TAVI after Ten Years of Experience

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Percutaneous Aortic Valve Replacement

April 16th, 2002: First human case description trans-catheter aortic valve

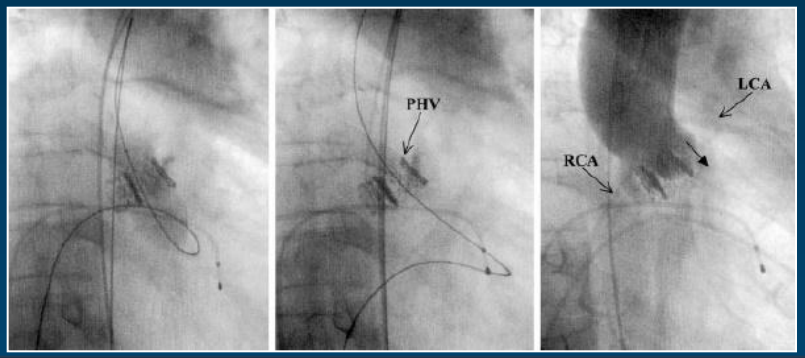
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association. Learn and Live.

Special Report

Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis

First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD



Neil Armstrong, Moon July 20, 1969

Percutaneous Device

CoreValve Revalving® System (CRS)

CE 0050

Edwards-SAPIEN™ Aortic Bioprosthesis

>30,000 patients

>30,000 patients

TAVR Initial Experiences

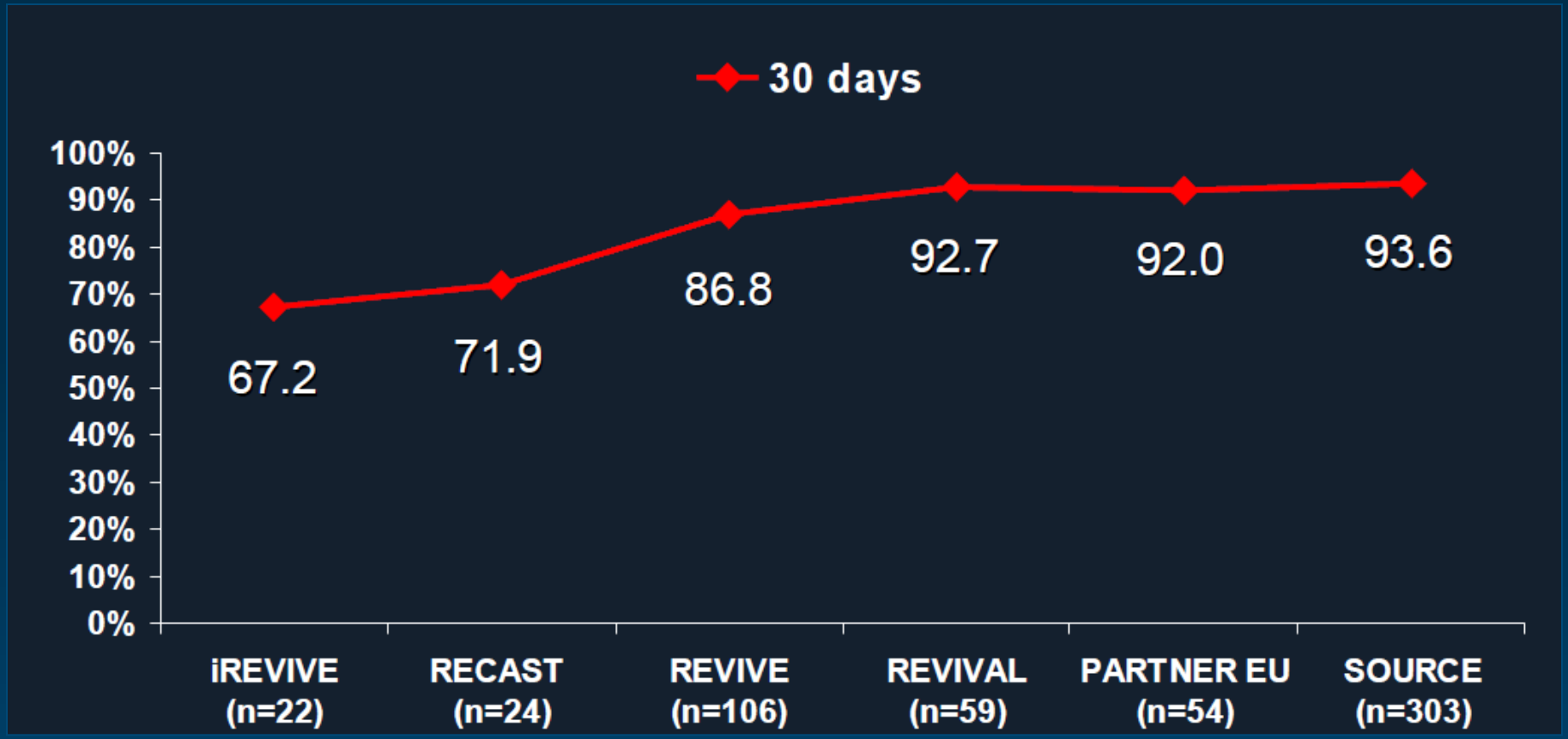
Table I Multicentre feasibility studies

Study	Enrollment	Number of patients	Approach	Device	Procedural success	30-day mortality
I-REVIVE/RECAST[6]	2003–2005	26	Transseptal	Edwards SAPIEN	85% (22/26)	16.7% (6/36)
		7	TF	Edwards SAPIEN	57% (4/7)	
Grube et al.[9]	2005–2007	86	TF	CoreValve	74% (64/86)	11.6% (10/86)
TRAVERCE[26]	2006–2008	168	TA	Edwards SAPIEN	95.8% (161/168)	14.9% (25/168)
REVIVAL[24,25]	2006–2008	40	TA	Edwards SAPIEN	100% (40/40)	12.5% (7/40)
	2005–2006	55	TF	Edwards SAPIEN	87% (48/55)	7.3% (4/55)

TF, transfemoral; TA, transapical; I-REVIVE, Initial Registry of EndoVascular Implantation of Valves in Europe trial; RECAST, Registry of Endovascular Critical Aortic Stenosis Treatment trial; REVIVAL, PeRcutaneous EndoVascular Implantation of VALves trial; TRAVERCE, The initial multicentre feasibility trial for TA-AVI.

Transfemoral TAVI

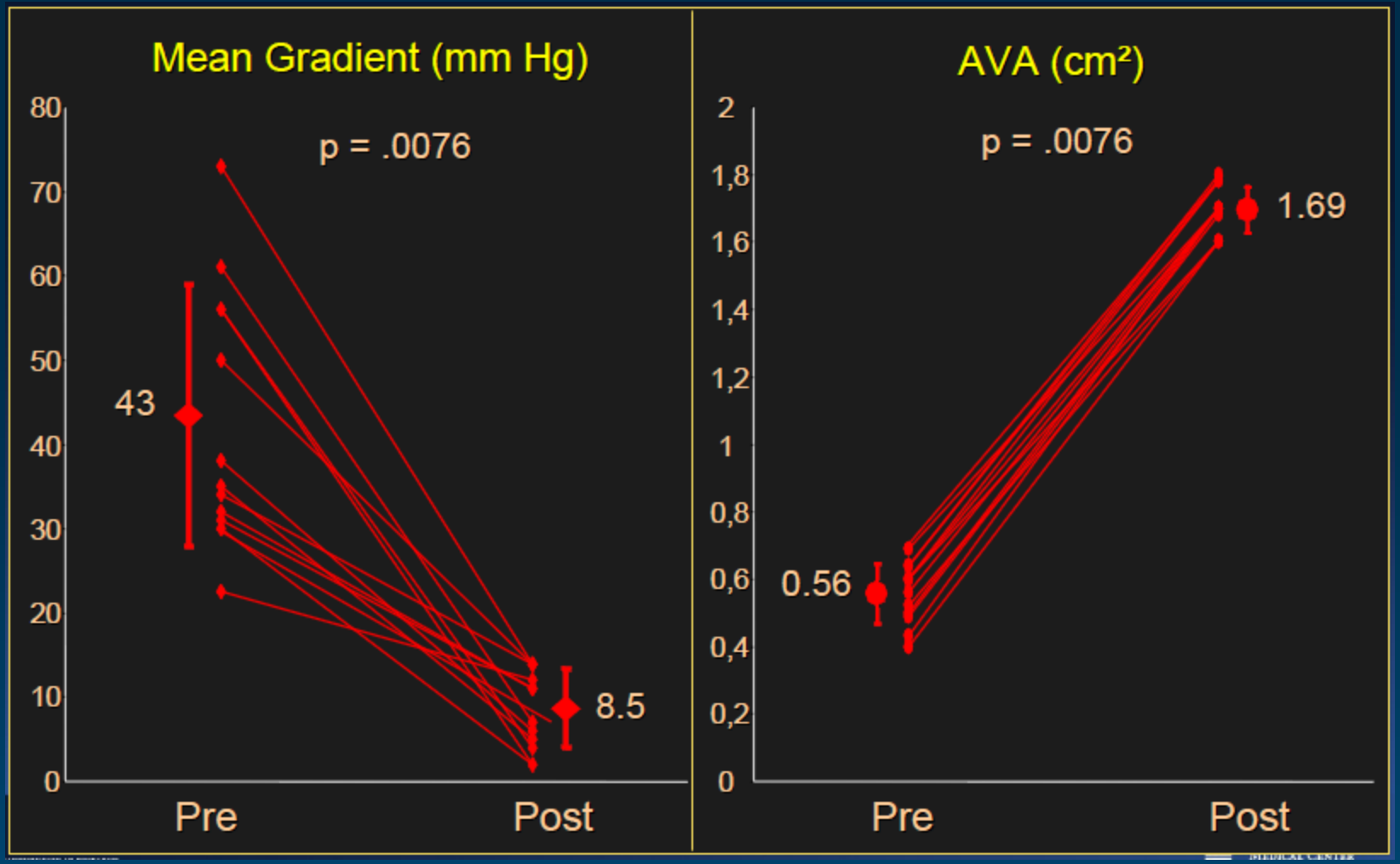
Survival at 1 month



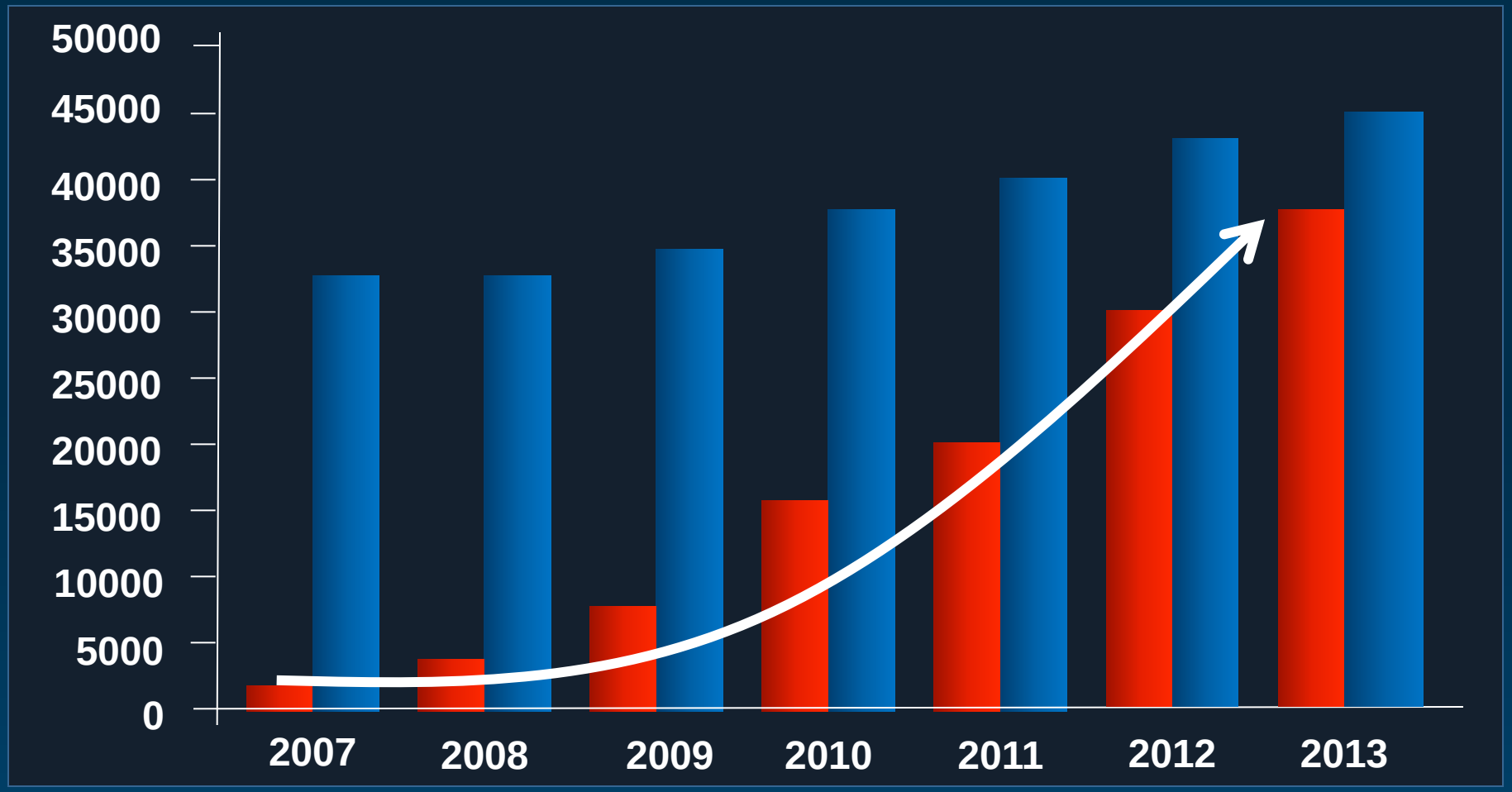
Early "evolution", then "stabilization"

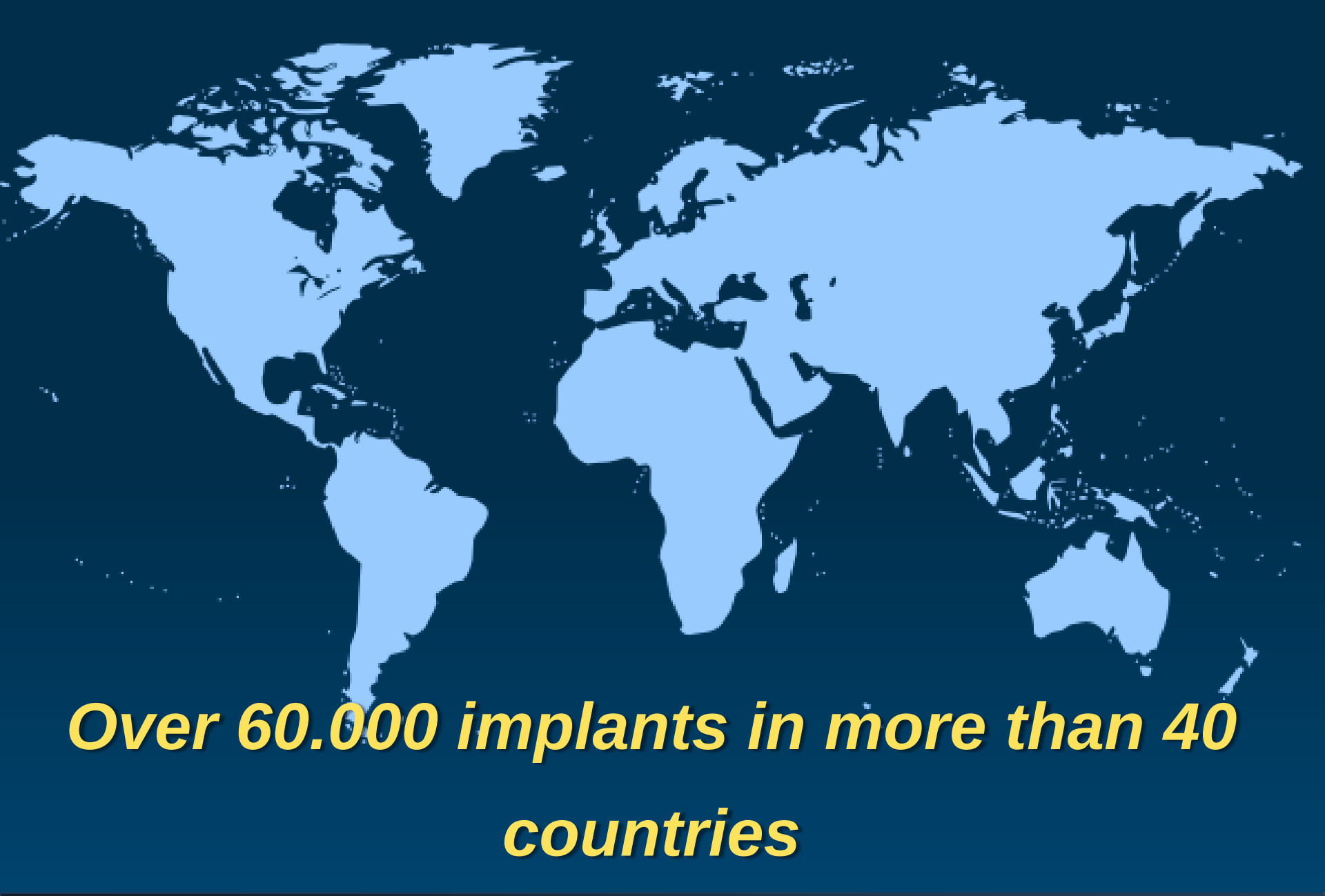
Cribier – Early TAVI Experience

Procedural Results (n=16)



TAVR vs SAVR in EU Centers





Over 60.000 implants in more than 40 countries

PARTNER IDE Trial

Population: High Risk/Non-Operable
Symptomatic, Critical Calcific Aortic Stenosis

ASSESSMENT: Operability

Total n= 1040

n= up to 690 pts

Yes

Cohort A

ASSESSMENT: Transfemoral Access

Yes

Cohort A TF Powered Independently

1:1 Randomization

Trans femoral vs **AVR Control**

No

Cohort A TA Powered to be Pooled with TF

1:1 Randomization

Trans apical vs **AVR Control**

Primary Endpoint: All Cause Mortality (Non-inferiority)

No

Cohort B

n=350 pts

ASSESSMENT: Transfemoral Access

Yes

1:1 Randomization

Trans femoral vs **Medical Management Control**

Primary Endpoint: All Cause Mortality (Superiority)

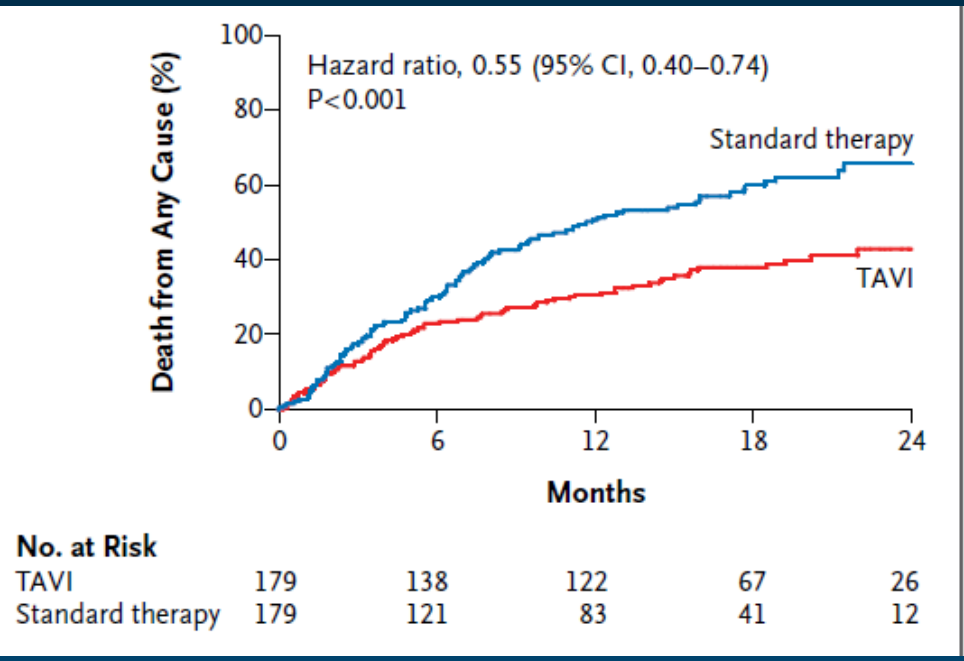
No

Not in Study

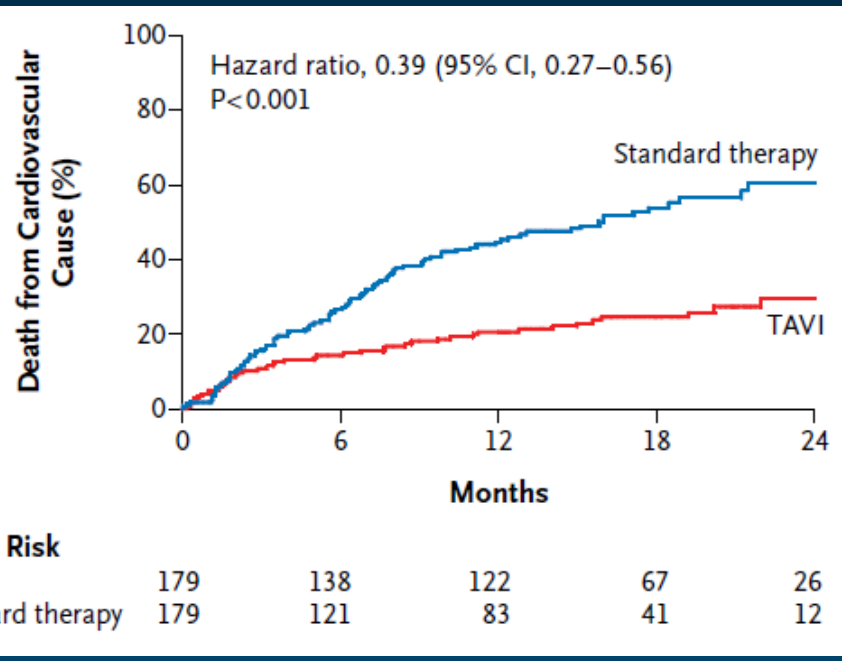
The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*



No. at Risk					
TAVI	179	138	122	67	26
Standard therapy	179	121	83	41	12



No. at Risk					
TAVI	179	138	122	67	26
Standard therapy	179	121	83	41	12

PARTNER IDE Trial

Population: High Risk/Non-Operable
Symptomatic, Critical
Calcific Aortic Stenosis

ASSESSMENT: Operability

Total n= 1040

Yes

n= 699 pts

Cohort A

ASSESSMENT: Transfemoral Access

Yes

Cohort A TF Powered Independently

1:1 Randomization

Trans femoral vs **AVR Control**

No

Cohort A TA Powered to be Pooled with TF

1:1 Randomization

Trans apical vs **AVR Control**

Primary Endpoint: All Cause Mortality (Non-inferiority)

No

Cohort B

n=350 pts

ASSESSMENT: Transfemoral Access

Yes

1:1 Randomization

Trans femoral vs **Medical Management Control**

No

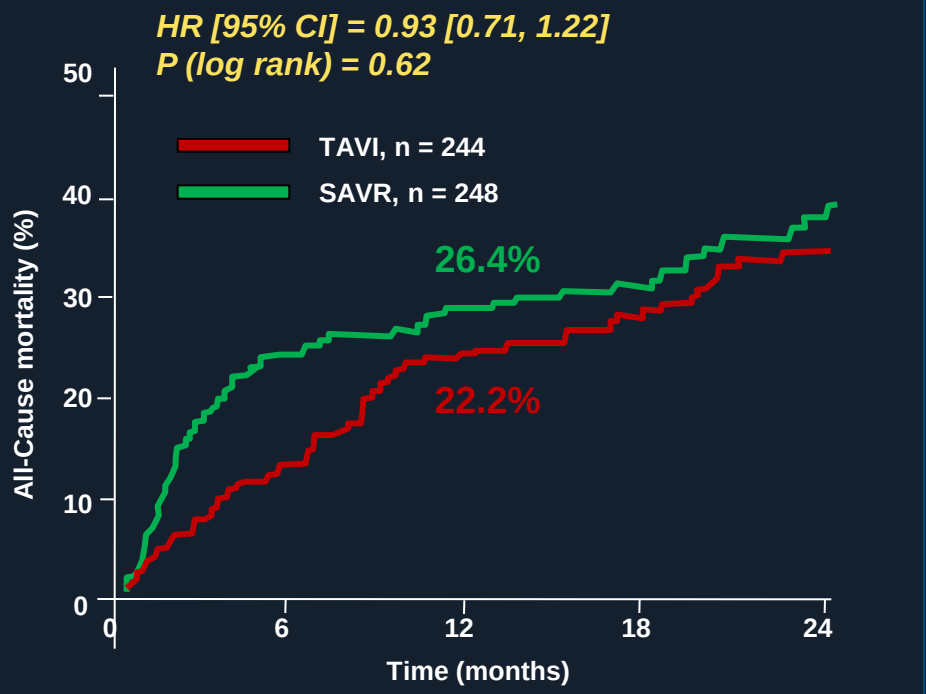
Not in Study

Primary Endpoint: All Cause Mortality (Superiority)

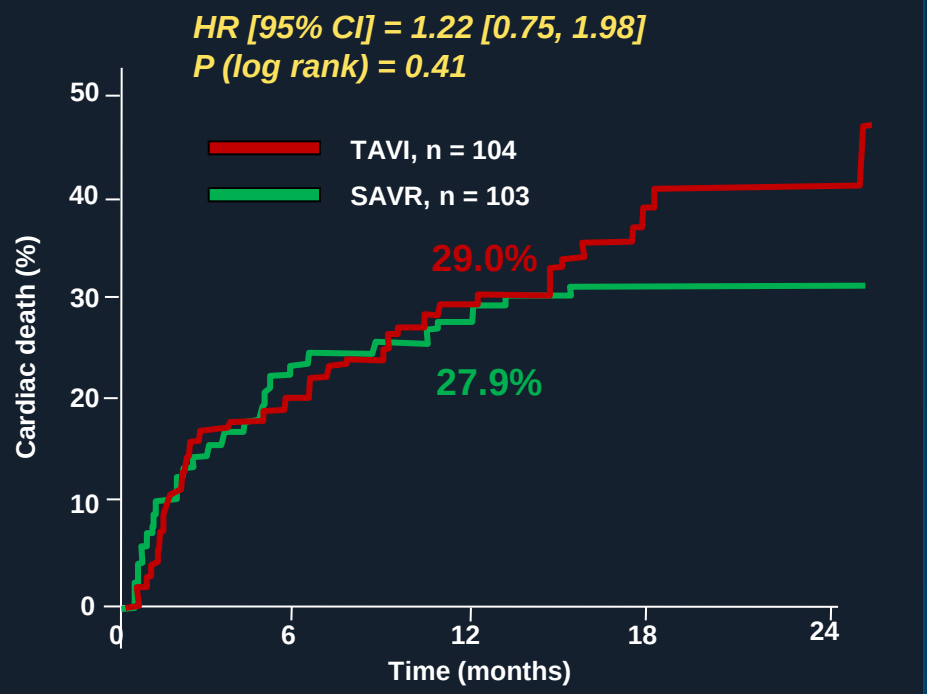
PARTNER Randomized Trial Cohort A

Kaplan-Meier All-Cause Mortality

Transfemoral (n=492)



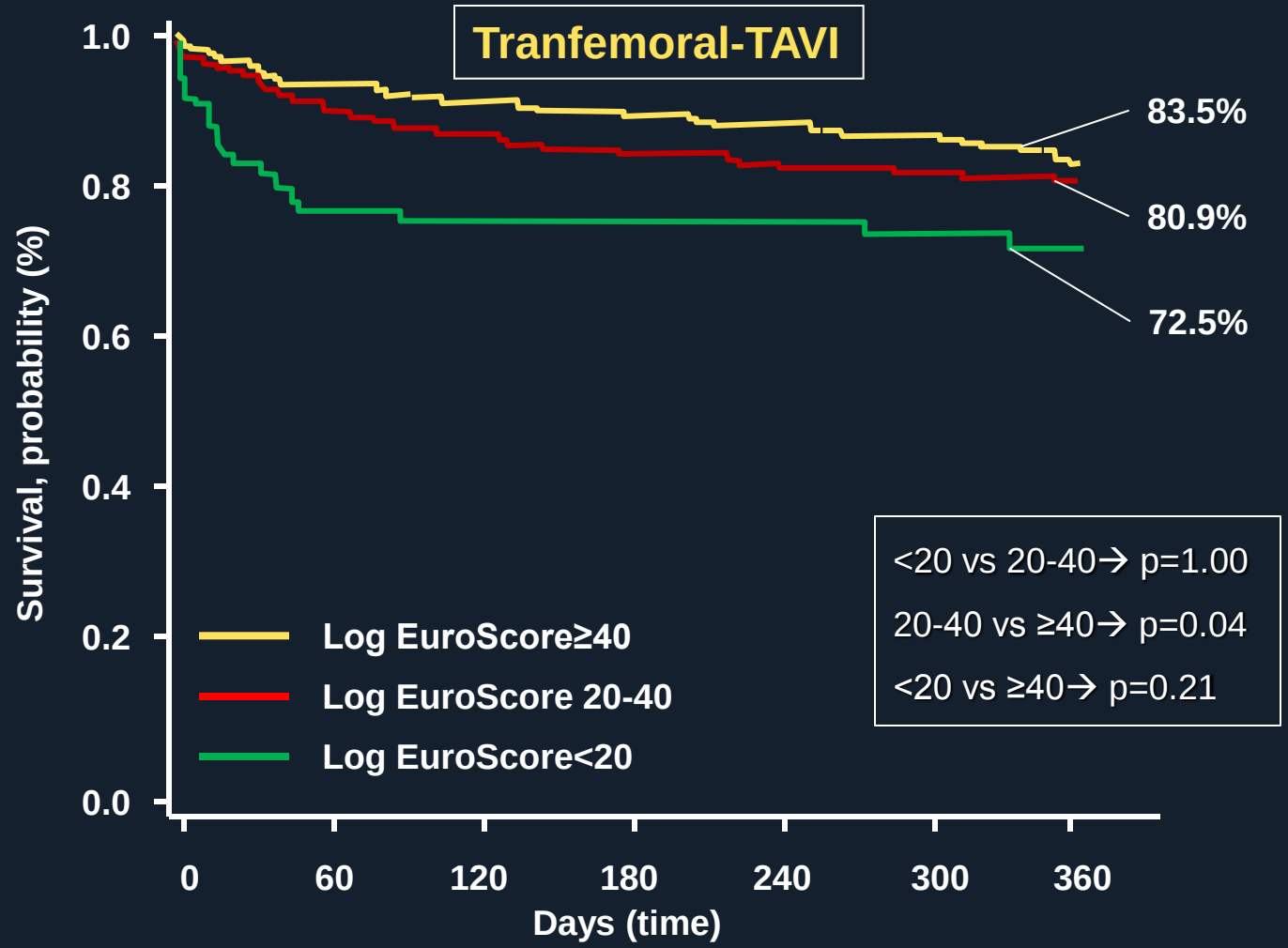
Transapical (n=207)



Smith CR, NEJM 2011

SOURCE Registry

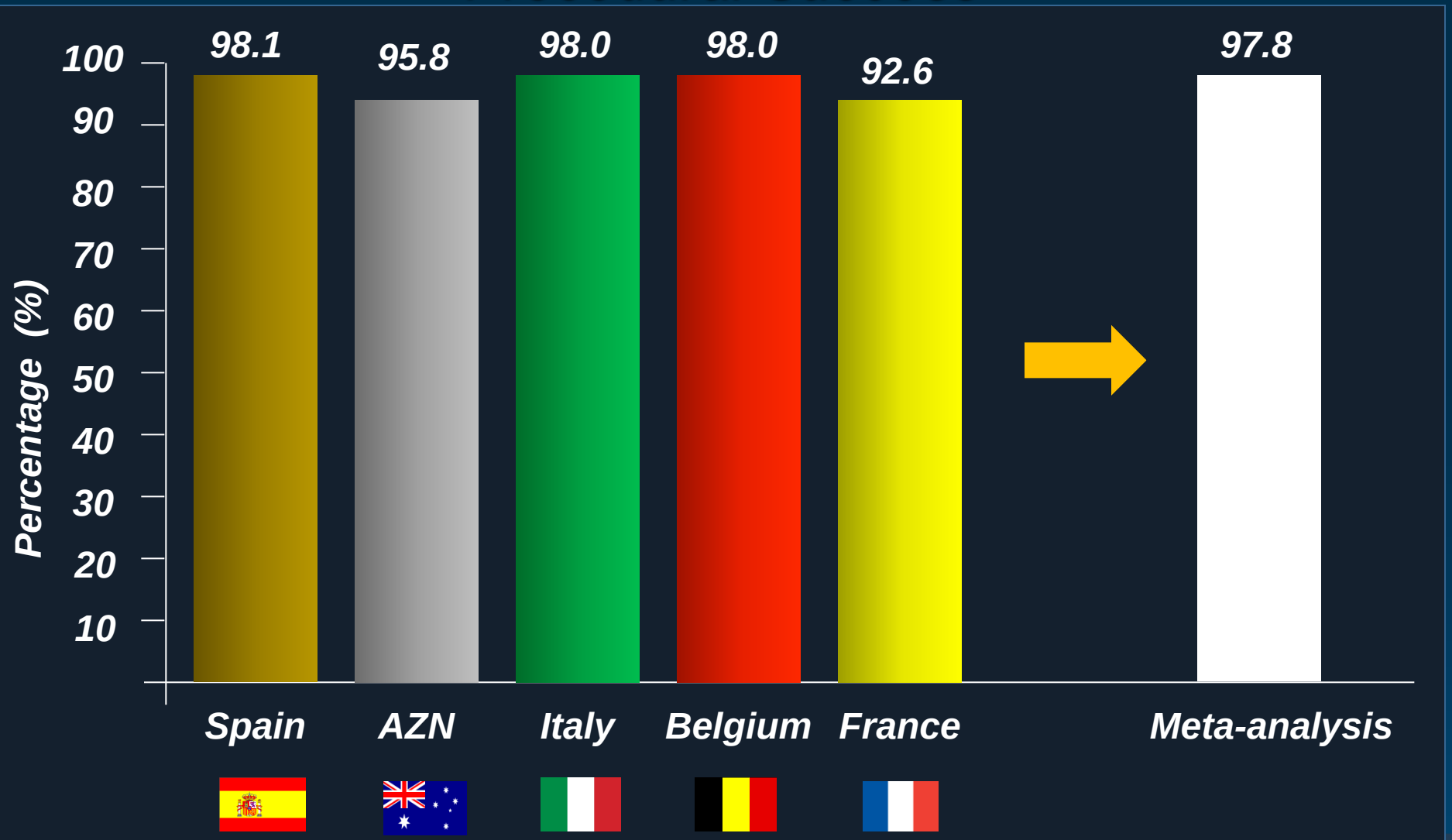
All cause Mortality by EuroScore strata



Thomas et al. Circulation 2011;124:425-33

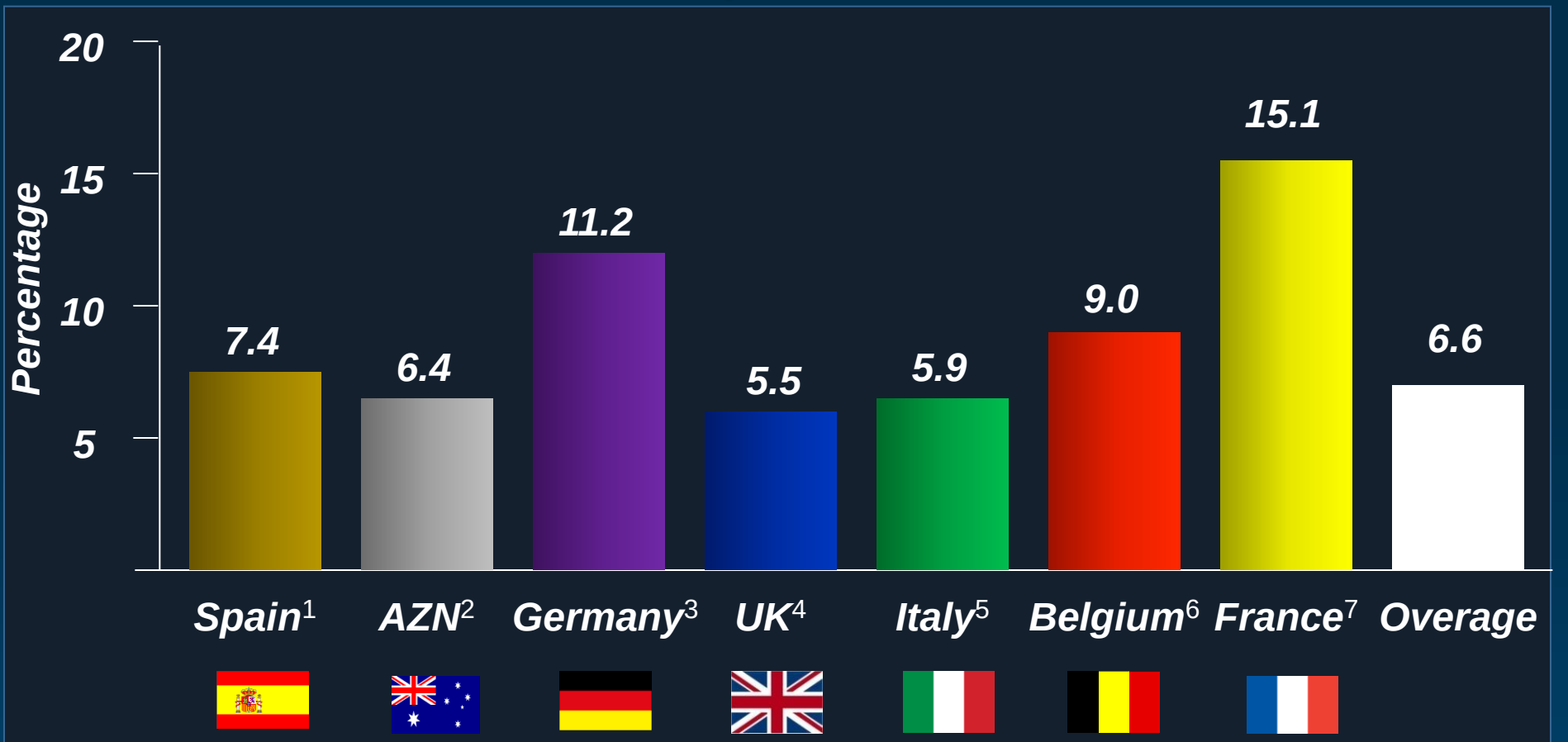
CRS Registries Results

Procedural Success



CRS Registries Results

30-day Survival



[1]Avanzas Rev Esp Cardiol 2010; [2]Meredith TCT2010; [3]Zahn EuroPCR 2010 [4]Moat EuroPCR 2010; [5]Tamburino Circulation 2011; [6]Bosmans EuroPCR 2010; [7]Eltchaninoff Eur Heart J 2010.

European Heart Journal Advance Access published January 12, 2012

European Heart Journal
doi:10.1093/eurheartj/ehr491

FASTTRACK
CLINICAL RESEARCH

Transcatheter aortic valve implantation: 3-year outcomes of self-expanding CoreValve prosthesis

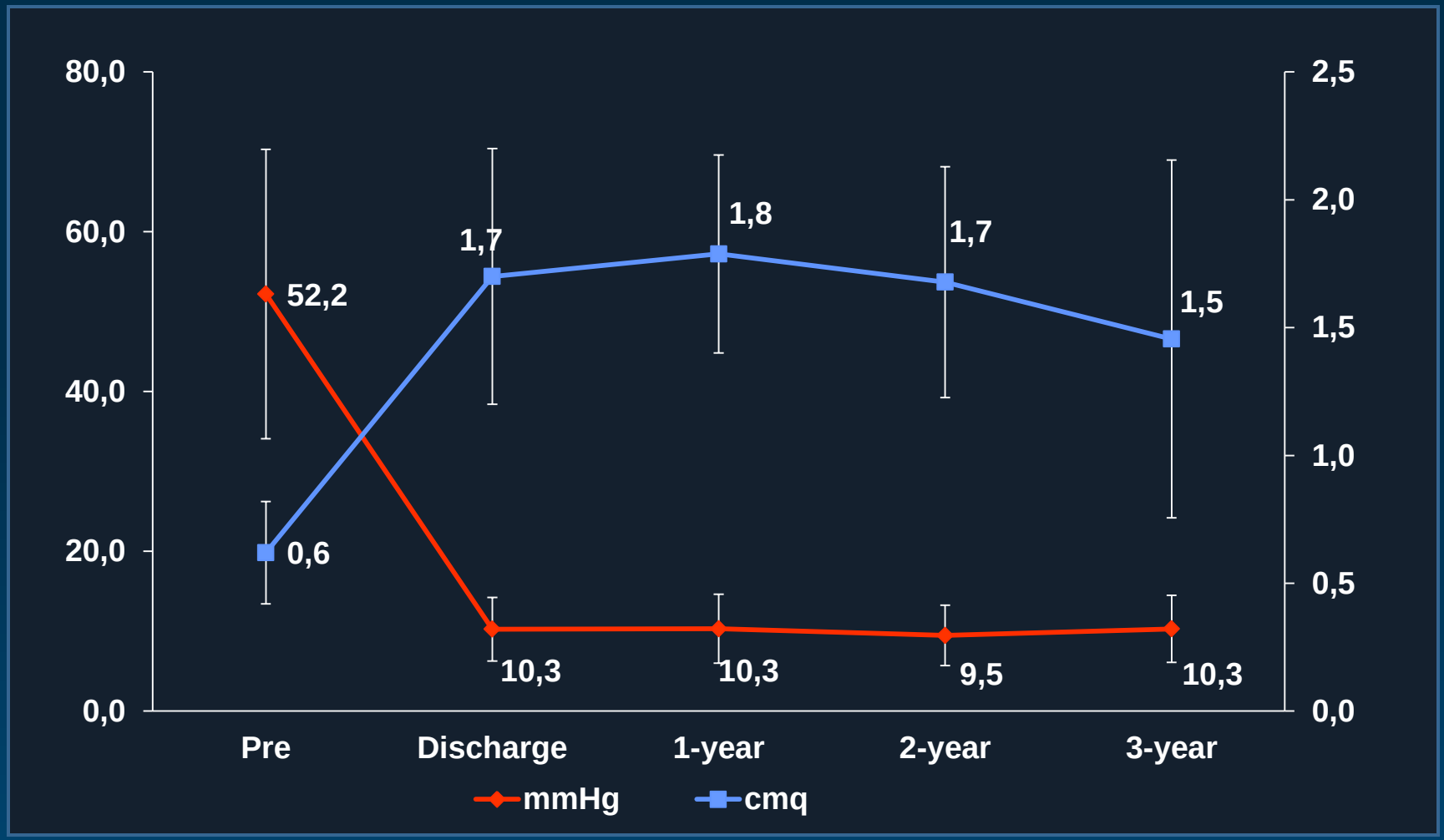
Gian Paolo Ussia[1,2]*, Marco Barbanti[1], Anna Sonia Petronio[3], Giuseppe Tarantini[4], Federica Ettori[5], Antonio Colombo[6], Roberto Violini[7], Angelo Ramondo[8], Gennaro Santoro[9], Silvio Klugmann[10], Francesco Bedogni[11], Francesco Maisano[6], Antonio Marzocchi[12], Arnaldo Poli[13], Marco De Carlo[3], Massimo Napodano[4], Claudia Fiorina[5], Federico De Marco[10], David Antoniucci[9], Emanuela de Cillis[14], Davide Capodanno[1,2], and Corrado Tamburino[1,2], on behalf of CoreValve Italian Registry Investigators

[1]Interventional Structural and Congenital Heart Disease Programme, Invasive Cardiology Division of Cardiology, Ferrarotto Hospital, University of Catania, Catania, Italy; [2]ETNA Foundation, Catania, Italy; [3]AOU Pisana, Pisa, Italy; [4]University of Padova, Padua, Italy; [5]Spedali Civili, Brescia, Italy; [6]Scientific Institute S. Raffaele, Milan, Italy; [7]Division of Interventional Cardiology, A.O. San Camillo Forlanini Hospital, Rome, Italy; [8]Division of Cardiology, Bassano del Grappa, Padua, Italy; [9]Careggi Hospital, Florence, Italy; [10]Niguarda Ca'Granda Hospital, Milan, Italy; [11]Clinical Institute S. Ambrogio, Milan, Italy; [12]Policlinico S. Orsola-Malpighi, University of Bologna, Bologna, Italy; [13]Ospedale Civile, Legnano, Italy; and [14]Division of Cardiovascular Surgery, Ospedale Policlinico, Bari, Italy

Received 22 October 2011; revised 1 December 2011; accepted 14 December 2011

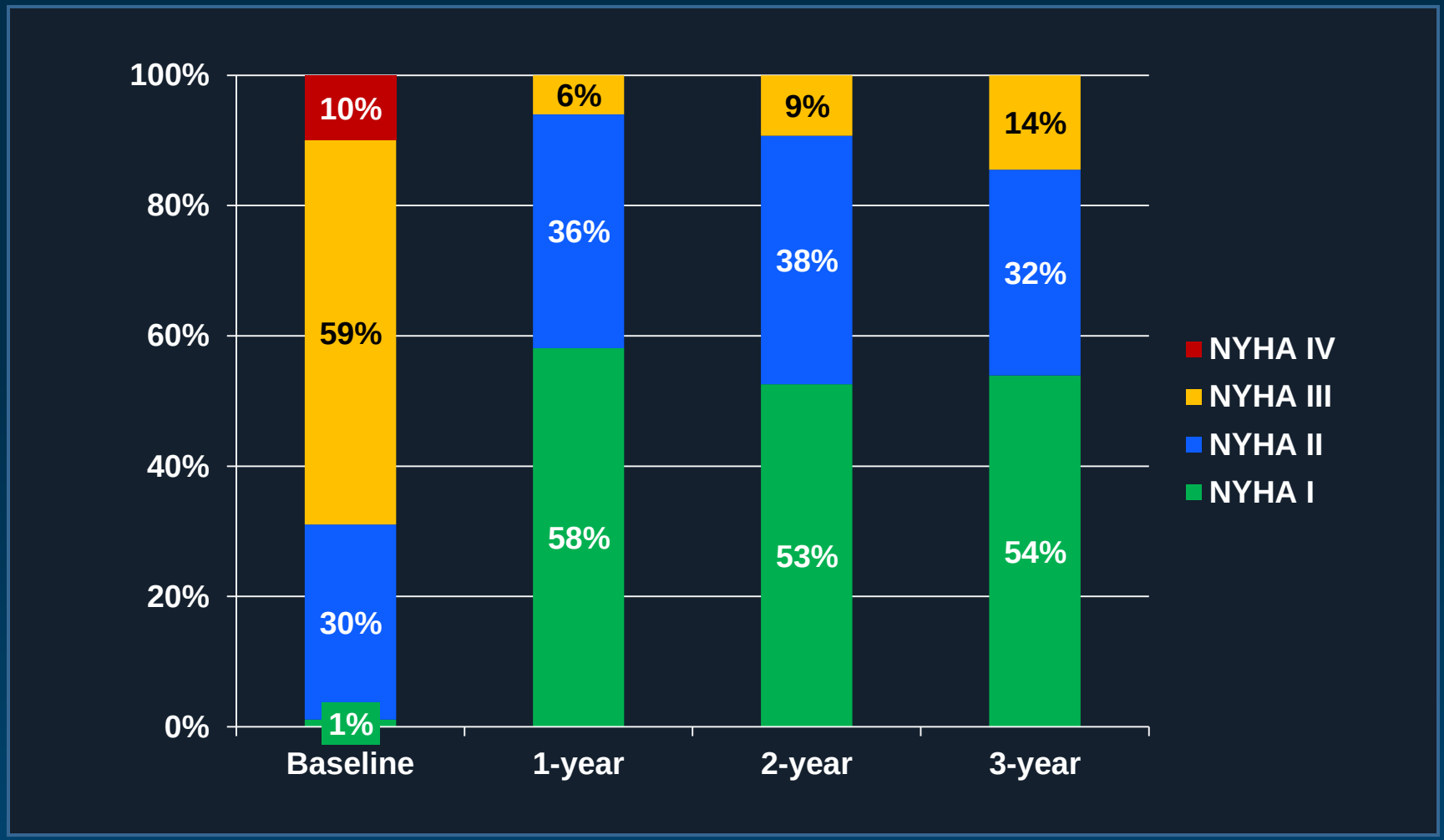
Long-term TAVI

3 year Italian experience



Long-term TAVI

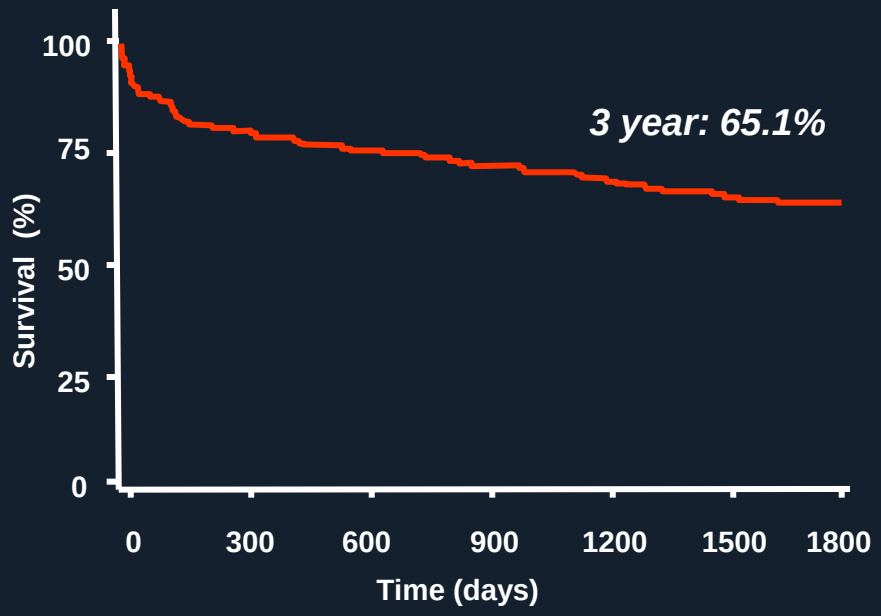
3 year Italian experience

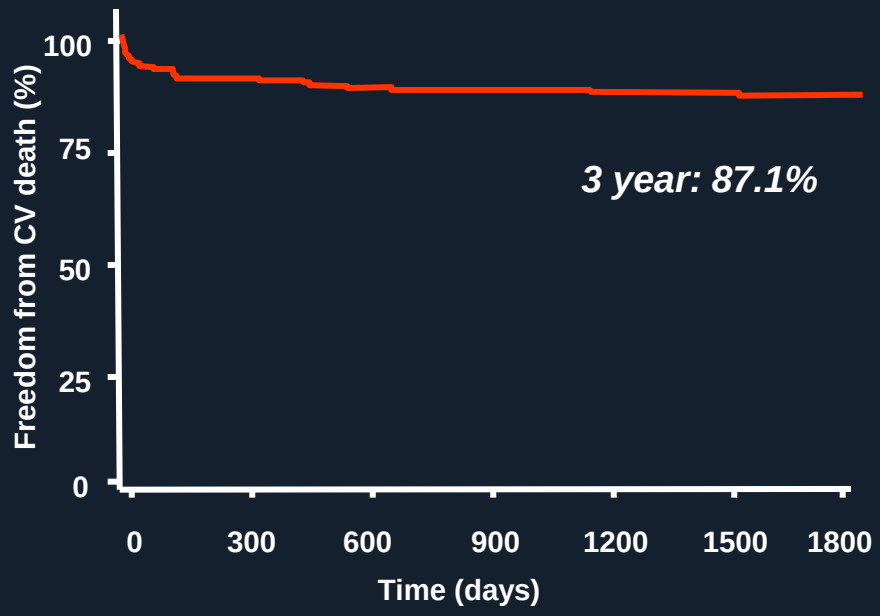


Italian TAVI Experience

3-year outcomes

- *181 patients enrolled with at least 3-year follow-up*
- *VARC definitions*
- *Less than 2% lost at follow-up*





New Data

The German Aortic Valve Registry (GARY)

Between Jan 1st 2011 and Dec 31st 2011

28% TAVI

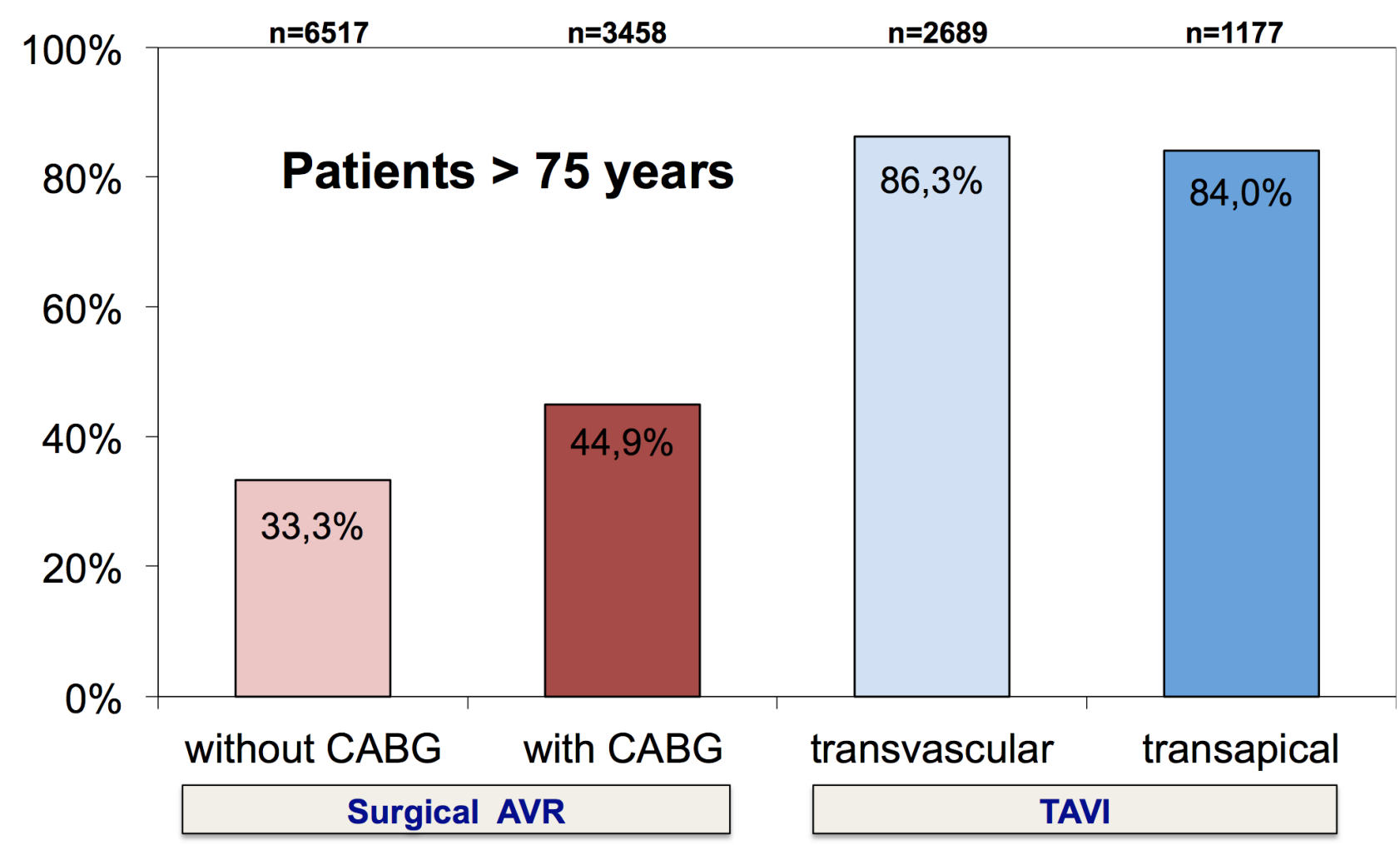
Cardiac surgery units
93

Cardiology units
59

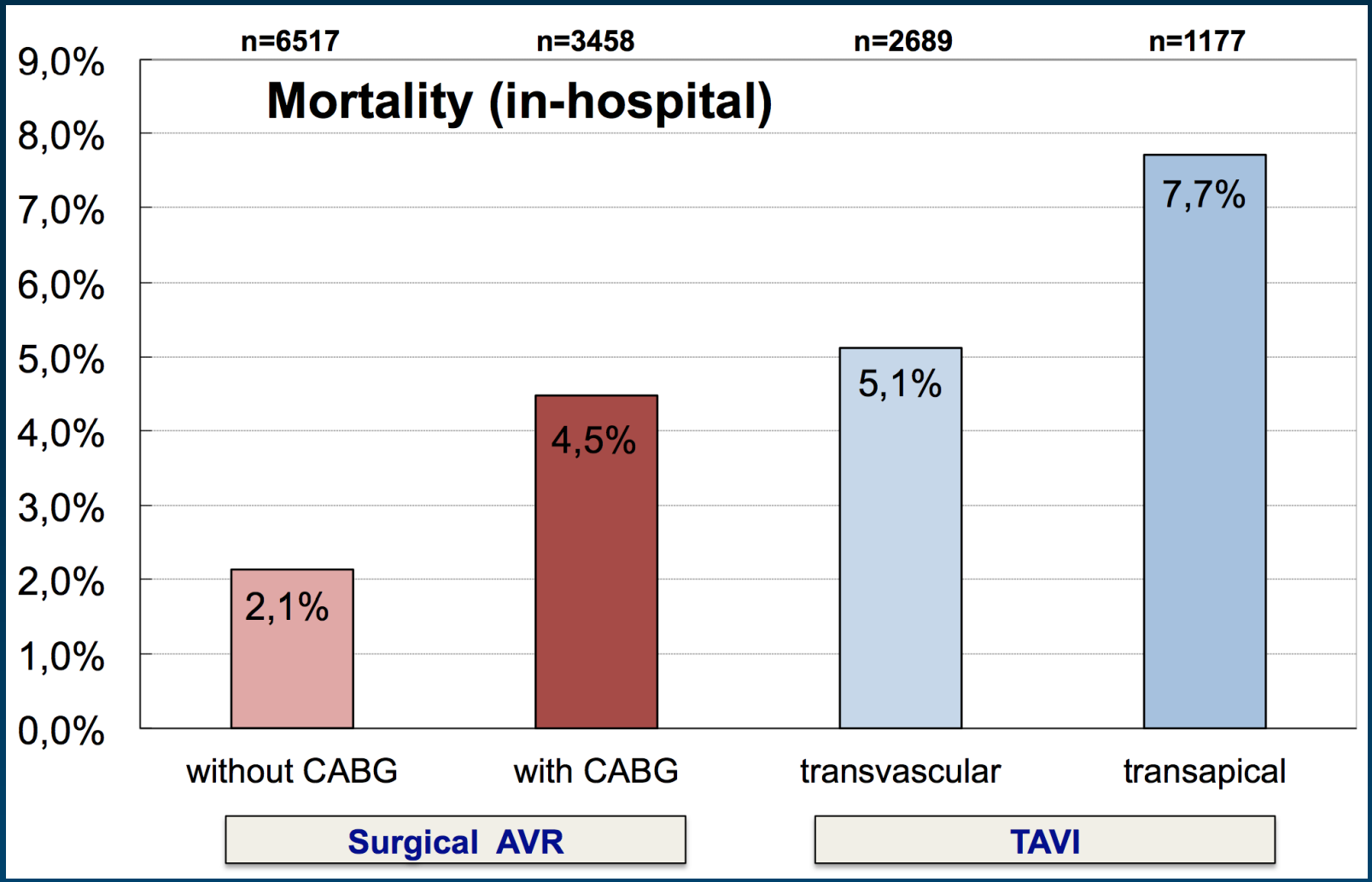
Patient (n)
13.860

sAVR only	sAVR + CABG	TAVI tansvasc.	TAVI Transapical
6.523	3.462	2.694	1.181

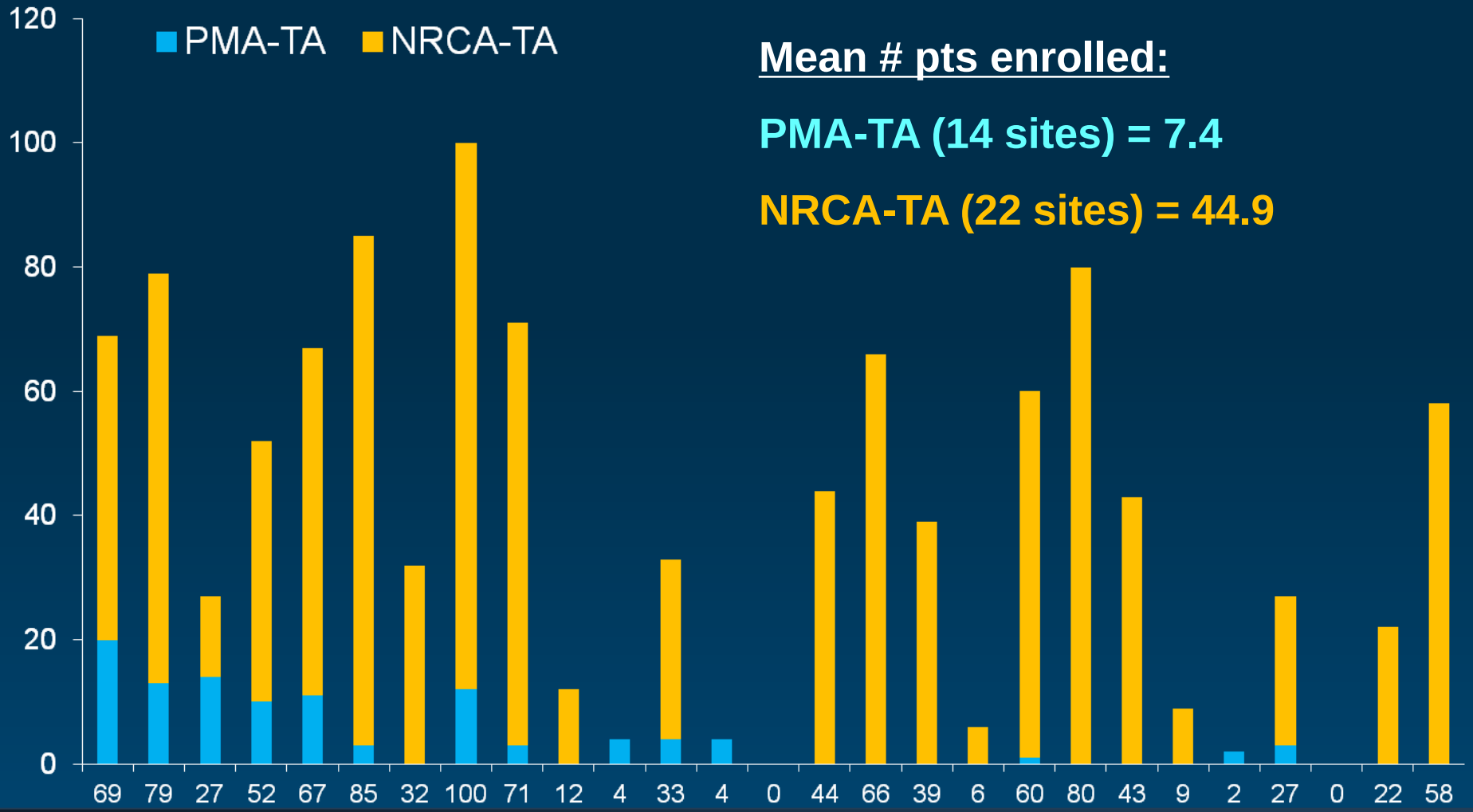
The German Aortic Valve Registry
Baseline Characteristics



The German Aortic Valve Registry
In-Hospital Outcomes



Transapical Enrollment per Site

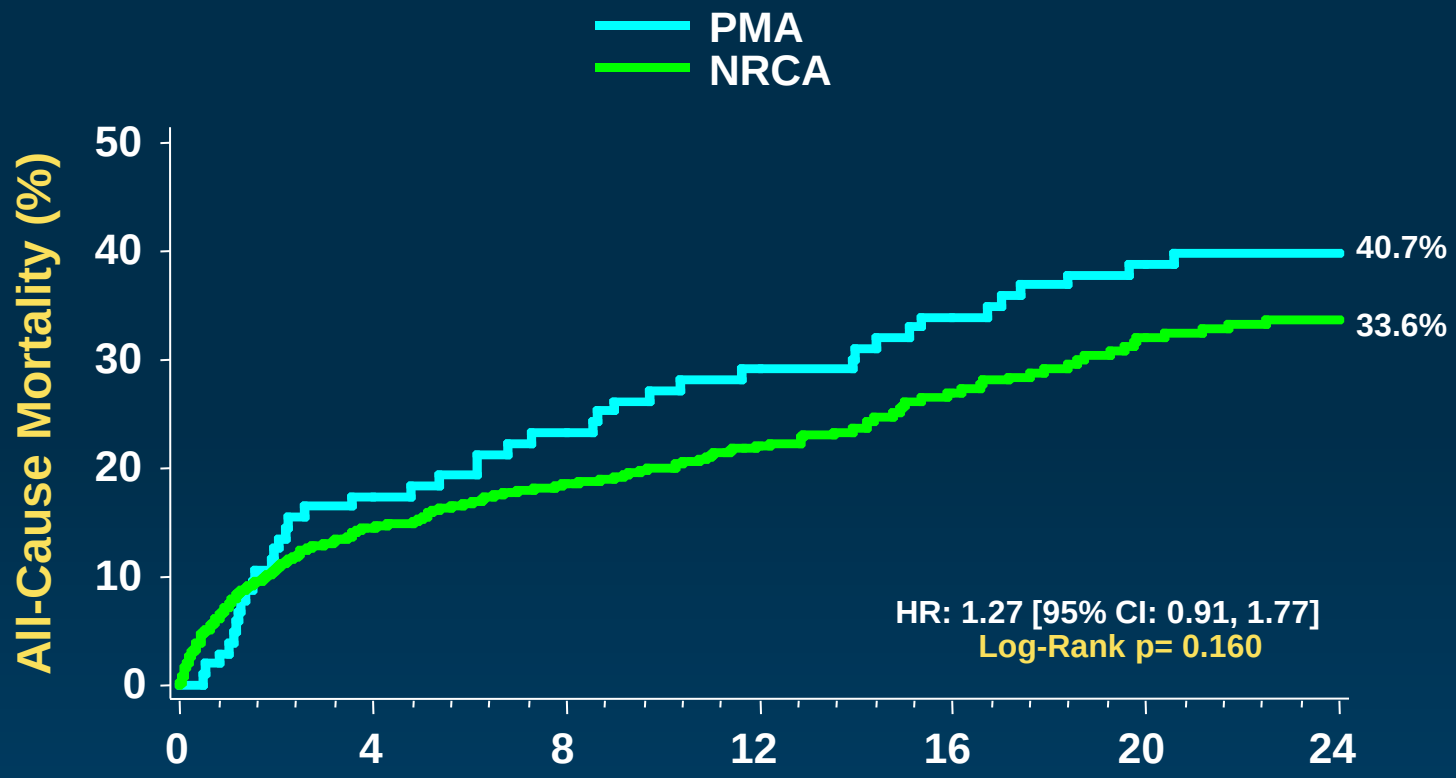


Mean # pts enrolled:

PMA-TA (14 sites) = 7.4

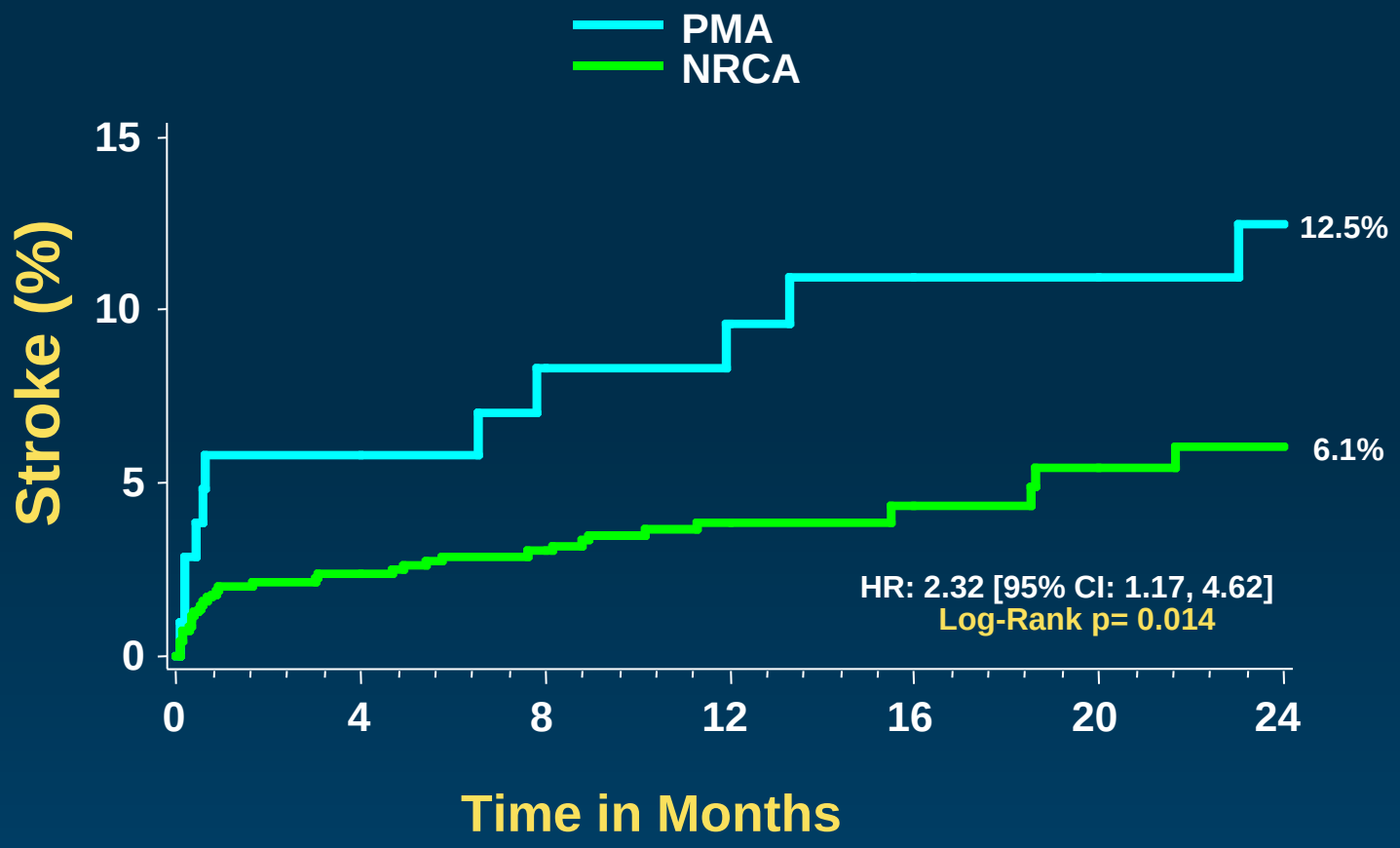
NRCA-TA (22 sites) = 44.9

2 Year Mortality following TA-TAVR



Number at risk							
PMA	104	85	79	73	68	63	60
NRCA	988	808	638	456	194	171	116

2-year Stroke following TA-TAVR



Number at risk							
PMA	104	80	73	68	63	59	55
NRCA	988	789	620	439	187	164	109

ADVANCE | Procedural Results

Procedural Parameters	
N=996	**%**
Successful vascular access, delivery & deployment of device & successful retrieval of the delivery system	97.5
Correct position of the device in the proper anatomical location	98.7
Mean aortic valve gradient < 20 mmHg*	96.2
Aortic Regurgitation ≤ 2* measured by angiography	97.9
Only one valve implanted in the proper anatomical location	96.0

Major Complications, Valve Related	
N=996	**%**
Annulus Rupture	0.0
Valve Embolization	0.2
Conversion to open AVR	0.1
Coronary Compromised	0.1

ADVANCE | Primary Endpoint

Endpoint	1 Month	1 Year
N=996	%*	%*
MACCE	8.0	21.2
All-cause Mortality	4.5	17.9
Myocardial Infarction	0.2	0.9
Emergent Cardiac Surgery or Percutaneous Re-intervention	1.3	1.6
Stroke	3.0	4.5
Minor	1.8	2.3
Major	1.2	2.2

*Kaplan-Meier Estimates

PCR london valves

ADVANCE | Additional VARC I Endpoints

Endpoint	1 Month	1 Year
N=996	%*	%*
Cardiovascular Mortality	3.4	11.7
Bleeding	29.0	32.0
Life Threatening or Disabling Bleeding	4.0	4.9
Major Bleeding	9.7	11.2
Minor Bleeding	17.4	19.3
Vascular Complications	20.7	21.9
Major	10.9	12.0
Minor	10.2	10.3
Acute Kidney Injury—Stage III†	0.4	0.6
New Pacemaker Implantation	26.3	29.2

*Kaplan-Meier Estimates

†New AKI that occurred outside of the 72 hr post-TAVI window are included

PCR EAPCI EUROPEAN SOCIETY OF CARDIOLOGY® KING'S HEALTH PARTNERS

TAVI - Conduction Distrubances

Up to 50% of TAVI patients develop conduction disturbances

- ✓ Complete AV block (4-11 % Edwards, 15-38% CoreValve)
- ✓ Left Bundle Branch Block LBBB (about 1/3)
- ✓ AV conduction disturbances (Variable percentage)

Para-valvular leak after TAVI

Impact on outcomes

Valvular Heart Disease

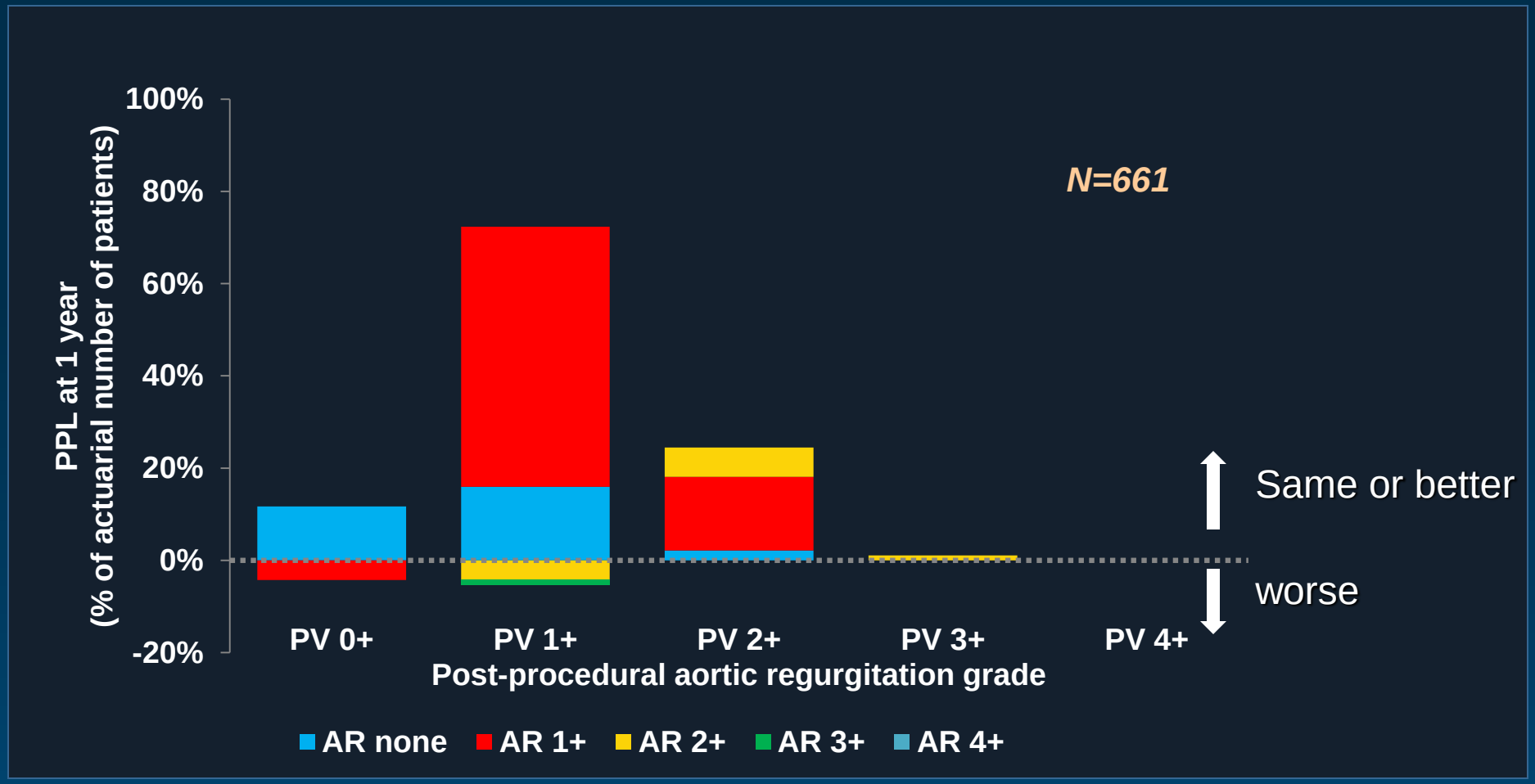
Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Corrado Tamburino, MD, PhD; Davide Capodanno, MD; Angelo Ramondo, MD; Anna Sonia Petronio, MD; Federica Ettori, MD; Gennaro Santoro, MD; Silvio Klugmann, MD; Francesco Bedogni, MD; Francesco Maisano, MD; Antonio Marzocchi, MD; Arnaldo Poli, MD; David Antoniucci, MD; Massimo Napodano, MD; Marco De Carlo, MD, PhD; Claudia Fiorina, MD; Gian Paolo Ussia, MD

Tamburino et al. Circulation 2011

Para-valvular leak after TAVI

Impact on outcomes



Para-valvular leak after TAVI

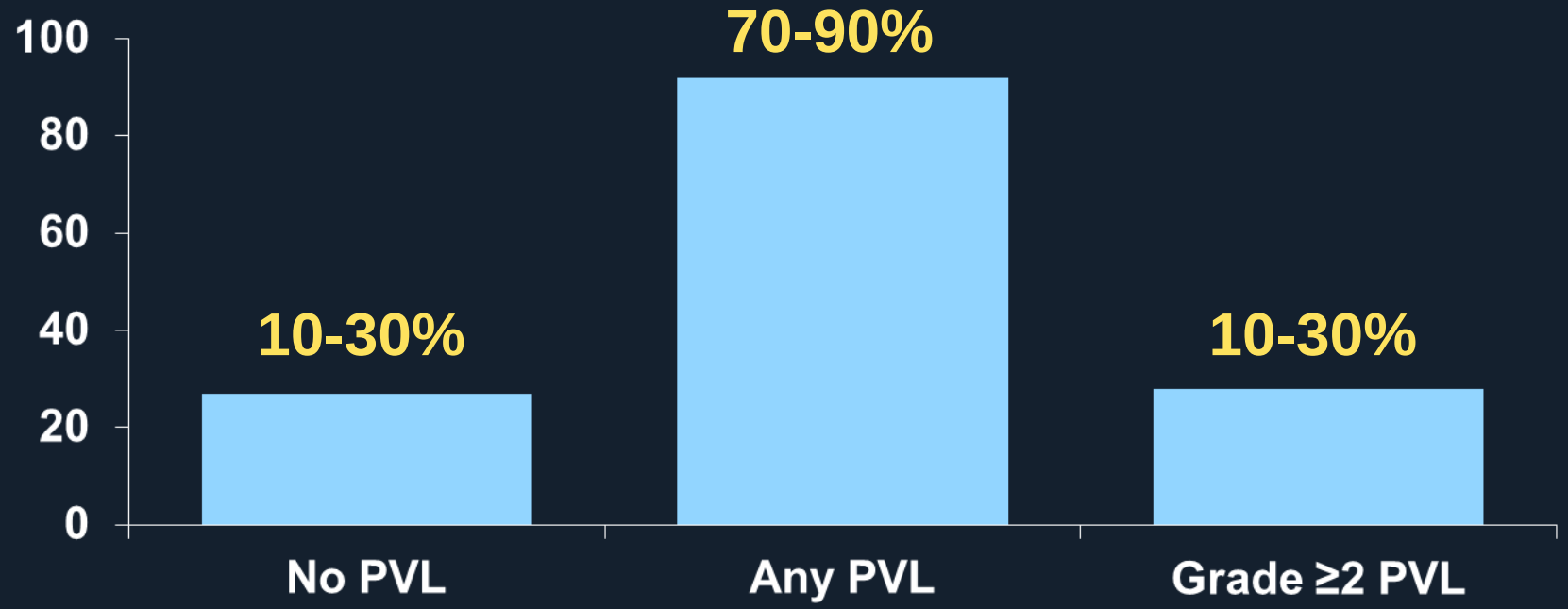
Impact on outcomes

Overall mortality	Hazard ratio	95% LCL	95% UCL	p value
Intraprocedural stroke	15.76	3.27	75.90	0.001
Pre-procedural mitral regurgitation 3+ or 4+	4.62	1.66	12.87	0.003
Systolic pulmonary artery pressure > 60 mmHg	3.21	1.19	8.71	0.02
Prior acute pulmonary edema	2.75	1.32	5.72	0.007
Diabetes mellitus	2.45	1.19	5.07	0.02
Early mortality	**Odds ratio**	**95% LCL**	**95% UCL**	**p value**
Conversion to open heart surgery	38.68	2.86	522.59	0.006
Cardiac tamponade	10.97	1.59	75.61	0.02
Major access site complications	8.47	1.67	42.82	0.01
Left ventricular ejection fraction < 40%	3.51	1.62	7.62	0.002
Prior balloon aortic valvuloplasty	2.87	1.24	6.65	0.01
Diabetes mellitus	2.66	1.26	5.65	0.01
Late mortality	**Hazard ratio**	**95% LCL**	**95% UCL**	**p value**
Prior stroke	5.468	1.47	20.39	0.01
Post-procedural paravalvular leak ≥2+	3.785	1.57	9.10	0.003
Prior acute pulmonary edema	2.696	1.09	6.68	0.03
Chronic kidney disease	2.532	1.01	6.35	0.048

Tamburino et al. Circulation 2011

Para-valvular leak after TAVI

Incidence, ES & CRS



Rajan et al. Catheter Cardiovasc Interv 2009

Jilaihawi et al. Eur Heat J 2009

Moss et al. JACC Cardiovasc Imag 2008

Clavel et al. J Am Coll Cardiol 2009

Himbert et al. J Am Coll Cardiol 2008

Detaint et al. JACC Cardiovasc Interv 2009

Stroke incidence from TAVI Registries

Table 2 Stroke After TAVR According to Access Site and Device Type: Major Published Data

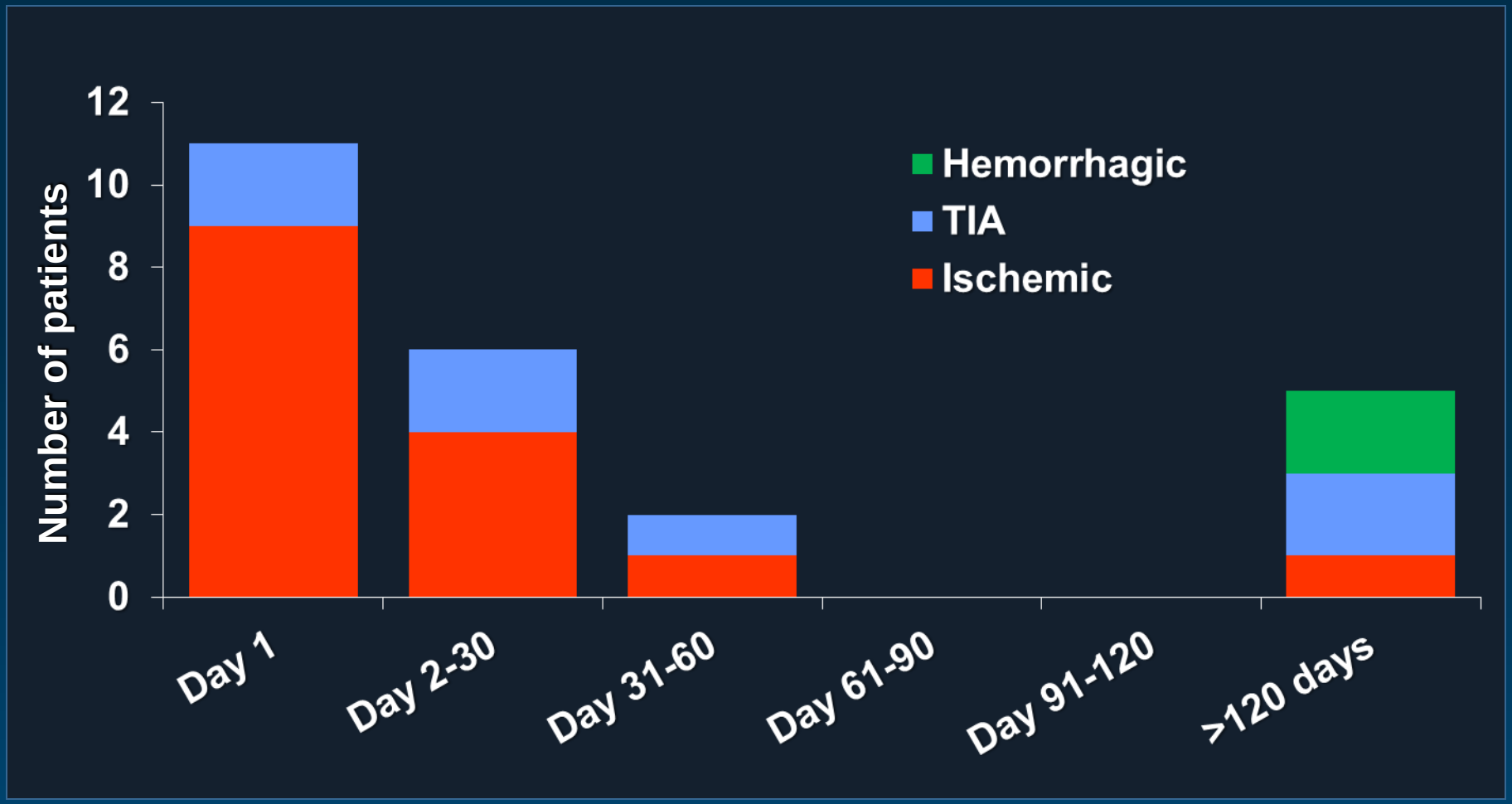
First Author (Ref. #)	Type of Study	n	STS	EuroSCORE	Follow-Up, Months	Death		Stroke	
						30-day	1-yr	30-day	1-yr
Edwards Sapien: TF									
Lefevre et al. (25)	Registry	61	11.3%	25.7%	12	8.2%	21.3%	3.3%	7.0%
Eltchaninoff et al. (21)	Registry	95	17.4%	25.6%	1	8.4%	—	4.2%	—
Himbert et al. (24)	Registry	51	15.0%	25.0%	12	8.0%*	19.0%	6.0%*	—
Rodes-Cabau et al. (22)	Registry	113	9.0%	—	24	9.5%	25.0%	3.0%	—
Thomas et al. (23)	Registry	463	—	14.5%	1	6.3%	18.9%	2.4%	—
Leon et al. (1)	RCT	179	11.2%	26.4%	12	5.0%	30.7%	6.7%†	10.6%†
Edwards Sapien: TA									
Walther et al. (26)								2.0%	5.0%
Svensson et al. (27)								5.0%	—
Lefevre et al. (25)								1.5%	10.3%
Eltchaninoff et al. (21)								2.8%	—
Himbert et al. (24)								0%*	—
Rodes-Cabau et al. (22)								1.7%	—
Thomas et al. (23)	Registry	575	—	16.3%	1	10.3%	27.9%‡	2.6%	—
Medtronic CoreValve: TF									
Grube et al. (29)	Registry	136	—	23.1%	12	12.5%	29.8%	4.4%	7.1%‡
Piazza et al. (31)	Registry	646	—	23.1%	1	8.0%	—	1.9%	—
Eltchaninoff et al. (21)	Registry	66	21.3%	24.7%	1	15.1%	—	4.5%	—
Petronio et al. (30)	Registry	460	—	19.4%	6	6.1%	11.4%	1.7%	—
Medtronic CoreValve: SC									
Eltchaninoff et al. (21)	Registry	12	21.0%	24.6%	1	8.3%	—	0%	—
Petronio et al. (30)	Registry	54	—	25.3%	6	0%	6.7%	1.9%	—
Zahn et al. (32)	Registry	697	—	20.5%	1	12.4%	—	2.8%*	—

30-day average → 2,9%
12-month average → 8,0%

Daneault et al. JACC 2011

Stroke after TAVI

High-Risk Period for CVE



Tay et al, JACC Cardiovasc Interv 2011

New onset AF after TAVI

A potential source of CVE after TAVI?

EXPEDITED PUBLICATIONS

Incidence, Predictive Factors, and Prognostic Value of New-Onset Atrial Fibrillation Following Transcatheter Aortic Valve Implantation

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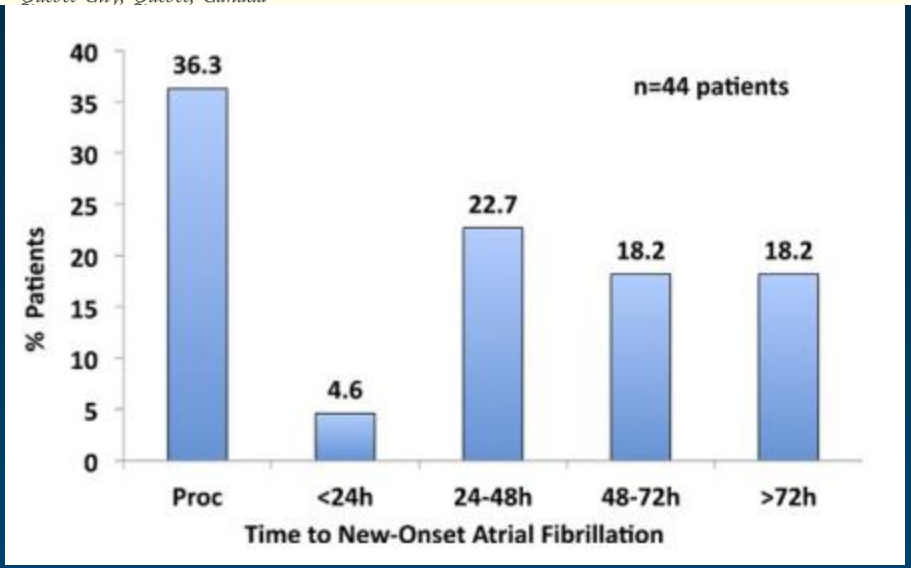
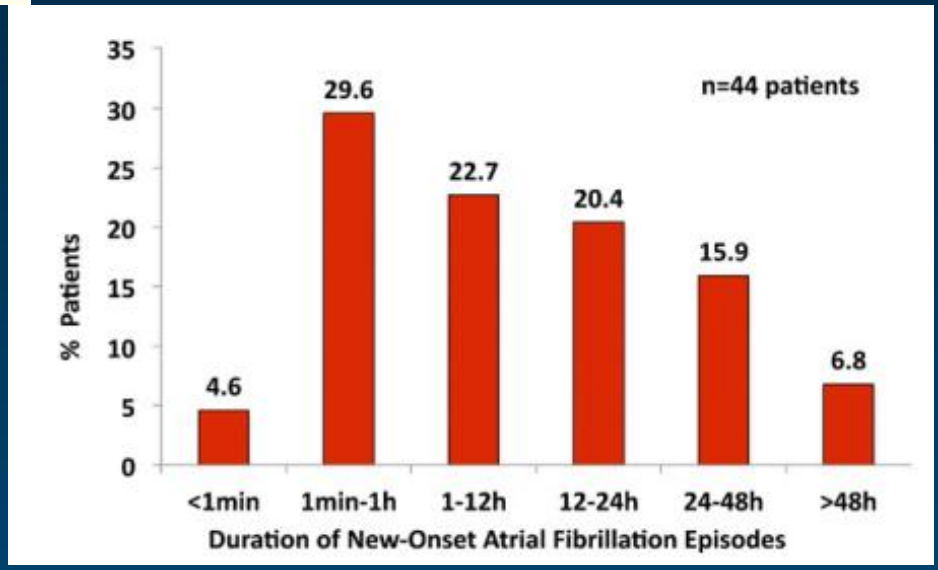
Quebec City, Quebec, Canada





Ferrarotto Hospital
University of Catania

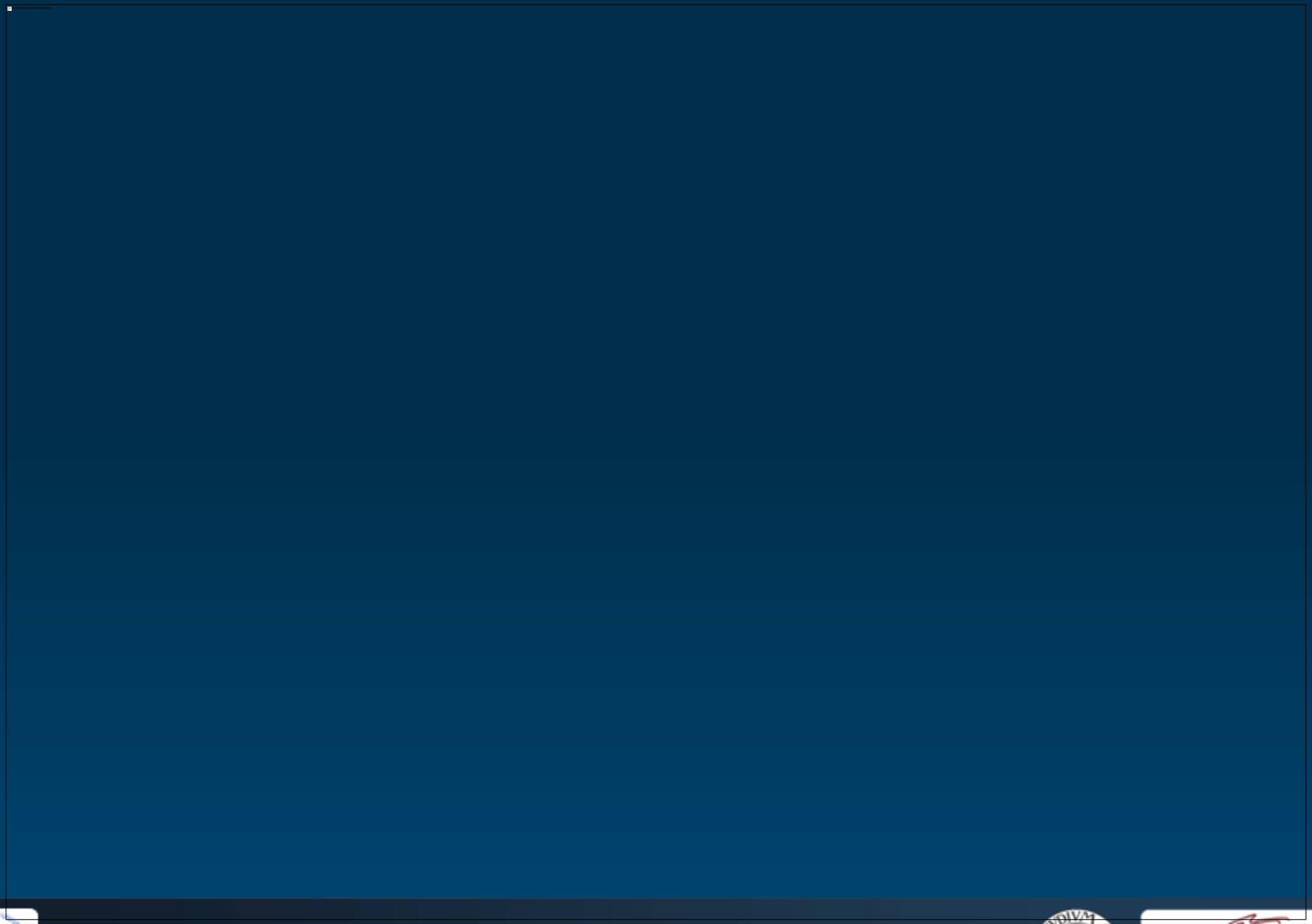
Amat-Santos et al.JACC 2012

OBSERVANT matched population

Baseline Clinical Characteristics	SAVR N=650 n (%)	TAVI N=650 n (%)	P value
Valve migration	-	15 (2.3)	-
Renal failure	64 (10.9)	36 (6.1)	0,004
Residual aortic regurgitation			
mild	44 (7.5)	239 (40.8)	
moderate	9 (1.5)	53 (9.1)	0,000
severe	3 (0.5)	4 (0.7)	
Cardiac tamponade	25 (3.9)	26 (4.1)	0,886
Permanent A-V block	23 (3.6)	98 (15.5)	0,000
AMI	5 (0.8)	3 (0.5)	0,479
Major vascular damage	3 (0.5)	48 (7.9)	0,000
Stroke	14 (2.2)	8 (1.3)	0,180
Infection			
wound	10 (1.6)	6 (1.0)	
lung or other organs	24 (3.9)	29 (4.7)	0,191
sepsis	11 (1.8)	4 (0.6)	
Emergency PCI	0 (0.0)	6 (0.9)	-
Transfusions: number of units	3.6±3.6	2.3±2.2	0,002
Mean gradient after procedure (mmHg)	13.6±6.7	10.3±5.6	0,000
ICU stay (days)	3.8±7.7	3.2±4.7	0,077
Hospital stay (days)	12.6±1.34	8.8±8.5	0,000
Postprocedural mortality (30 days)	24 (3.8)	20 (3.2)	0,546
Log EuroScore	10.2±9.2	9.5±7.1	0,104

New Routes

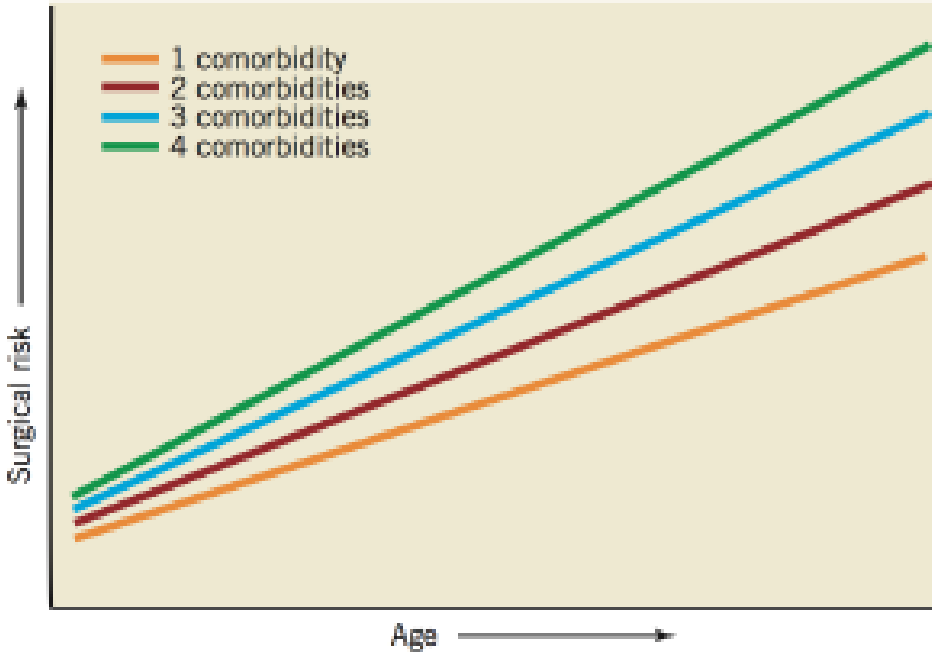
TRANSAORTIC APPROACH



Expanding indications to ideal (i.e. intermediate risk) patient?

How can we define the intermediate risk?

SURTAVI model Rationale



Low risk

- ≥70 years and <2 risk factors
- ≥75 years and no risk factors

Intermediate risk

- ≥70 years and 2 or 3 risk factors
- ≥75 years and 1 or 2 risk factors
- ≥80 years and ≤1 risk factor

High risk

- ≥70 years and >3 risk factors
- ≥75 years and >2 risk factors
- ≥80 years and >1 risk factor

Van Mieghem N et al. EuroIntervention 2012;8:258-66

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EXPEDITED PUBLICATION

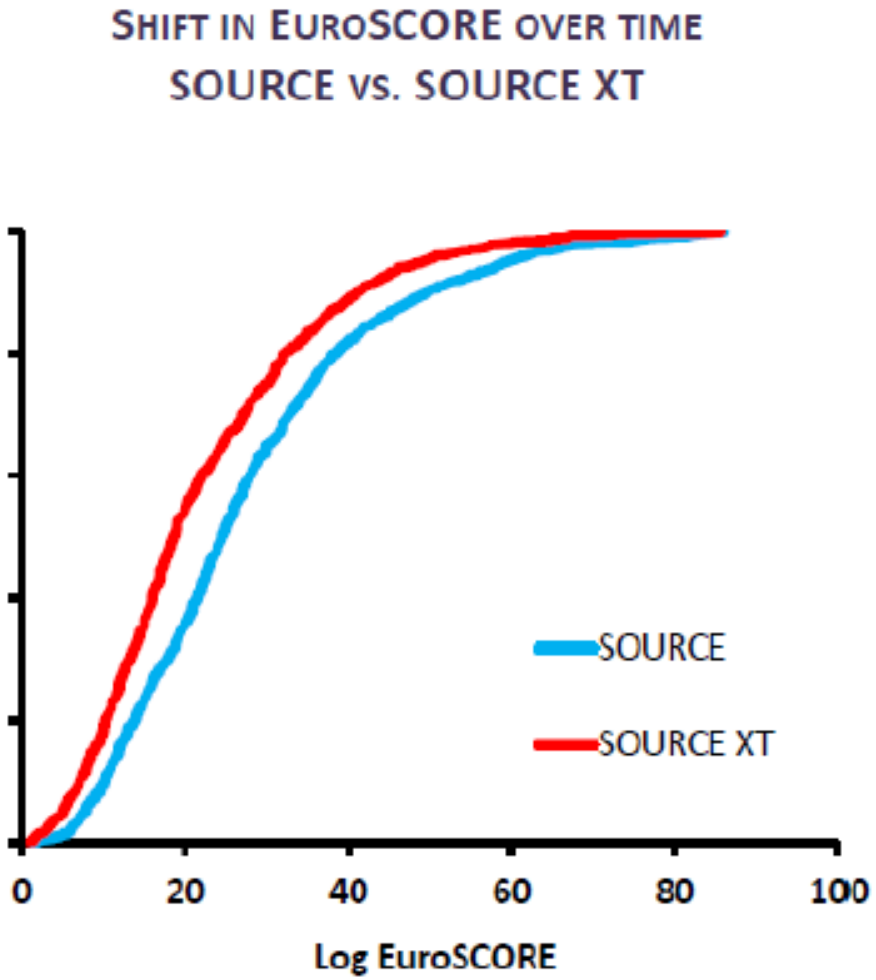
Improvements in Transcatheter Aortic Valve Implantation Outcomes in Lower Surgical Risk Patients

A Glimpse Into the Future

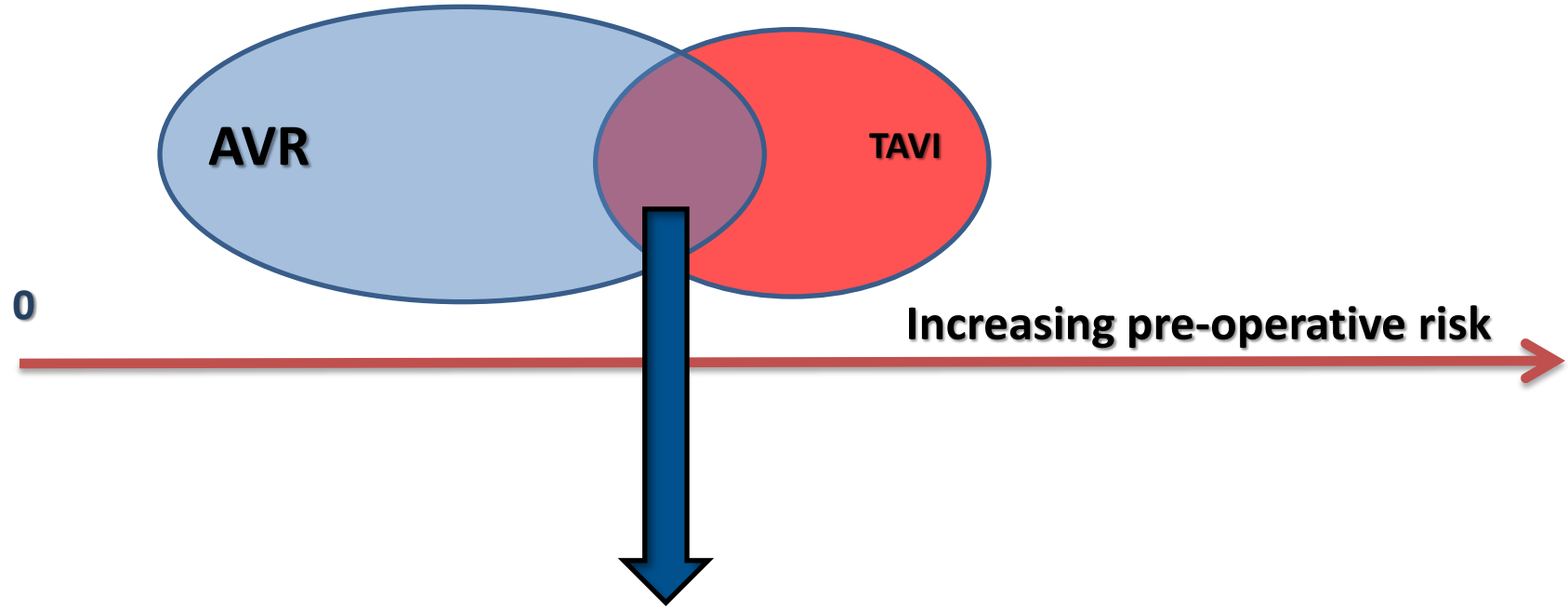
Table 1 Baseline Characteristics for the Overall Cohort and Quartiles 1 to 4

	Overall Cohort	Q1	Q2	Q3	Q4	p Value
Age, yrs	80.3 ± 7.1	81.11 ± 7.00	81.1 ± 7.2	80.19 ± 6.20	78.9 ± 7.9	0.09
Female	265 (63)	58 (55.2)	63 (60)	76 (72.4)	68 (64.8)	0.065
Logistic EuroSCORE, %	20.17 ± 13.00	25.44 ± 16.0	18.9 ± 10.0	18.3 ± 11.0	17.8 ± 12.0	<0.001*
STS-PROM, %	6.1 ± 4.1	7.13 ± 5.4	6.2 ± 3.5	5.8 ± 3.9	4.8 ± 2.6	<0.001†
NYHA functional class III or IV	406 (96.7)	104 (99)	99 (94.3)	101 (96.2)	102 (97.2)	0.27

Change in EuroSCORE over time

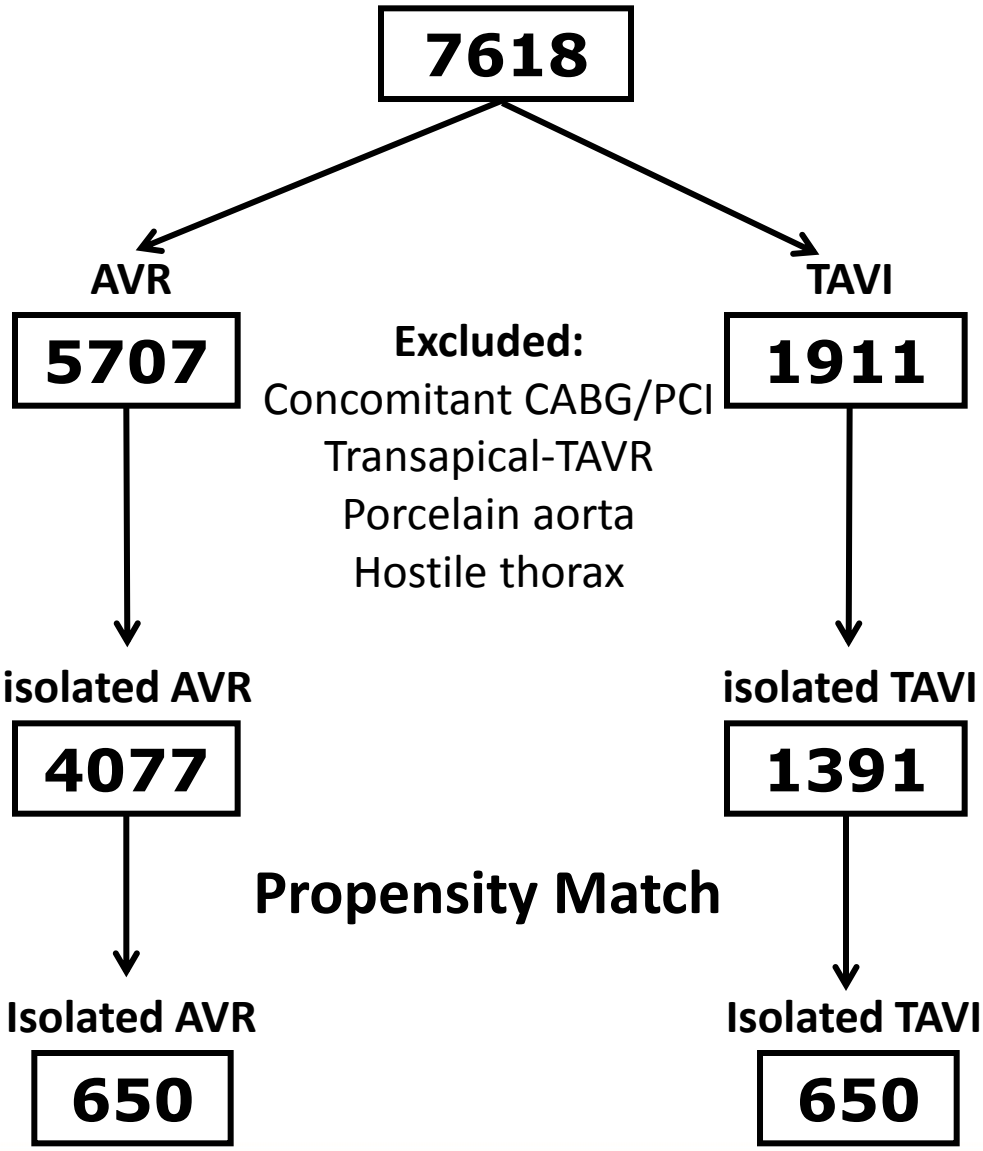


Propensity Approach



The purple area represents the subgroup of patients potentially eligible to both procedures

OBSERVANT Population



OBSERVANT matched population

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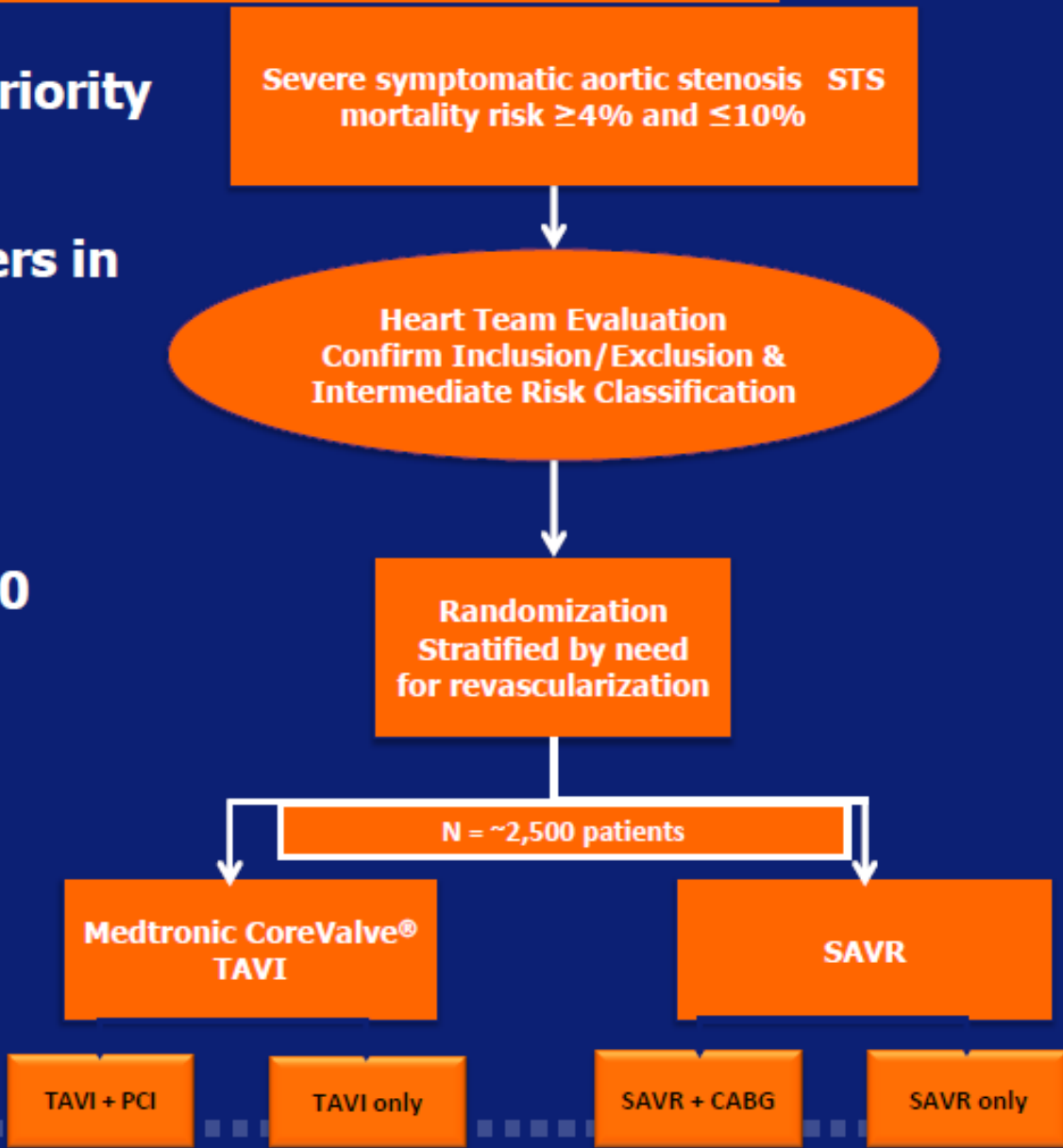
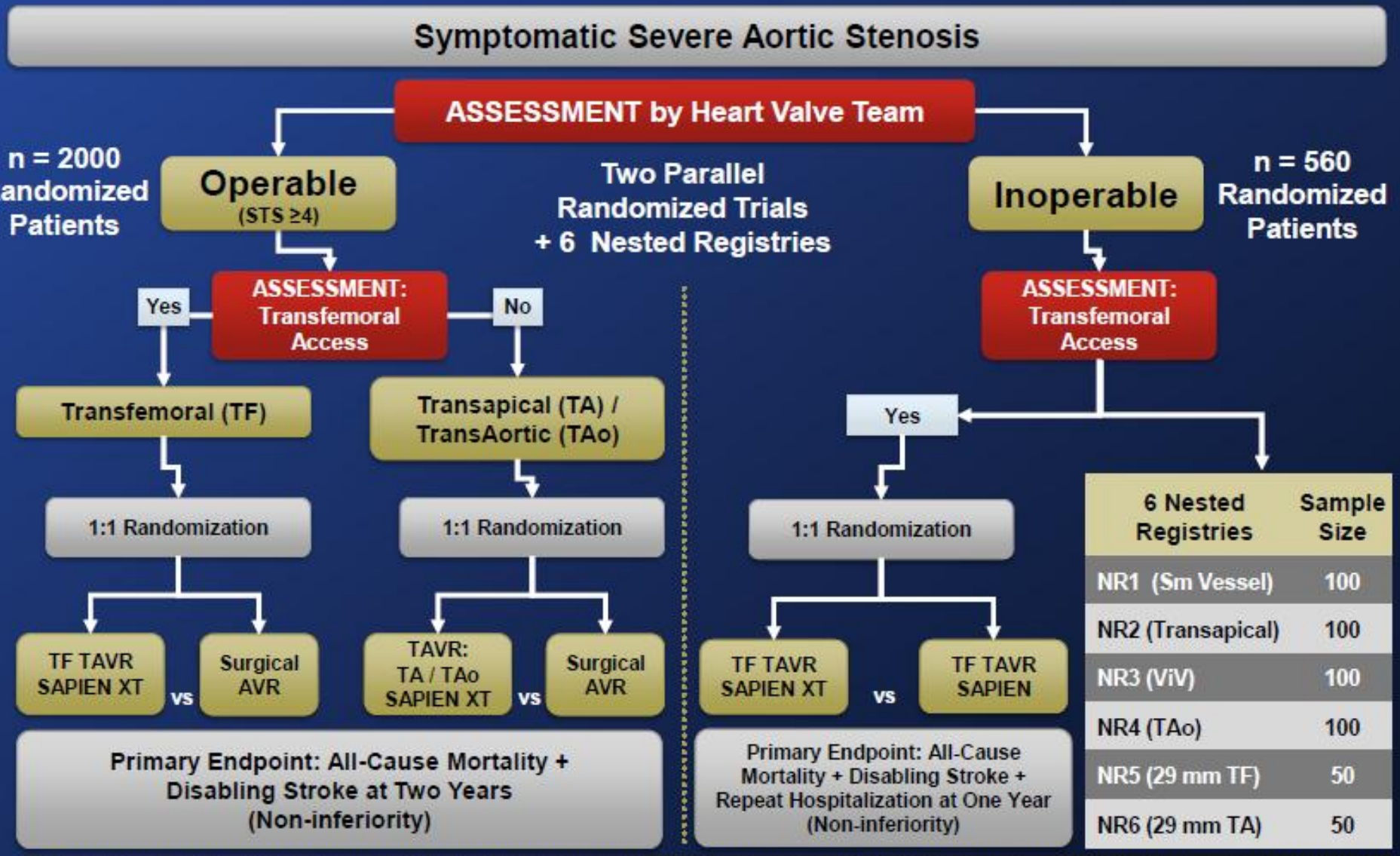
CoreValve® SURTAVI Trial

Erasmus MC

- Randomized 1:1, non-inferiority study
- Multicenter up to 75 centers in
  - Europe
  - Canada
  - United States
- Sample size: Approx. 2,500
- 5-year FU



The PARTNER II Trial
Study Design



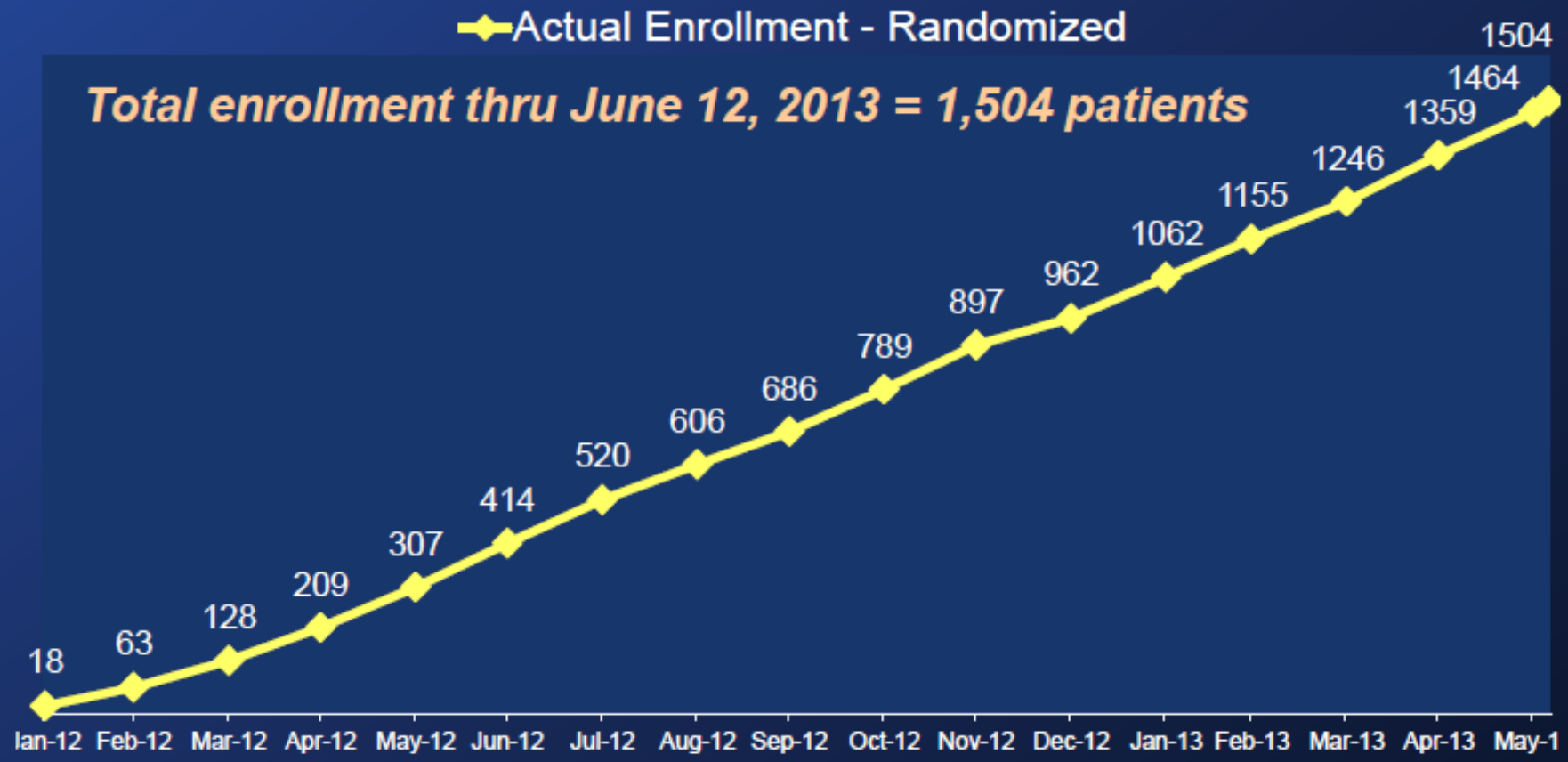
6 Nested Registries	Sample Size
NR1 (Sm Vessel)	100
NR2 (Transapical)	100
NR3 (ViV)	100
NR4 (TAo)	100
NR5 (29 mm TF)	50
NR6 (29 mm TA)	50

PARTNER IIA Intermediate Risk

Enrollment thru June 12, 2013

THE PARTNER TRIAL

Actual Enrollment - Randomized



Leon MB, TVT 2013

Take Home Message

- ✓ TAVI procedure showed over ten years to be a safe and reliable technique
- ✓ Both self expandable and balloon expandable device show the same efficacy result in short and medium term follow-up
- ✓ New randomized controlled trials are searching to expand indication of TAVI
- ✓ New device iteration will certainly improve current outcomes reducing all potential drawbacks and complications