

AORTIC VALVE DISEASE

RANDOMISED TRIALS

COMPARING

TAVI WITH SAVR



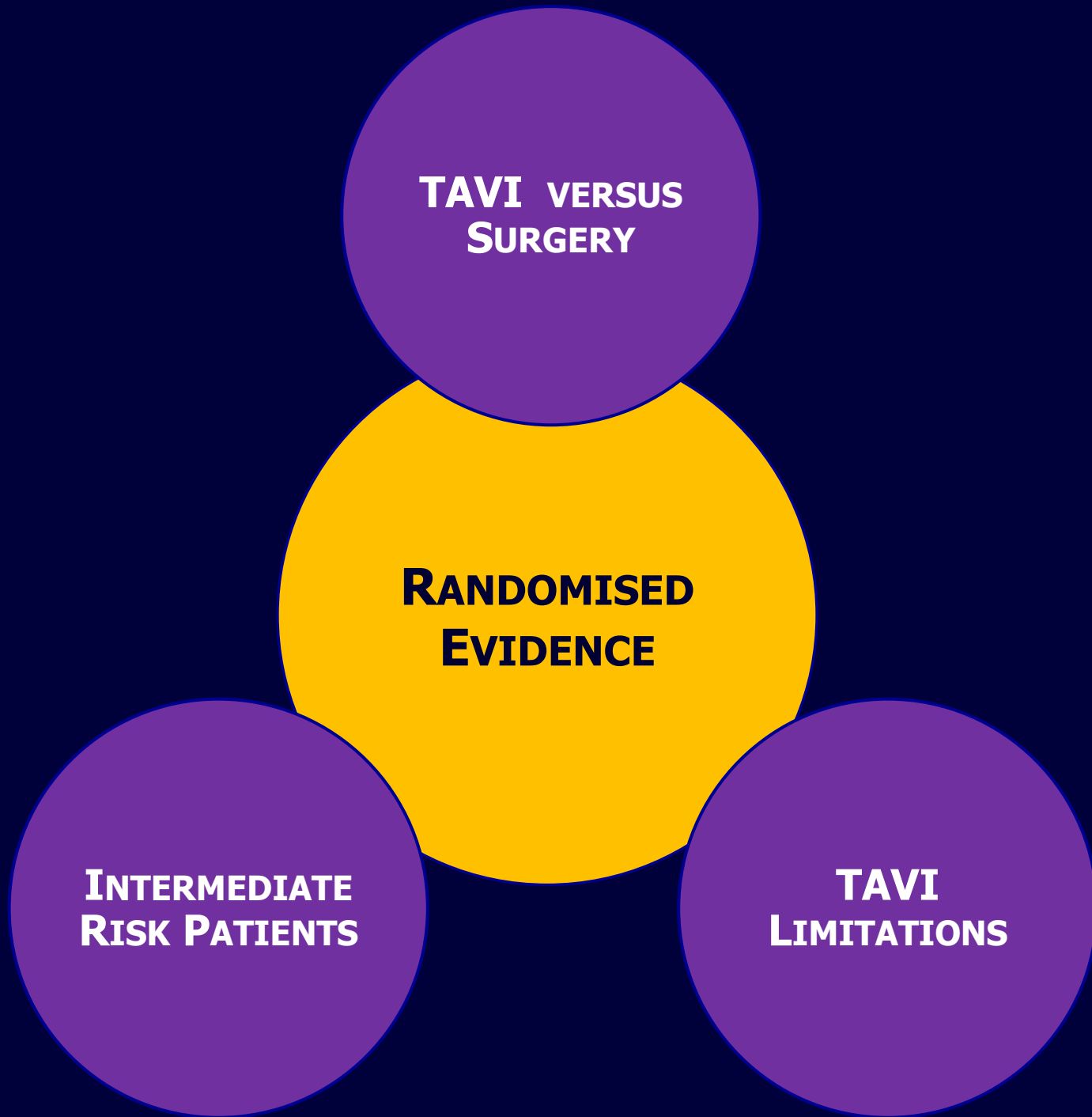
STEPHAN WINDECKER



DEPARTMENT OF CARDIOLOGY

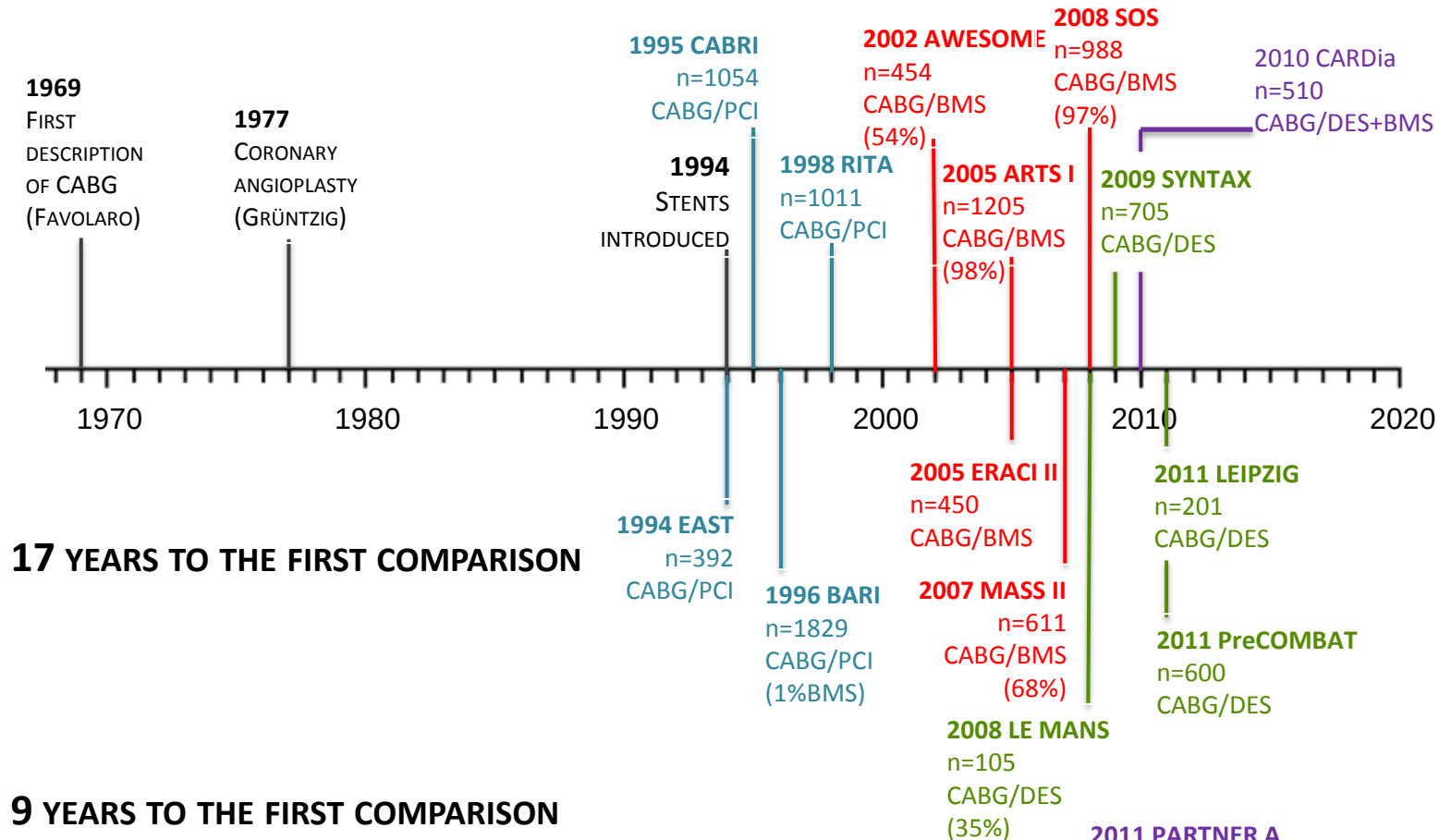
SWISS CARDIOVASCULAR CENTER AND CLINICAL TRIALS UNIT BERN

BERN UNIVERSITY HOSPITAL, SWITZERLAND



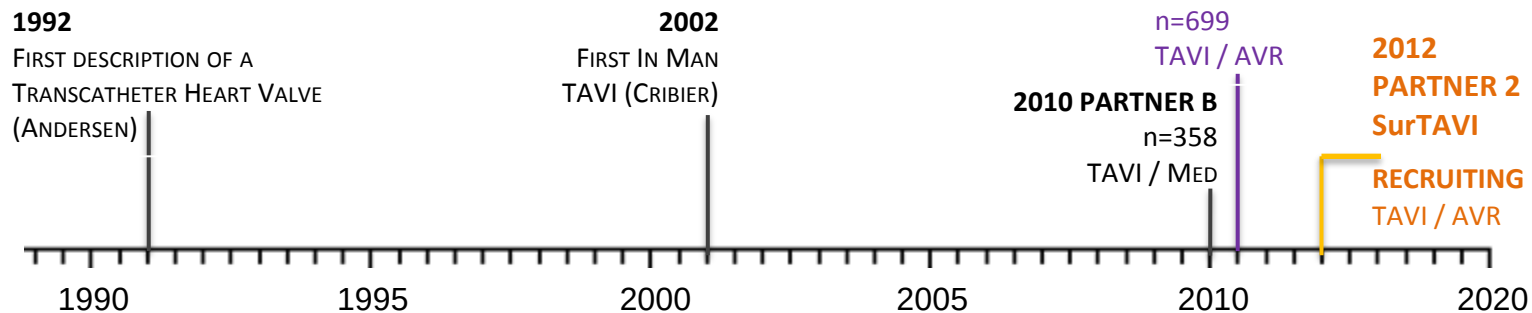
PCI vs. CABG AND TAVI vs. AVR

PCI vs. CABG



TAVI vs. AVR

9 YEARS TO THE FIRST COMPARISON



10 YEARS OF DEVELOPMENT

THE PROCEDURE

2012

ADAPTABLE TF ACCESS

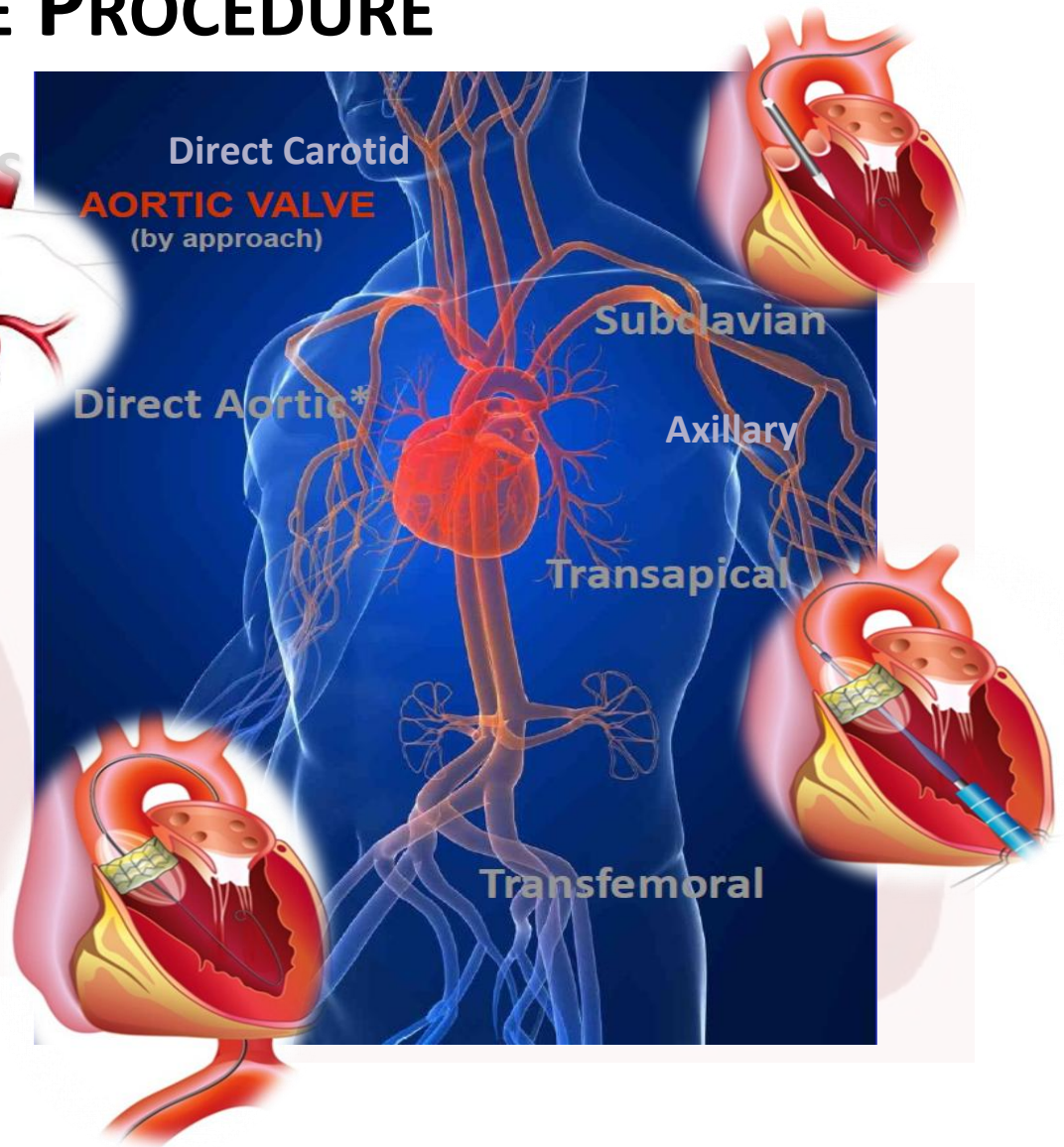
PATIENT - ADAPTED

ACCESS SITE SELECTION

ACCORDING TO

INDIVIDUAL ANATOMICAL

CHARACTERISTICS



Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium[†]

Martin B. Leon*, Nicolo Piazza, Eugenia Nikolsky, Eugene H. Blackstone, Donald E. Cutlip, Arie Pieter Kappetein, Mitchell W. Krucoff, Michael Mack, Roxana Mehran, Craig Miller, Marie-angèle Morel, John Petersen, Jeffrey J. Popma, Johanna J.M. Takkenberg, Alec Vahanian, Gerrit-Anne van Es, Pascal Vranckx, John G. Webb, Stephan Windecker,



European Heart Journal (2012) 33, 2403–2418
doi:10.1093/eurheartj/ehs255

FASTTRACK CLINICAL

Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document[†]

A. Pieter Kappetein*, Stuart J. Head, Philippe Généreux, Nicolo Piazza, Nicolas M. van Mieghem, Eugene H. Blackstone, Thomas G. Brott, David J. Cohen, Donald E. Cutlip, Gerrit-Anne van Es, Rebecca T. Hahn, Ajay J. Kirtane, Mitchell W. Krucoff, Susheel Kodali, Michael J. Mack, Roxana Mehran, Josep Rodés-Cabau, Pascal Vranckx, John G. Webb, Stephan Windecker, Patrick W. Serruys, and Martin B. Leon

PROCEDURAL SUCCESS

COREVALVE
EDWARDS SAPIEN



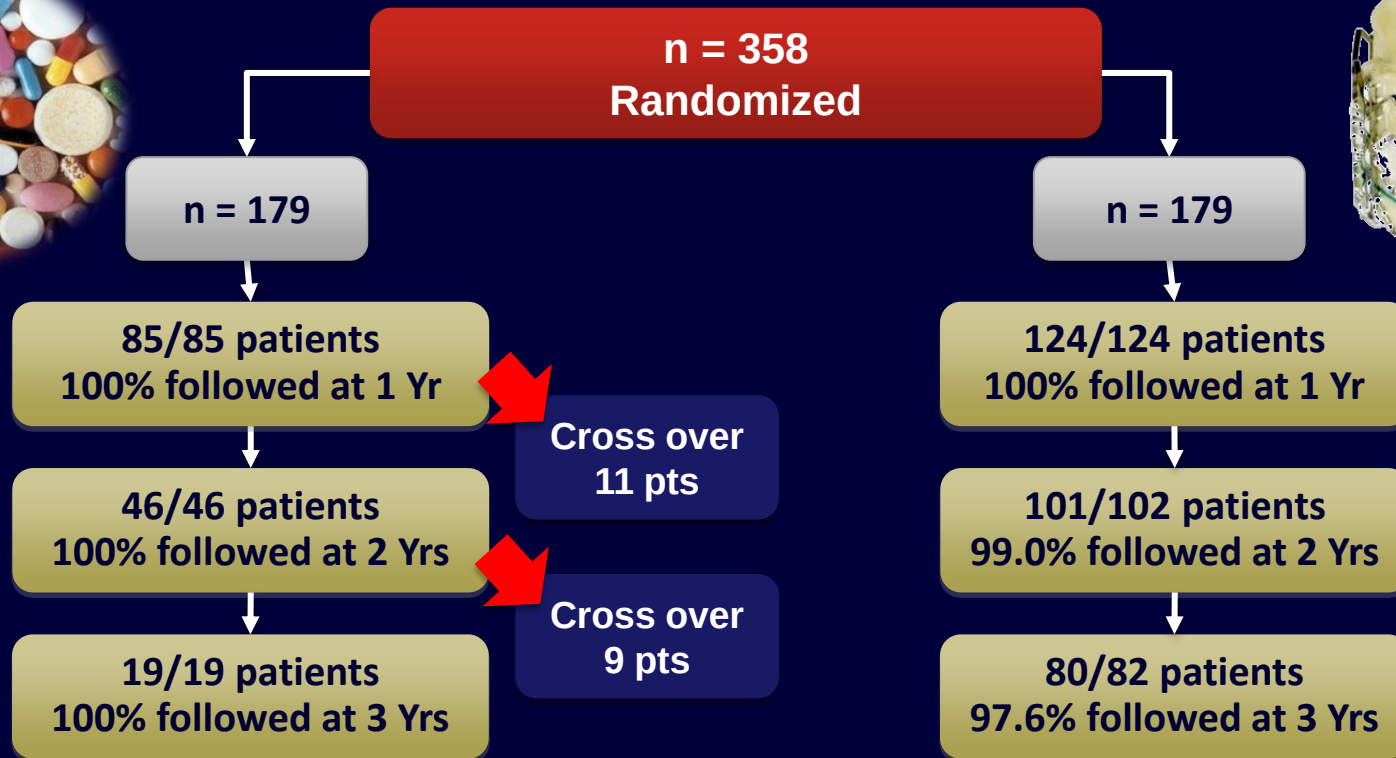
PARTNER B

Leon et al. *N Engl J Med* 2010 Oct 21;363(17):1597-607

INOPERABLE PATIENTS
WITH SYMPTOMATIC AS

MEDICAL TREATMENT

TAVI



TAVI vs. MEDICAL TREATMENT

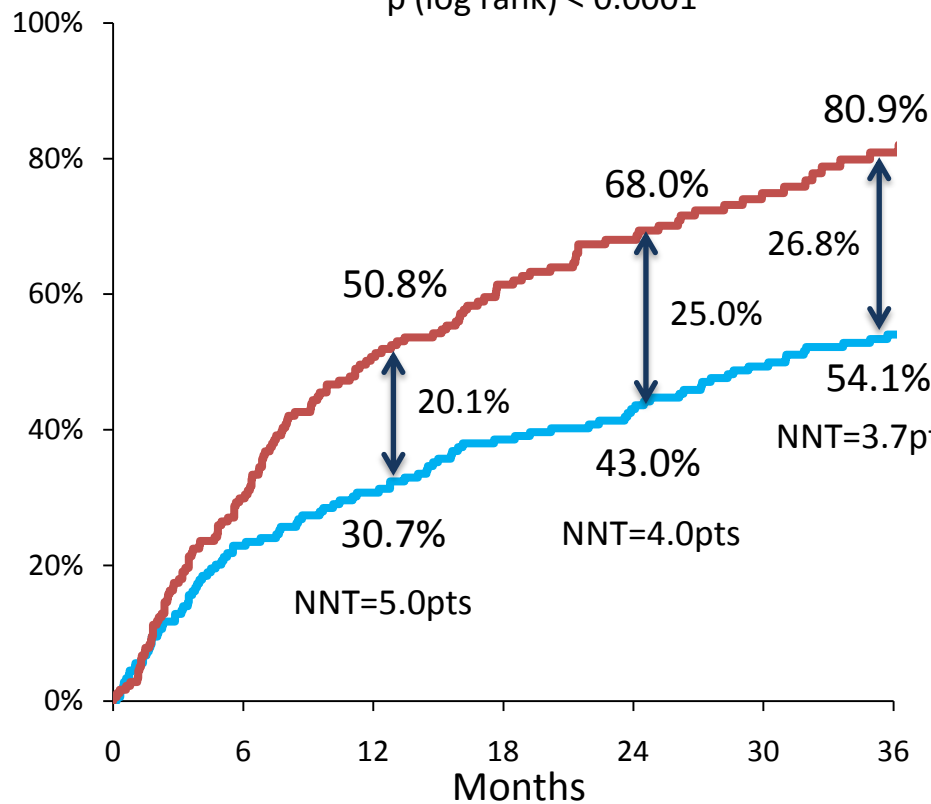
IN INOPERABLE PATIENTS – 3 YEAR F/U

LEON MB ET AL. NEJM 2010; PRESENTED AT TCT 2012, MIAMI

ALL – CAUSE DEATH

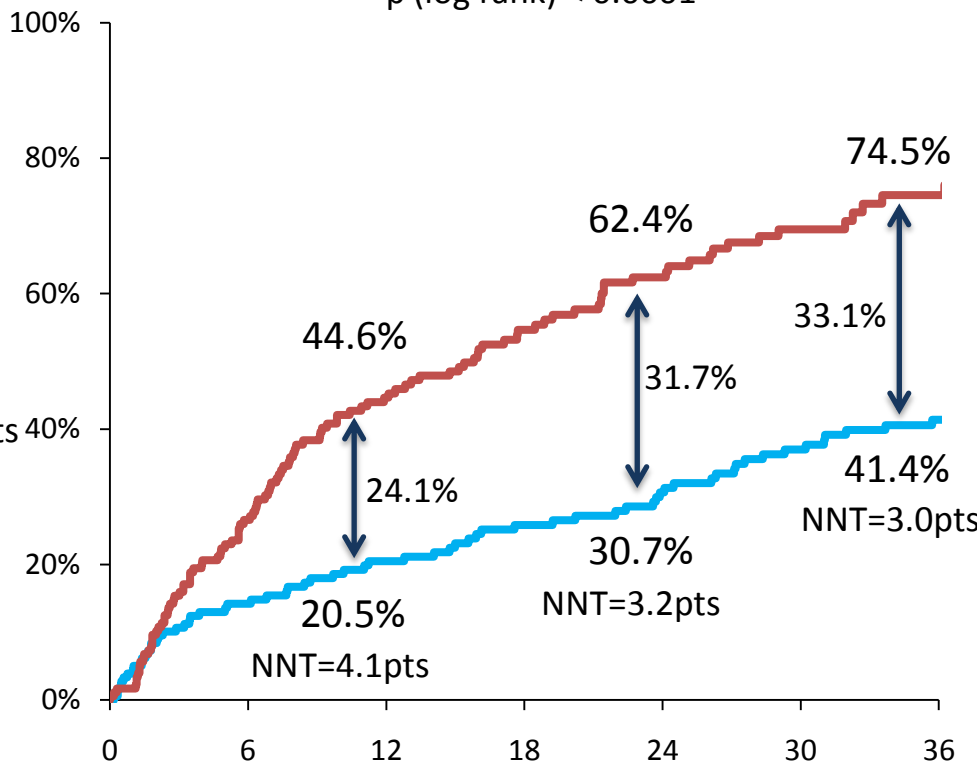
HR [95% CI] = 0.53 [0.41, 0.68]
p (log rank) < 0.0001

Standard Rx
TAVI



CARDIAC DEATH

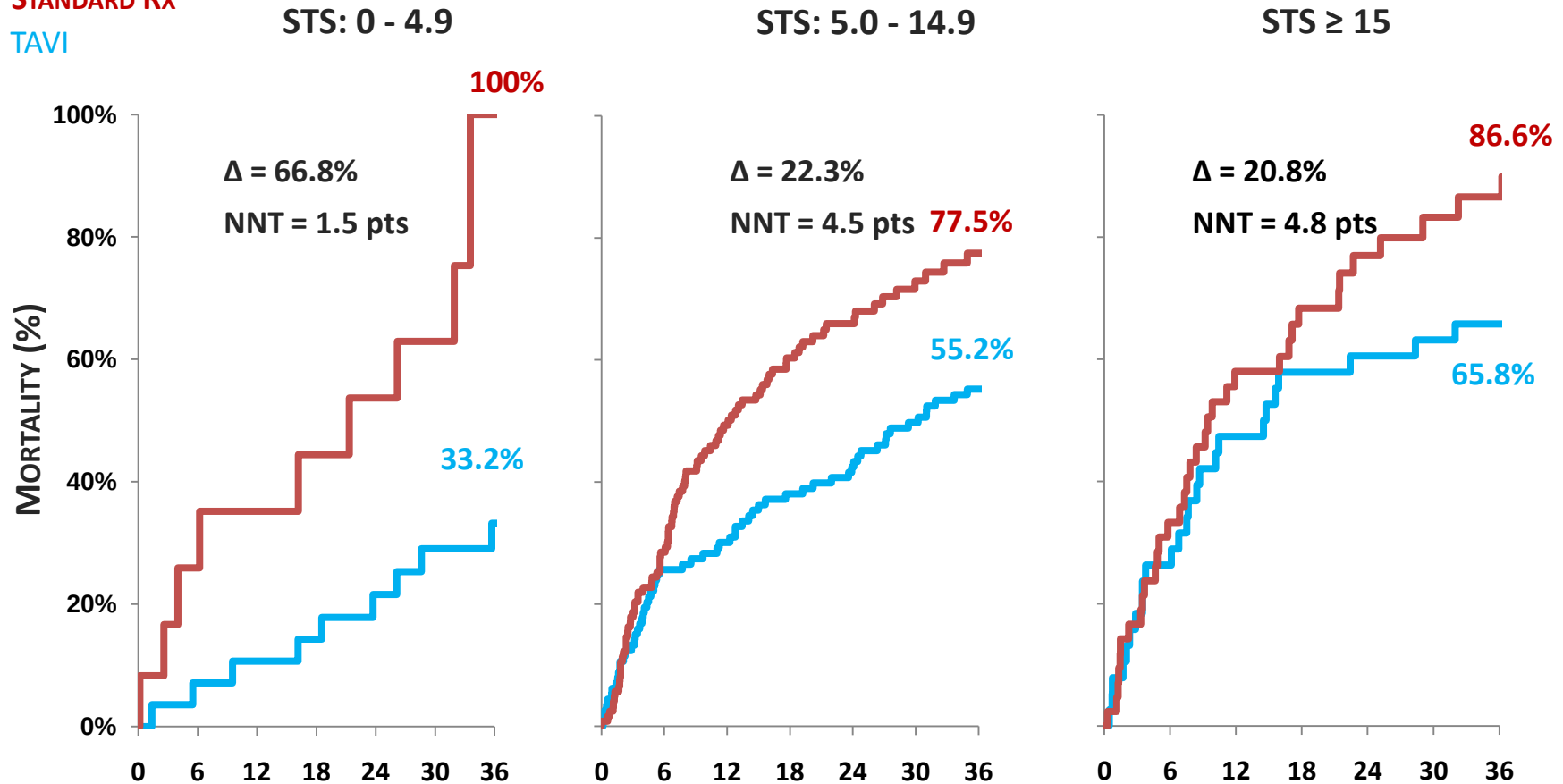
HR [95% CI] = 0.41 [0.30, 0.56]
p (log rank) < 0.0001



MORTALITY STRATIFIED BY STS SCORE (ITT)

LEON MB ET AL. NEJM 2010; PRESENTED AT TCT 2012, MIAMI

— STANDARD RX
— TAVI



Numbers at Risk

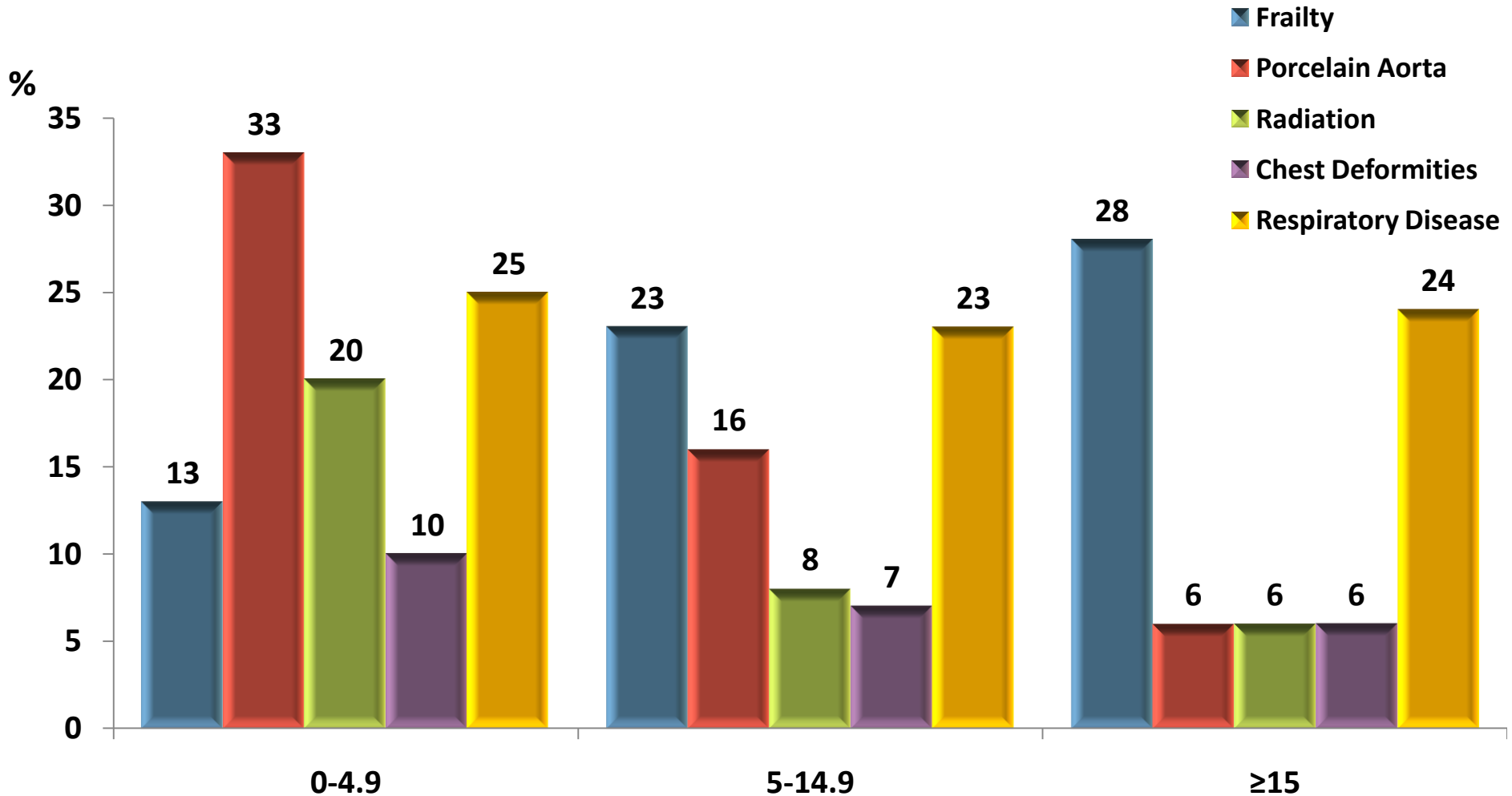
Standard Rx	12	8	7	6	5	3	0
TAVR	28	26	25	24	21	19	16

123	86	61	44	33	19	13
113	84	79	70	65	55	44

43	27	17	12	8	5	4
38	28	20	16	15	14	10

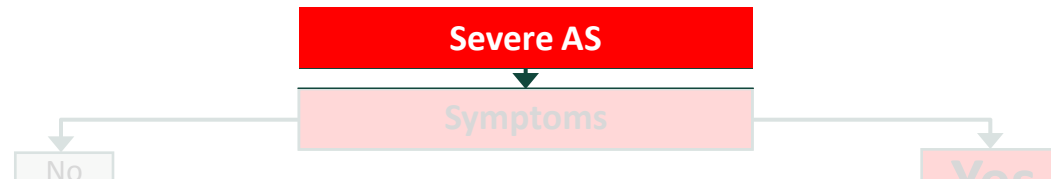
INOPERABILITY CONDITIONS BY STS RISK SCORE

Makkar et al. *N Engl J Med* 2012;366:1696-704



MANAGEMENT OF SEVERE AORTIC STENOSIS

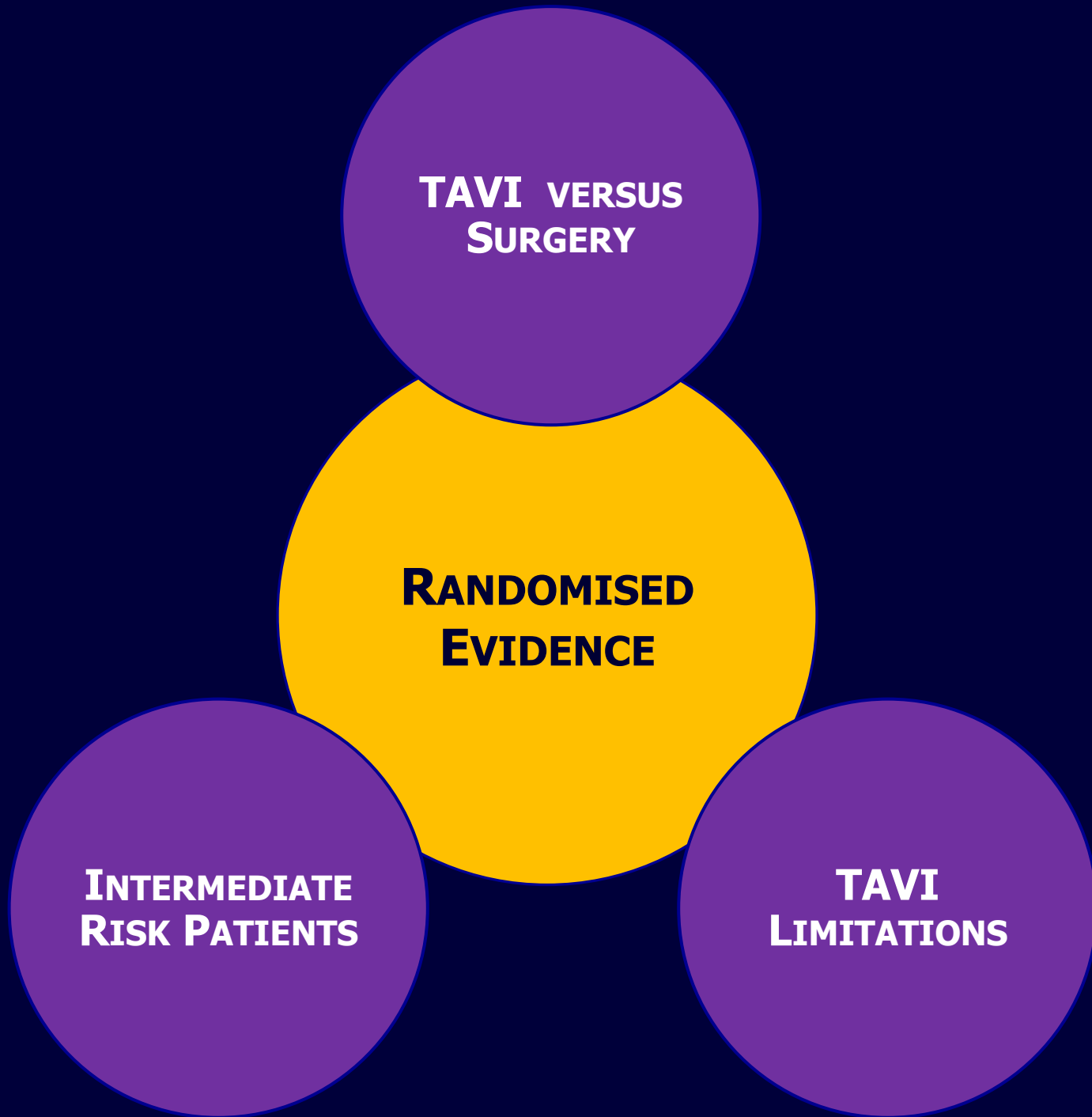
ESC GUIDELINES ON VALVULAR HEART DISEASE 2012



	Class	Level
TAVI should only be undertaken with a multidisciplinary “heart team” including cardiologists and cardiac surgeons and other specialists if necessary.	I	C
TAVI should only be performed in hospitals with cardiac surgery on-site.	I	C
TAVI is indicated in patients with severe symptomatic AS who are not suitable for AVR as assessed by a “heart team” and who are likely to gain improvement in their quality of life and to have a life expectancy of more than 1 year after consideration of their comorbidities.	I	B
TAVI should be considered in high risk patients with severe symptomatic AS who may still be suitable for surgery, but in whom TAVI is favoured by a “heart team” based on the individual risk profile and anatomic suitability.	Ila	B


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graph TD
    Line[ ] --> No1[No]
    Line --> Yes1[Yes]
    Line --> AVR1[AVR]
    Line --> AVRorTAVI[AVR or TAVI]
    Line --> TAVI1[TAVI]
    No1 --> ReEvaluate[Re-evaluate in 6 months]
    Yes1 --> AVR2[AVR]
  
```

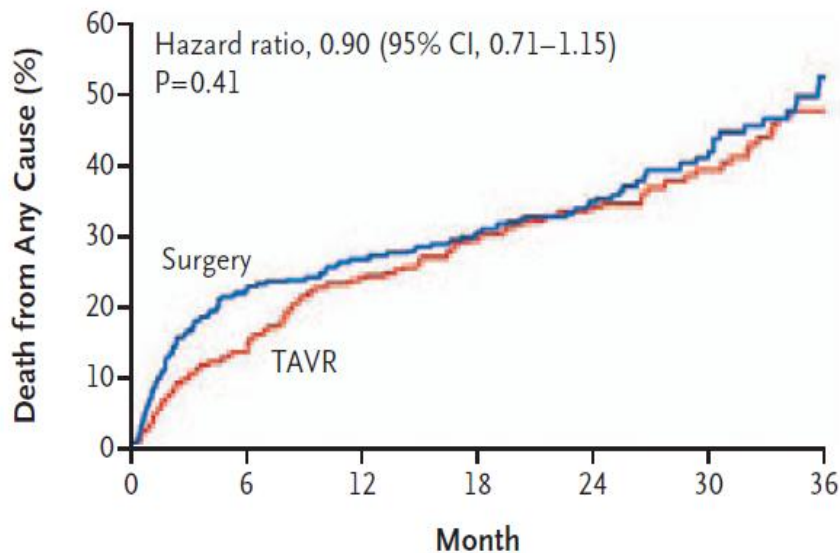


TAVI vs. SURGERY

ALL – CAUSE DEATH

Kodali et al. *N Engl J Med* 2012;366:1686-95

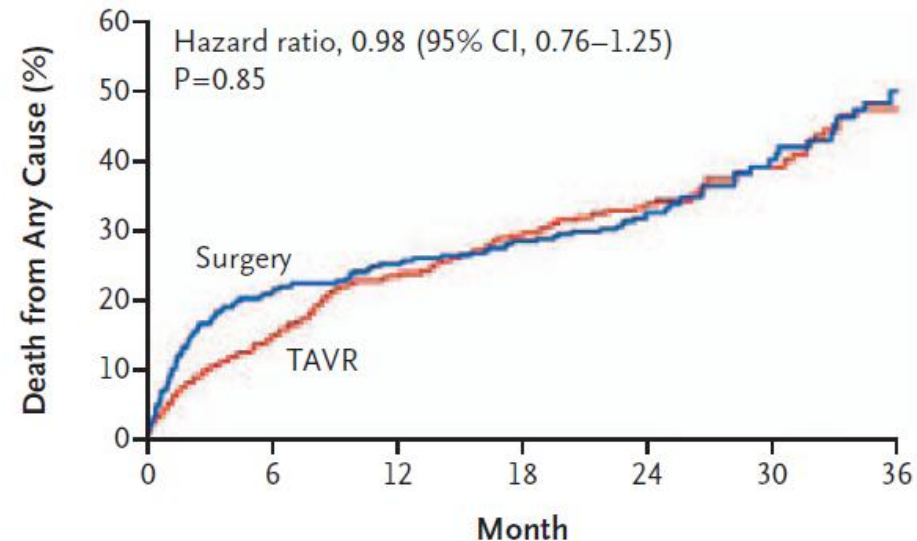
INTENTION TO TREAT POPULATION



No. at Risk

TAVR	348	298	260	234	172	70	31
Surgery	351	252	236	217	165	65	32

AS TREATED POPULATION



344	291	259	232	155	70	29
313	243	229	211	143	63	28

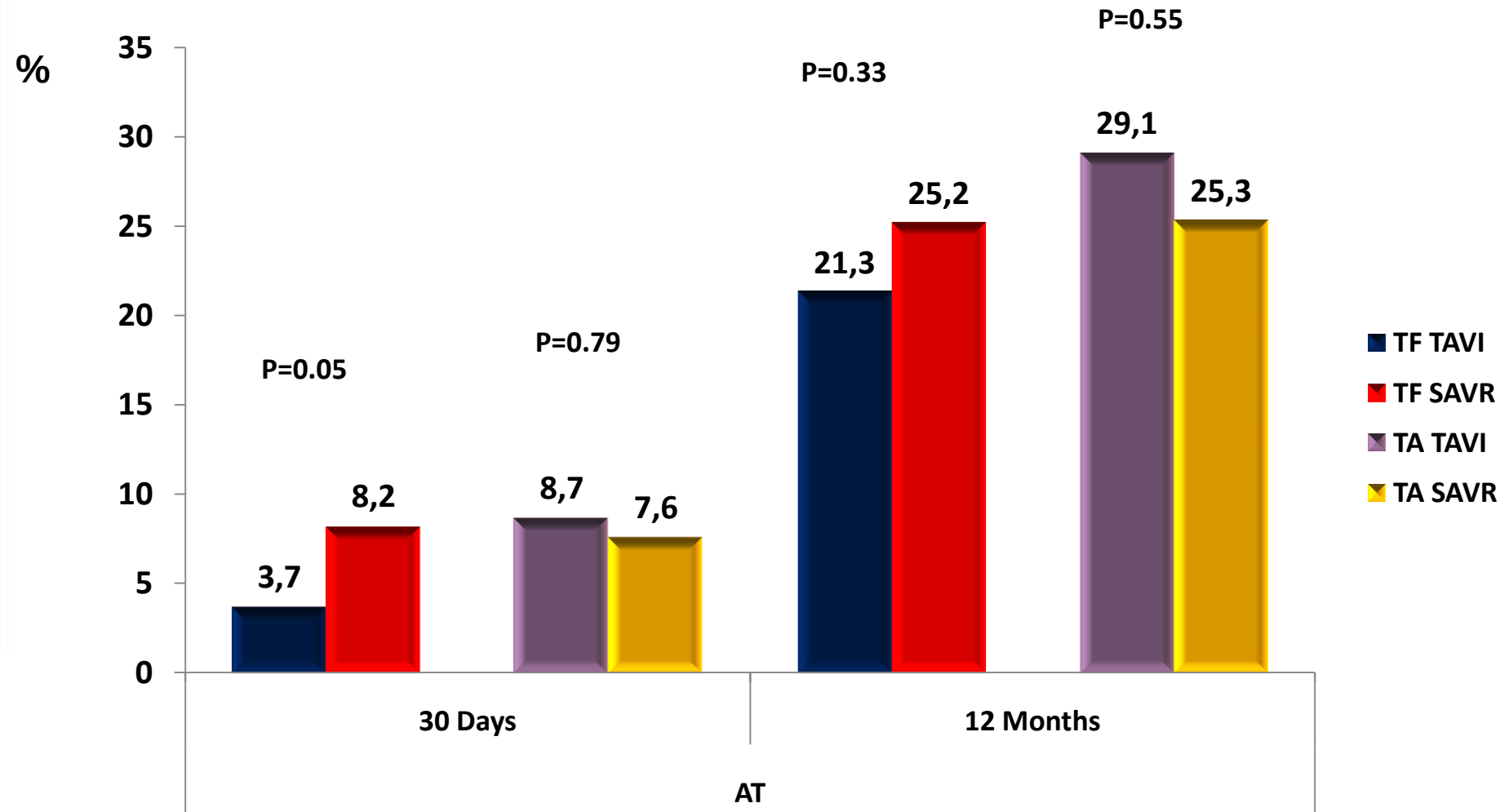
TAVI vs. SURGERY

ALL – CAUSE DEATH

Smith C et al. *N Engl J Med* 2011;364:2187-98



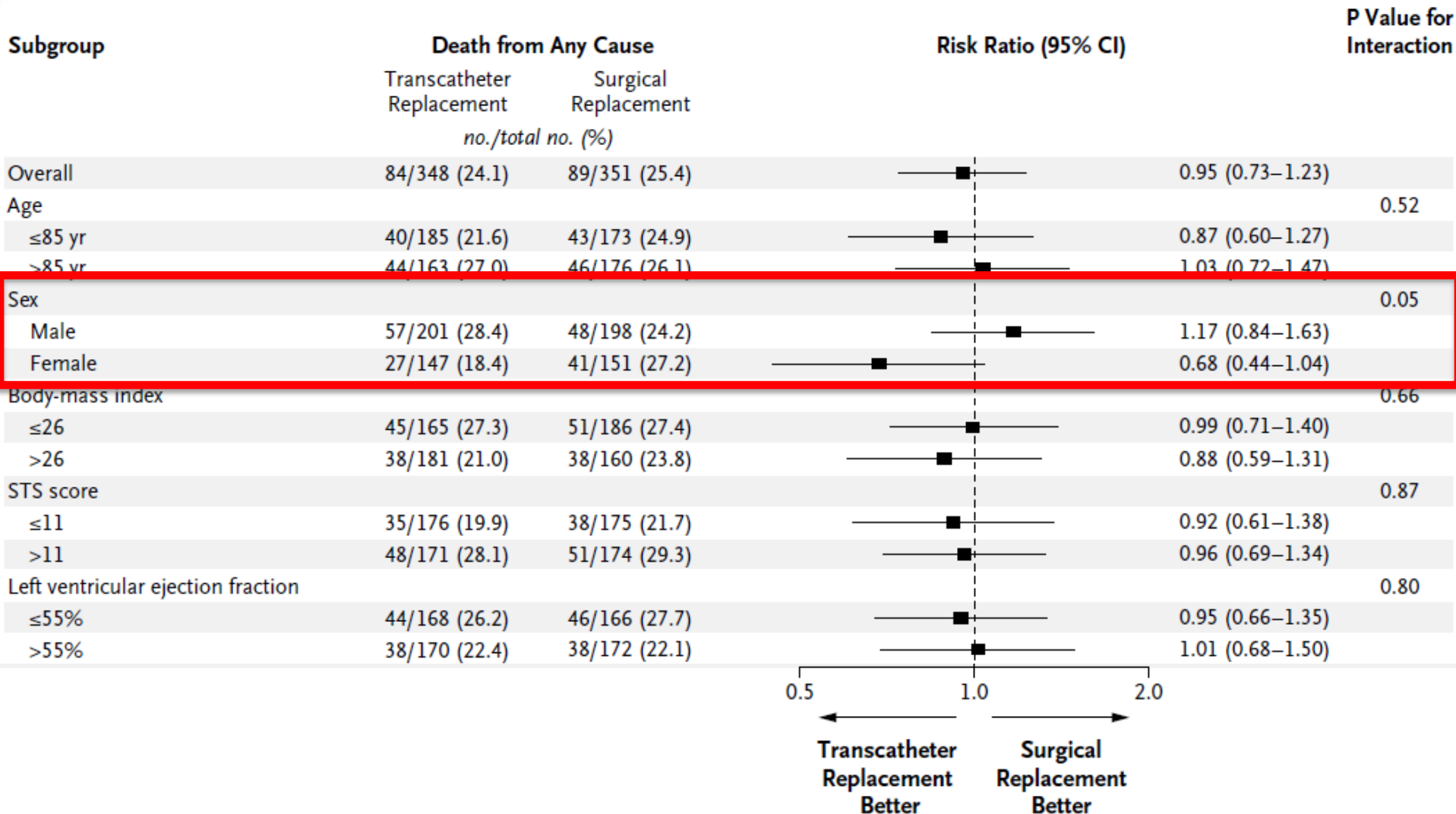
AS TREATED PATIENT POPULATION



TAVI vs. SURGERY

SUBGROUP ANALYSES OF TREATMENT EFFECT

Smith C et al. *N Engl J Med* 2011;364:2187-98

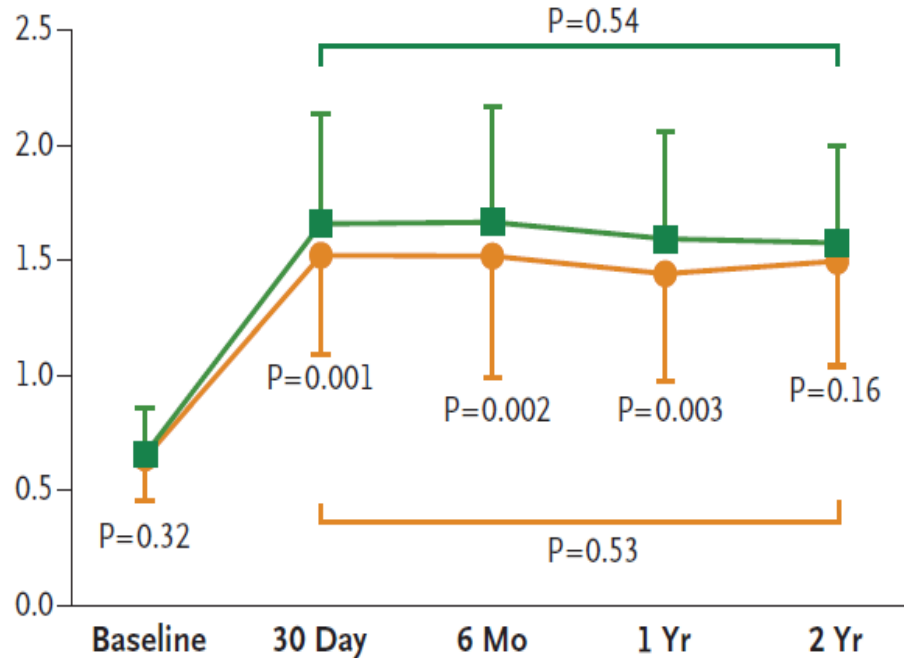


TAVI vs. SURGERY

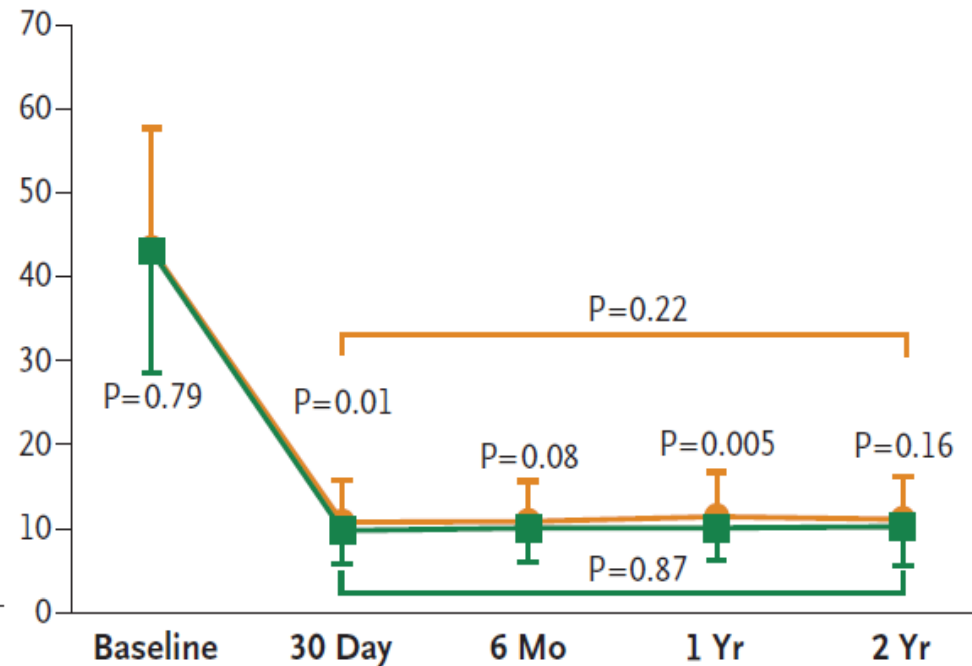
ECHOCARDIOGRAPHIC FINDINGS

Kodali et al. *N Engl J Med* 2012;366:1686-95

AORTIC VALVE AREA



MEAN AORTIC GRADIENT



TAVI	290	224	163	151	110	290	224	163	151	110
SAVR	301	269	223	210	139	301	269	223	210	139

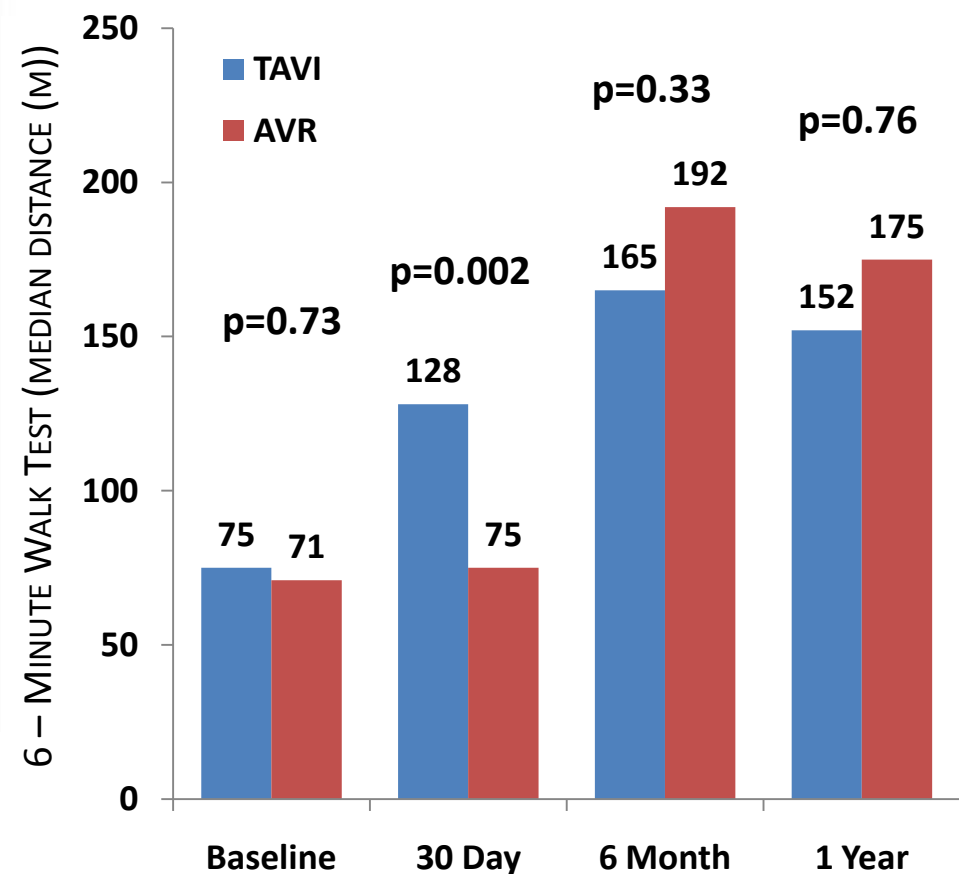
—■— TAVI —●— SAVR

TAVI vs. SURGERY

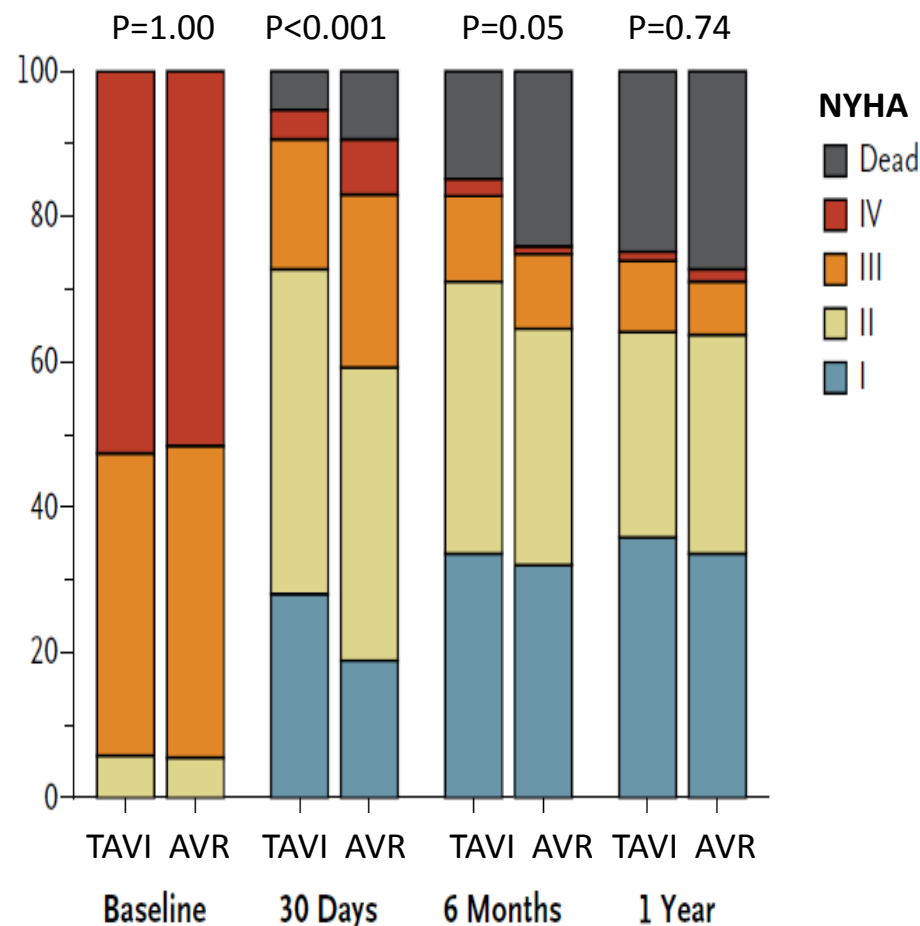
EFFECT OF TAVI ON QoL AT 12 MONTHS

Reynolds MR et al. *J Am Coll Cardiol* 2012;50:548-58

FUNCTIONAL CAPACITY



NYHA FUNCTIONAL CLASS



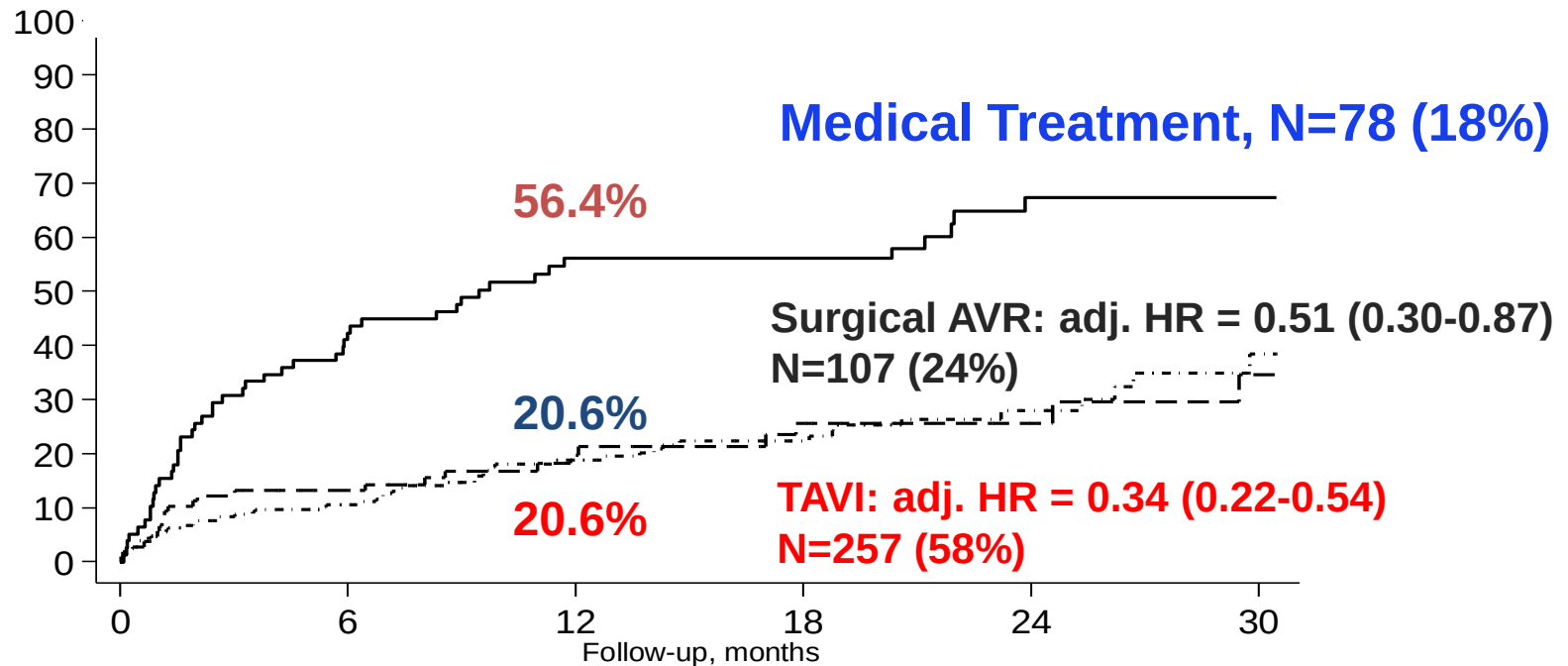
ROLE OF TAVI IN ROUTINE CLINICAL PRACTICE



Wenaweser P et al. *J Am Coll Cardiol* 2011;58:2151-62

All Cause Mortality

N=452

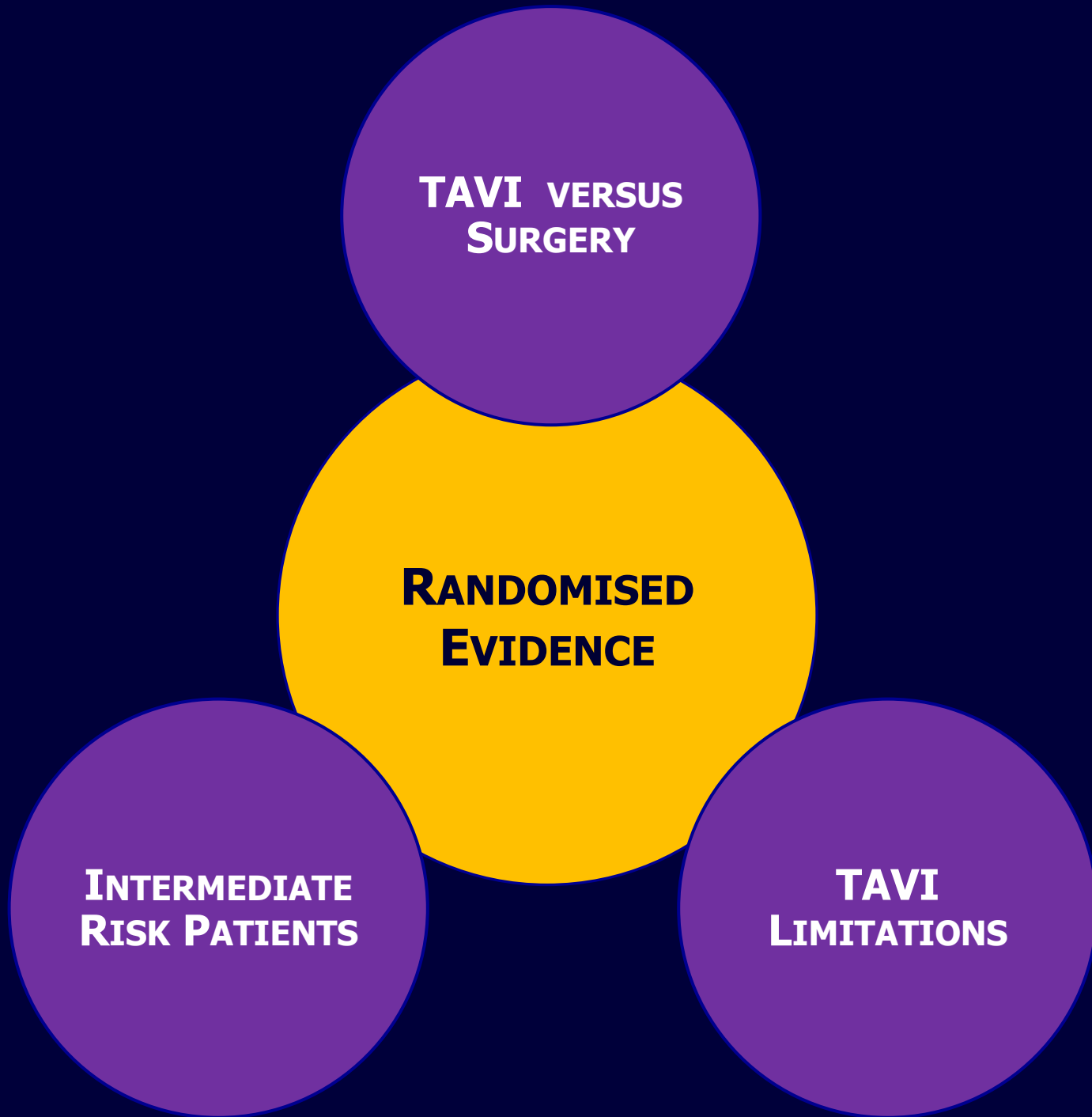


No. at risk

Medical	78	46	29	26	13	9
Surgical	107	82	53	34	22	13
TAVI	254	187	121	88	43	17

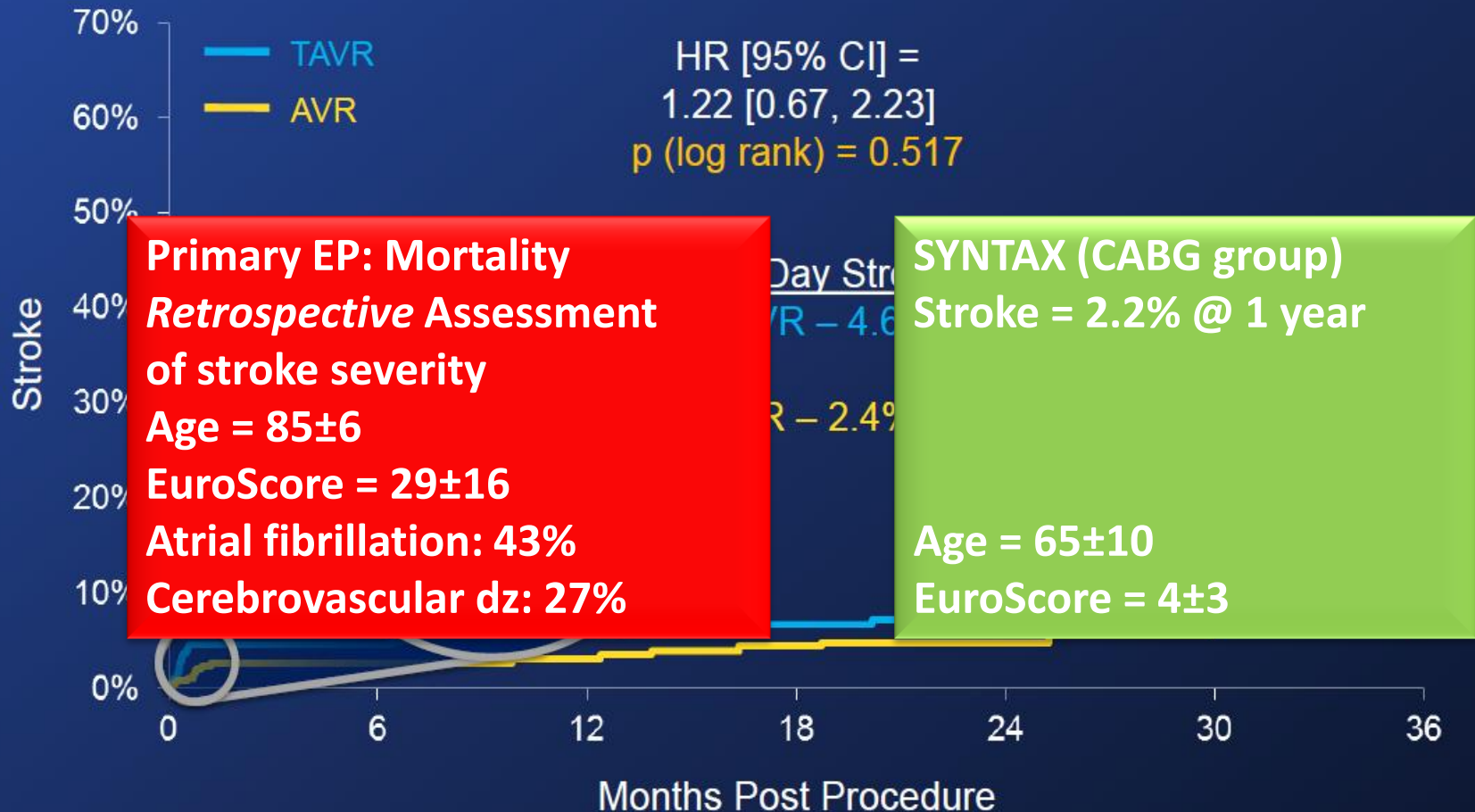
ESC RECOMMENDATIONS FOR THE TREATMENT OF VALVULAR HEART DISEASE

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TAVI vs. SAVR

CEREBROVASCULAR ACCIDENTS (ITT)



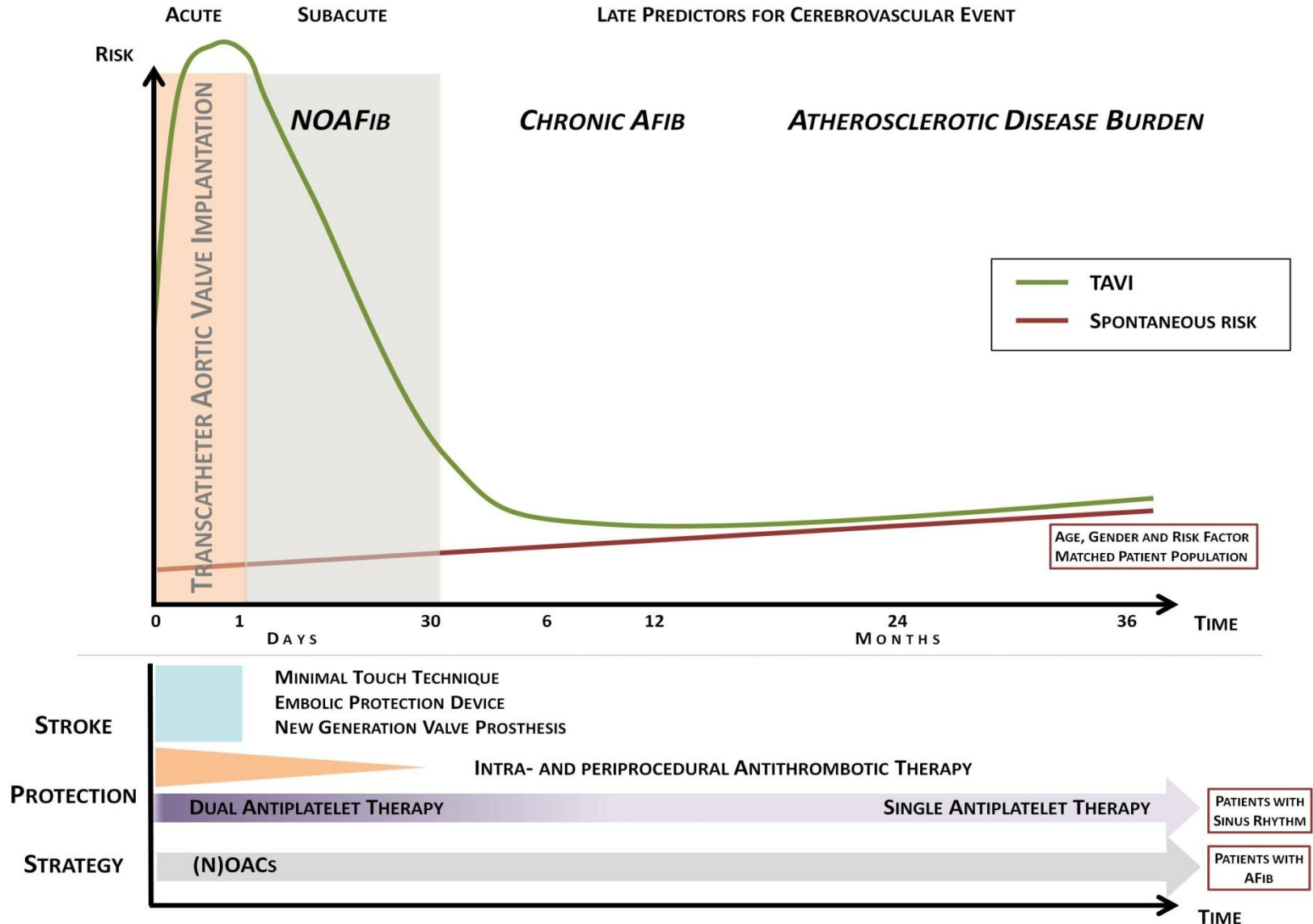
Numbers at Risk

TAVR	348	287	249	224	162	65	28
AVR	351	246	230	211	160	62	31

TRANSCATHETER AORTIC VALVE IMPLANTATION AND Cerebrovascular Events

STORTECKY S, WINDECKER S CIRCULATION 2012;126:2921-4

LATE PREDICTORS FOR Cerebrovascular EVENT



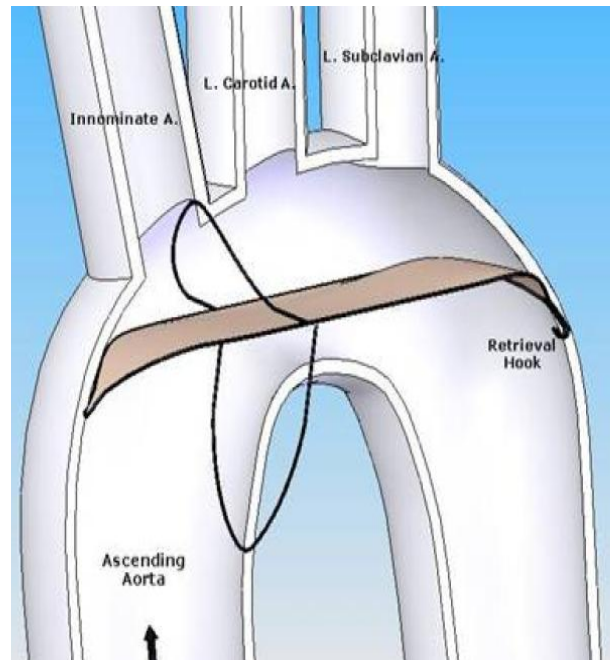
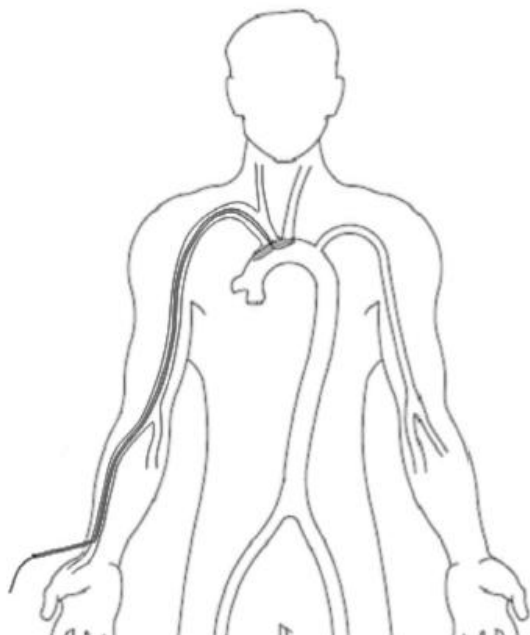
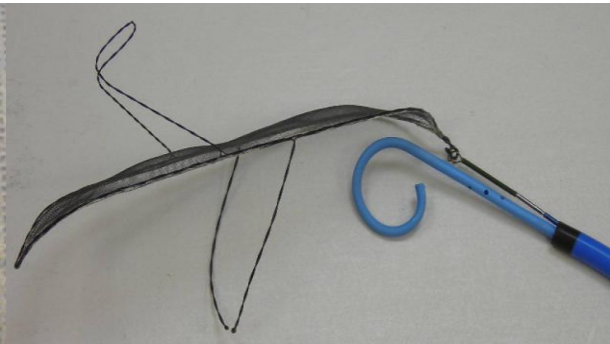
EMBOLIC PROTECTION DEVICES

EMBOLIC DEFLECTOR DEVICES

RADIAL ACCESS

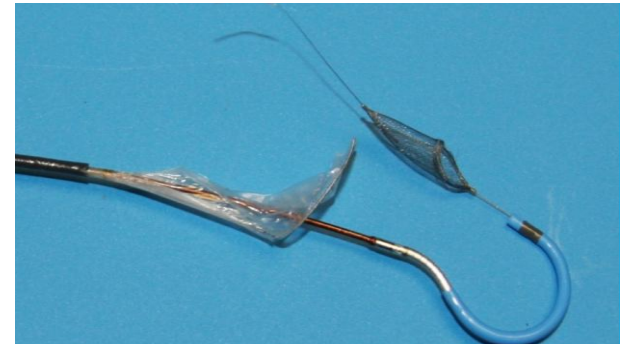


FEMORAL ACCESS



EMBOLIC FILTER DEVICE

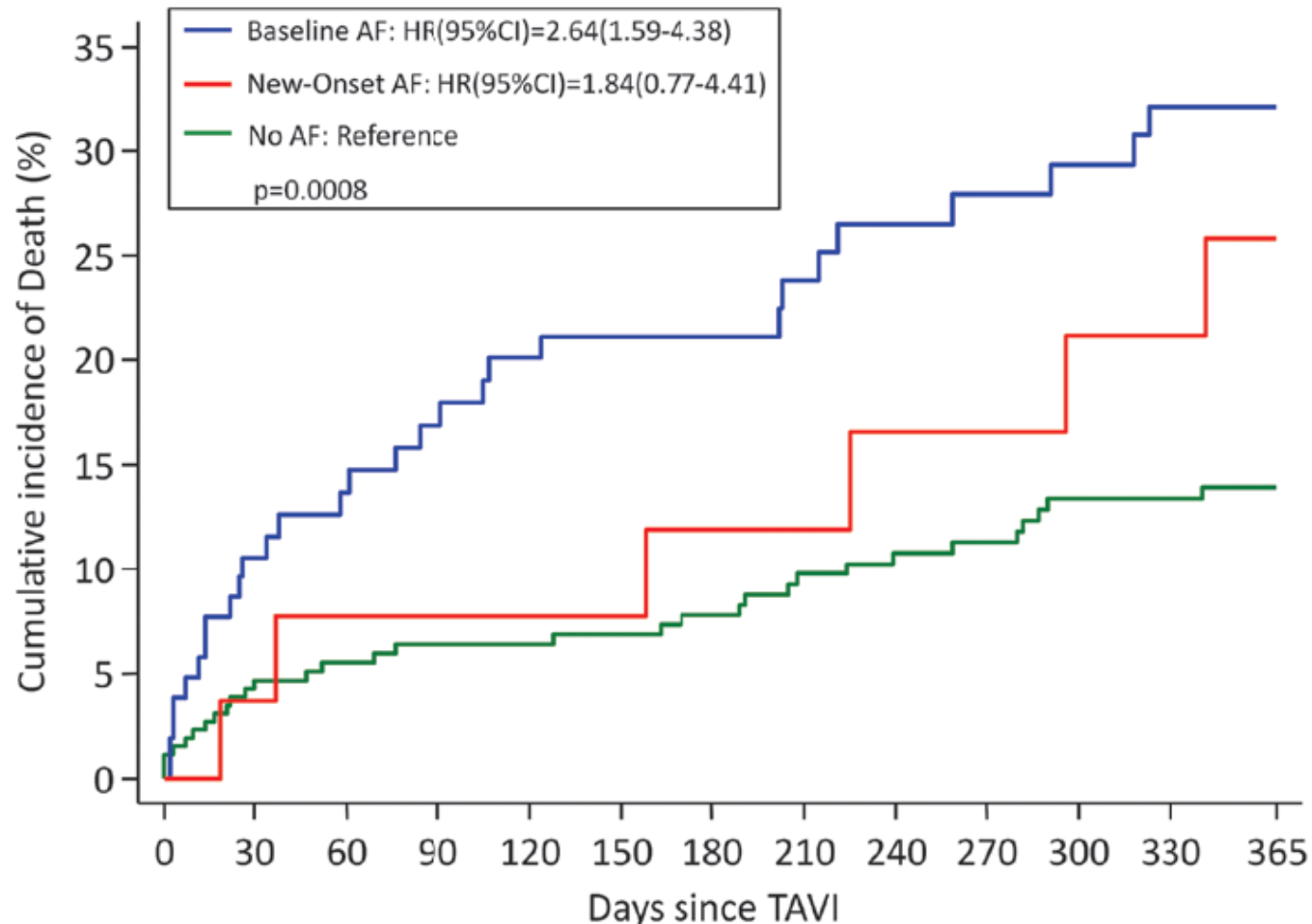
RADIAL ACCESS



AORTIC STENOSIS AND ATRIAL FIBRILLATION IN PATIENTS UNDERGOING TAVI

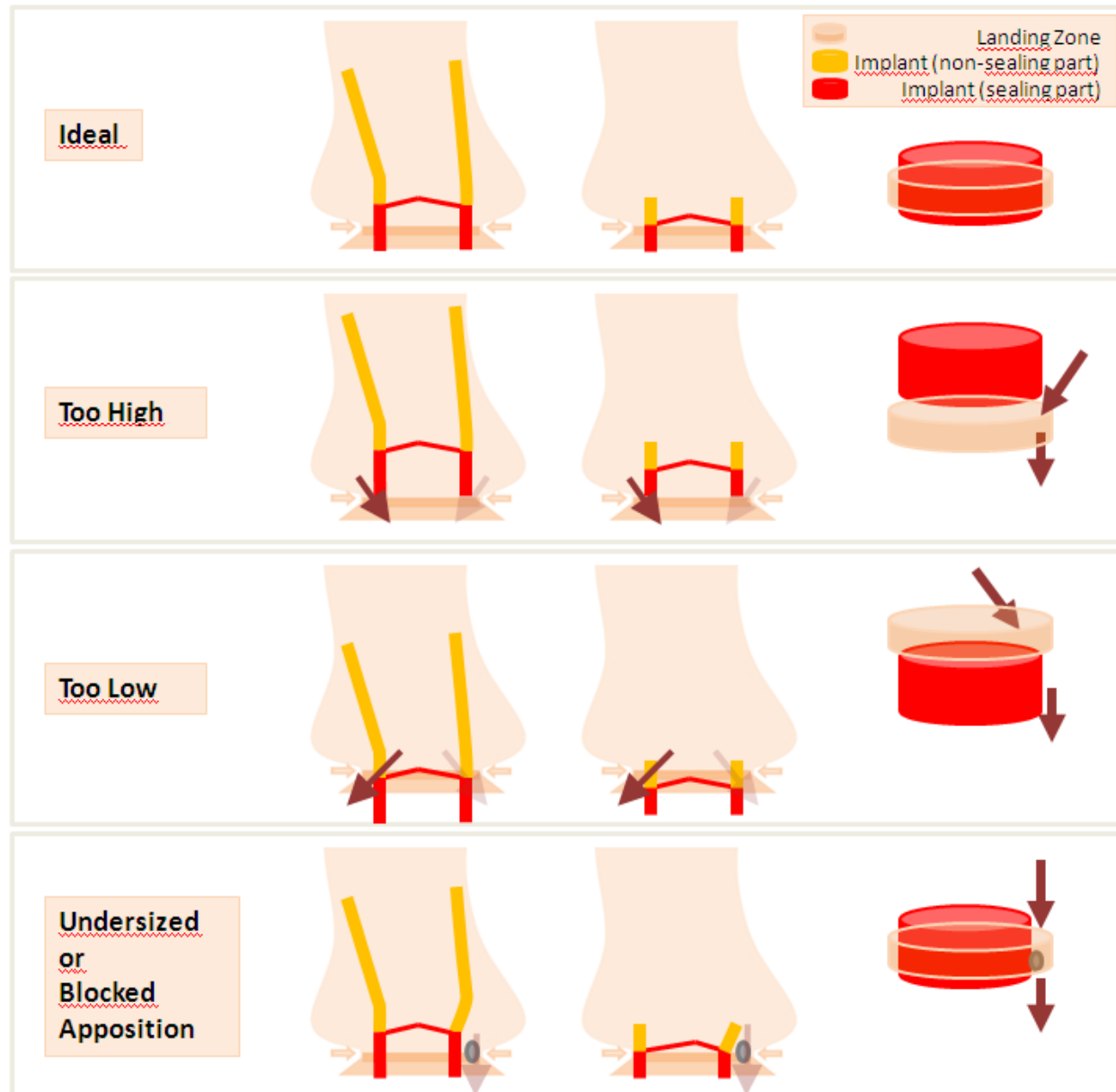
STORTECKY S ET AL. CIRC CARDIOVASC INTERV FEB 2013; [EPUB AHEAD OF PRINT]

BERN TAVI REGISTRY N=389; AGE 83 ± 6 YEARS; 58% FEMALE GENDER



MECHANISMS OF AORTIC REGURGITATION

Buellesfeld L et al. JACC Cardiovasc Interv 2012;5:578-81

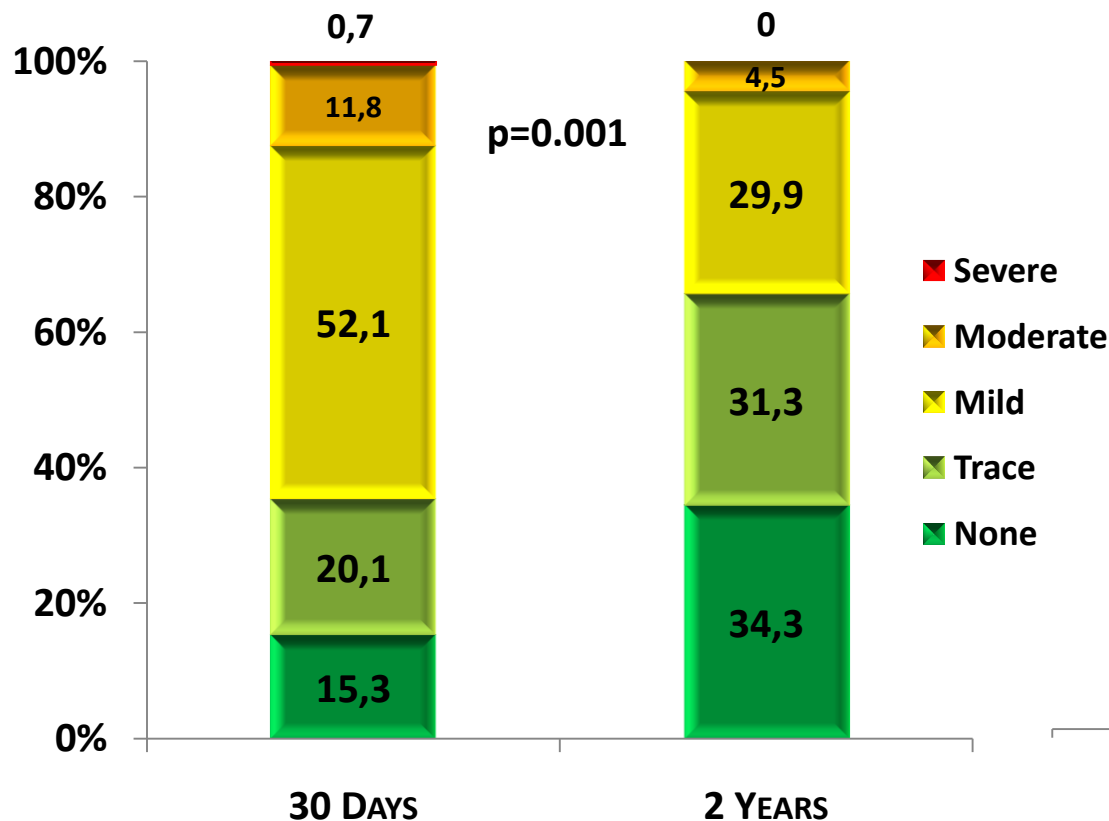


TAVI vs. MEDICAL TREATMENT

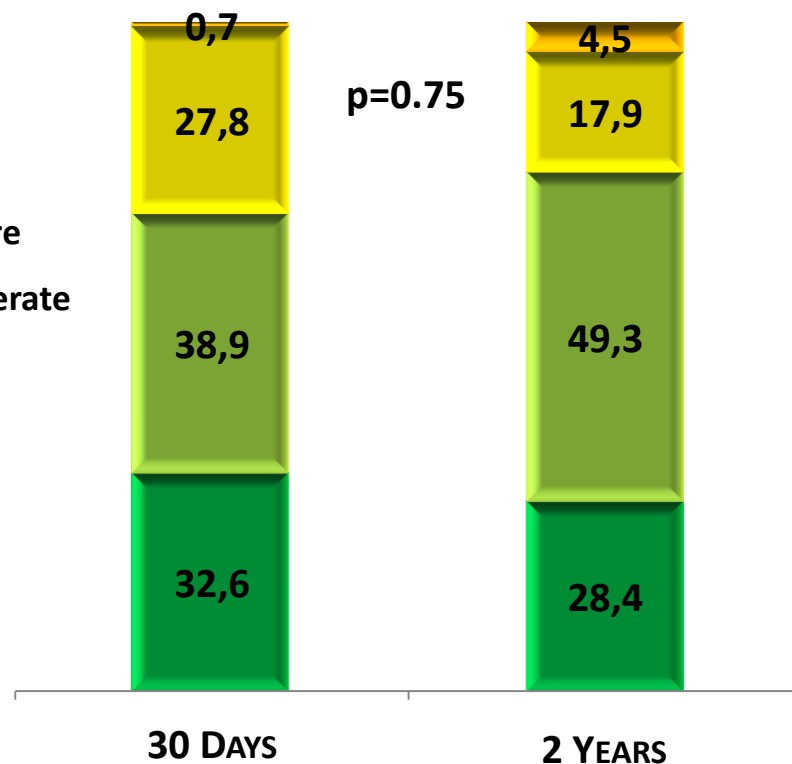
ECHOCARDIOGRAPHIC OUTCOMES – TAVI COHORT

Makkar et al. *N Engl J Med* 2012;366:1696-704

PARAVALVULAR AR



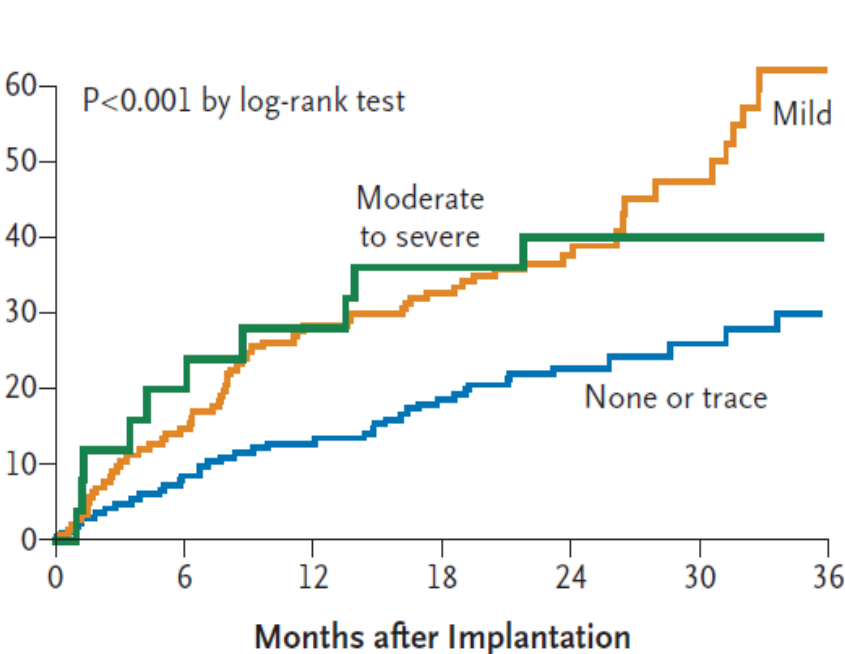
TRANSVALVULAR AR



AORTIC REGURGITATION AND IMPACT ON OUTCOMES

Kodali SK et al. N Engl J Med. 2012;366:1686-95

PARAVALVULAR AR

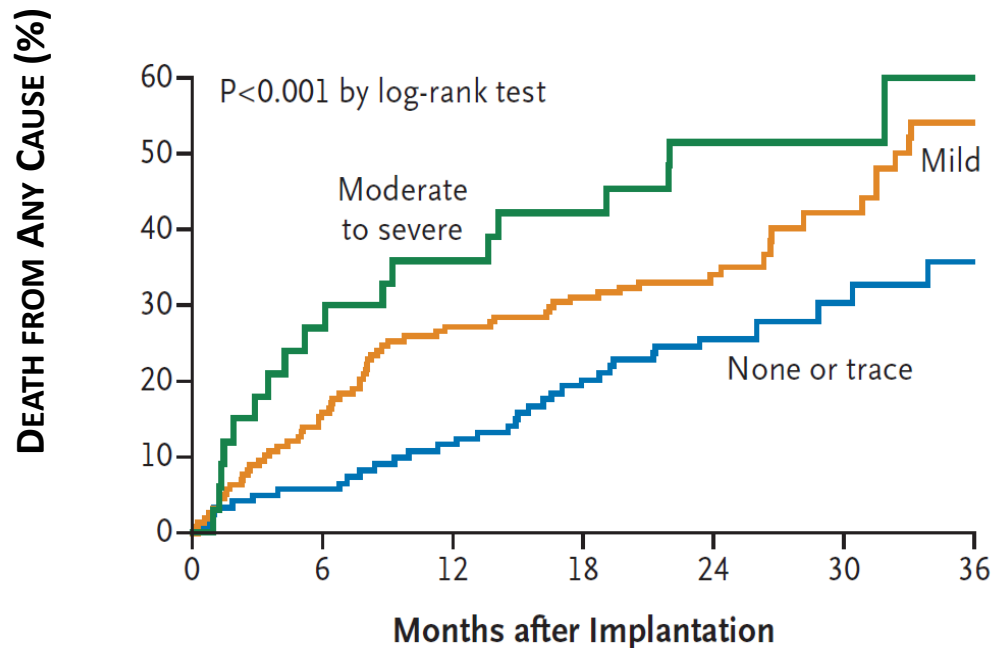


158	142	134	121	84	39	15
136	115	95	86	51	21	10
24	19	17	15	13	5	2

No. at Risk

None or trace	125
Mild	162
Moderate to severe	34

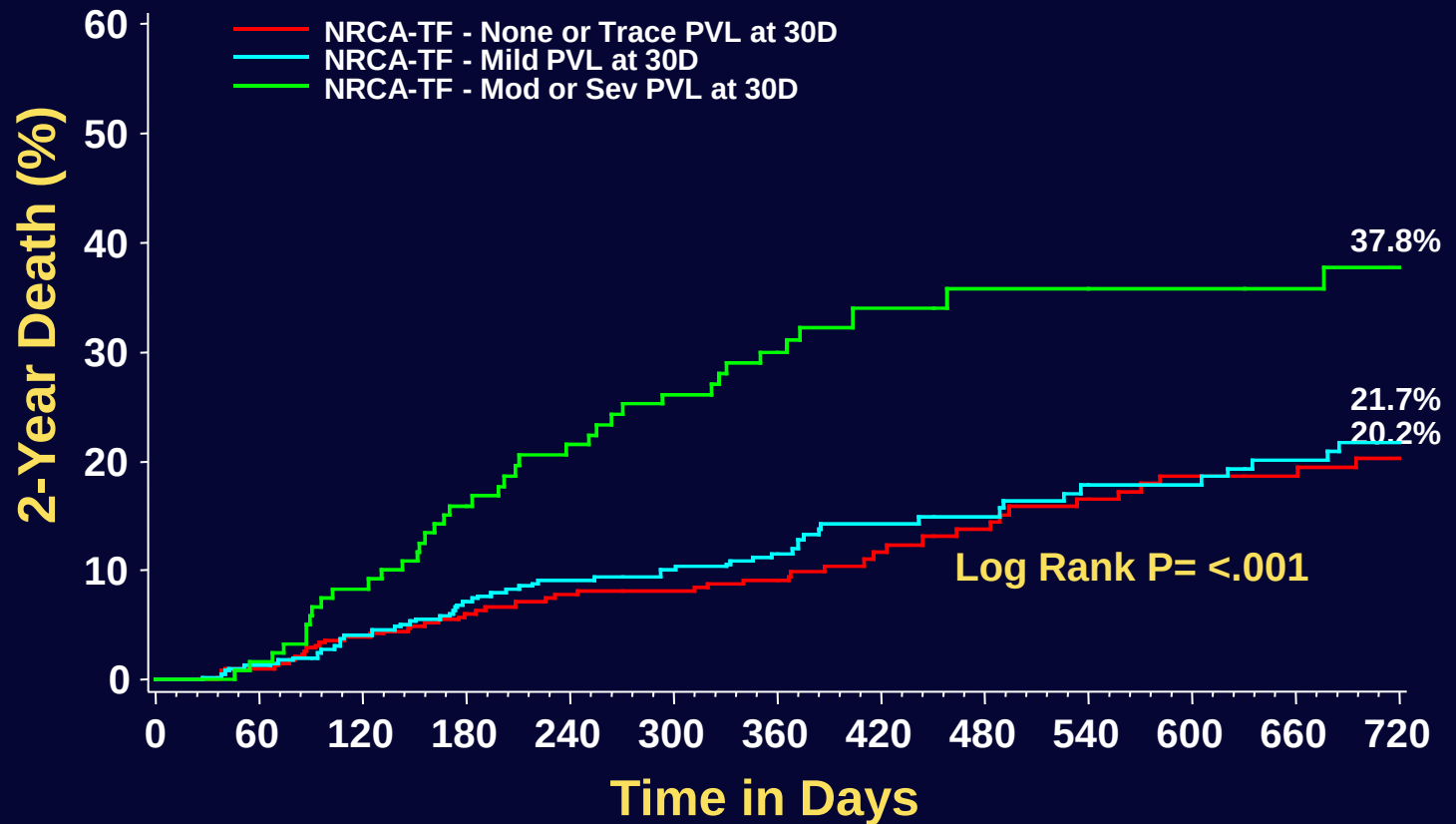
OVERALL AR



None or trace	125	117	108	95	64	29	10
Mild	162	136	118	109	70	31	15
Moderate to severe	34	25	22	19	15	6	2

PARTNER 1 NRCA ONLY

MORTALITY & PARAVALVULAR LEAK



Number At Risk

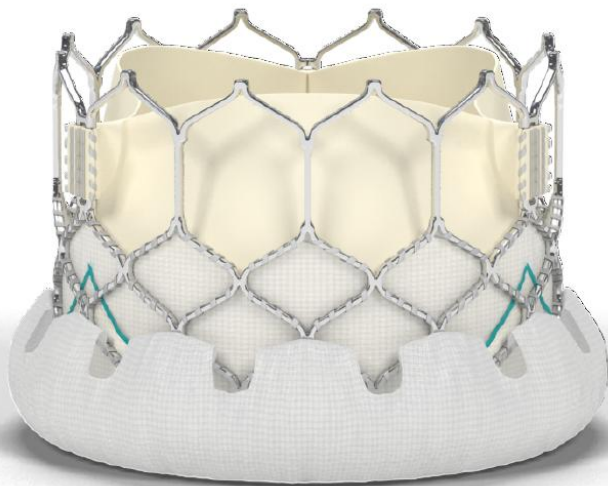
None or Trace PVL	388	373	339	300	238	127	119	112	76
Mild PVL	400	388	350	303	247	125	114	106	74
Mod or Sev PVL	120	113	97	81	66	37	34	32	23

* Events adjudicated to one year

NEW GENERATION TAVI DEVICES

EFFECT ON PARAVALVULAR AR?

EDWARDS SAPIEN 3



**SEALING CUFF
TECHNOLOGY**

MEDTRONIC ENGAGER

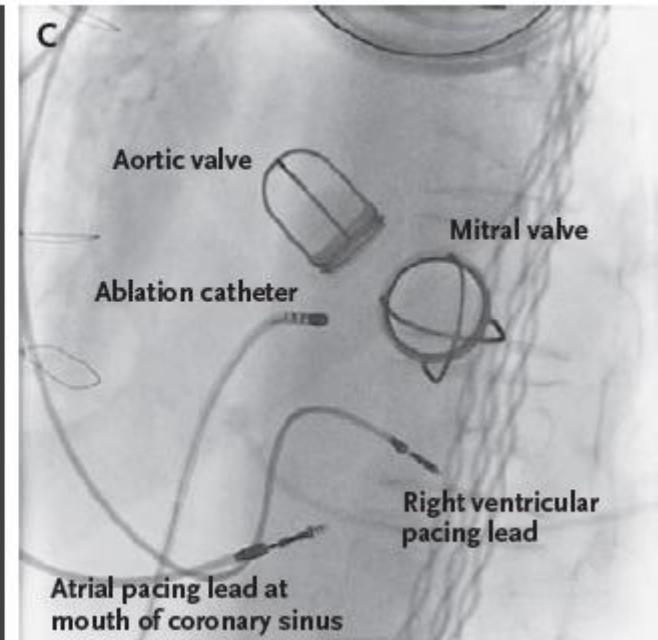
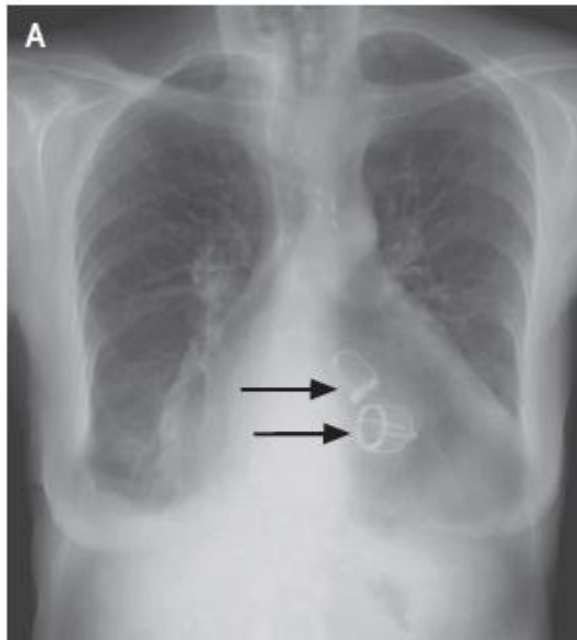
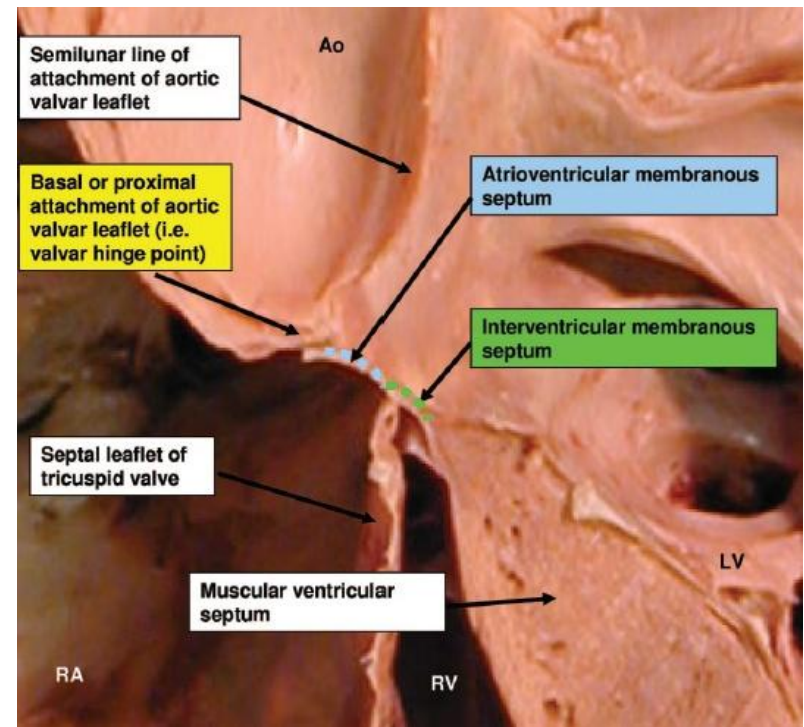


**NATIVE VALVE CLIPPING
MECHANISM**

RELATIONSHIP OF THE AORTIC VALVE AND THE CONDUCTION SYSTEM

EPSTEIN A ET AL. *N ENGL J MED* 2007;357:2706

PIAZZA N ET AL. *CIRC CARDIOVASC INTERV* 2008;1:74-81



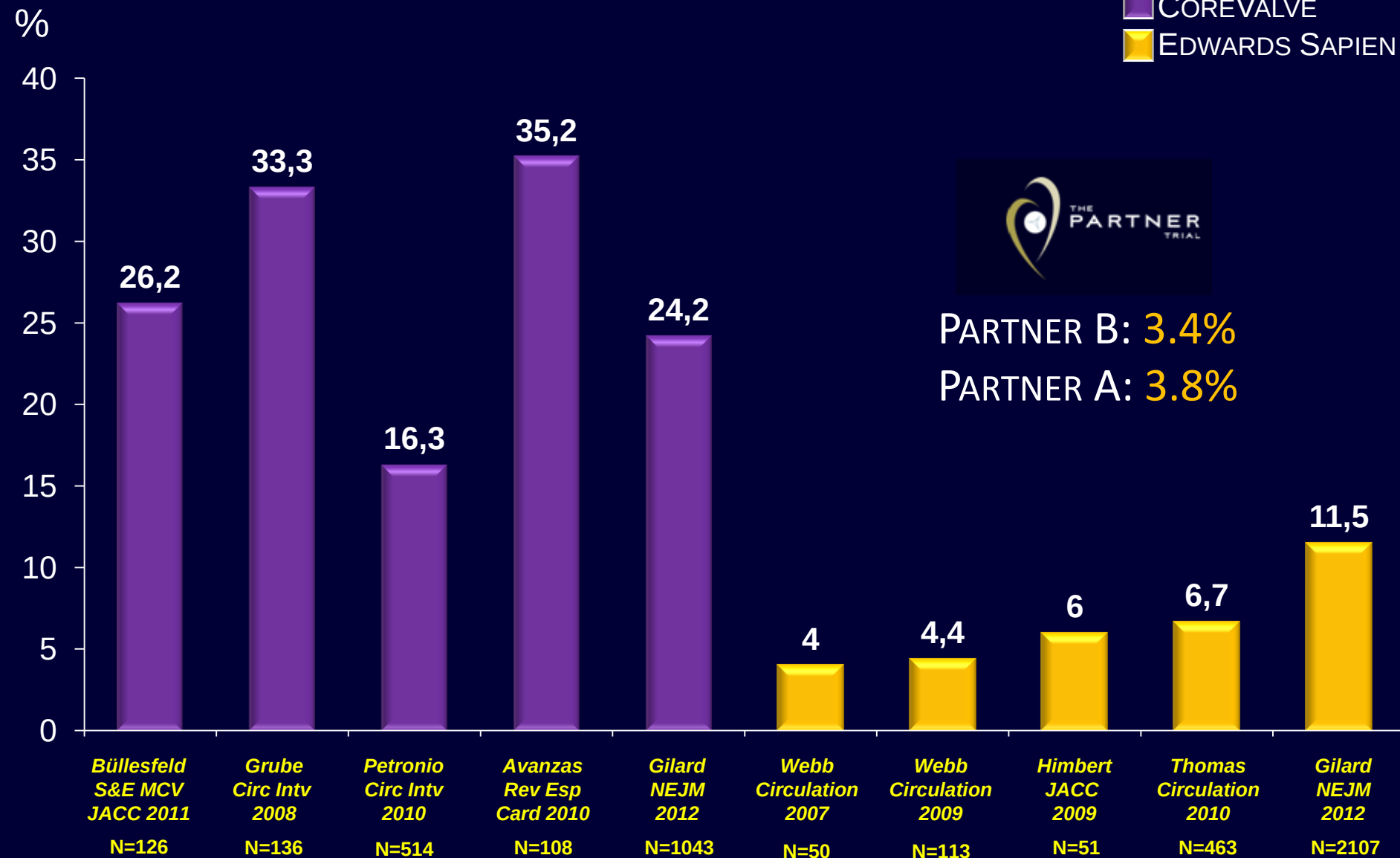
PERMANENT PACEMAKER IMPLANTATION

 COREVALVE
 EDWARDS SAPIEN



PARTNER B: 3.4%

PARTNER A: 3.8%

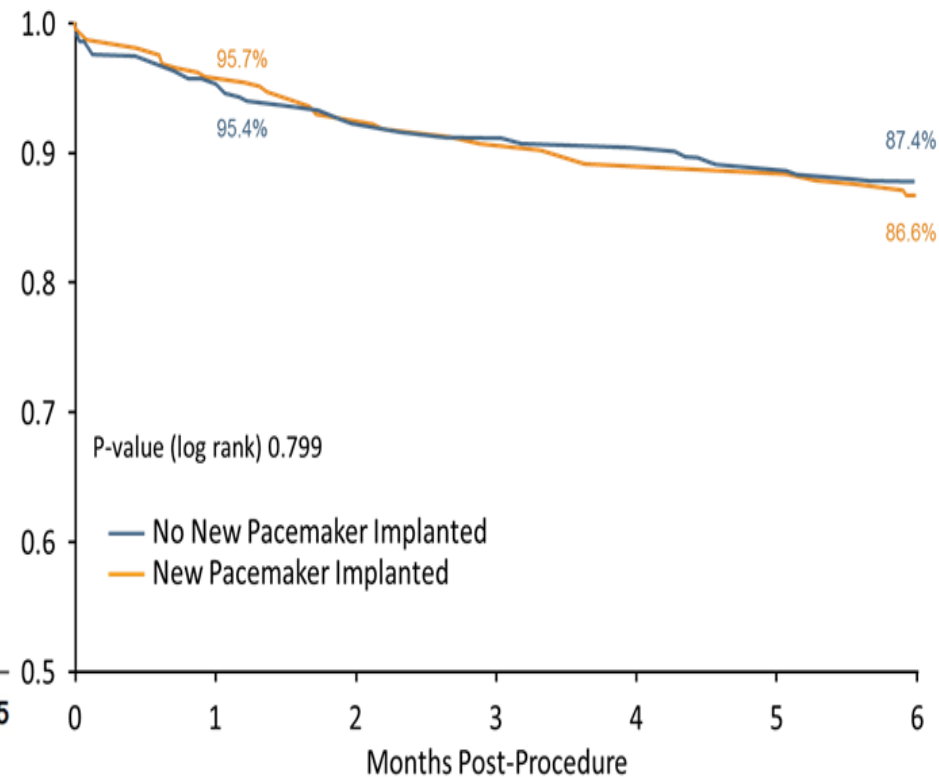
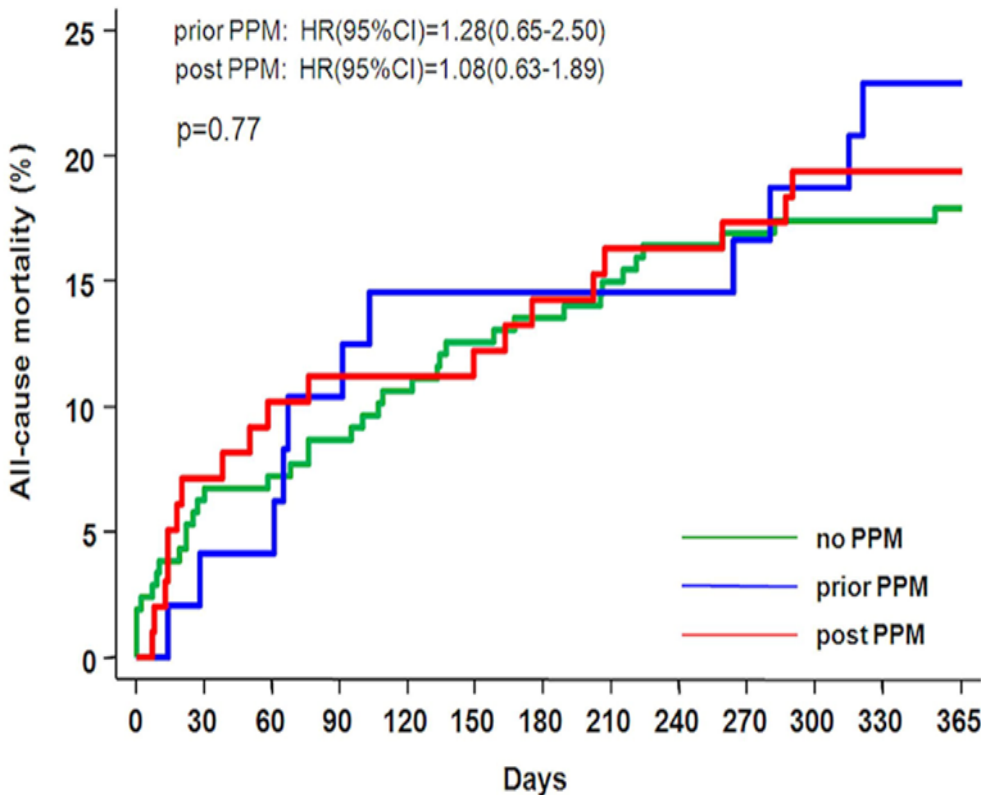


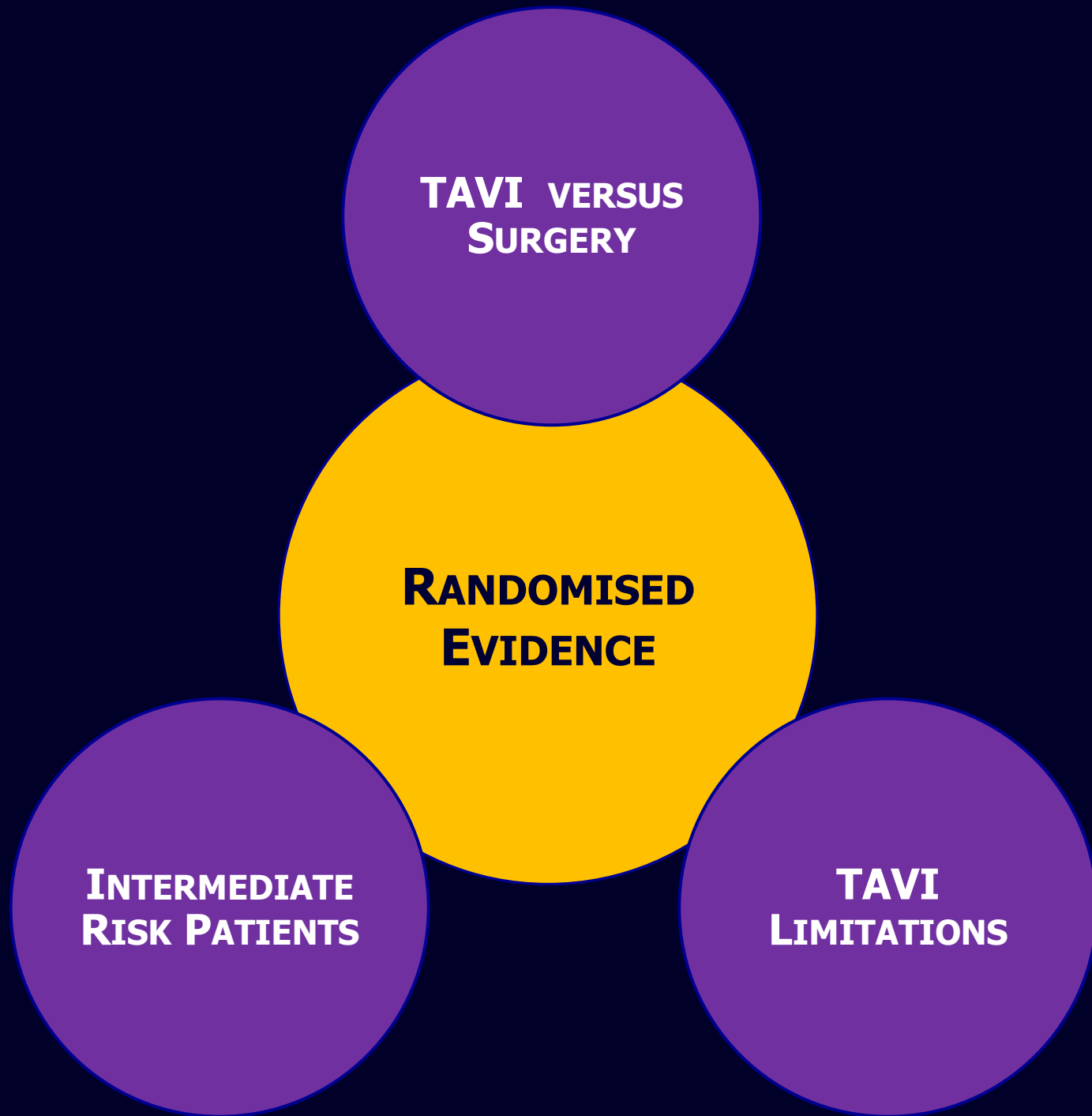
IMPACT OF PERMANENT PACEMAKER IMPLANTATION ON CLINICAL OUTCOMES AFTER TAVI

BUELLESFELD L ET AL. J AM COLL CARDIOL 2012;60:493-501

COREVALVE ADVANCE

PRESENTED BY BAUERNSCHMITT R. AT EUROPCR 2012





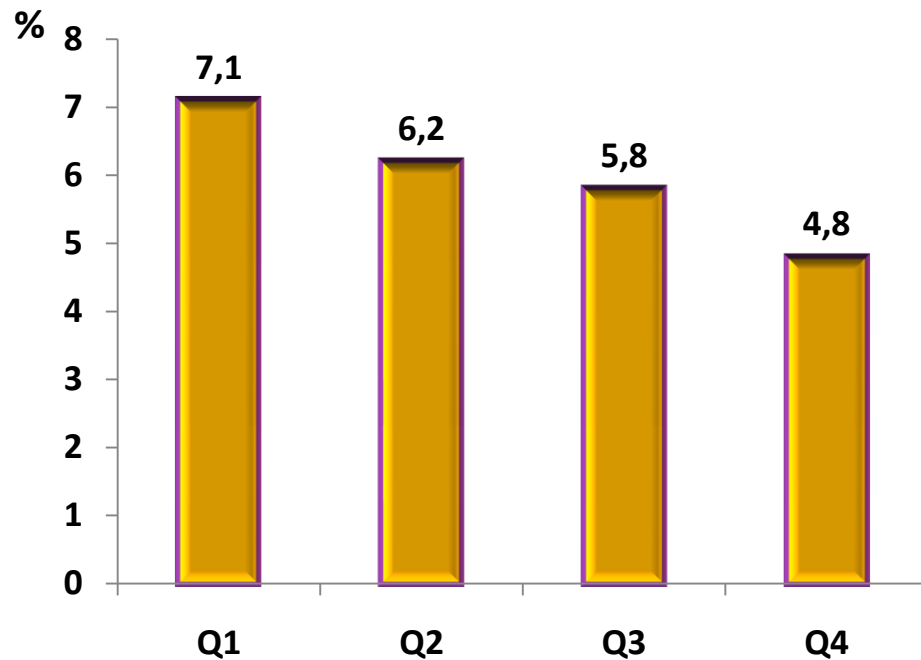
Improvements in Transcatheter Aortic Valve Implantation Outcomes in Lower Surgical Risk Patients

A Glimpse Into the Future

Ruediger Lange, MD, PhD, Sabine Bleiziffer, MD, Domenico Mazzitelli, MD, Yacine Elhmidi, MD, Anke Opitz, MD, Marcus Krane, MD, Marcus-Andre Deutsch, MD, Hendrik Ruge, MD, Gernot Brockmann, MD, Bernhard Voss, MD, Christian Schreiber, MD, Peter Tassani, MD, PhD, Nicolo Piazza, MD, PhD

Munich, Germany

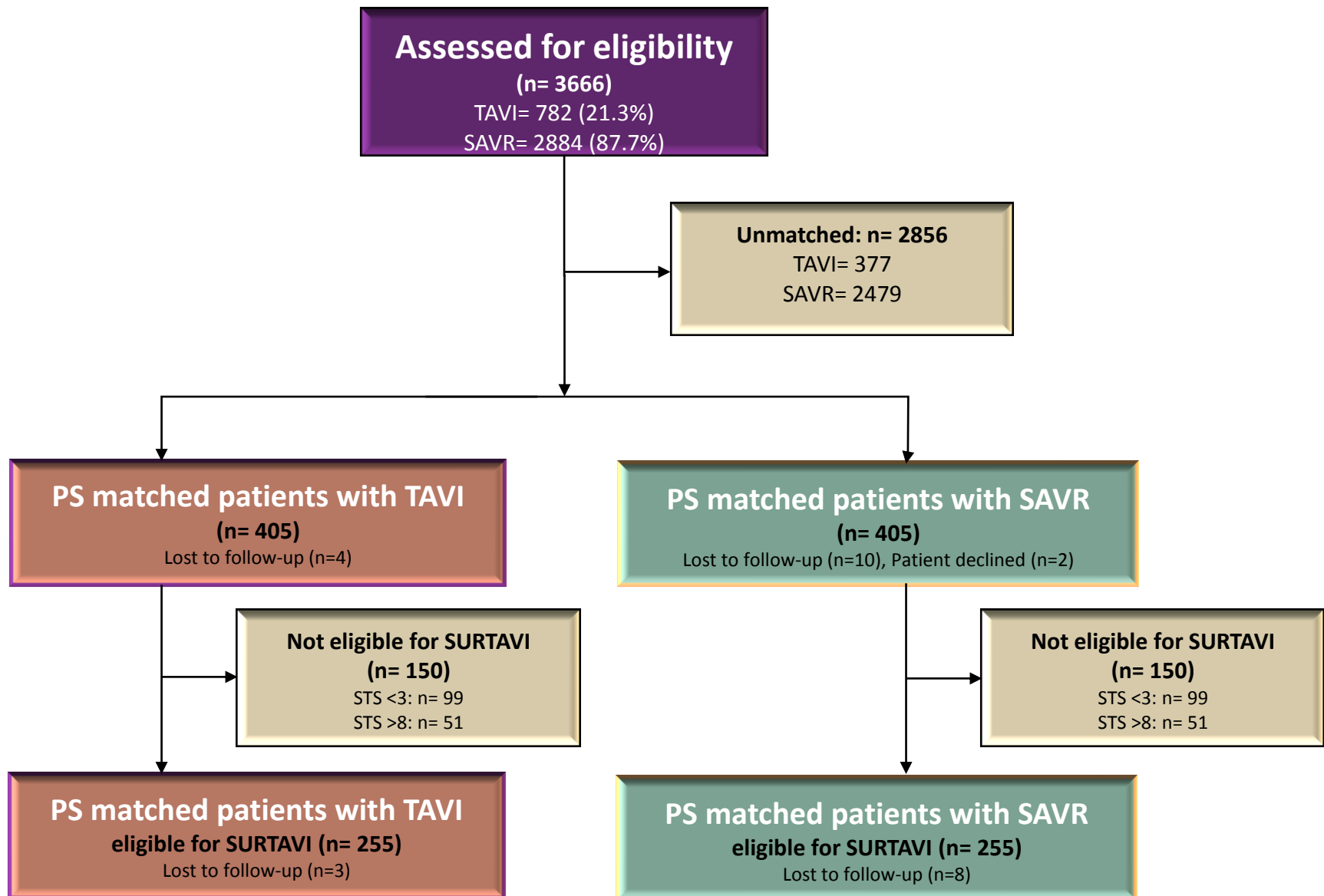
HEART TEAM DECISION STS - SCORE



BERMUDA – PATIENT FLOW



PIAZZA N ET AL. JACC CARDIOVASC INTERV. 2013; AHEAD OF PRINT

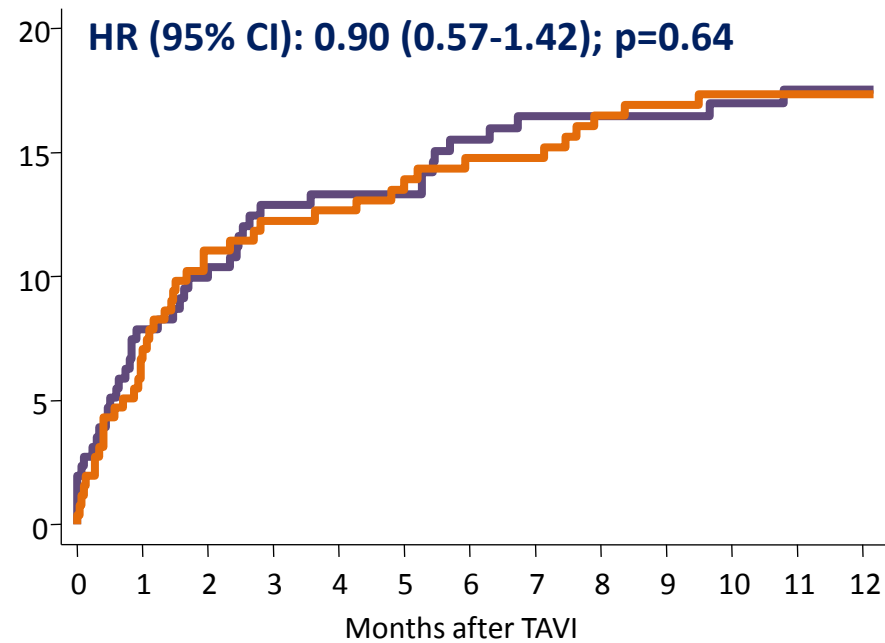


A map of Europe highlighting the Schengen Area. The area is outlined in blue and includes the following countries: United Kingdom, Ireland, France, Belgium, Luxembourg, Germany, Netherlands, Switzerland, Austria, Italy, Spain, Portugal, Greece, and Slovenia. The flags of these countries are shown: United Kingdom (Union Jack), Ireland (Tricolor), France (Tricolor), Belgium (Tricolor), Luxembourg (Tricolor), Germany (Tricolor), Netherlands (Tricolor), Switzerland (Cross), Austria (Horizontal stripes), Italy (Vertical stripes), Spain (Vertical stripes), Portugal (Vertical stripes), Greece (Horizontal stripes), and Slovenia (Diagonal stripes). The map also shows the borders of non-Schengen countries like Denmark, Poland, Czech Republic, Slovakia, Hungary, Romania, Bulgaria, and Turkey.

PROPENSITY SCORE MATCHED PATIENT POPULATION

All – Cause Death @ 30 Days

**All – Cause Death
@ 12 Months**

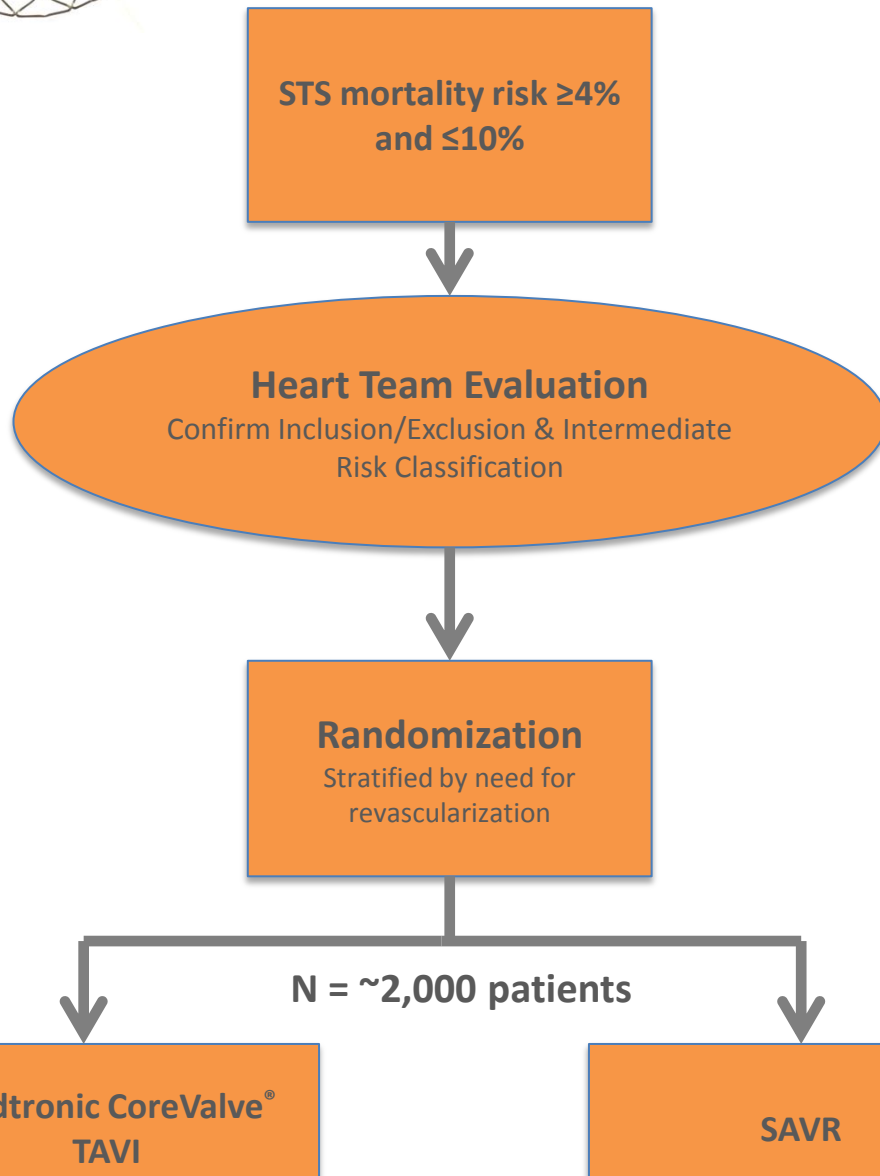


NO. AT RISK		Days after TAVI							Months after TAVI											
		0	30	60	90	120	150	180	3	6	9	12	15	18	21	24	27	30	33	36
TAVI	255	248	246	242	239	237	233	255	233	215	206	203	199	186	171	161	157	153	149	143
SAVR	255	250	248	244	243	241	237	255	237	223	216	211	205	200	199	194	191	189	188	183

— TAVI — SAVR



SURTAVI – STUDY DESIGN



- Randomized 1:1, non-inferiority study
- Up to 75 worldwide centers
 - ✓ Europe
 - ✓ Canada
 - ✓ United States
- Approx 2,000 total number of trial subjects
- Long-term follow-up through 5 years

PARTNER II TRIAL UPDATE

LEON MB, PRESENTED AT TCT 2012

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

n=2000
Randomized
Patients

Operable
(STS ≥ 4)

Two Parallel
Randomized Trials
+5 Nested Registries

n=500
Randomized
Patients

Inoperable

**ASSESSMENT:
Transfemoral
Access**

Yes

No

Transfemoral (TF)

Transapical (TA)

1:1 Randomization

1:1 Randomization

TF TAVR
SAPIEN
XT

VS

Surgical
AVR

TAVR:
TA / TAO

VS

Surgical
AVR

Primary Endpoint: All-Cause Mortality +
Major Stroke at Two Years
(Non-inferiority)

**ASSESSMENT:
Transfemoral
Access**

Yes >7mm

Yes 6-7mm

No

1:1 Randomization

6-7mm
Registry

TF TAVR
SAPIEN
XT

VS

TAVR
SAPIEN

TA
Registry

TAO
Registry

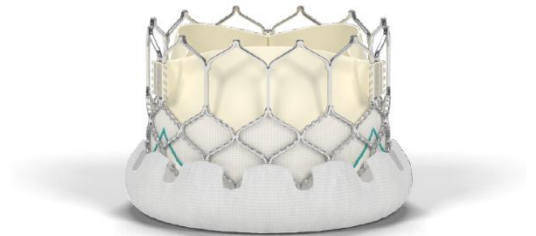
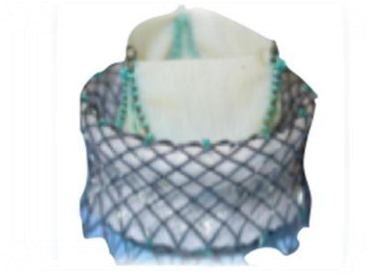
Primary Endpoint: All-Cause
Mortality + Disabling Stroke +
Repeat Hospitalization at One Year
(Non-inferiority)

29 mm valve
Registry

Additional
Registry:

Transcatheter Valve-in-Surgical Valve Registry

NEW GENERATION TAVI DEVICES



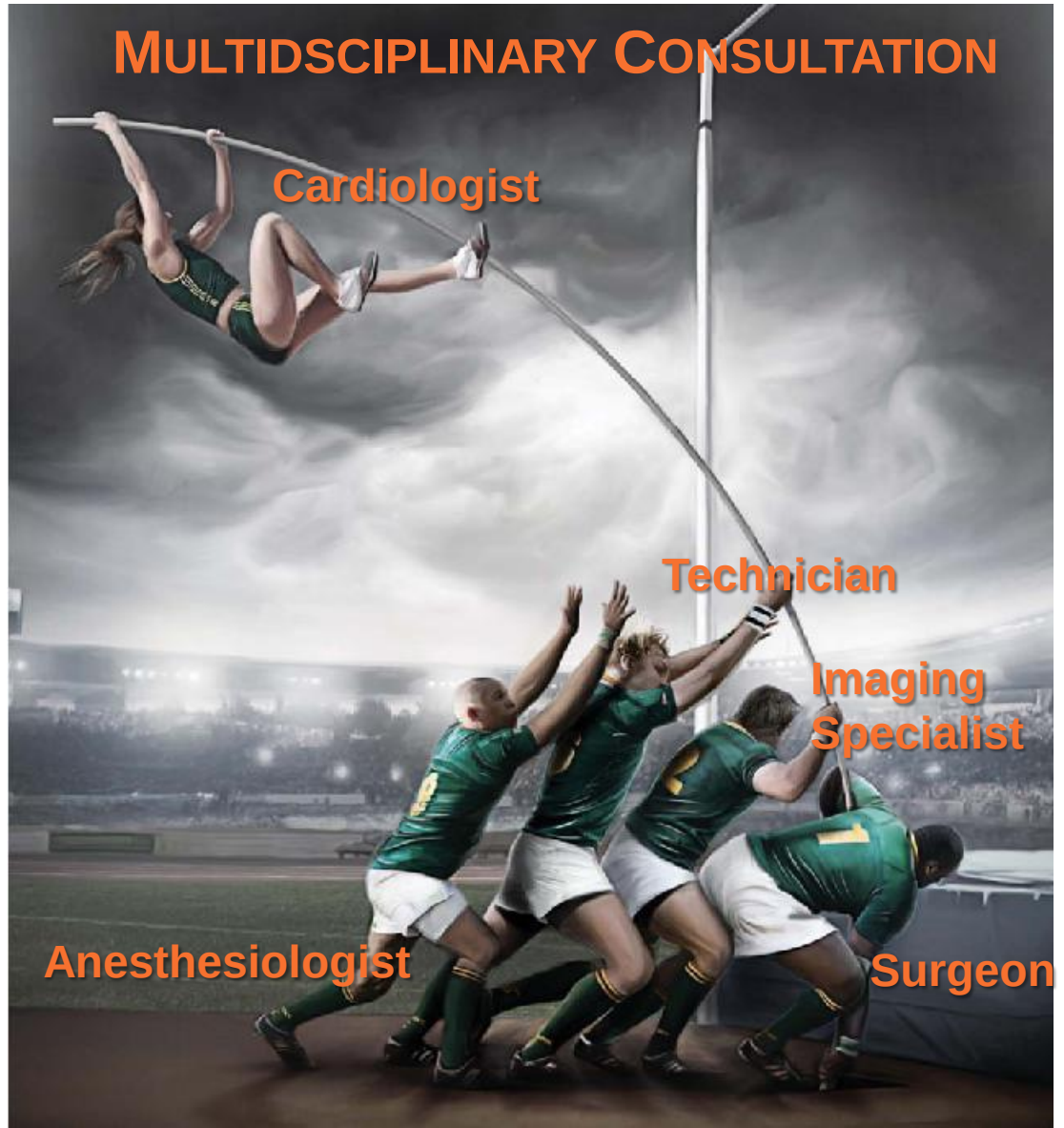
TAVI IN INTERMEDIATE RISK PATIENTS

PRIORITY SURTAVI & PARTNER II

HEART TEAM APPROACH

“Surgeons and cardiologists must work as a team to select appropriate candidates, perform the procedure, and, finally, evaluate the results.”

Vahanian A et al. Eur Heart J. 2008;29:1463-70



10 YEARS TAVI

WHAT DID WE LEARN FROM CLINICAL TRIALS

- **TAVI IMPROVES**

- TAVI is superior to surgical a

- **STROKE AFTER**

- Cerebrovascu
- and have a su

- **VALVE DURABI**

- is maintained
- Aortic regurgi

- **HEALTH RELAT**

- TAVI effective
- and improves

TAVI vs. SURGERY

EFFECT OF TAVI ON QoL AT 12 MONTHS

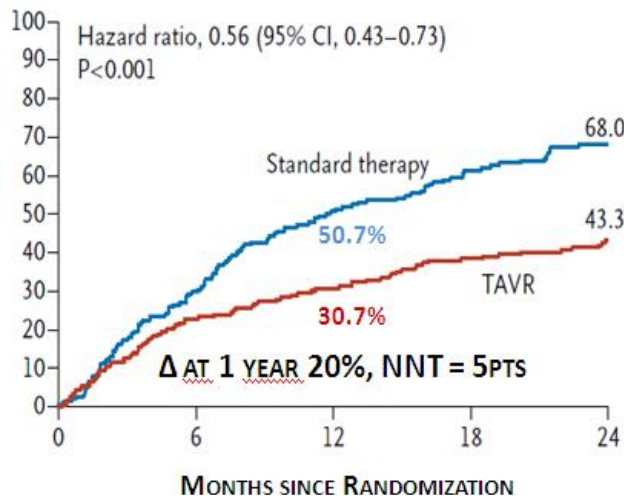
Reynolds MR et al. *J Am Coll Cardiol* 2012;50:548-58



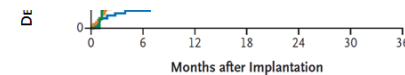
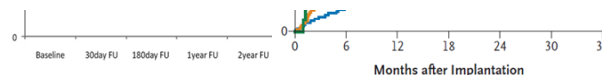
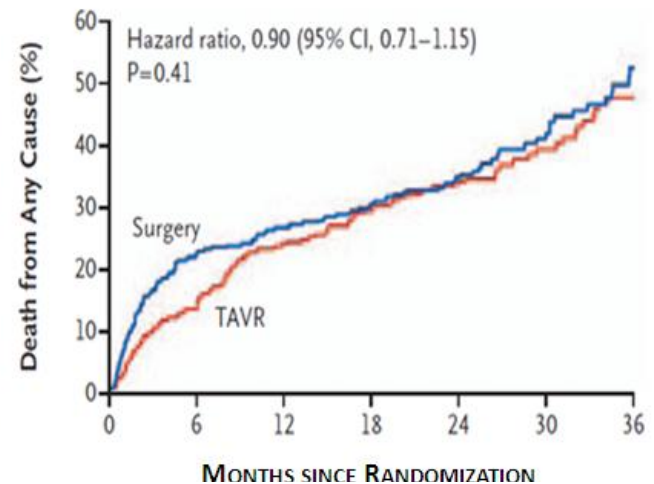
● TRANSFEMORAL VS. ■ TRANSAPICAL TAVI

red

PARTNER B



PARTNER A



0
76
42

10 YEARS TAVI

WHAT DID WE LEARN FROM CLINICAL TRIALS

- **TAVI IS SAFE**

- TAVI is superior compared to medical treatment and non-inferior compared to surgical aortic valve replacement.

- **STROKE AFTER TAVI IS AN ISSUE**

- Cerebrovascular events are frequent early after TAVI

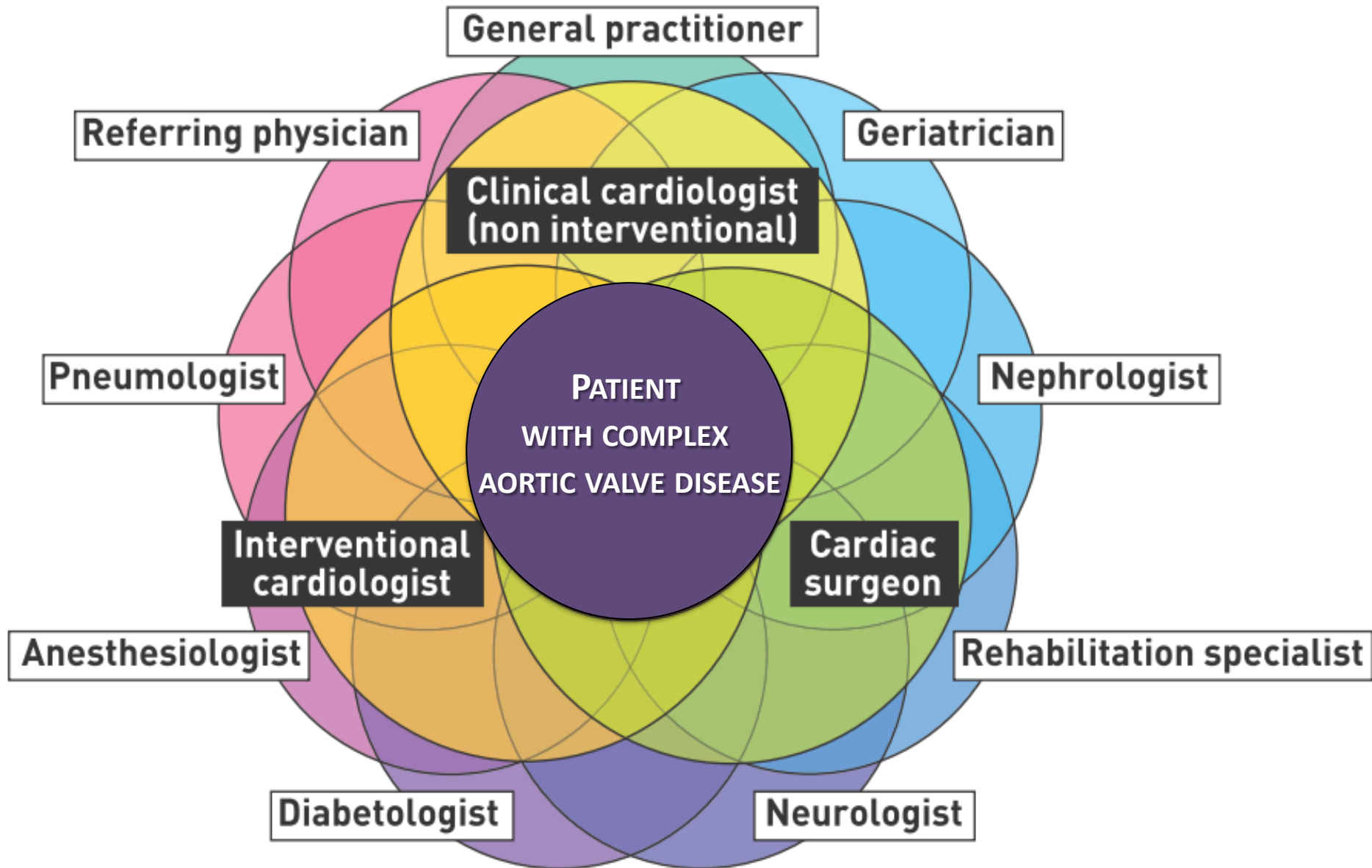
- **VALVE DURABILITY**

- is maintained beyond 2 years of follow-up
- Aortic regurgitation impacts on outcomes and needs to be improved

- **HEALTH RELATED QUALITY OF LIFE**

- TAVI effectively alleviates symptoms
- and improves health-related quality of life

HEART TEAM APPROACH



**10 YEARS OF
TAVI**

**TAVI VERSUS
SURGERY**

**TAVI
LIMITATIONS**

**COST
EFFECTIVENESS**

**INTERMEDIATE
RISK PATIENTS**

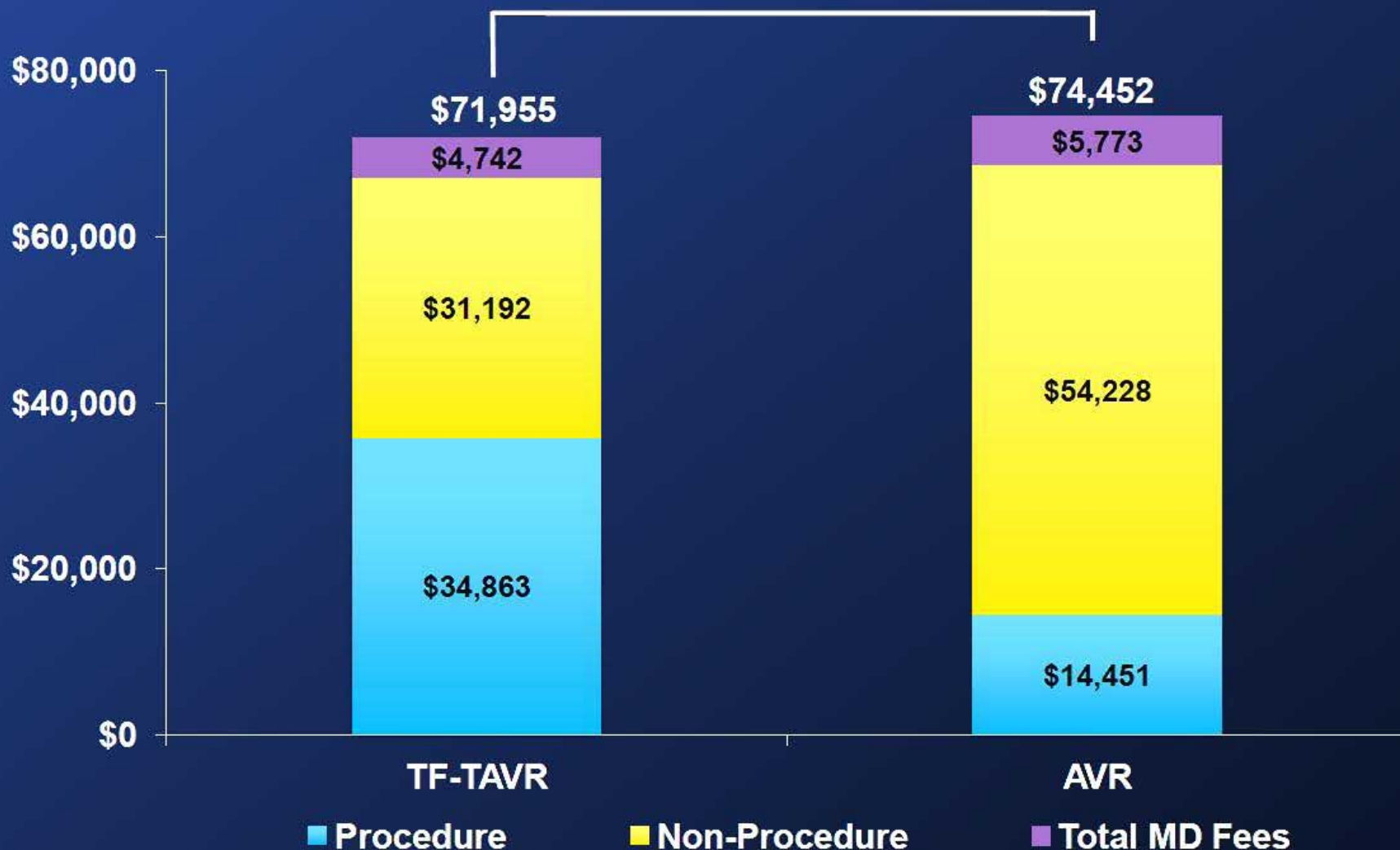
**RANDOMISED
EVIDENCE**

Index Admission Costs

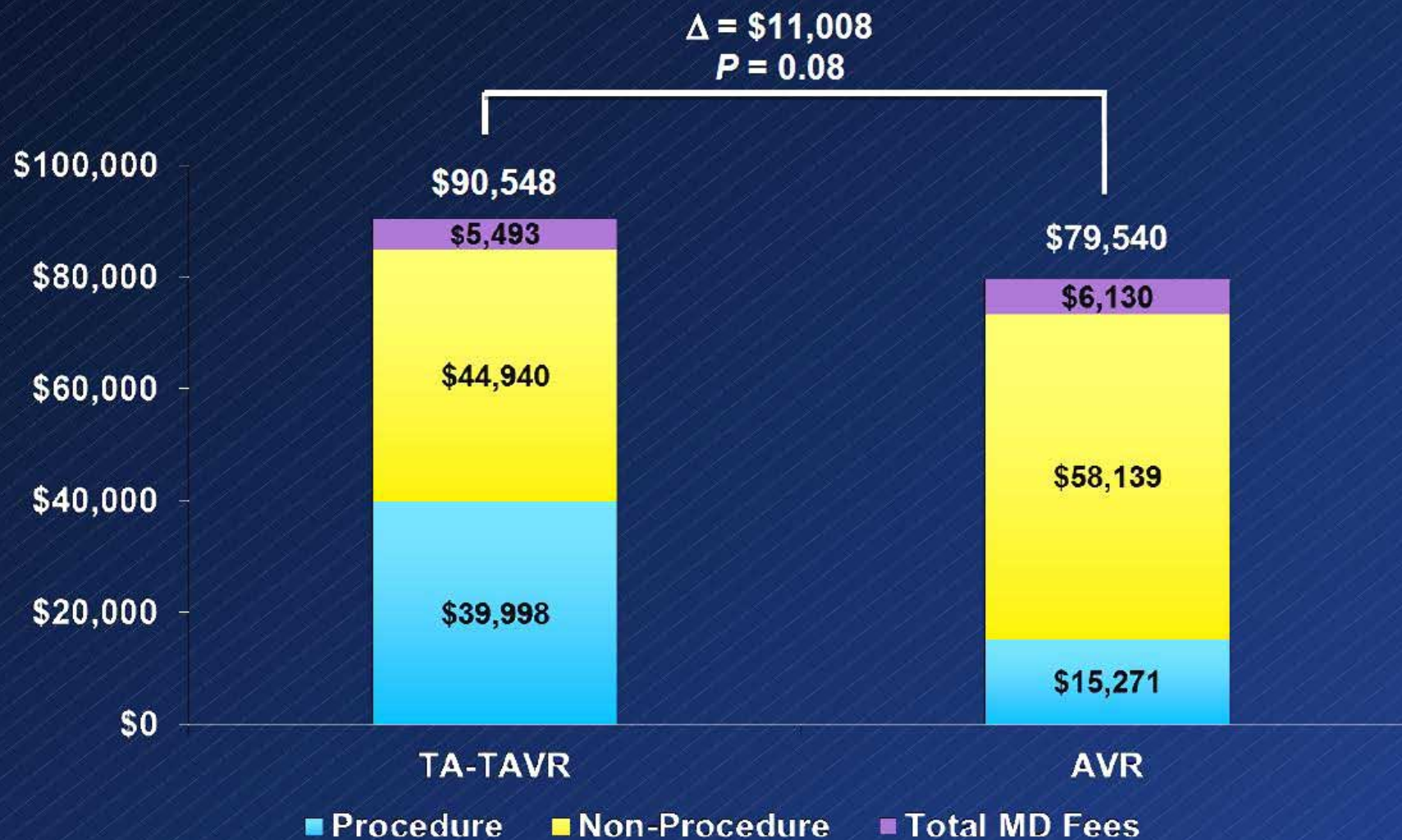
Transfemoral



$\Delta = (\$2,496)$
 $P = 0.53$

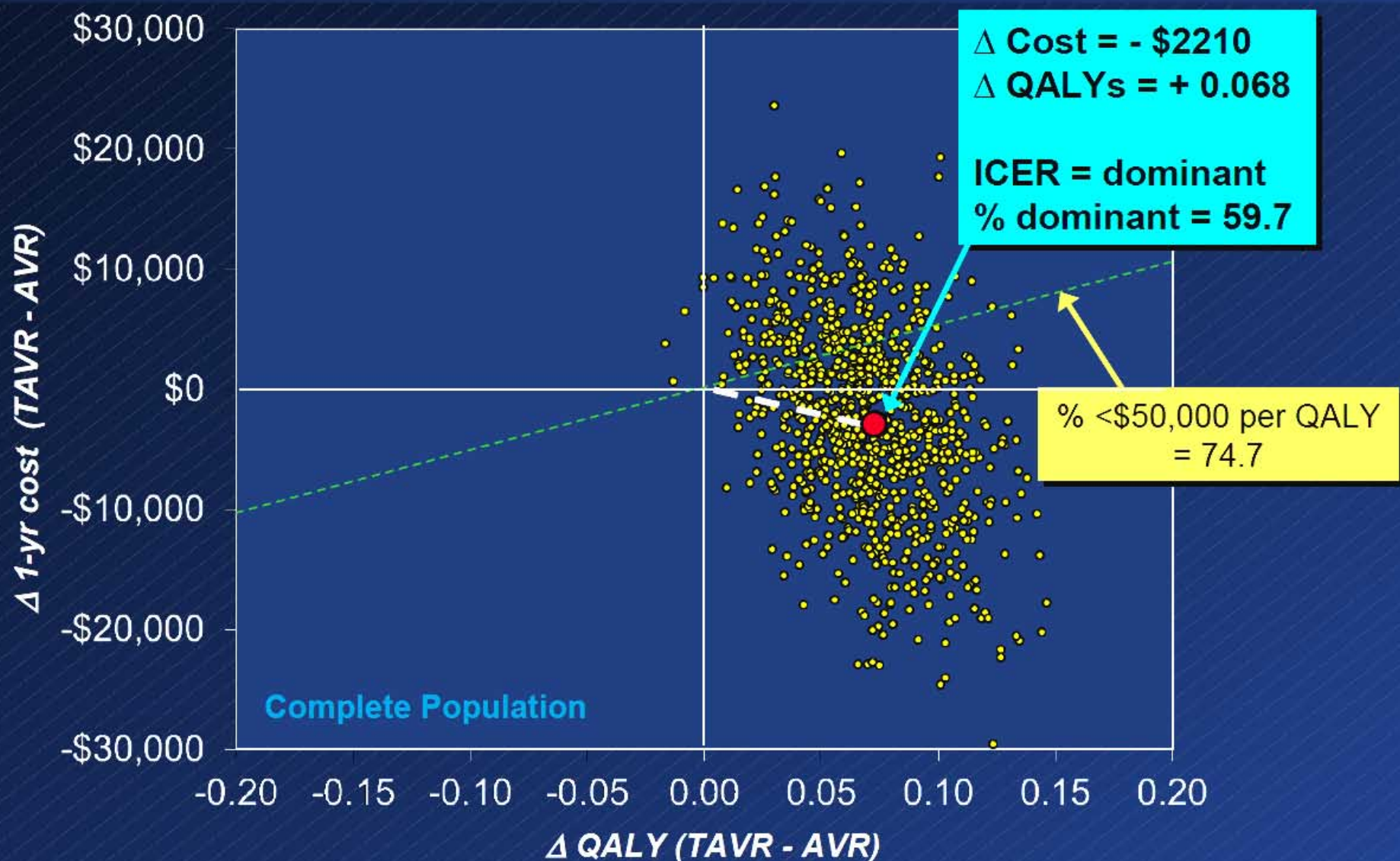


Index Admission Costs Transapical



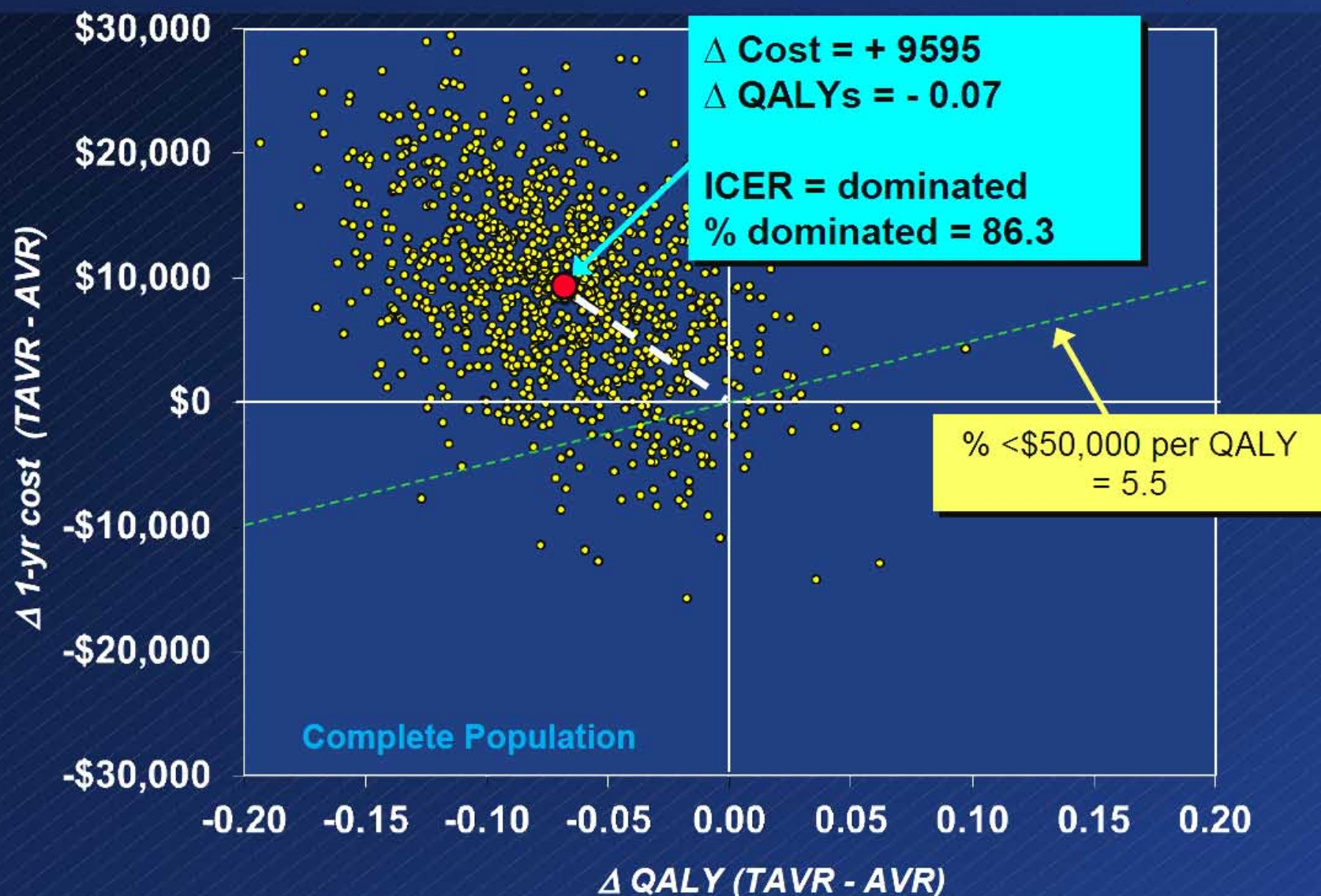
TAVR vs. AVR: Transfemoral

Cost per QALY gained



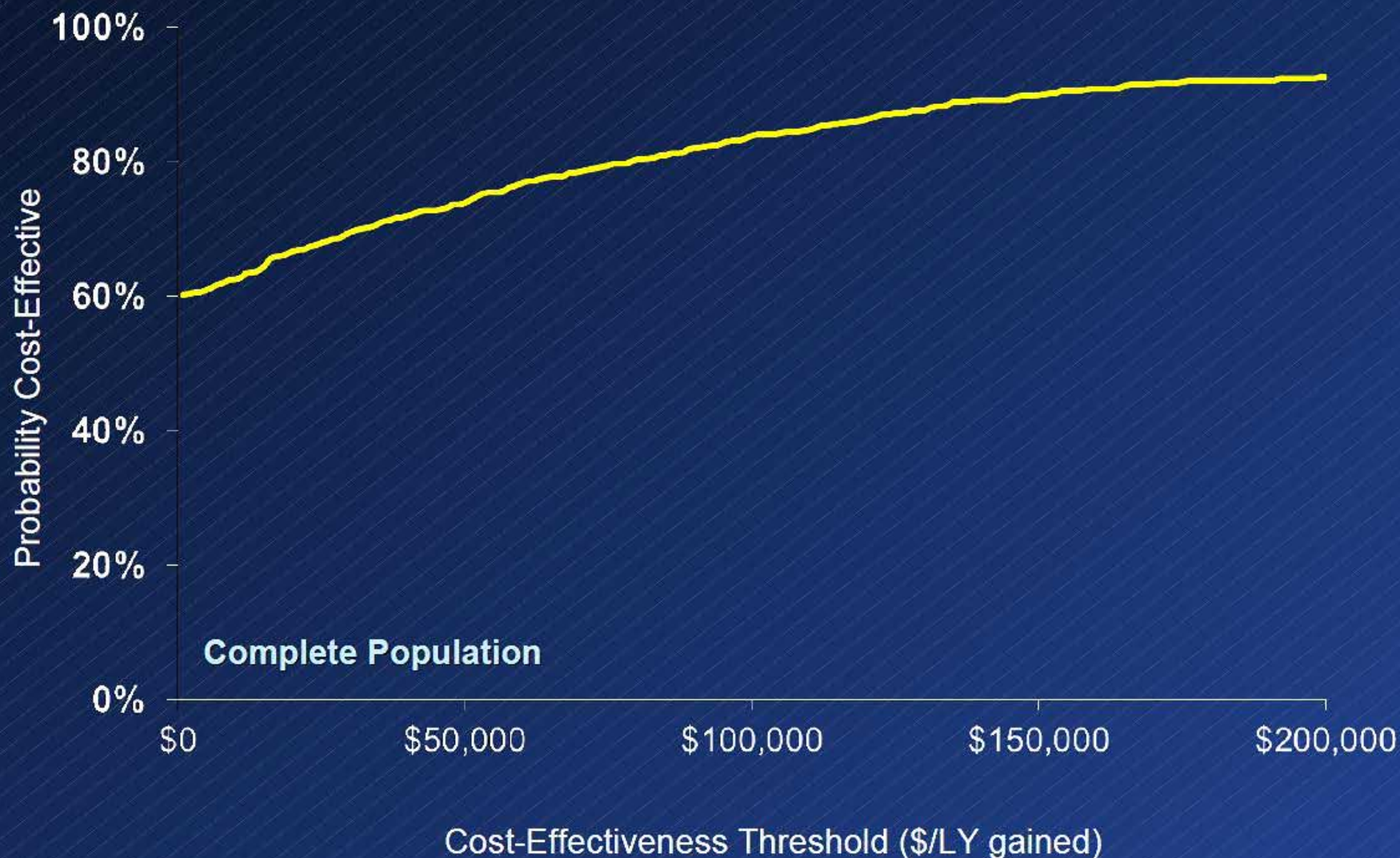
TAVR vs. AVR: Transapical

Cost per QALY gained



Cost-Effectiveness of TAVR vs. AVR

Transfemoral (cost per LY gained)



Cost-Effectiveness of TAVR vs. AVR

Transapical (cost per LY gained)



Complete Population