

Is TAVI ready for prime time in:

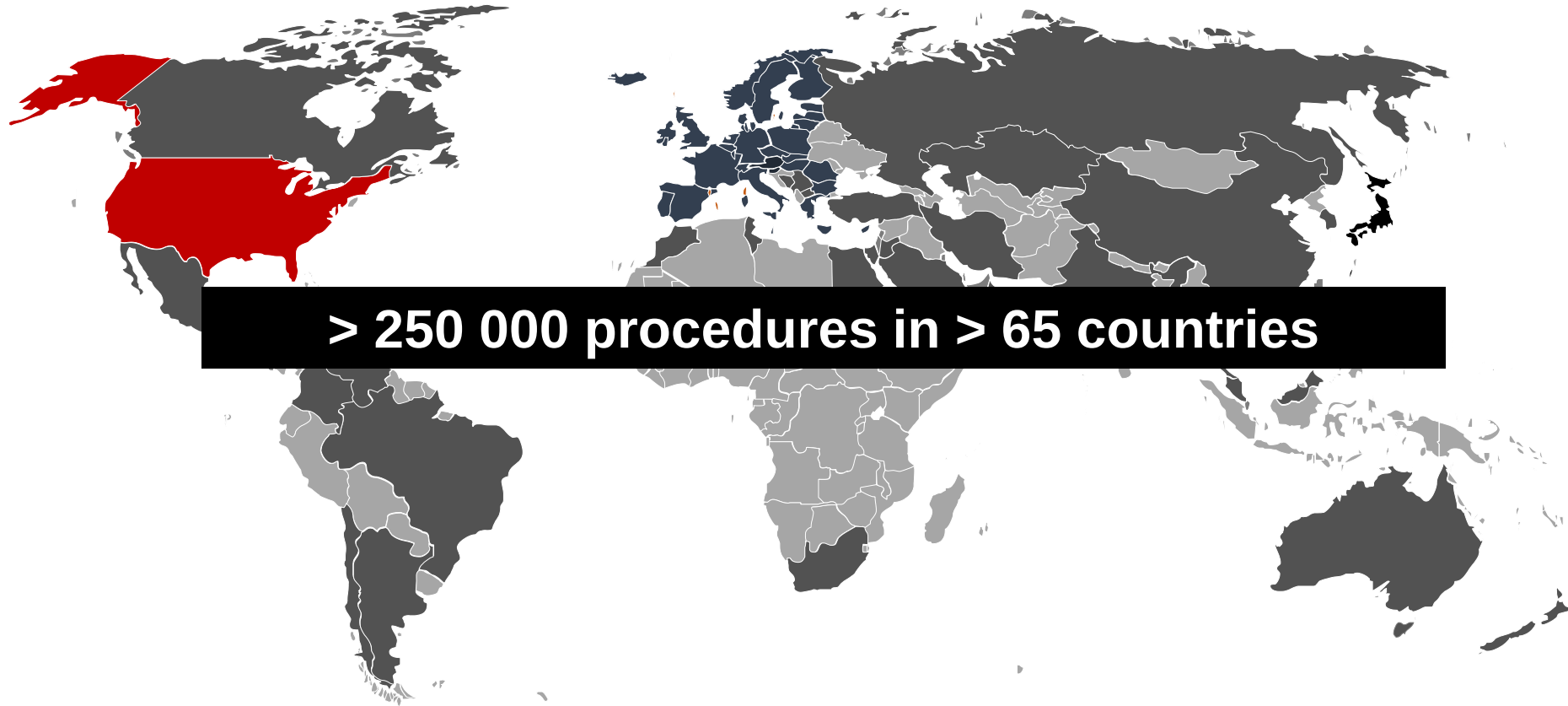
- Intermediate risk patients?**
- Low risk patients?**

Didier TCHETCHE, MD.
Clinique PASTEUR, Toulouse, France,

Conflicts of interest:

- Consultant for Edwards LifeSciences
- Consultant for Medtronic
- Consultant for Boston Scientific

TAVI procedures worldwide



What do we know about

TAVI in intermediate-risk patients

?

Key Message

We are already treating intermediate risk patients

2014 ACC/AHA guidelines

	Low Risk (Must Meet ALL Criteria in this column)	Intermediate Risk (Any 1 criterion in this column)	High Risk (Any 1 criterion in this column)	Prohibitive Risk (Any 1 criterion in this column)
STS PROM*	<4% AND	4% to 8% OR	>8% OR	Predicted risk with surgery of death or major morbidity (all- cause) >50% at 1 y OR
Frailty†	None AND	1 Index (mild) OR	≥ 2 Indices (moderate to severe) OR	
Major organ system compromise not to be improved postoperatively	None AND	1 Organ system OR	No more than 2 organ systems OR	≥ 3 Organ systems OR
Procedure- specific impediment	None	Possible procedure- specific impediment	Possible procedure- specific impediment	Severe procedure- specific impediment

How frequent is a lower risk profile?

	TAVR Group (N = 394)	Surgical Group (N = 401)
Age — yr	83.2±7.1	83.5±6.3
Female sex — no. (%)	183 (46.4)	189 (47.1)
NYHA class — no. (%)		
Class II	56 (14.2)	53 (13.2)
Class III	258 (65.5)	277 (69.1)
Class IV	80 (20.3)	71 (17.7)
STS PROM estimate†		
Mean estimate — %	7.3±3.0	7.5±3.2
<4% — no. (%)	33 (8.4)	42 (10.5)
4–10% — no. (%)	308 (78.2)	288 (71.8)
>10% — no. (%)	53 (13.5)	71 (17.7)
Logistic EuroSCORE — %‡	17.6±13.0	18.4±12.8

Adams et al. NEJM 2014

Intermediate-risk patients are already referred to TAVI



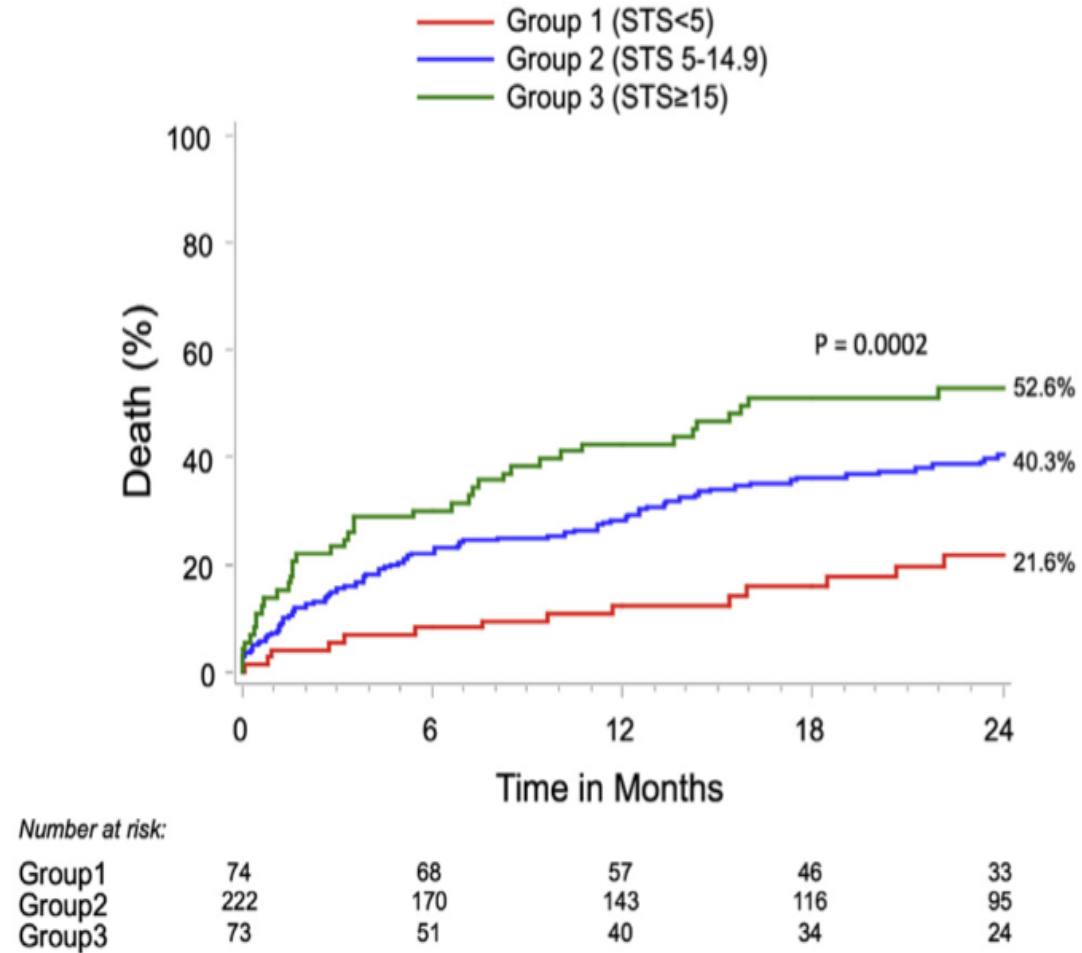
Discussion

The prospective PRAGMATIC AS survey represents a snapshot of contemporary management of patients with degenerative AS in selected countries in Europe and highlights the following. 1) Risk estimation was primarily based on Heart Team decision. 2) Overall, nearly half of the patients were considered at low operative risk (these patients were predominantly sent for SAVR), a quarter of patients were at intermediate risk (two thirds of these underwent TAVI), and almost all patients at high risk were sent for TAVI. 3) Overall, 30-day all-cause mortality was low, being highest for patients at higher operative risk, and neurological events were rare. 4) TAVI was associated with more permanent pacemaker implantations and shorter hospital stay compared to SAVR.

Key Message

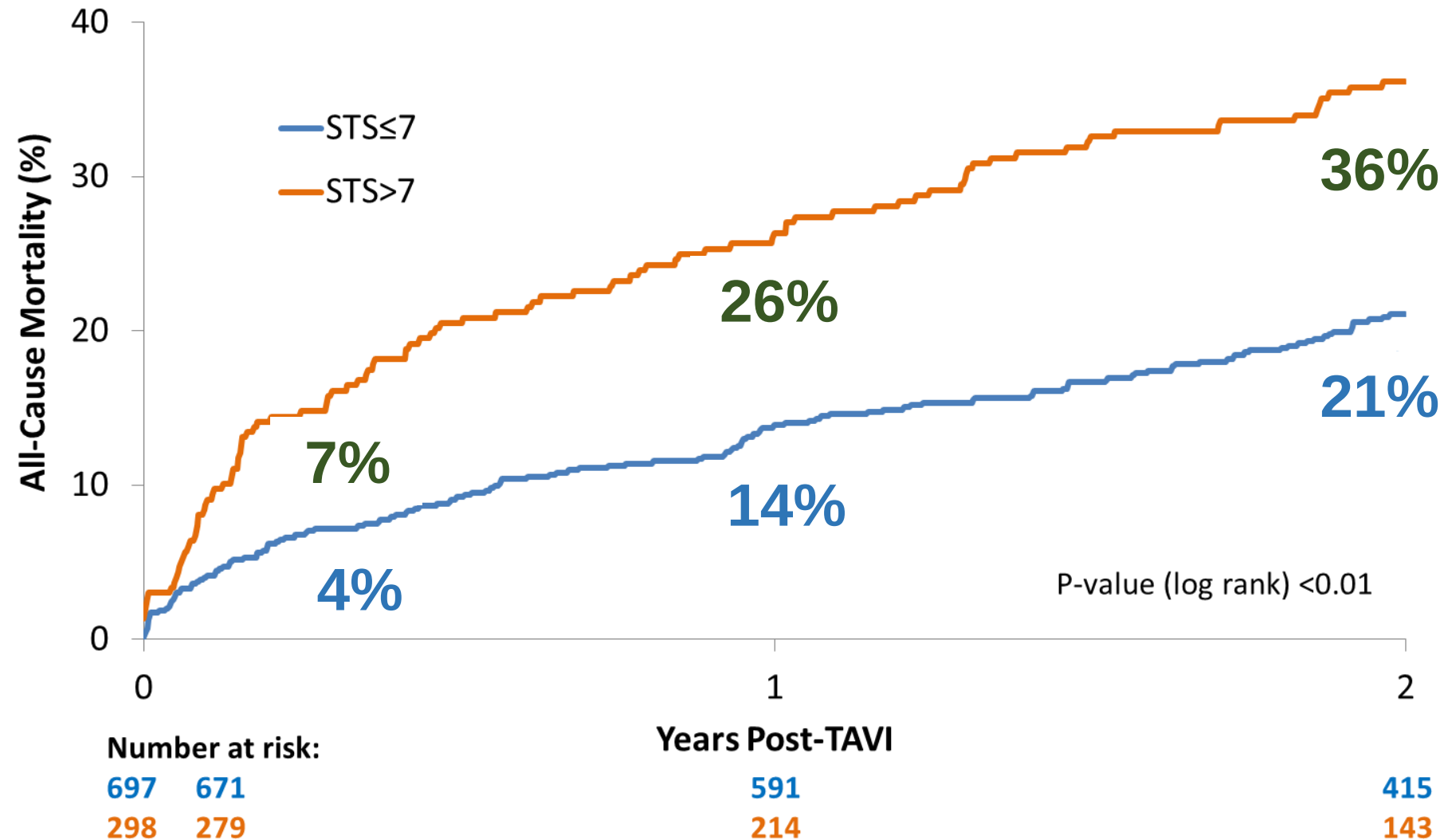
Intermediate risk patients have a better outcome

PARTNER 1B



R. Makkar et al. JACC 2014;63:901-911

2-Year All-Cause Mortality CoreValve ADVANCE Registry



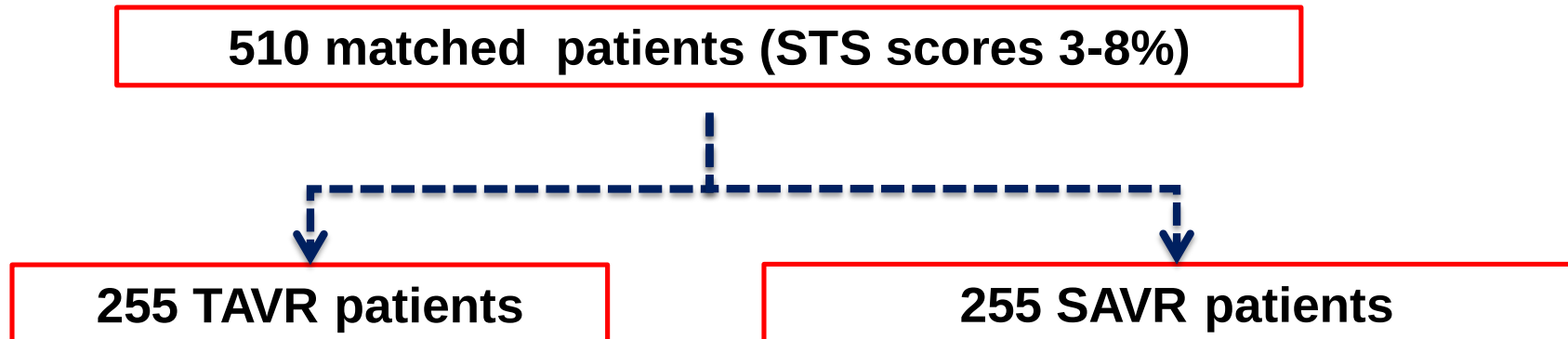
Key Message

TAVI is comparable to surgery in Intermediate risk patients

BERn-MUnich-rotterDAm

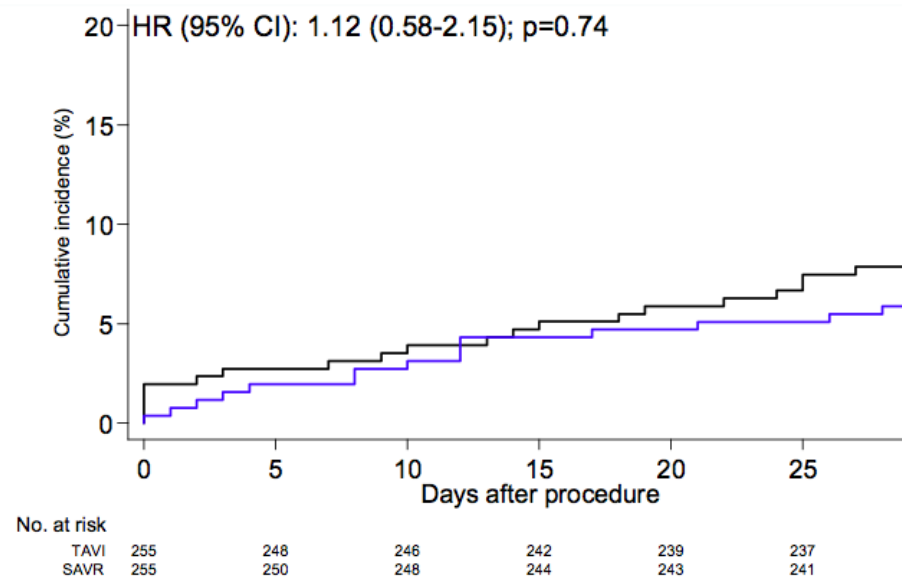
A 3-Center Comparison of 1-Year Mortality Outcomes Between Transcatheter Aortic Valve Implantation and Surgical Aortic Valve Replacement on the Basis of Propensity Score Matching Among Intermediate-Risk Surgical Patients

BERMUDA

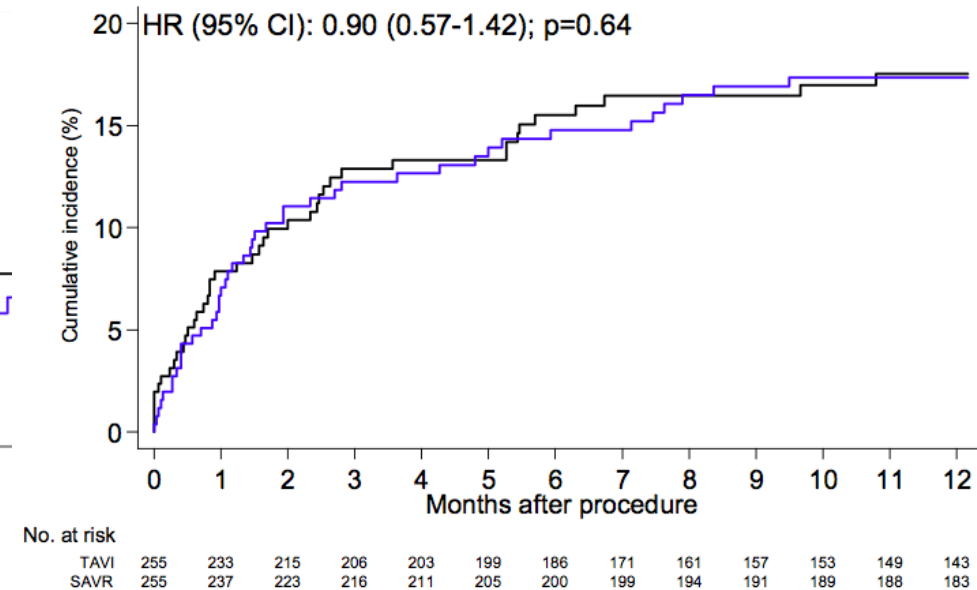


BERn-MUnich-rotterDAm

30-day All-cause mortality



1-year All-cause mortality



 TAVI
  SAVR

PARTNER II

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

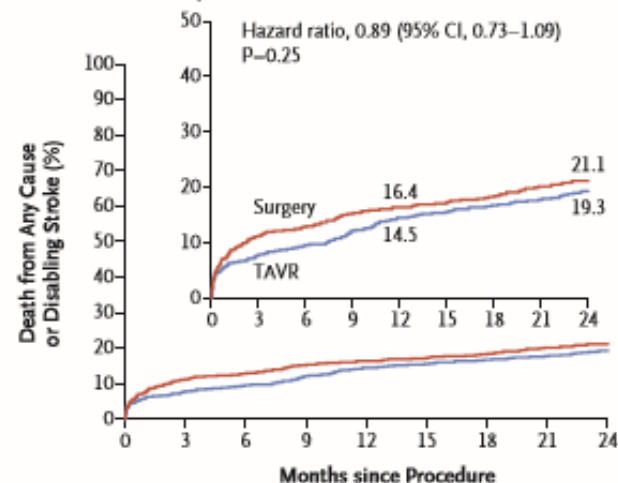
Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D.,

Table 1. Characteristics of the Patients at Baseline.*

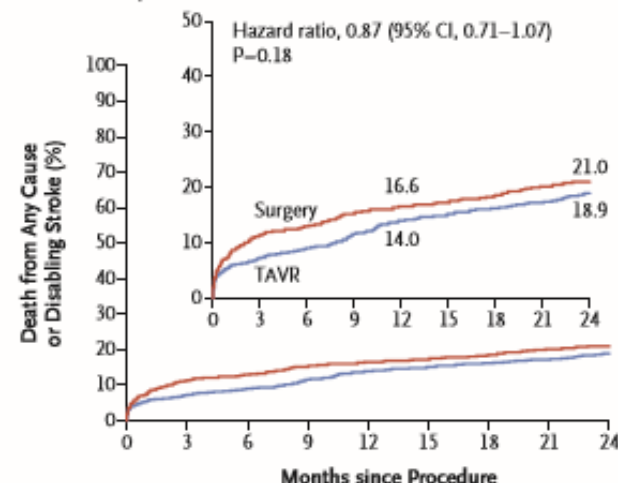
Characteristic	TAVR (N=1011)	Surgery (N=1021)
Age — yr	81.5±6.7	81.7±6.7
Male sex — no. (%)	548 (54.2)	560 (54.8)
Body-mass index†	28.6±6.2	28.3±6.2
STS risk score‡	5.8±2.1	5.8±1.9

A Intention-to-Treat Population



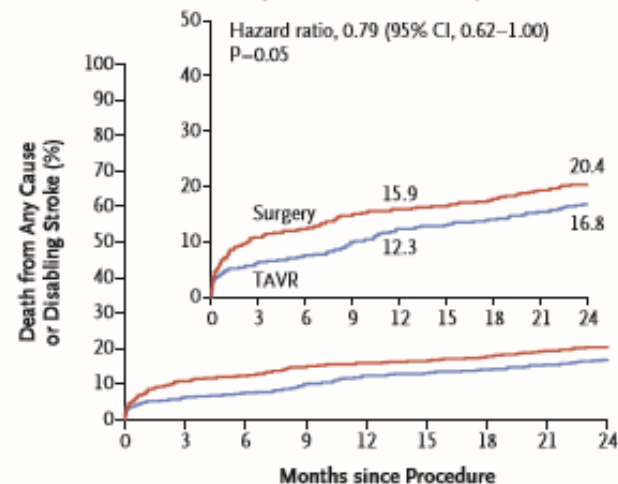
No. at Risk	1011	918	901	870	842	825	811	801	774
TAVR	1021	838	812	783	770	747	735	717	695

B As-Treated Population



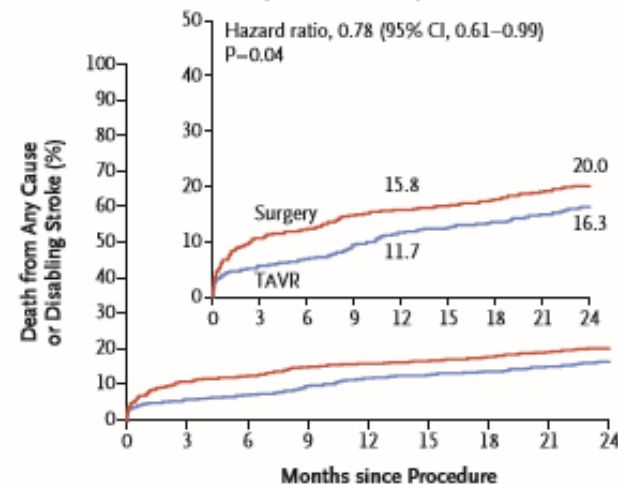
No. at Risk	994	917	900	870	842	825	811	801	774
TAVR	944	826	807	779	766	743	731	715	694

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



No. at Risk	775	718	709	685	663	652	644	634	612
TAVR	775	643	628	604	595	577	569	557	538

D Transfemoral-Access Cohort, As-Treated Analysis

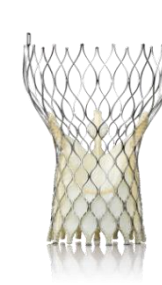


No. at Risk	762	717	708	685	663	652	644	634	612
TAVR	722	636	624	600	591	573	565	555	537

Key Message

TAVI seems promising in low risk patients

Low Risk



The NOTION trial was the first to randomize TAVI with CoreValve to SAVR in low and intermediate risk patients

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<http://dx.doi.org/10.1016/j.jacc.2015.03.014>

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis



1-Year Results From the All-Comers NOTION
Randomized Clinical Trial

Hans Gustav Hørsted Thyregod, MD,* Daniel Andreas Steinbrüchel, MD, DMSc,* Nikolaj Ihlemann, MD, PhD,†
Henrik Nissen, MD, PhD,‡ Bo Juel Kjeldsen, MD, PhD,§ Petur Petursson, MD,|| Yanping Chang, MS,¶
Olaf Walter Franzen, MD,† Thomas Engstrøm, MD, DMSc,† Peter Clemmensen, MD, DMSc,† Peter Bo Hansen, MD,#
Lars Willy Andersen, MD, DMSc,# Peter Skov Olsen, MD, DMSc,* Lars Søndergaard, MD, DMSc†

The NOTION Trial

Randomized Low-Risk Patients



Main inclusion criteria

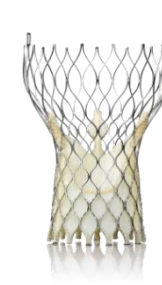
- Severe AS
- Age ≥ 70 years
- Life expectancy ≥ 1 year
- Suitable for TAVR & SAVR

Main exclusion criteria

- Severe CAD
- Severe other valve disease
- Prior heart surgery
- Need for acute treatment
- Recent stroke or MI
- Severe lung disease
- Severe renal failure

The NOTION Trial

Randomized Low-Risk Patients

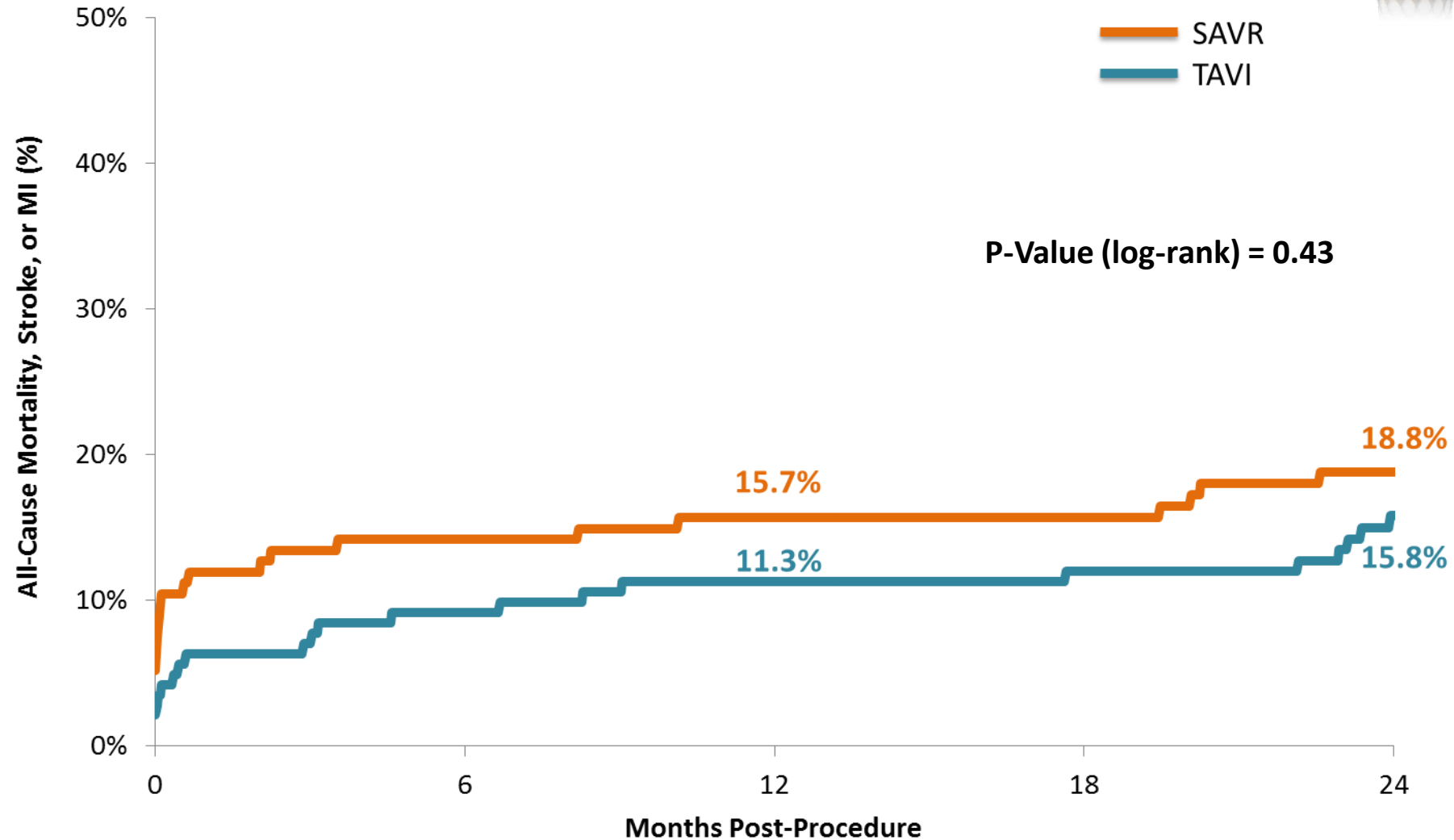


NOTION Trial | Select Baseline Characteristics

Characteristic, % or mean $\pm$ SD	TAVI n=145	SAVR n=135	p-value
Age (yrs)	79.2 $\pm$ 4.9	79.0 $\pm$ 4.7	0.71
Male	53.8	52.6	0.84
STS Score	2.9 $\pm$ 1.6	3.1 $\pm$ 1.7	0.30
STS Score < 4%	83.4	80.0	0.46
NYHA class III or IV	48.6	45.5	0.61

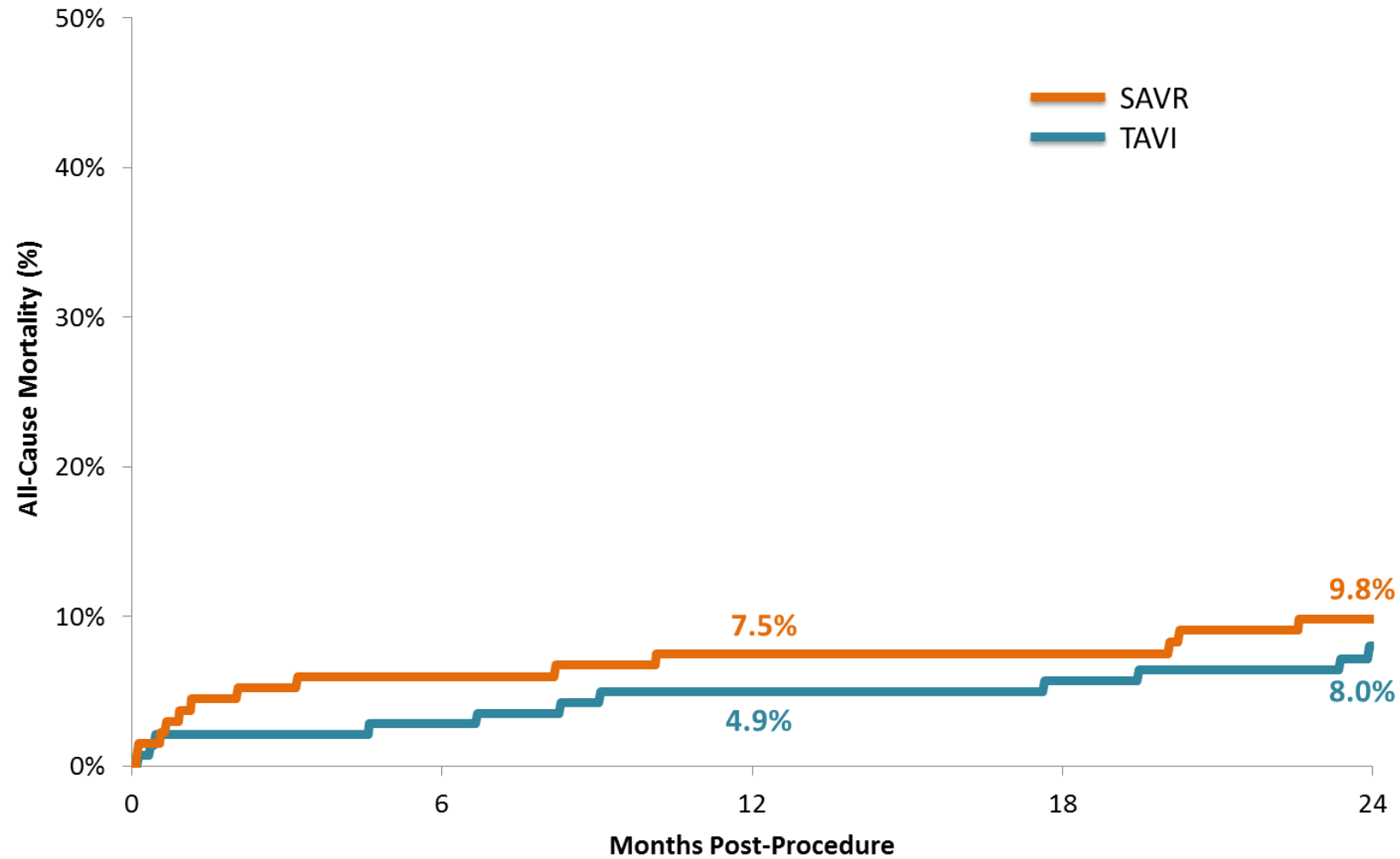
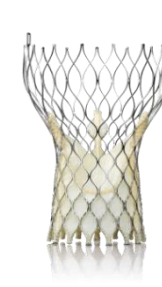
The NOTION Trial

Randomized Low-Risk Patients



The NOTION Trial

Randomized Low-Risk Patients



Key Message

FDA approved randomized trial for low risk patients:

- TAVI vs SAVR

- Age $\geq$ 65

- Medtronic / Evolut R

- Edwards LifeScience/ Sapien 3

- Boston Scientific / Lotus

Key Message

Remaining issues to solve before expanding TAVI indications

Important limitation for expanding TAVI to low risk patients

1-Unknown Durability

2-Pacemaker

3-Stroke

4-Access to coronary arteries

5-Vascular complications

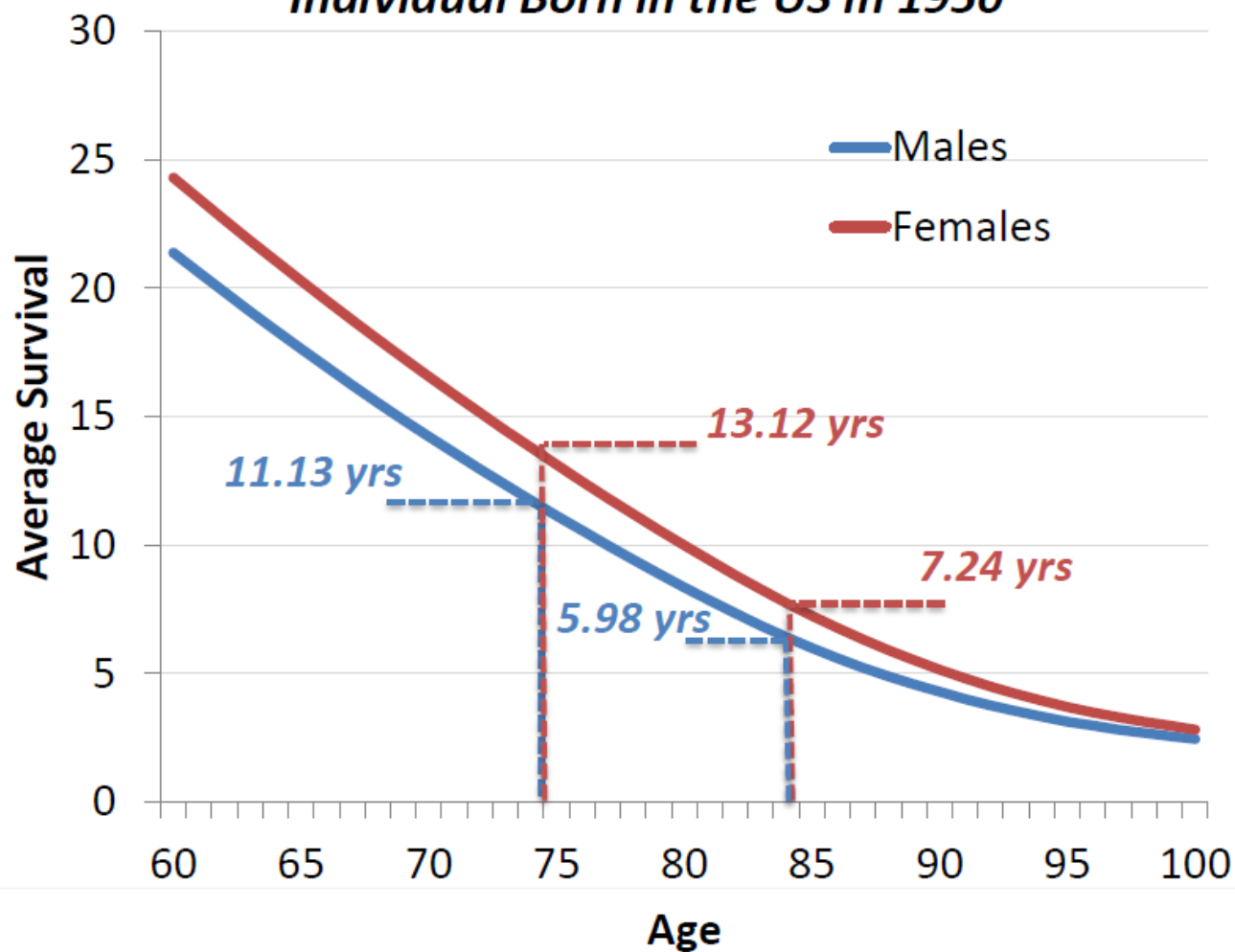
6-TAVI in bicuspid valves

What do we know about

TAVI durability

?

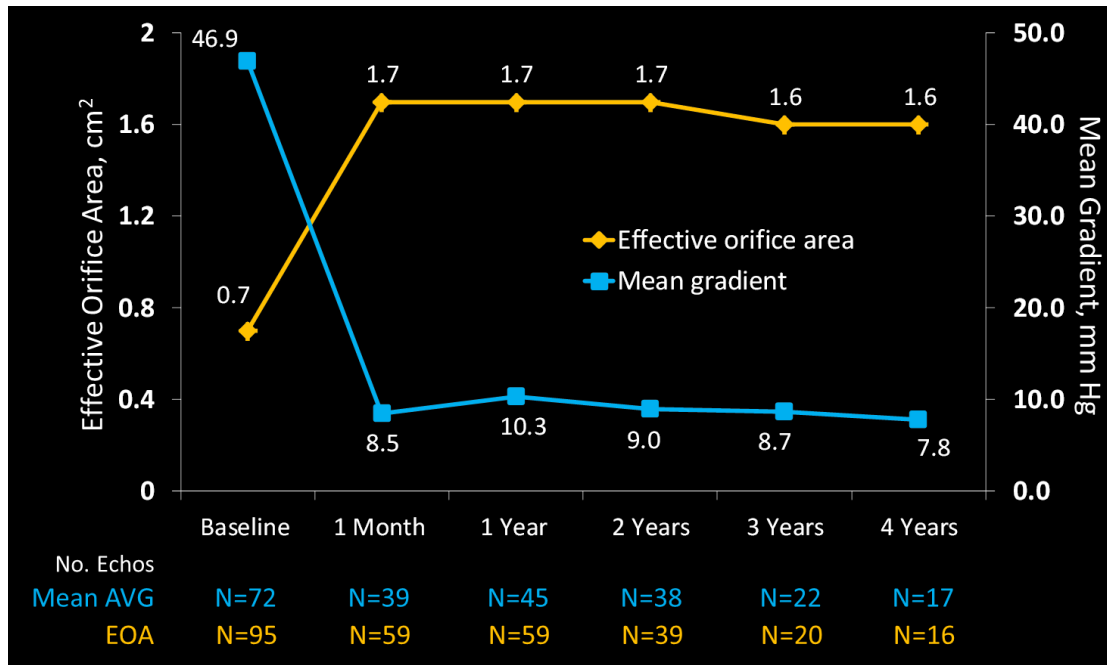
Average Survival for an Individual Born in the US in 1950



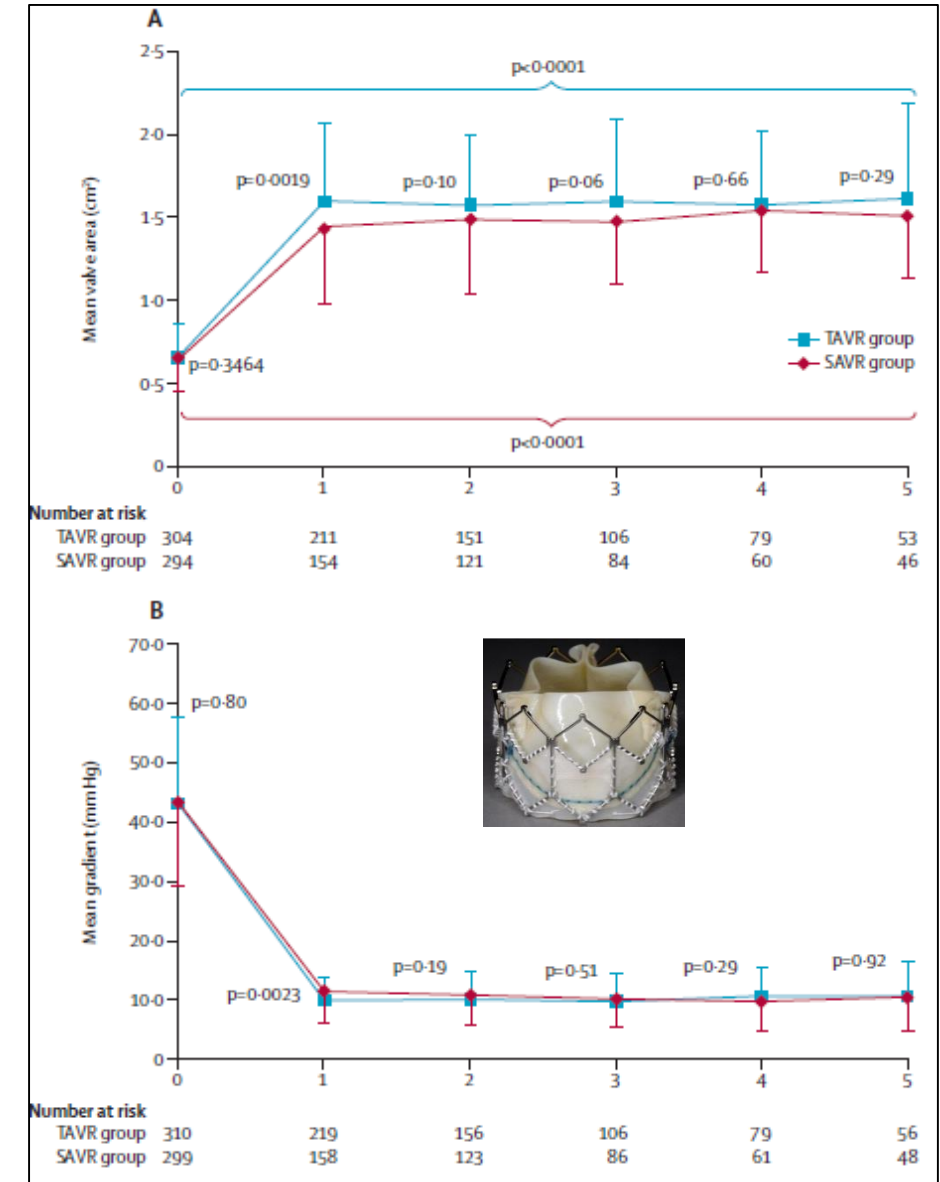
* Adapted from
United States
Social Security Life
Tables (F. Bell and
M. Miller)

TAVI durability up to 5 years

CoreValve CE Pivotal Trial



Kovac, Presented at ACC 2014



Mack et al., Lancet 2015

7 years follow-up of our CoreValve and SAPIEN XT patients



90 y.o.

NYHA I

No cardiovascular event

EOA: 1.7 cm² / Mean gradient 9 mmHg

Trace AR / LVEF 50%



86 y.o.

NYHA I

No cardiovascular event

EOA: 1.78 cm² / Mean gradient 8 mmHg

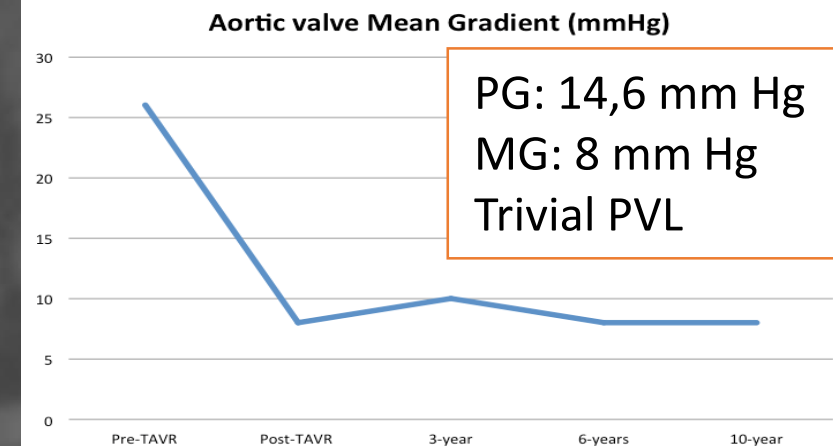
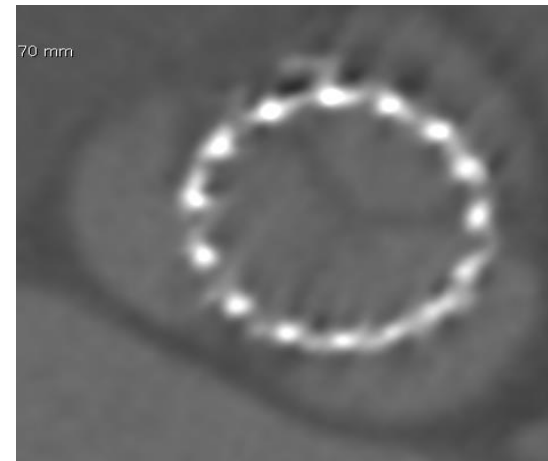
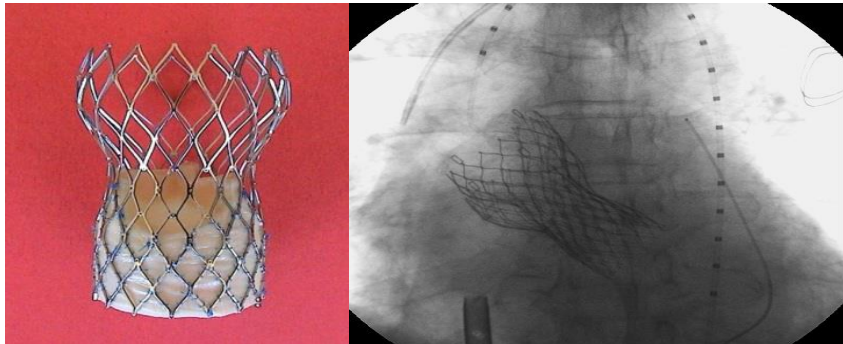
No AR / LVEF 48%

Corevalve Durability Example

2005: CoreValve case in Caracas.
Jose Condado, MD.

2015: 10 y Follow up

CoreValve 25 Fr



The News

Two-Month Follow-up of first South-American patient shows 58-year-old female is fully recovered and has resumed normal activity after non-surgical replacement of defective aortic heart valve using Corevalve's breakthrough ReValving™ procedure

04/04/2005

One of an ongoing series of early cases that demonstrate CoreValve's ReValving™ approach is a successful alternative to open-heart surgery

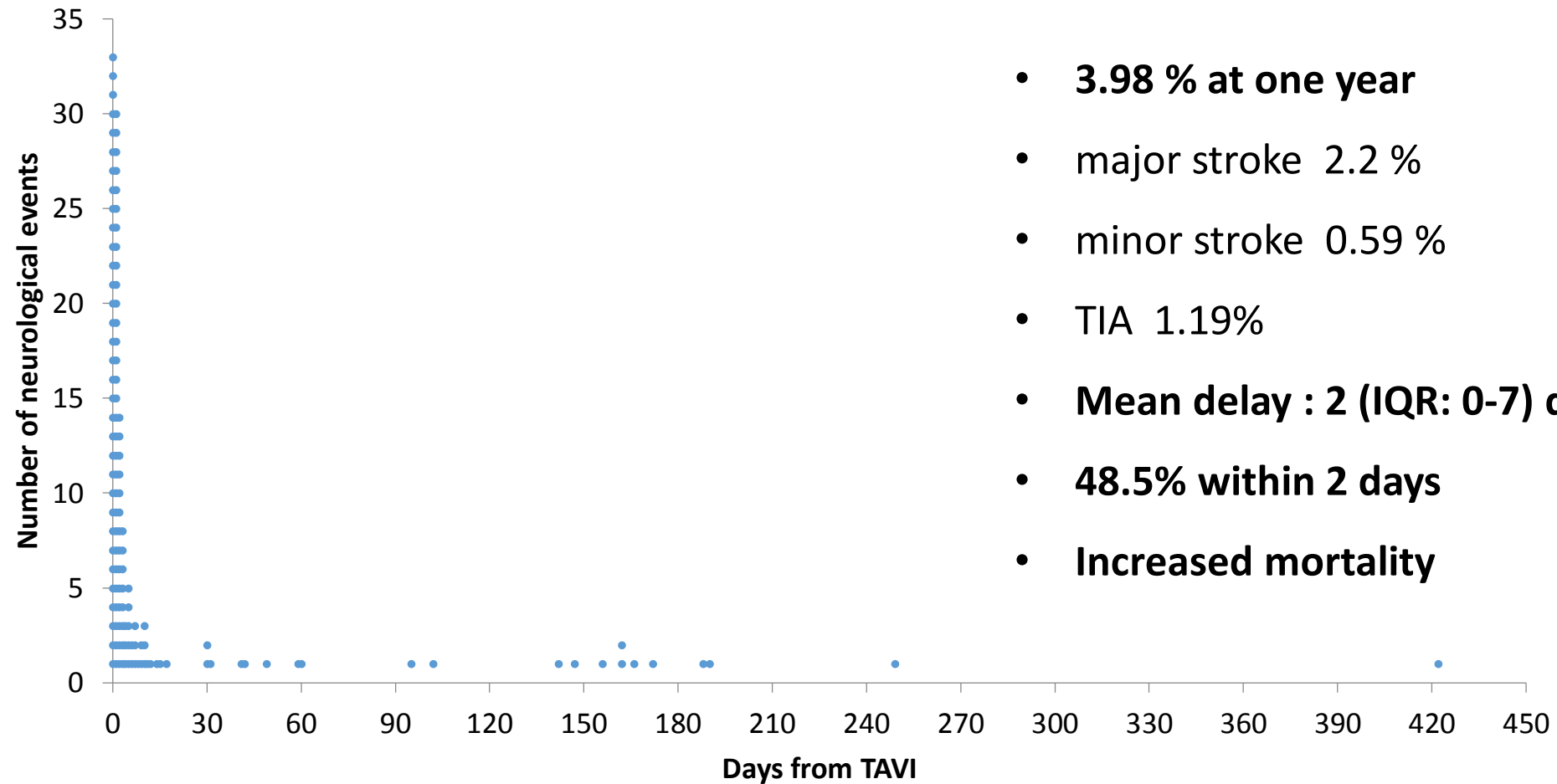
"This patient's life has been transformed—without surgery—from being significantly debilitated to normal-functioning as a direct result of ReValving. The procedure was performed in a hospital cathlab (not a cardiac OR) and avoided

What do we know about

Stroke post TAVI

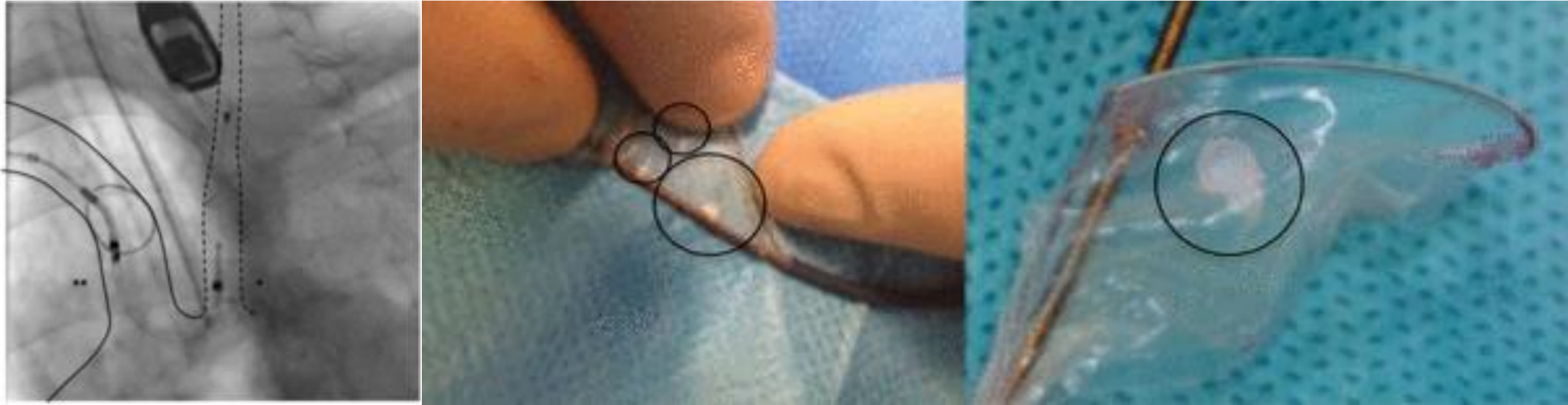
?

FRANCE 2 registry (n=3191)



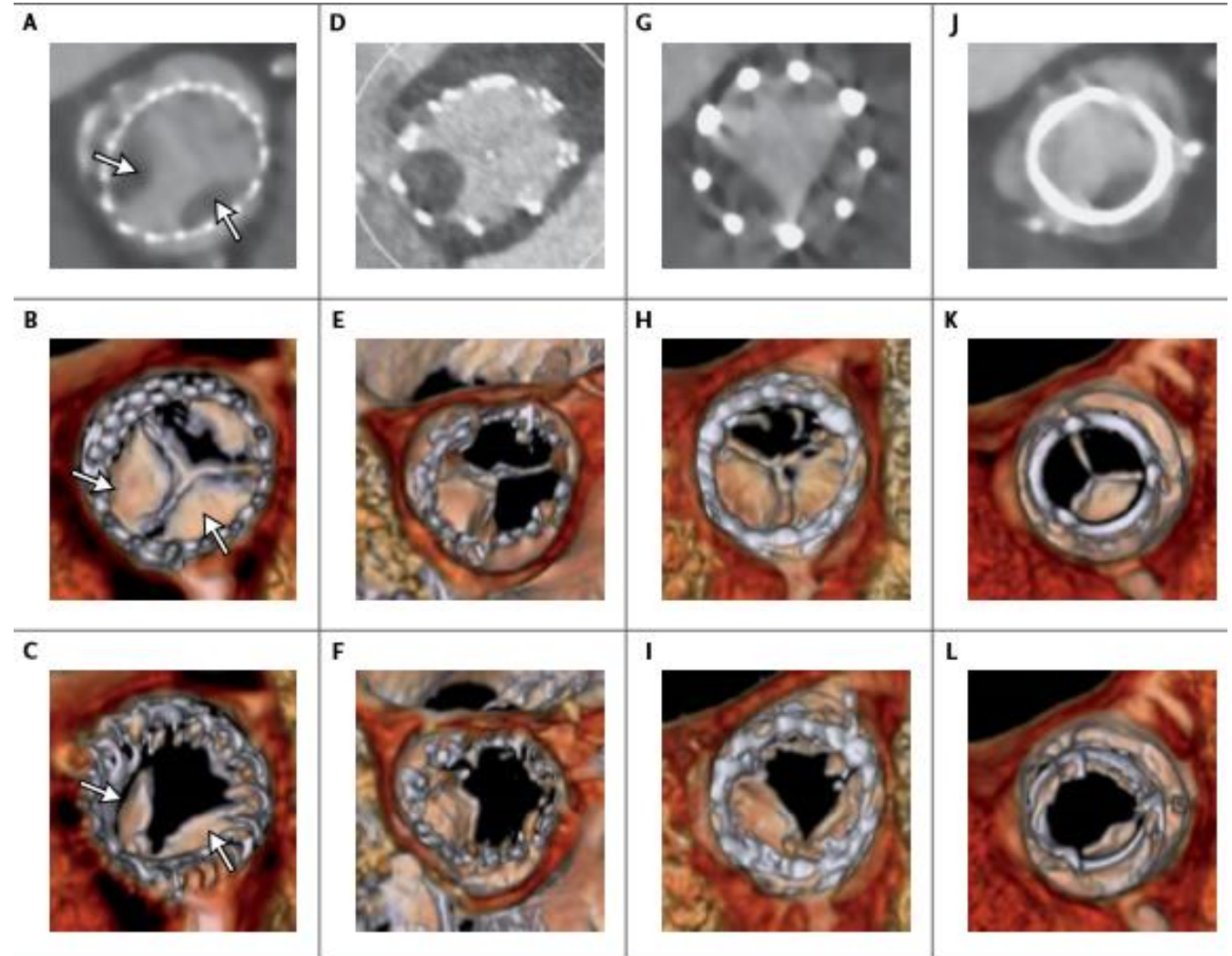
- **3.98 % at one year**
- major stroke 2.2 %
- minor stroke 0.59 %
- TIA 1.19%
- **Mean delay : 2 (IQR: 0-7) days**
- **48.5% within 2 days**
- **Increased mortality**

Embolic protection devices



Conclusions—Embolitic debris traveling to the brain was captured in 75% of transcatheter aortic valve replacement procedures where a filter-based embolic protection device was used. The debris consisted of fibrin, or amorphous calcium and connective tissue derived most likely from either the native aortic valve leaflets or aortic wall. (*Circulation*. 2013;127:2194-2201.)

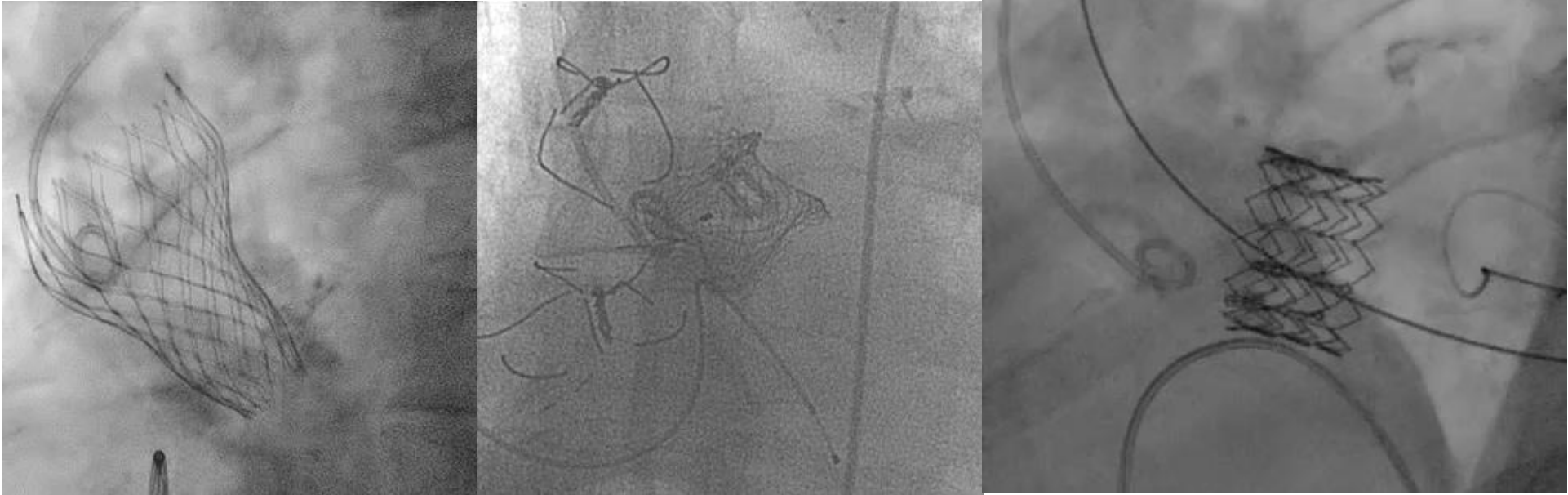
Leaflets thrombosis



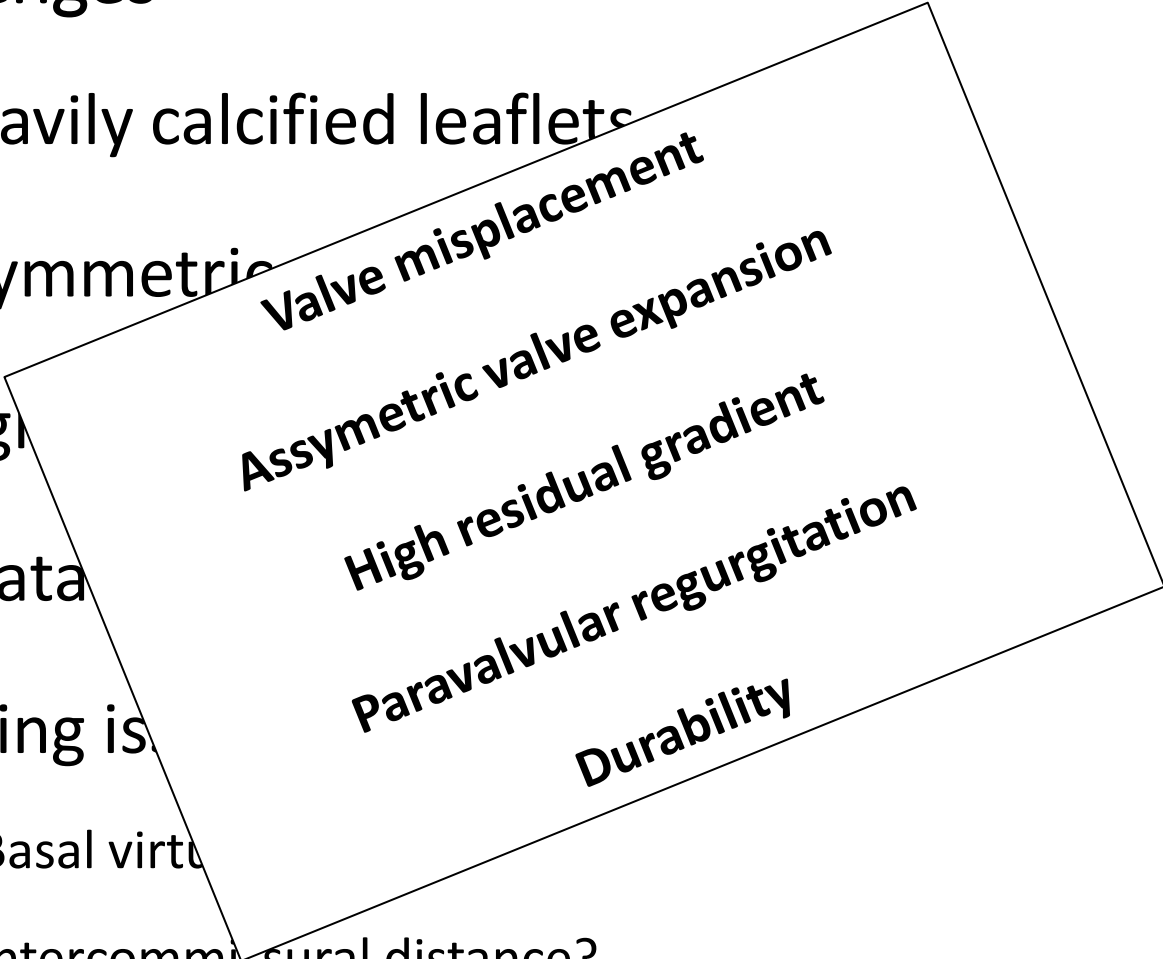
What do we know about

TAVI in bicuspid valves

?



Procedural Challenges

- Heavily calcified leaflets
 - Asymmetric
 - High
 - Dilata
 - Sizing is
 - Basal vort
 - Intercommissural distance?
- 
- Valve misplacement
Assymetric valve expansion
High residual gradient
Paravalvular regurgitation
Durability

What do we know about

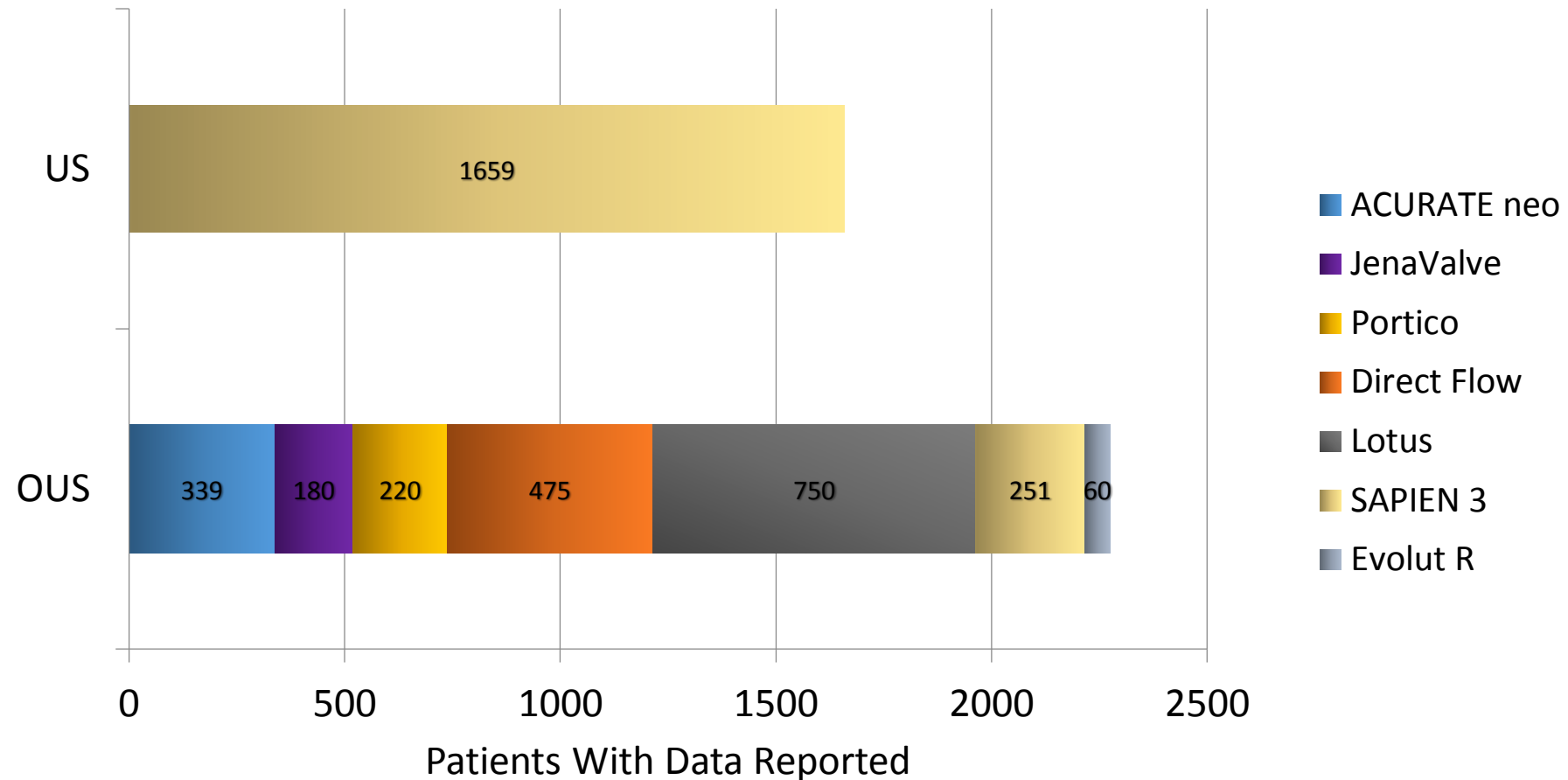
New generation TAVI devices

?

Evidence Base

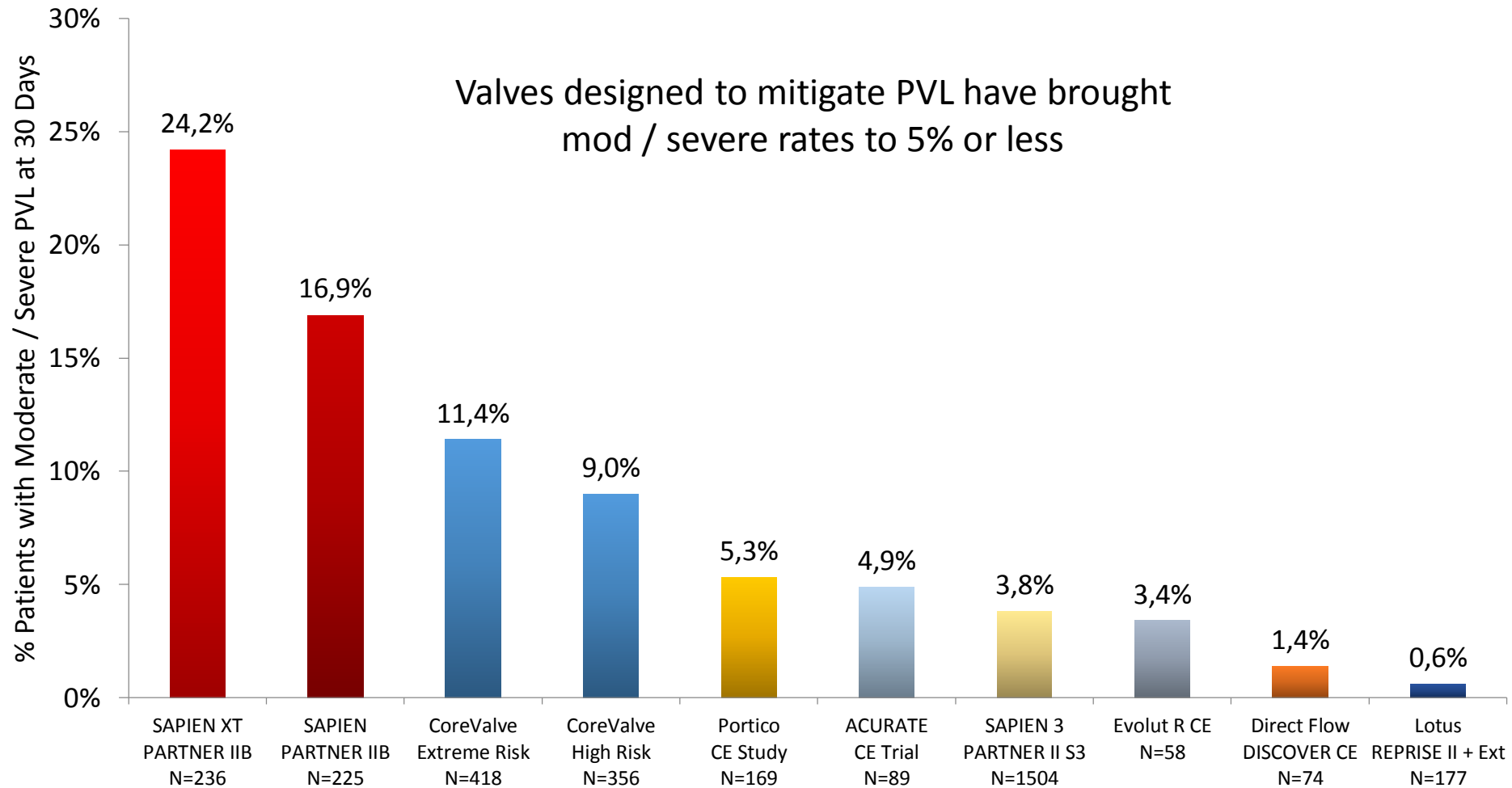
New Technologies

- The evidence base with these new devices is growing rapidly. In 2015, data from almost 4,000 patients implanted with new valve systems has been reported
- Both clinical trial and real-world data are available for some systems



Paravalvular Leak

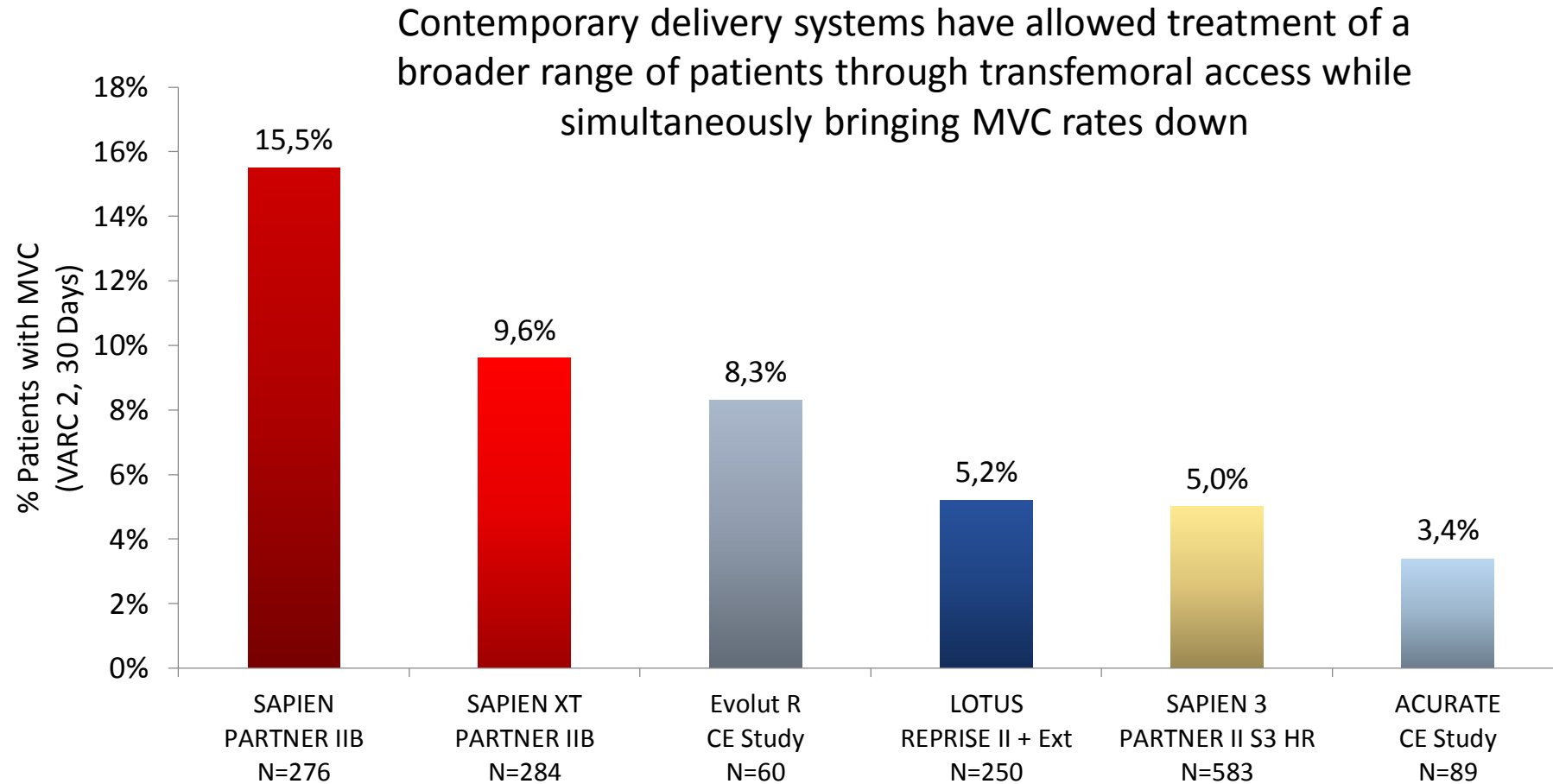
Moderate / Severe at 30 Days



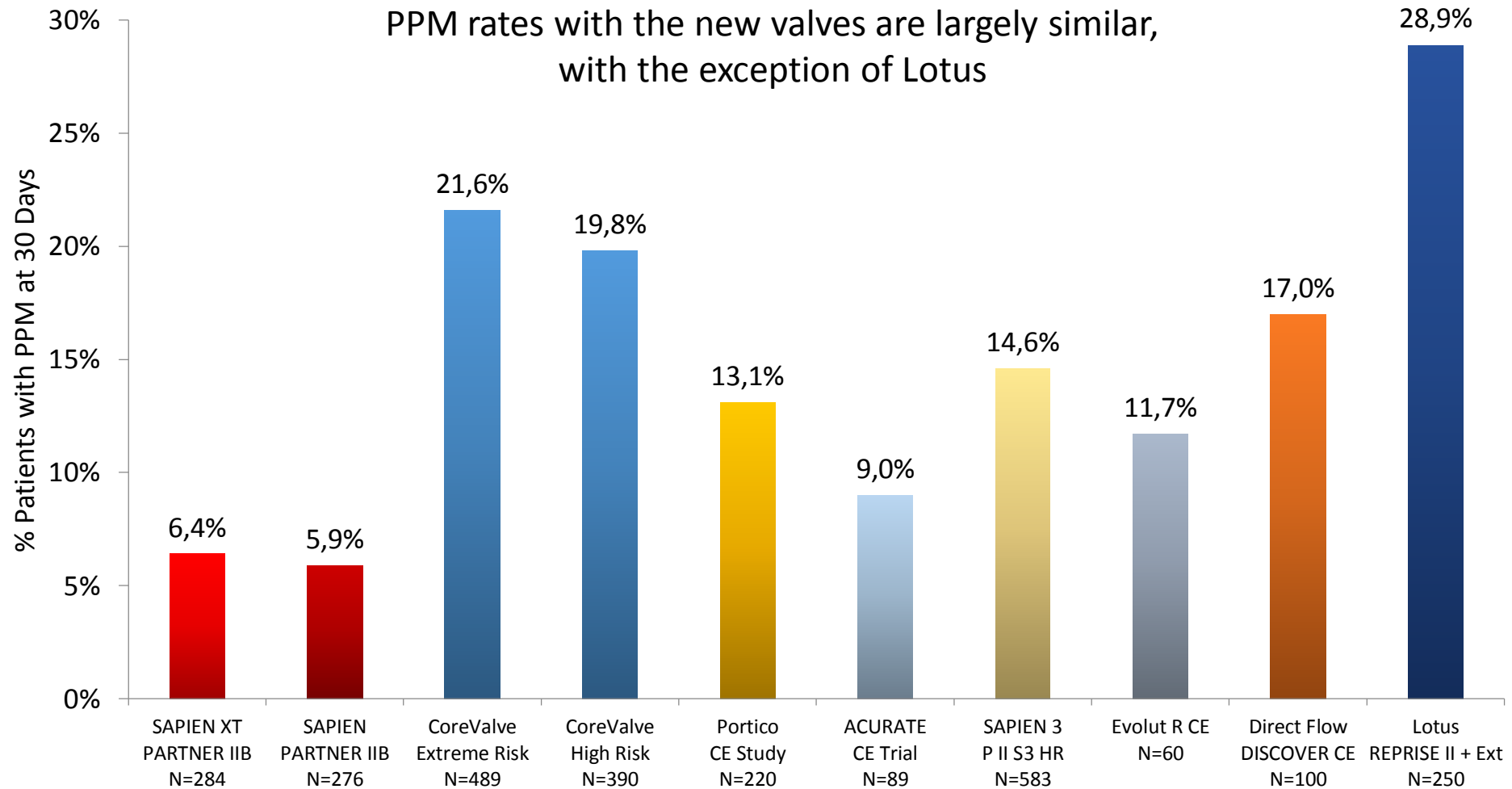
¹Leon, et. al. presented at ACC 2013; ²Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ³Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ⁴Linke, et. al. presented at PCR London Valves 2015; ⁵Abizaid, et al., presented at CRT 2015; ⁶Kodali, et al., presented at ACC 2015; ⁷Manoharan, et al., presented at TCT 2015; ⁸Naber, et al., presented at EuroPCR 2015; ⁹Vahanian, et al., presented at EuroPCR 2015; ¹⁰Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; ¹¹Meredith, et al., presented at PCR London Valves 2014

Major Vascular Complications

Rates According to VARC 2



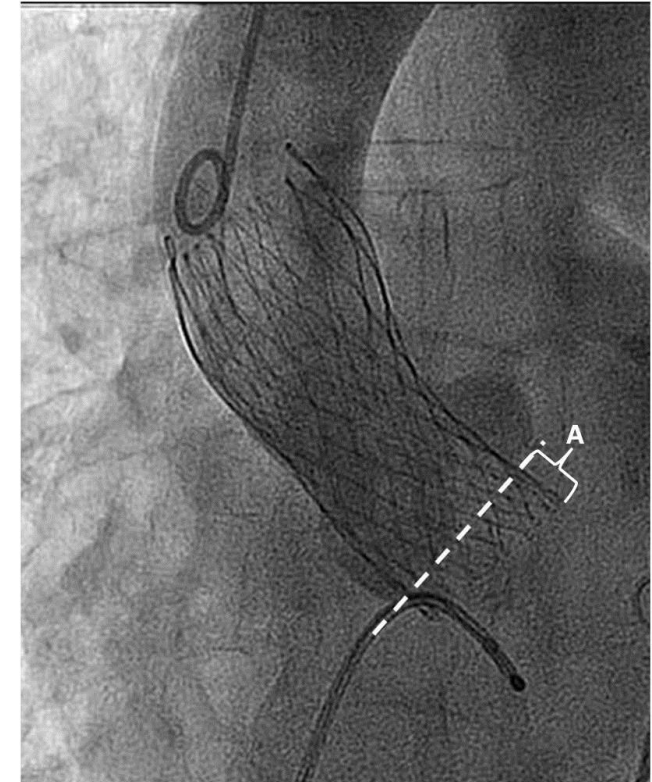
Permanent Pacemakers Rate at 30 Days



¹Leon, et. al. presented at ACC 2013; ²Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; ³Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ⁴Linke, et. al. presented at PCR London Valves 2015; ⁵Abizaid, et al., presented at CRT 2015; ⁶Kodali, et al., presented at ACC 2015; ⁷Manoharan, et al., presented at TCT 2015; ⁸Naber, et al., presented at EuroPCR 2015; ⁹Vahanian, et al., presented at EuroPCR 2015; ¹⁰Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; ¹¹Meredith, et al., presented at PCR London Valves 2014

Predictors of AV block after TAVI

- Pre existing RBBB
- Non coronary cusp calcification
- Depth of biosprothesis implantation
- QRS duration after TAVI (QRSd).



Piazza et al EuroIntervention (2008) ;4:242-249

Bleiziffer et al JACC Cardiovascular Intervention 2010; 3:524-530

Latsios et al Catheterization and Cardiovascular Interventions 76:431-439 (2010)

Tchetche et al EuroIntervention 2012;8:556-562

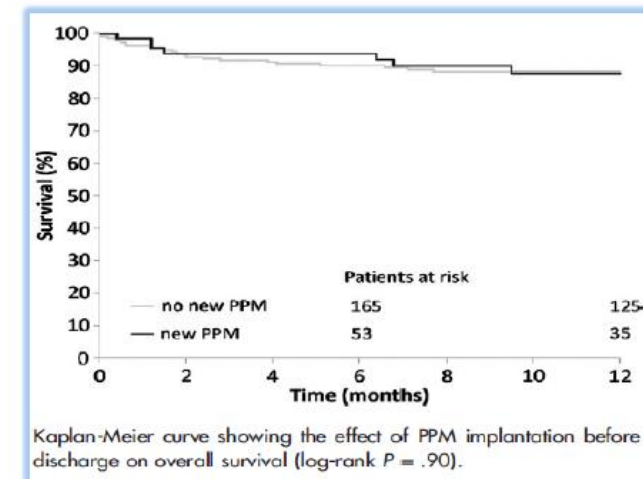
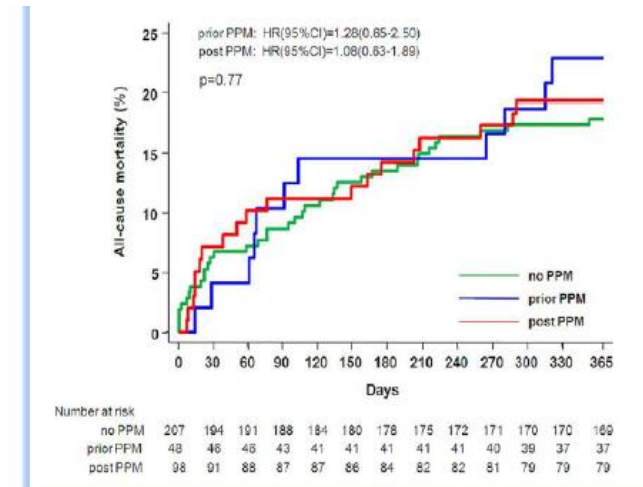
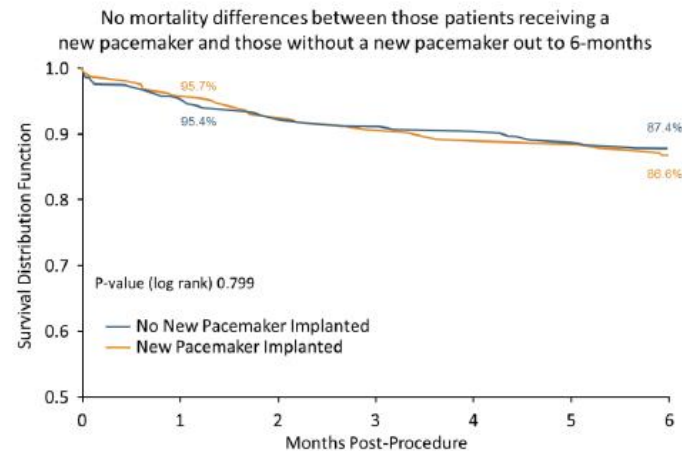
Mouillet et al Catheterization and Cardiovascular Interventions 81:882-887 (2013)

Baan et al

Pacemaker after TAVI: no impact on mortality

Three large studies demonstrate no association between pacemaker implantation and mortality

Buellesfeld, et. al. JACC 2012; Bauernschmitt, et. al. EuroPCR 2012; De Carlo, et. al. AHJ 2012.



CONCLUSION

- **TAVI is equal to surgery in intermediate risk patients.**
- **TAVI seems is safe in low-risk patients**
- **TAVI prostheses are durable up to five years and probably beyond.**
- **Examples of patients with functioning prosthesis up to 12 years**
- **TAVI is ready for prime time in intermediate risk patients**
- **Remaining issues to solve befor expanding indiatons to low risk patients**

THANK YOU