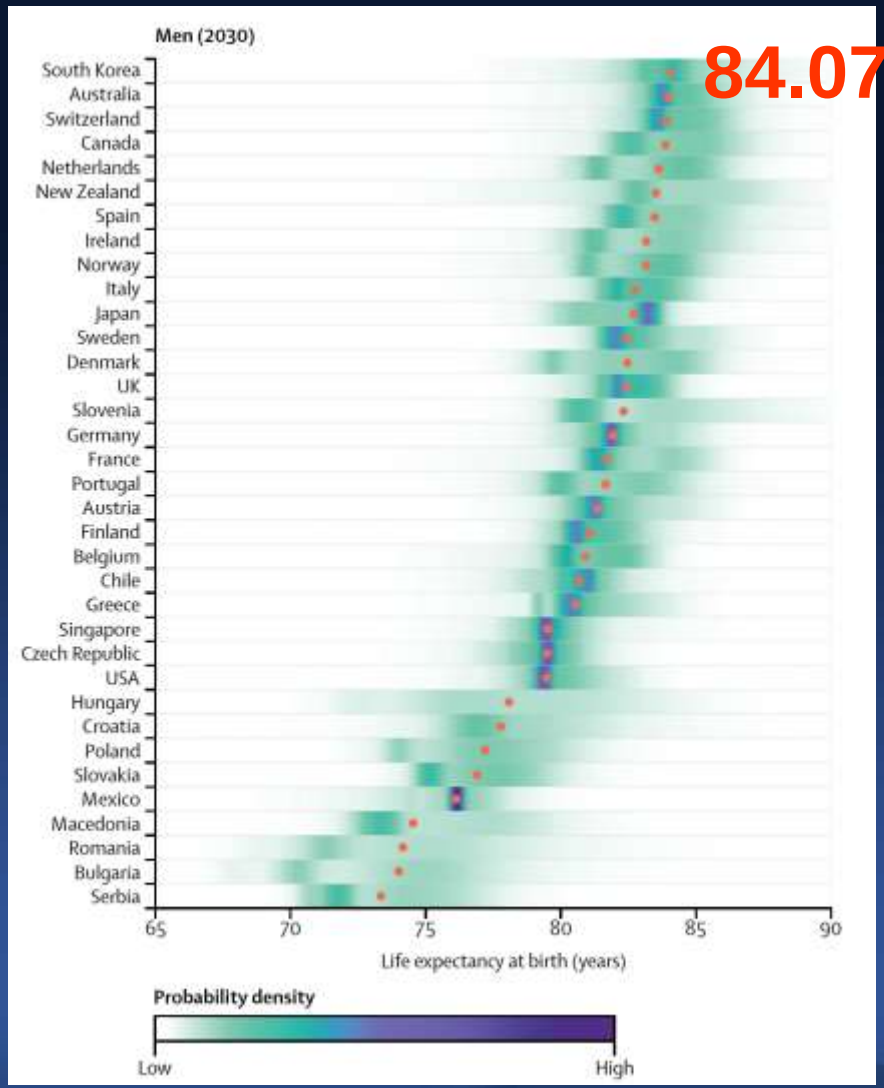
Life expectancy may exceed durability in low-risk, younger patients



Bagur et al. Heart 2017

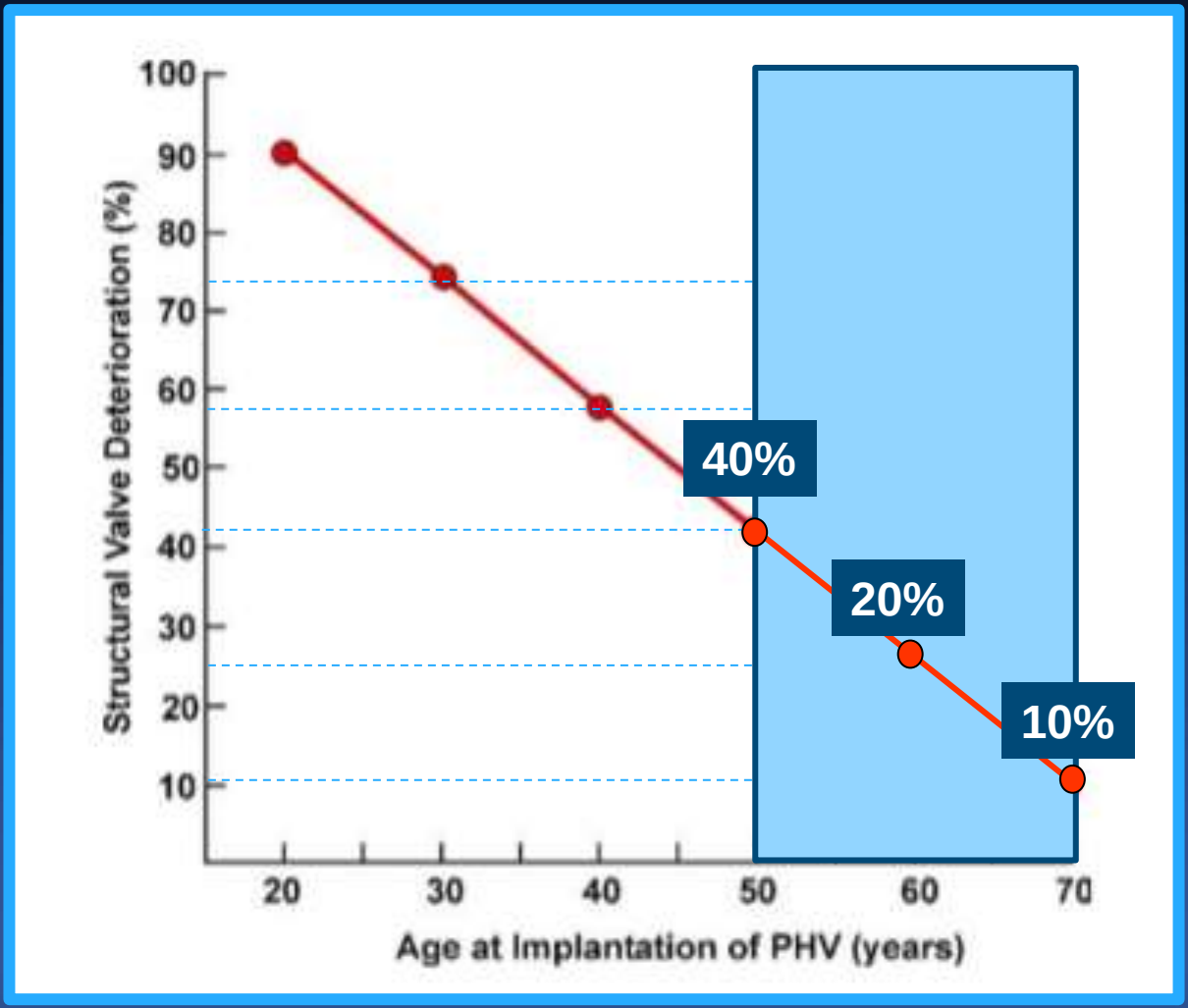
Life Expectancy of Korean
No #1 in the World at 2030





Vasilis Kontis et al. Lancet 2017;389:1323-35

Inverse Association Between Risk of SVD and Age



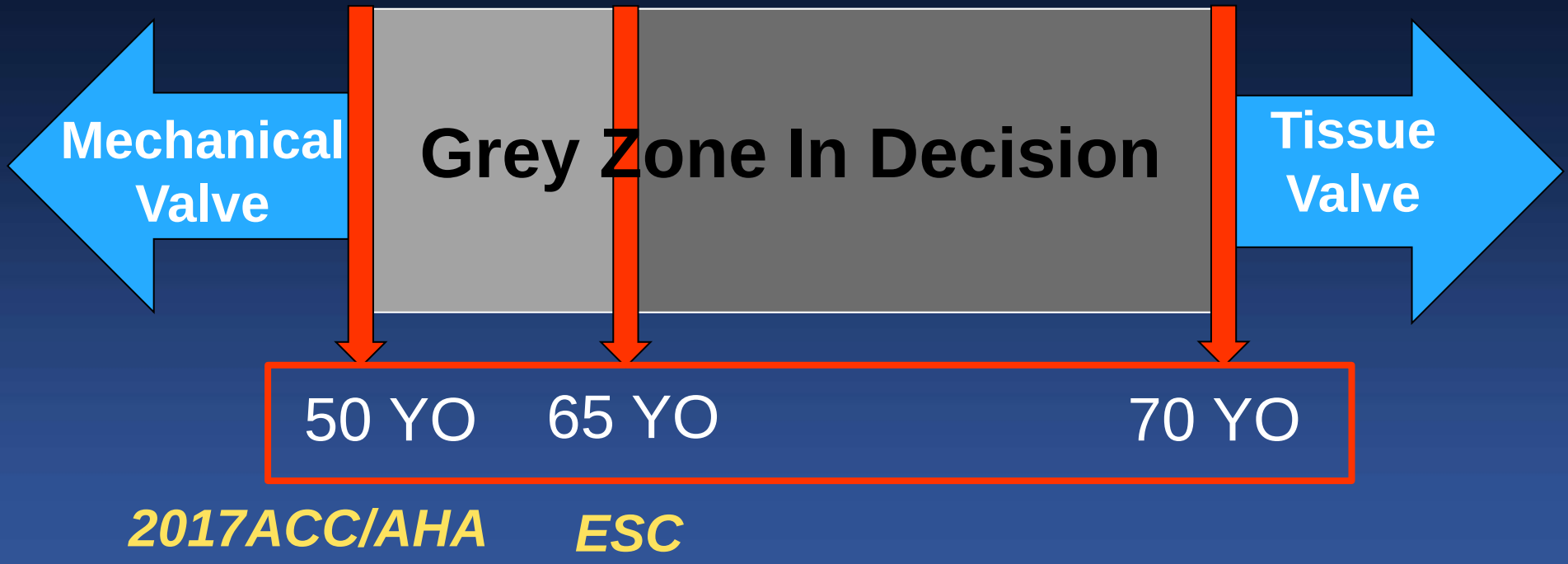
True Story,

The Terminator, Arnold Schwarzenegger, had heart valve surgery on April 16, 1997 at his age of **50 year old**.

Schwarzenegger apparently opted against a mechanical valve, the only permanent solution available at the time of his surgery, but **chose a tissue valve because mechanical valve would have sharply limited his physical activity and capacity to exercise**.

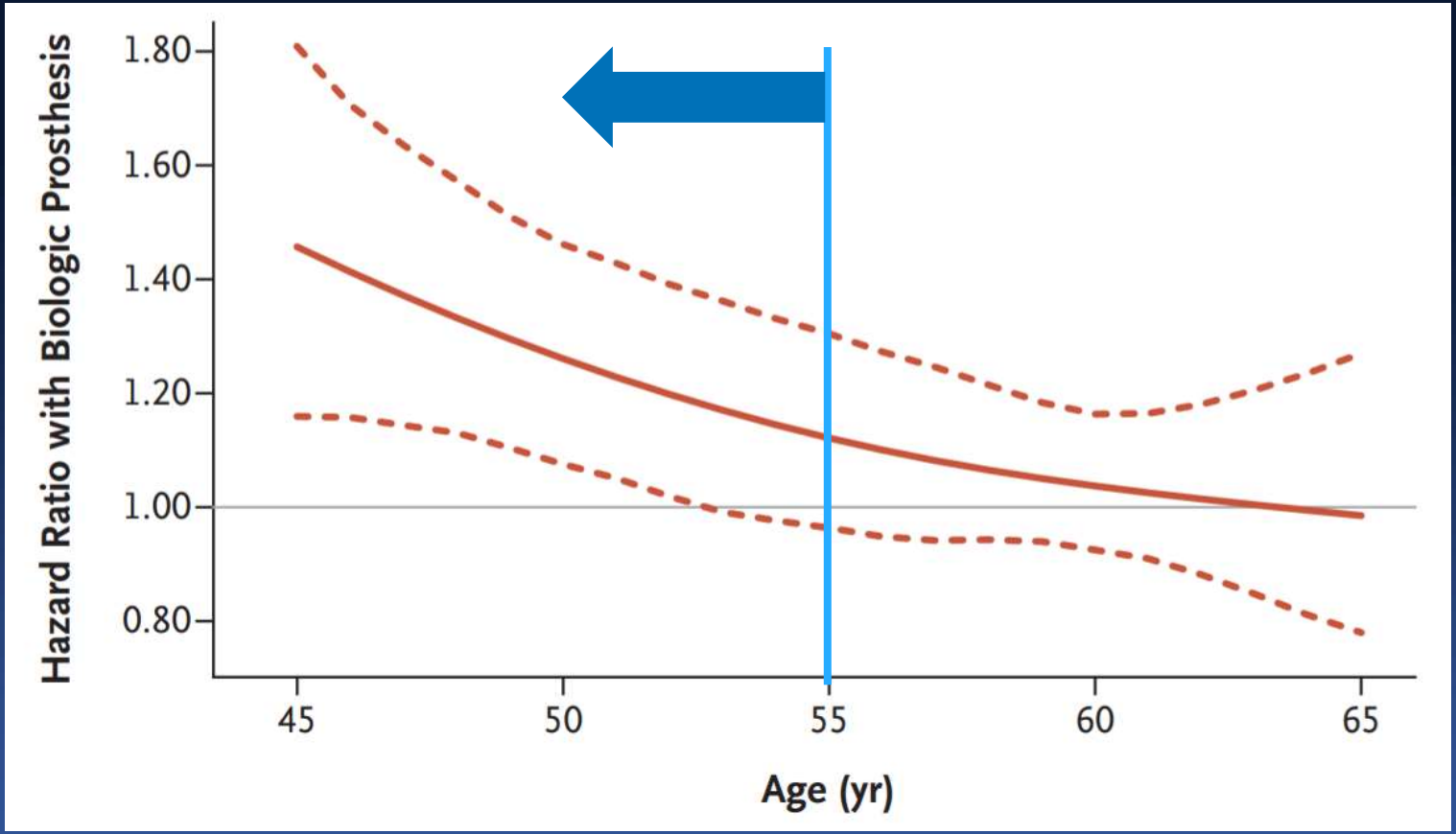
Medical experts predicted he would require reoperation in the following 3-8 years as his valve would progressively degrade.

Young Patients With Low Risk Surgical Valve Recommendation



California Registry

Age-Dependent Hazard of Death with a Biologic Prosthesis compared to Mechanical Prosthesis



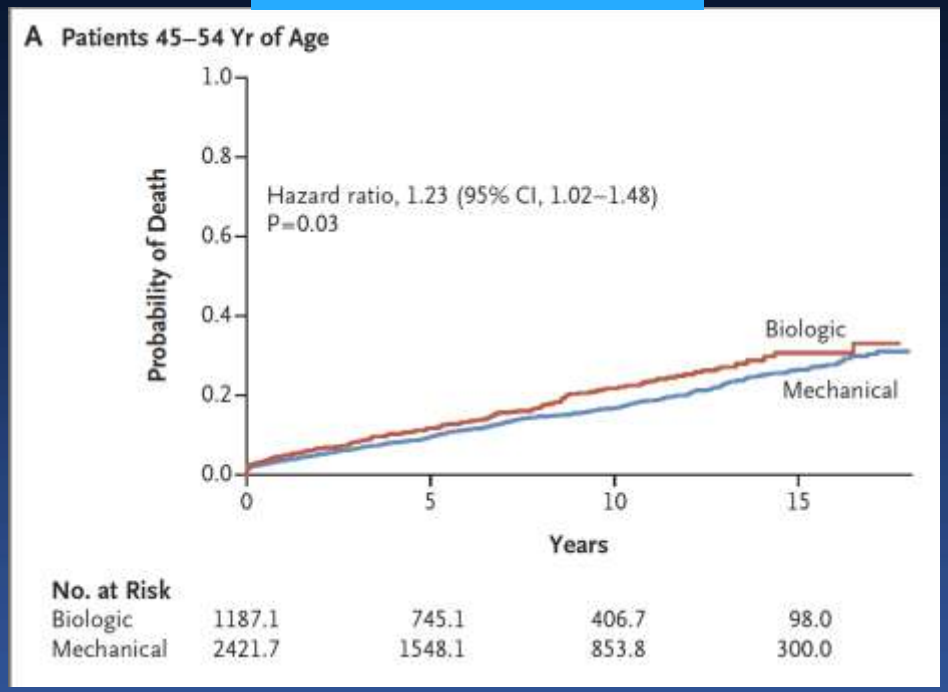
Mechanical Valve Better Survival < 55 YO in AV

N Engl J Med 2017;377:1847-57

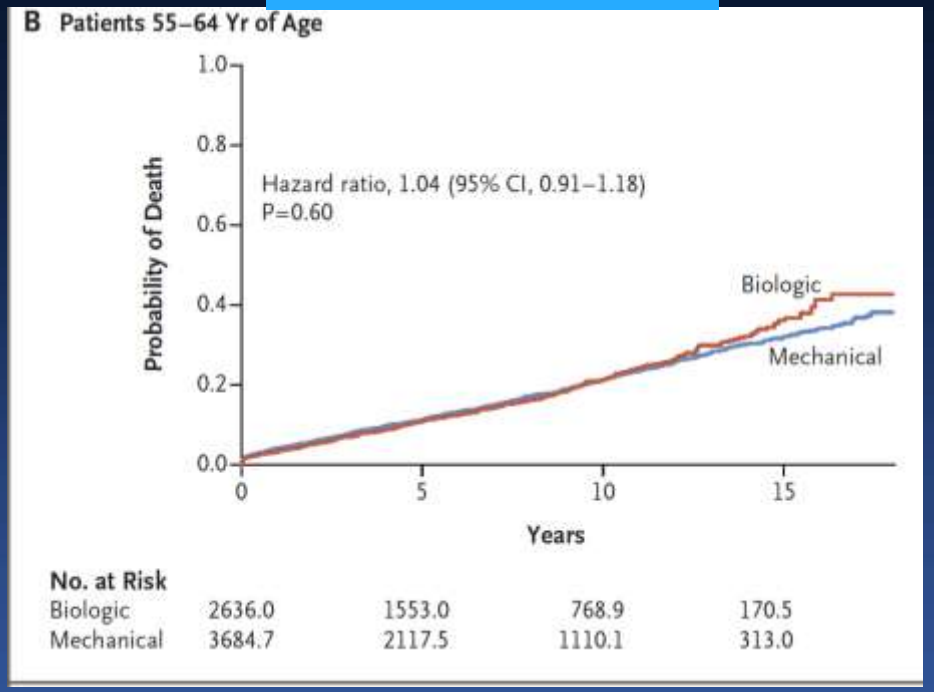
California Registry

Mechanical Valve Better Survival < 55 YO in Aortic Valve

<55 YO



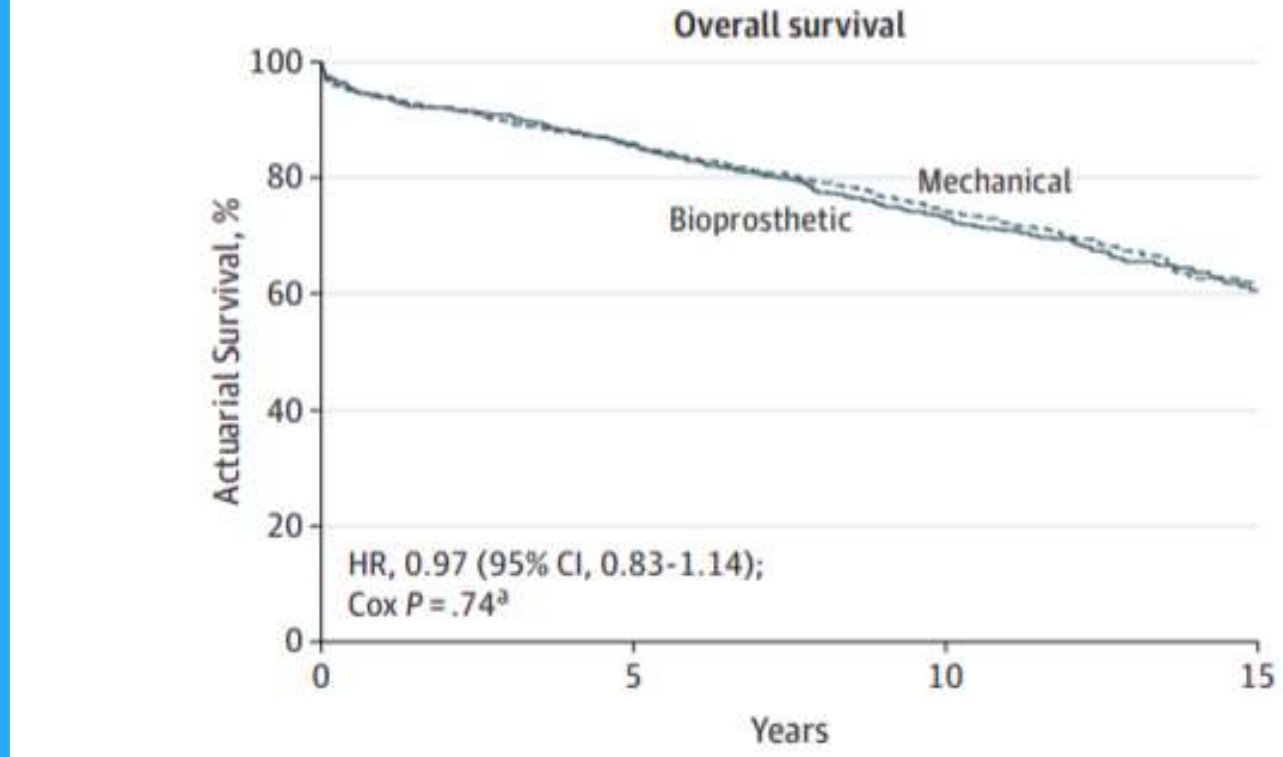
>55 YO



N Engl J Med 2017;377:1847-57

50-69 Years Old

US: New York State Registry



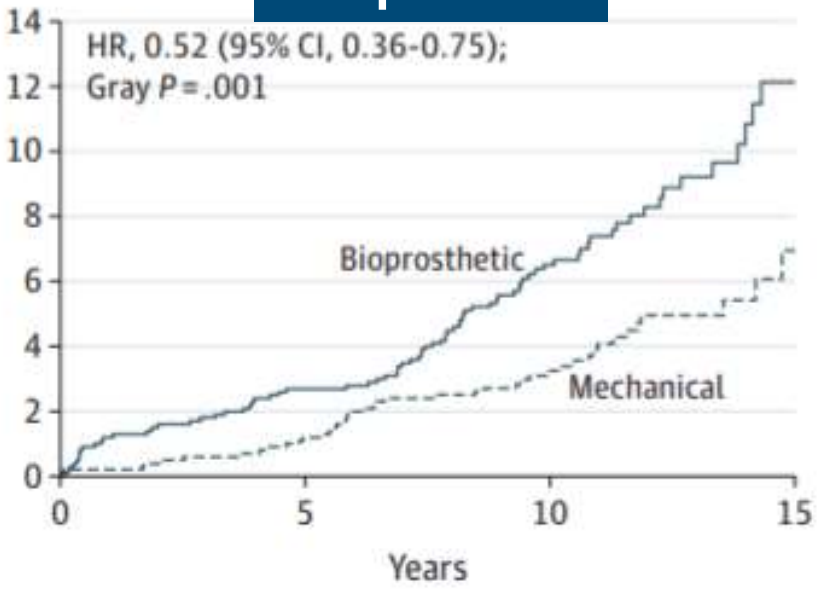
JAMA. 2014;312(13):1323-1329.

50-69 Years Old

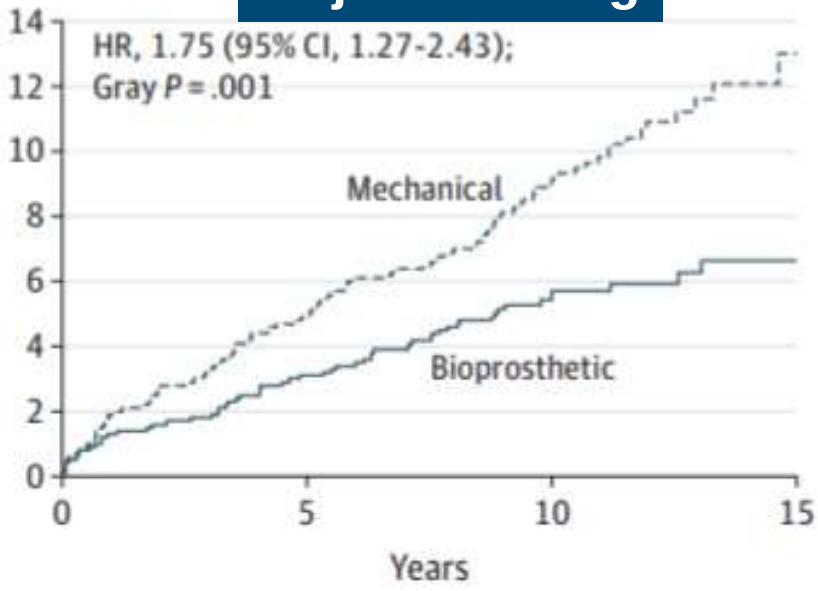
New York State Registry

Trade-Off

Reoperation ⟷ **Major Bleeding**



1001	845	456	37
1001	847	487	49

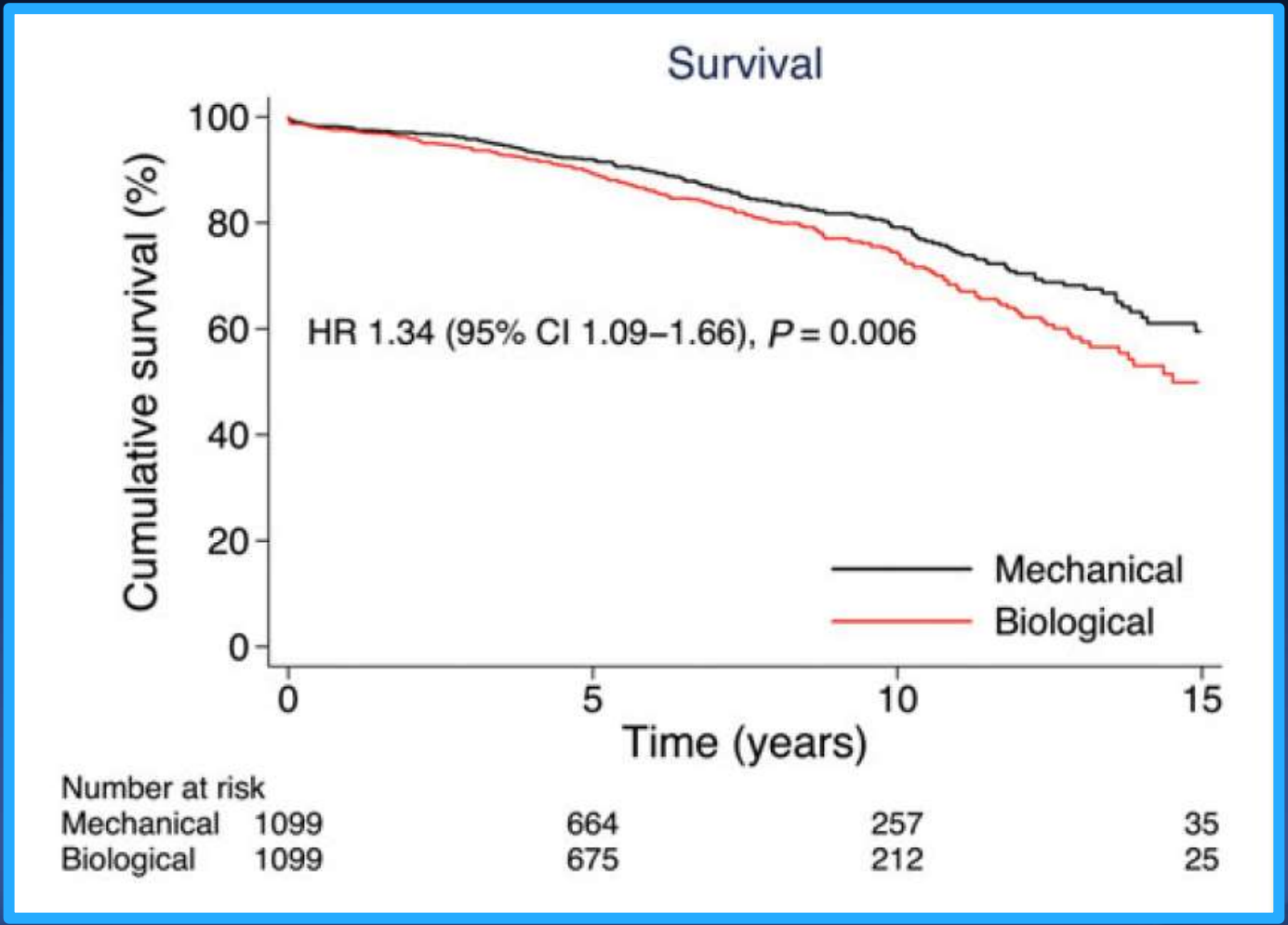


1001	838	463	39
1001	819	468	46

JAMA. 2014;312(13):1323-1329.

50-69 Years Old

Sweden Registry – Conflicting Data



European Heart Journal (2016) 37, 2658–2667

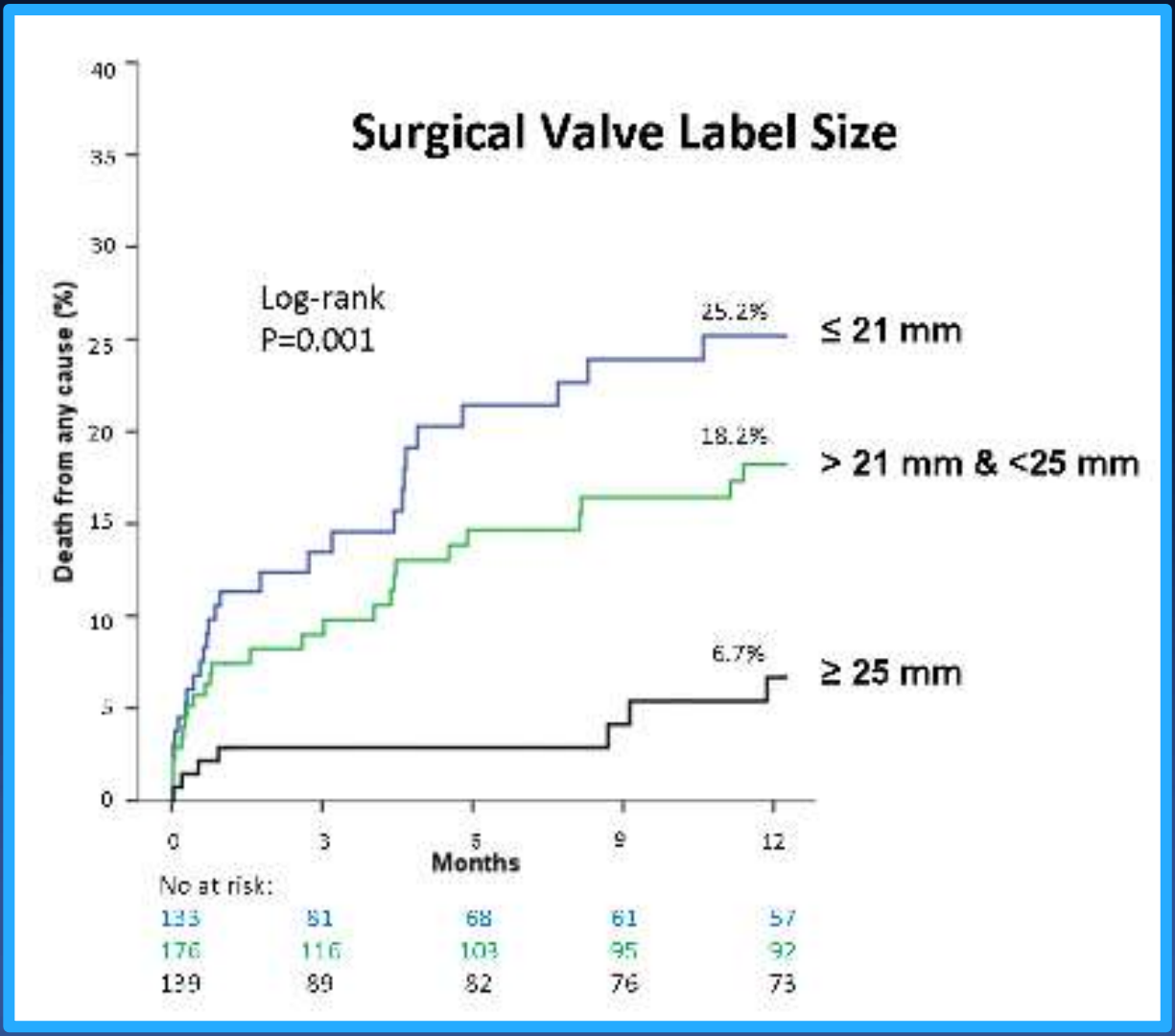
Why We Should Be More Careful for Younger Age Beyond Valve Degeneration itself?

Valve-in-Valve is Not Risk-Free

Complications	Valve-in-Valve		Conventional TAVR
Elevated post-procedural gradients *SAPIEN*	+++	>	+
Coronary obstruction	+++	>	+
Malpositioning	++	>	+
Vascular complications	++		++
Permanent pacemaker	+	<	++
Paravalvular leak	–		++
Annulus rupture	–		+

Jean-Michel Paradis et al. J Am Coll Cardiol 2015;66:2019–37

Mortality After Aortic ViV

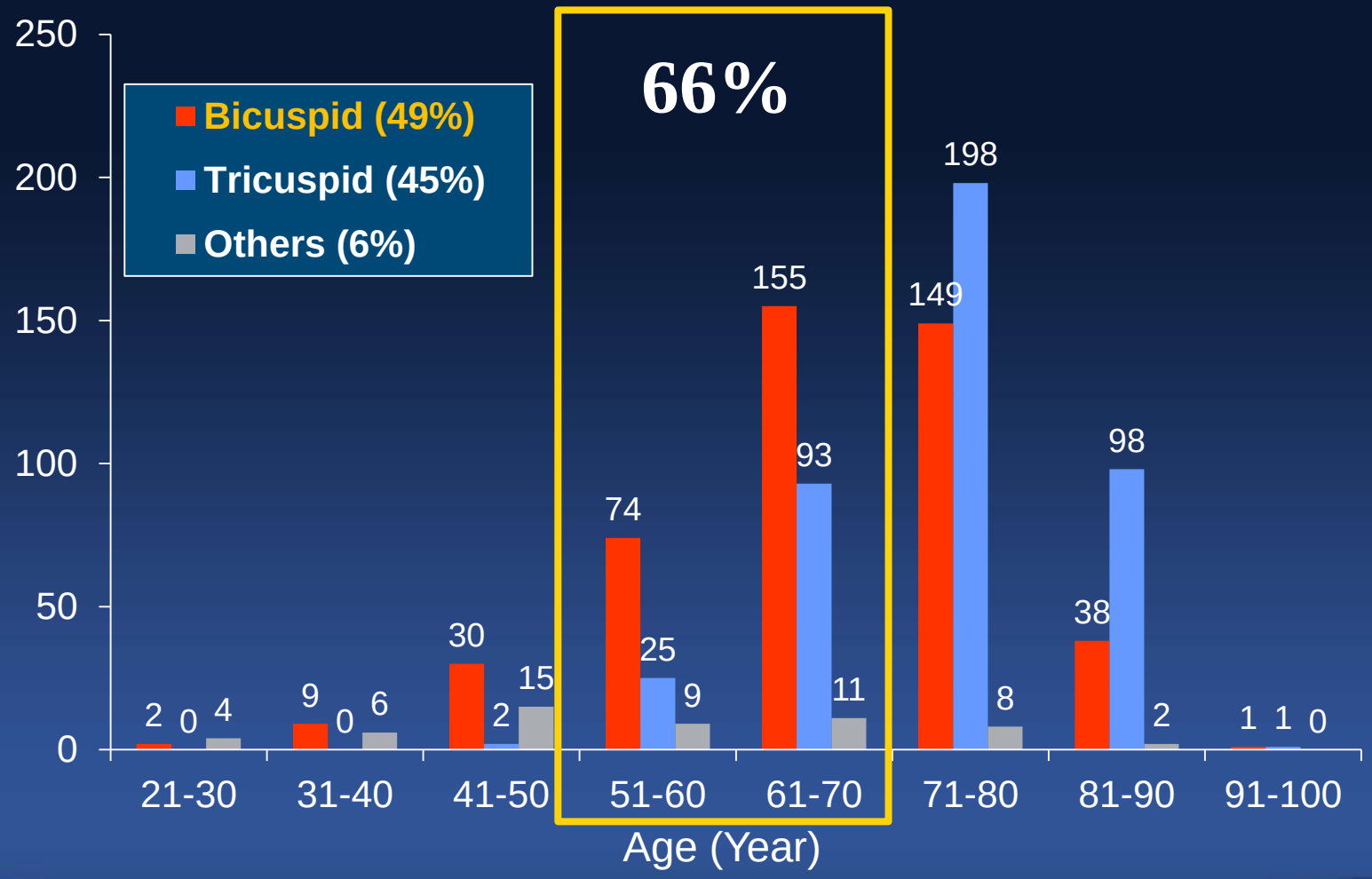


Dvir D et al. JAMA. 2014;312(2):162-170.

Bicuspid
In Younger Age

Incidence of Bicuspid AV in isolated AVR

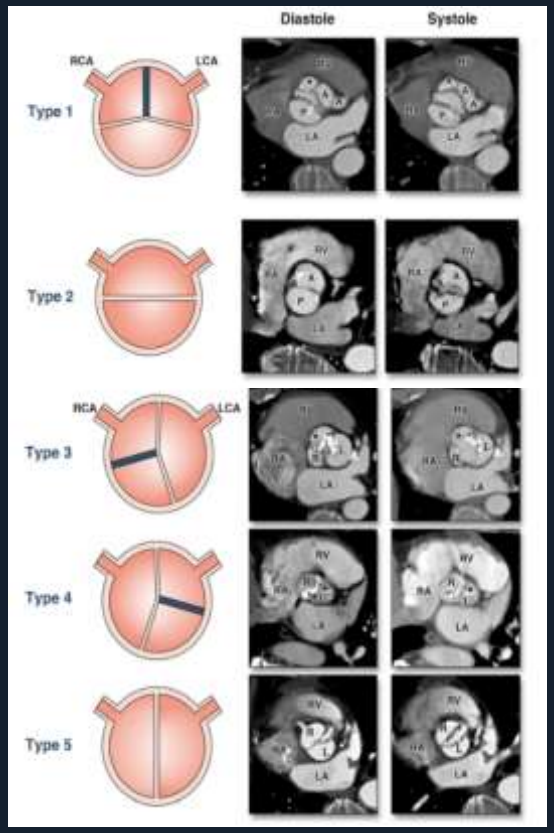
584 men and 348 women from USA (Baylor University)



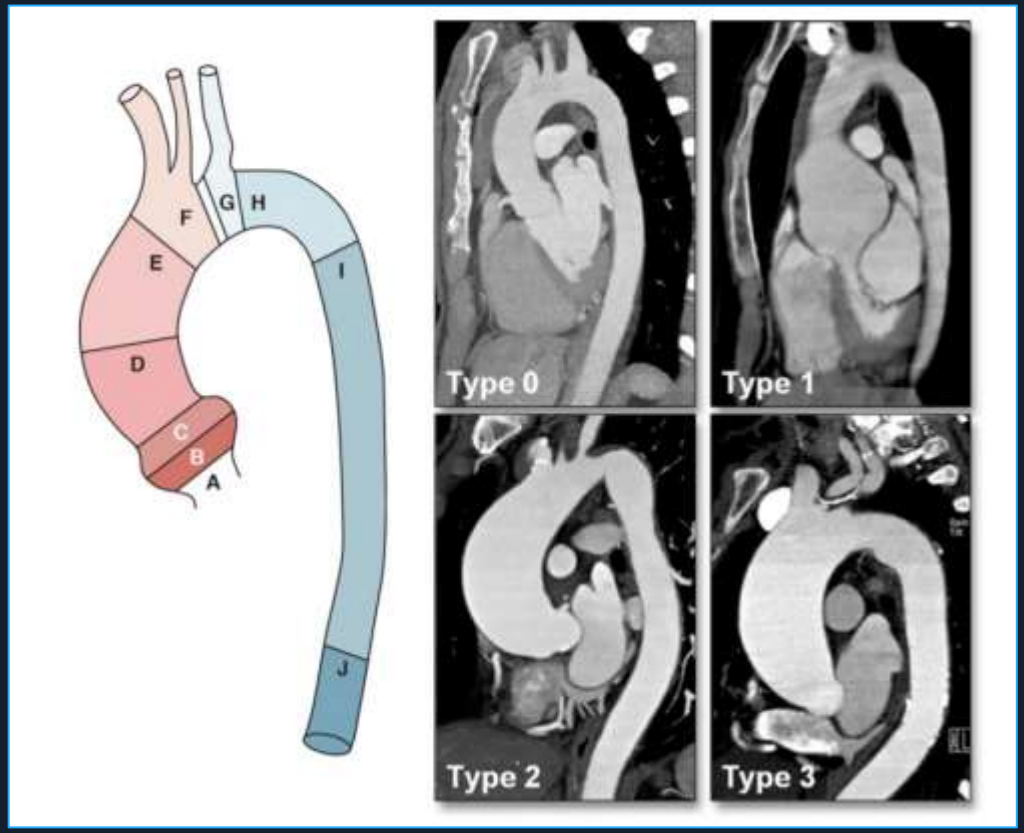
William Roberts, Circulation 2005;111:920-925

Spectrum of BAV Disease

Aortic Valve Morphology



Combined Aortopathy



TAVR for Bicuspid AV is Not Risk-Free

Anatomical Concern

- Annular eccentricity
- Asymmetrical heavy valve calcification
- Unequally-sized leaflets
- Calcified raphe
- Concomitant aortopathy
- Lack of Standardized Annulus Measurement

Procedural Concern

- Elliptical deployment
- Impaired Bioprosthesis Durability
- Residual Aortic Regurgitation
- Annulus Rupture
- Coronary Obstruction
- Aortic Complication

Zhao ZG et al. Nat. Rev. Cardiol 2015;12:123-128

CardioVascular Research Foundation
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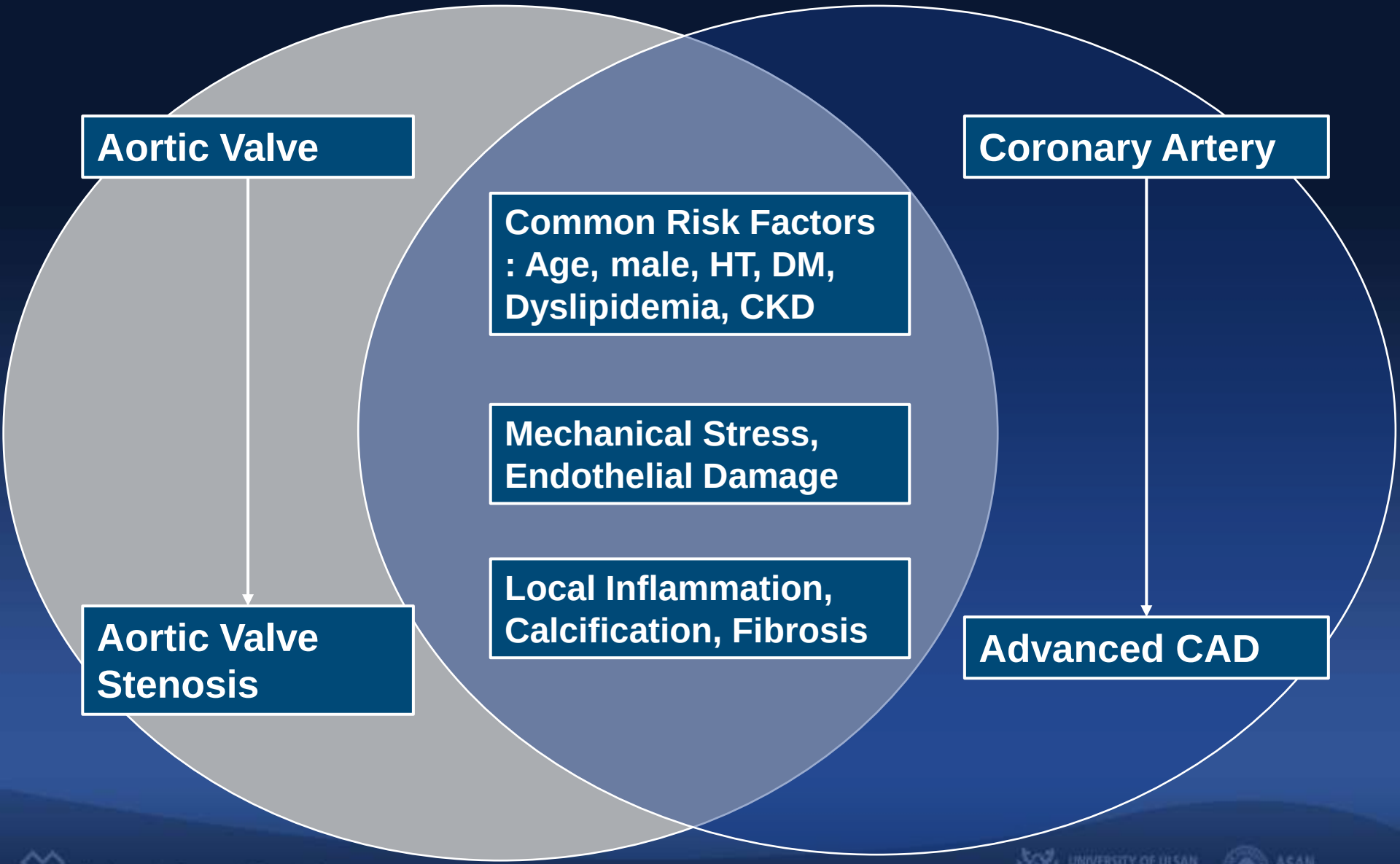
ASAN Medical Center

Post TAVR PCI Chance In Younger Age

Common Pathophysiology



Milin AC et al, J Am Heart Assoc. 2014 Sep;5:e001111

Post TAVR PCI

	Kerckhoff-Klinik	Segeberg Registry	UK Registry	TAVR-LM Registry
Incidence	35 / 1,000 (**3.5%**)	17 / 296 (**5.7%**)	18 / 2,588 (**0.7%**)	9 / 6,405 (**0.1%**)
ACS Indication	11.4%	37.5%	65%	78%
Time to PCI	233 ± 158 days	17.7 months (range: 1-72)	136 days (range: 1-1092)	368 days (IQR: 204-534)
Type of TAV Implanted			Not Reported	
CoreValve	29%	100%		44%
SAPIEN XT	54%			55%
JenaValve	3%			
Symetis	11%			
Portico	3%			
Procedural Success	***74%***	***95.8%***	Not Reported	100%

[1]Blumenstein, et al., *Clin Res Cardiol* 2015; 104:632-39; [2]Allali, et al., *Cardiovasc Revasc Med* 2016; epub ahead of print; [3]Snow, et al., *Int J Cardiol* 2015; 199:253-60; [4]Chakravarty, et al., *J Am Coll Cardiol* 2016; 67:951-60

Cardiovascular Research Foundation
University of Ulsan College Medicine
Asan Medical Center

Valve Thrombosis In Younger Age

TAVR ~13% SAVR ~5%

Valve Thrombosis and Stroke

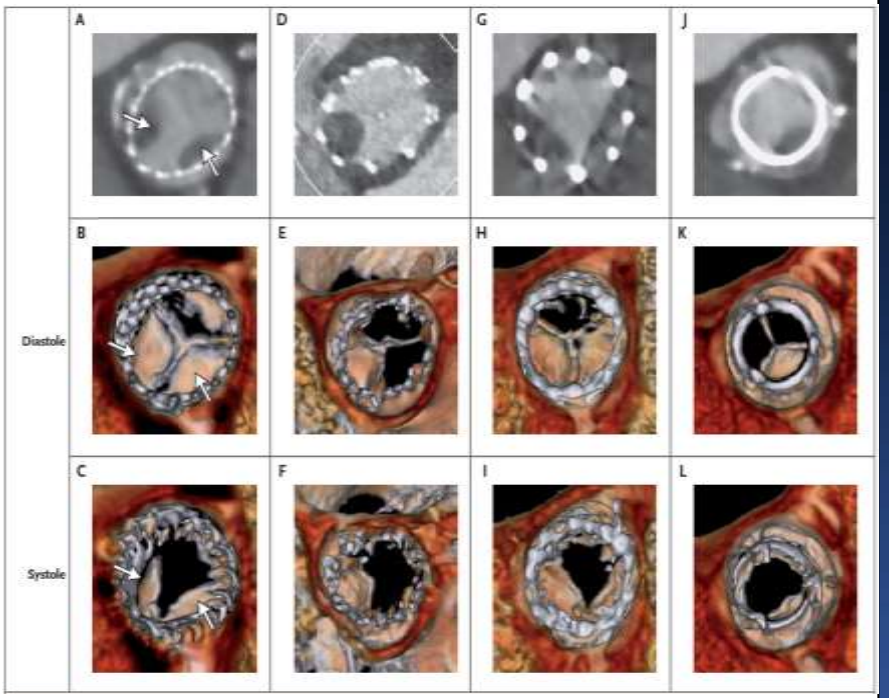
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

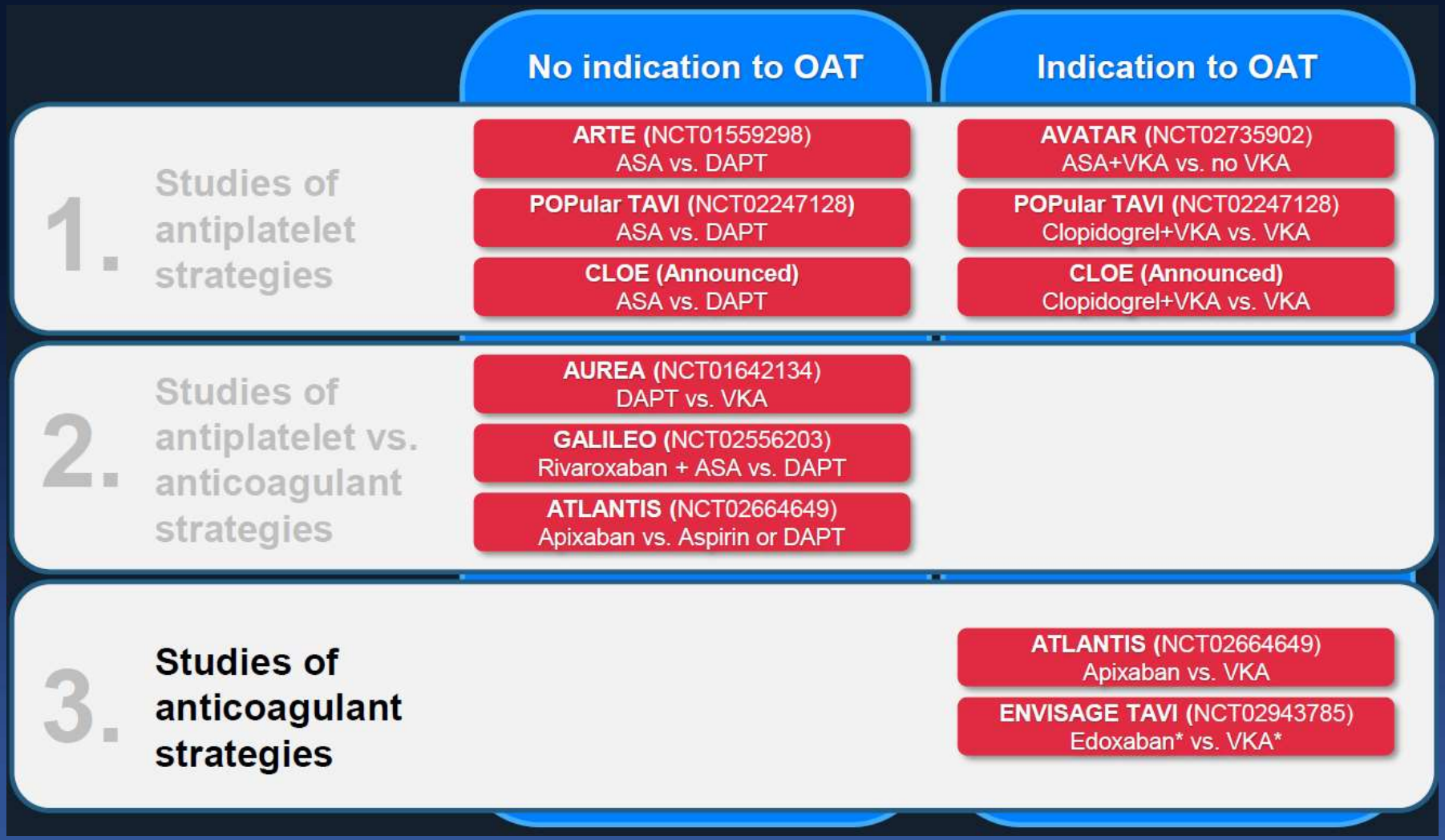
Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

R.R. Makkar, G. Fontana, H. Jilaihawi, T. Chakravarty, K.F. Kofoed, O. De Backer, F.M. Asch, C.E. Ruiz, N.T. Olsen, A. Trento, J. Friedman, D. Berman, W. Cheng, M. Kashif, V. Jelnin, C.A. Kliger, H. Guo, A.D. Pichard, N.J. Weissman, S. Kapadia, E. Manasse, D.L. Bhatt, M.B. Leon, and L. Søndergaard

ABSTRACT



Warfarinization

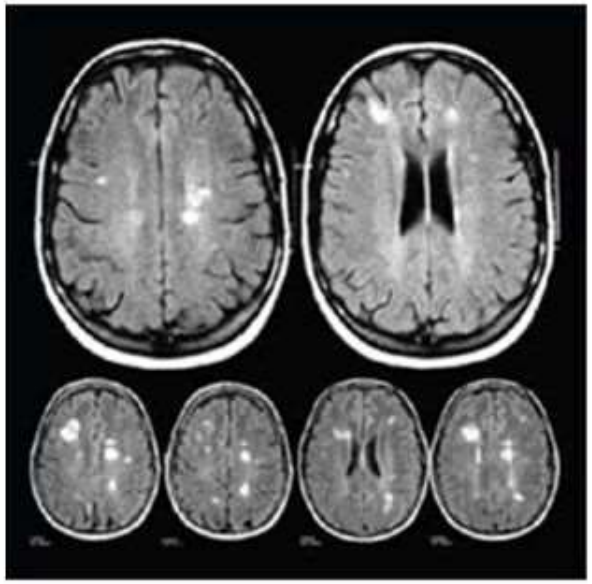


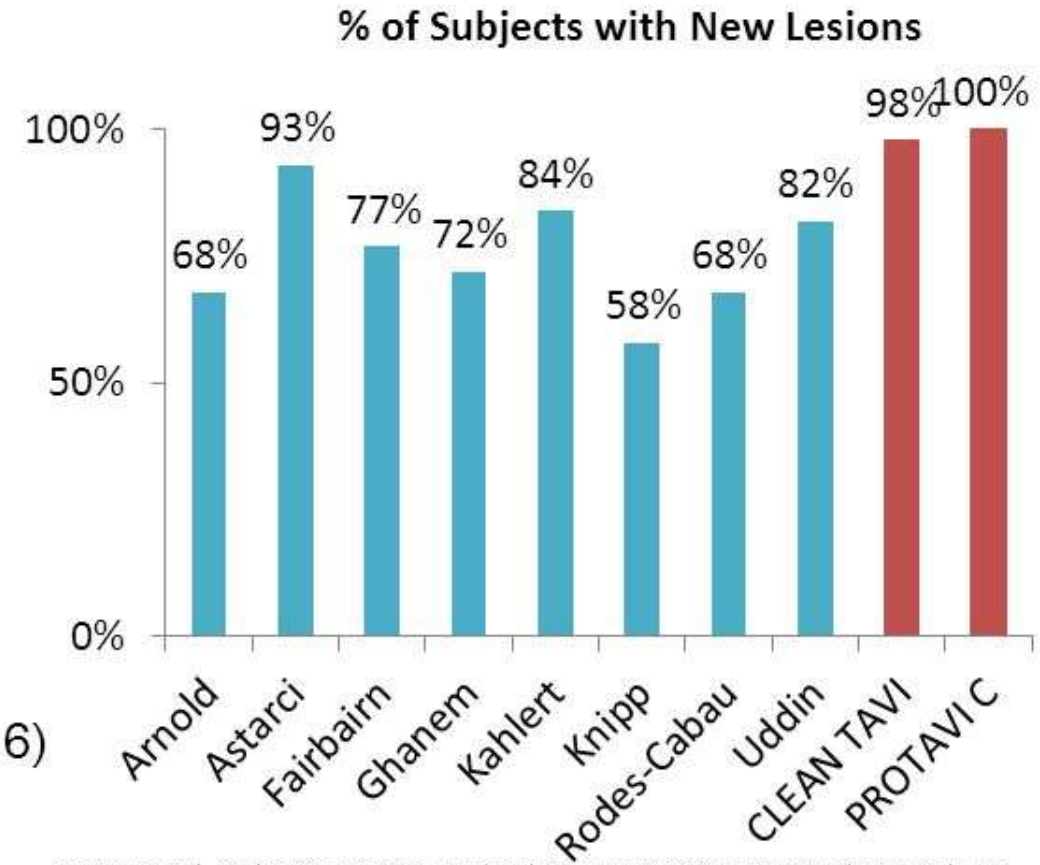
Capodanno, et al., presented at London Valves 2017

Silent Stroke
In Younger Age

Stroke Will Be a Major Concern in *Young* Patients

Silent Embolic Events on DW-MRI after TAVR

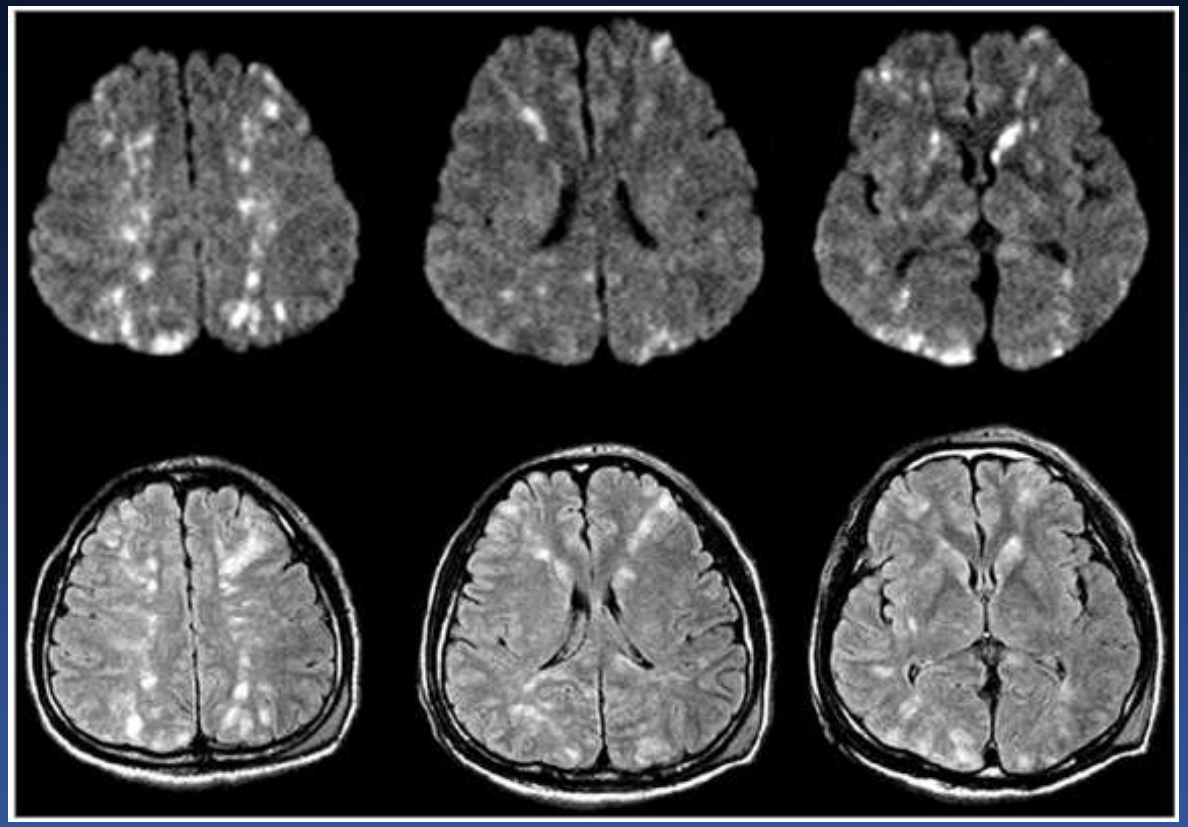


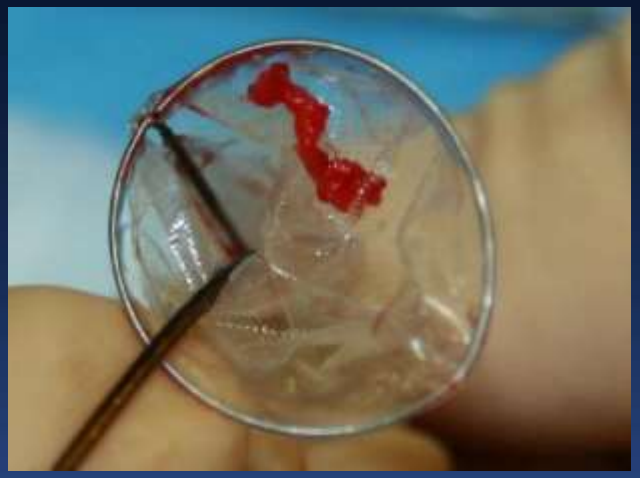


- Affect 58-100% of patients
- Multiple infarcts (≤36, $\bar{x}$ = 4.6)
- Associated with:
  - Neurocognitive decline
  - >2 fold risk of dementia
  - **>3 fold risk of stroke**

Restrepo et al. *Stroke* 2002;33:2909, Lund et al. *Eur Heart J.* 2005;26:1269, Schwarz et al. *Am Heart J* 2011;162:756, Knipp et al. *Ann Thorac Surg* 2008;85:872, Vermeer et al. *NEJM* 2003; 348:1215, Vermeer et al. *Stroke* 2003; 34:1126, Arnold et al. *JACC Cardiovasc Interv.* 2010;3:1126, Astarci et al. *J Heart Valve Dis.* 2013;22:79, Fairbairn et al. *Heart* 2012;98:18, Ghanem et al. *EuroIntervention.* 2013;8:1296, Kahlert et al. *Circ.* 2010;121:870, Knipp et al. *Interact Cardiovasc Thorac Surg.* 2013;16:116, Linke et al. TCT 2014, Rodes-Cabau et al. *JACC Cardiovasc Interv.* 2014;7:1146

Stroke Will Be a Major Concern in *Young* Patients



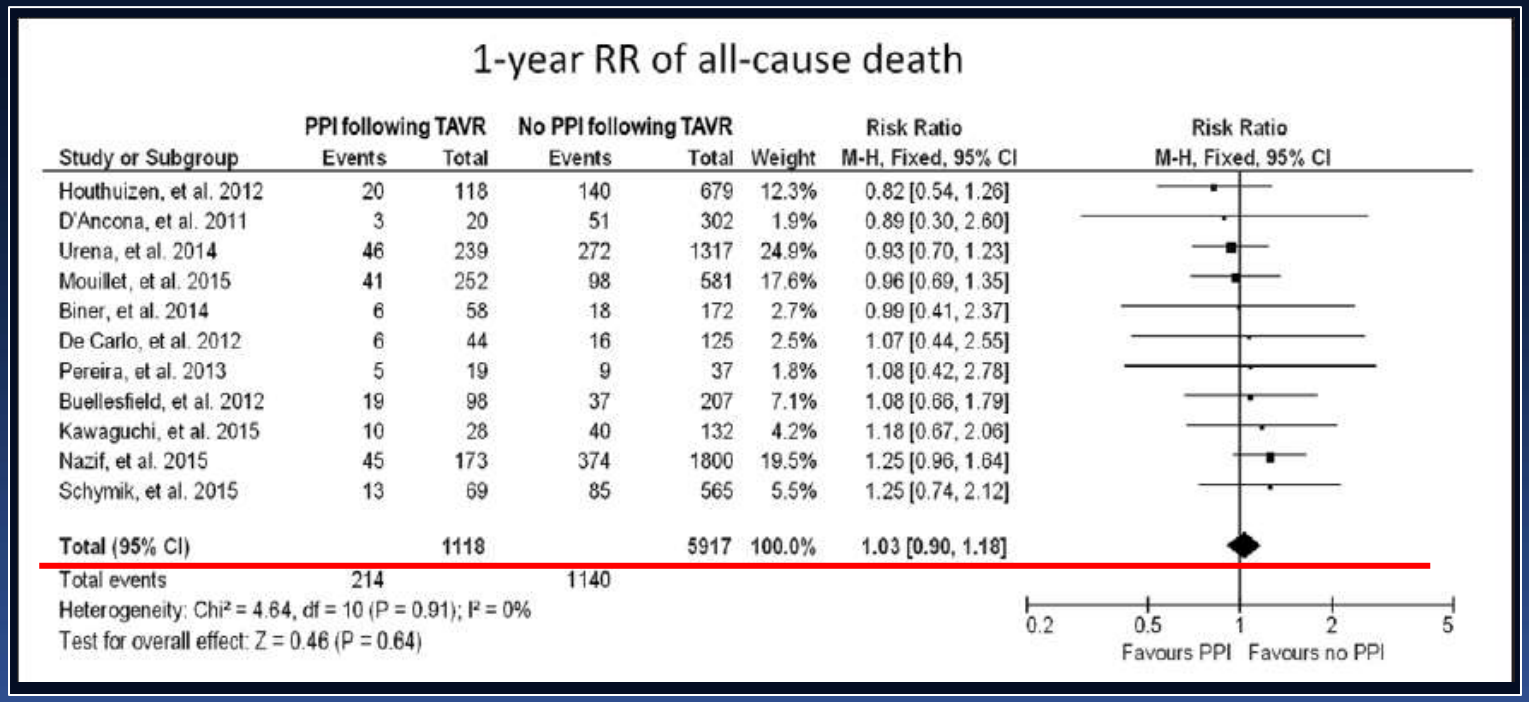


Captured by embolic protection devices in 80-85% TAVI patients

Permanent Pacemaker In Younger Age

Clinical Impact of PPM after TAVR

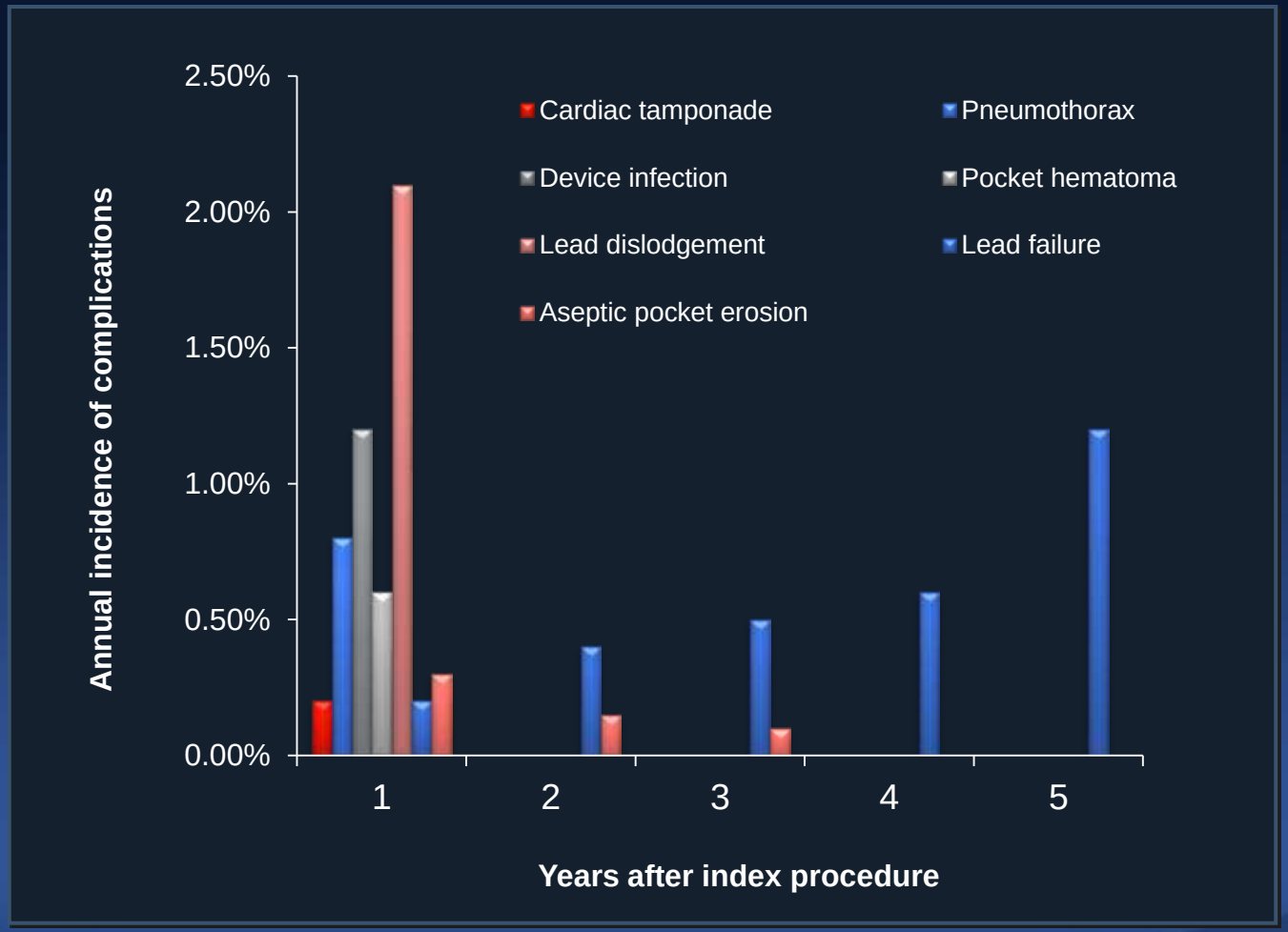
No Impact of Mortality



Rigueiro, A, et al. Circ Cardiovas Interv 2016;9:e003635

Clinical Impact of PPM after TAVR

Small But Significant Complications



Palmisano P, et al., Europace. 2013 Apr;15(4):531-40.

TAVR in Low-Risk, Younger Age

30 Year Life Expectancy and Long Journey for TAVR Valve

Procedural and Residual Risk in Young Patients

- Reintervention: ~ 20% at 15-20 years
- High Incidence of Bicuspid AS: 60%
- Risk of PCI after TAVR: feasible but not 100% success
- Risk of valve thrombosis and Stroke:
  Undetermined anticoagulation strategy
- Pacemaker implantation risk: : ~ 10-15%
- Long term effect of >mild PVL

Summary – TAVR in Low Risk How Much Younger?

- On the basis of chain of RCTs, TAVR become the standard procedure in low-risk patients with severe AS.

- Heat-team should be the mandatory decision-maker.
  - Age >75: Consider TAVR as the default treatment.
  - Age 70-75: Consider TAVR first if patient want less invasive procedure.
  - Age 65-70: balanced think in the heart-team and patient's want.
  - Age <65: still SAVR before long-term (>10 years) patency of TAVR is guaranteed.